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Original Article / Özgün Araştırma

Evaluation of Adults' Knowledge on Dental Caries and Oral Habits and Perception on the Oral-Systemic Relationship

Bireylerin Diş Çürüğü Gelişimi ve Oral Hijyen Alışkanlıkları Hakkındaki Bilgi Düzeyleri ile Genel Sağlık-Ağız ve Diş Sağlığı İlişkisinde Farkındalık Düzeylerinin Değerlendirilmesi

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Keywords

Dental caries, oral hygiene, oral health, toothbrushing, demographic and health surveys

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Abstract

Objective: This study aimed to evaluate the patients' awareness of the relationship between oral and systemic health based on their oral hygiene habits and knowledge. Materials and Methods: A 21-item questionnaire was administered to 500 patients who had been referred to the Istanbul University Department of Restorative Dentistry. The questionnaire consisted of specific questions to evaluate the sociodemographic data and frequency of oral habits and to examine existing systemic diseases. The questionnaires were administered through interviews by the same dentist, and collected data were statistically evaluated using chi-square tests. Results: Of the 500 patients (aged 18-78 years), deficiencies in tooth brushing (70.6%) and diet (50.2%) were related to dental caries. The effects of inadequate tooth brushing on caries development were not significantly different when analyzed by patients' gender and age groups (p>0.05), whereas significant results were observed in the educational status (p<0.05). Moreover, 19% of the patients indicated that oral symptoms did not play a crucial role in the early diagnosis of systemic health problems, 41% stated that it was important, and 40% had no idea. Patients' awareness of the relationship between oral and systemic health is significantly altered by their educational status (p<0.001).

Conclusion: Knowledge on the relationship between oral and systemic health is inadequate. Thus, patients should be educated on the importance of oral health awareness, as it is an inseparable part of general health. Referrals from health professionals to dentists may improve patients' access to dental care.

Öz

Amaç: Bu çalışmanın amacı, bireylerin ağız hijyeni alışkanlıklarına ve diş çürüğü gelişimine ilişkin bilgi düzeylerinin ölçülmesi ve genel sağlık-ağız ve diş sağlığı ilişkisi hakkındaki farkındalıklarının incelenmesidir.

Gereç ve Yöntemler: İstanbul Üniversitesi Restoratif Diş Tedavisi Anabilim Dalı'na başvuran 500 hasta, 21 sorudan oluşan anketi cevaplamıştır. Tüm anketler bir diş hekimi tarafından röportaj şeklinde gerçekleştirilmiştir. Anket, katılımcıların sosyodemografik değerlerini belirlemek, oral alışkanlıklarının sıklığını değerlendirmek

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ve mevcut sistemik hastalıklarını incelemek için ayrıntılı sorular içermiştir. Sonuçlar ki-kare testleri kullanılarak istatistiksel olarak değerlendirilmiştir.

Bulgular: 18-78 yaş arasındaki 500 hastaya göre, yetersiz diş fırçalama (%70,6) ve beslenme (%50,2) diş çürüğü gelişimi ile direkt ilişkilidir. Yetersiz diş fırçalamanın diş çürüğü gelişimine neden olacağını belirten bireyler, cinsiyet ve yaş grupları açısından anlamlı olarak farklılık göstermezken (p>0,05), eğitim durumları istatistiksel olarak anlamlı farklılık göstermiştir (p<0,05). Katılımcıların %19'u genel sağlık sorunlarının erken teşhisinde oral semptomların önemli bir rol oynamadığını belirtirken, %41'i bunun önemli olduğunu belirtmiştir. Bireylerin genel sağlık-ağız ve diş sağlığı ilişkisindeki farkındalık düzeyleri eğitim durumlarına göre anlamlı derecede farklılık göstermiştir (p<0,001).

Sonuç: Bireylerin genel sağlık-ağız ve diş sağlığı ilişkisi hakkında yeterli bilgiye sahip olmadığı görülmüştür. Ağız-diş sağlığının, genel sağlıktan farklı olarak görülmemesi ve bu bilincin yaygınlaştırılması konusunda bireylerin eğitilmesi gerekmektedir. Bu hususta özellikle sistemik hastalığa sahip olan bireylerin teşhisin ardından tıp hekiminden, diş hekimine yönlendirilmesi büyük önem taşımaktadır. Sağlık profesyonellerinden diş hekimlerine sevk ile bireylerin dental hizmetlere erişimi kolaylaşacaktır.

Introduction

According to World Health Organization, dental caries and periodontal pathologies are still the most common diseases all over the world which are affected by lack of oral hygiene habits and dental knowledge (1). In the USA, 85% of the adults older than 18 years and 44% of the 5-year-olds are affected by dental caries (2). Likewise, the rate of dental caries was 73.8%, and periodontal diseases were 62% among adults aged between 35 and 44 in Turkey (3). As dental problems affect patients without any age or gender exceptions and could only be solved by basic oral hygiene procedures, the higher ratios show a deficiency in promoting oral health. Generally, the prevalence was taken from nationwide surveys so that there could be greater numbers when these surveys investigate only special populations such as patients with systemic diseases.

The Fédération Dentaire Internationale first defended oral health as a fundamental human right and an inseparable part of systemic health in 2013 (4). Then, in 2016, oral health was identified as reflecting the physiological, social, and psychological attributes necessary to a quality life (5). Recent studies proved there are systemic diseases with probable oral symptoms as well as oral diseases that could affect the general condition of the body (6-8). Today, many systemic diseases are connected to oral problems such as cardiovascular diseases (9), diabetes (10), rheumatoid arthritis (11), asthma (12), and respiratory diseases (13). Thus, dentists and physicians should work collaboratively in order to increase patients' quality of life. That approach would ensure the health and economic and social needs of the population.

Furthermore, it is crucial to implant the idea of maintaining optimum oral health to provide better general health; also, good oral knowledge could lead to early diagnosis of oral and systemic diseases. Last but not least, with the knowledge of oral diseases, patients could first change their oral beliefs into actions and later into oral habits.

The aim was to measure the oral behavior, knowledge, and perception of the oral and systemic health relation of a group of dental patients who applied for public dental service. This is the first study evaluating the factors affecting caries development among adults and comparing the results over age, gender, and educational levels. The present survey's hypotheses include the following; (1) There were no significant differences in the knowledge on factors affecting dental caries among participants' gender, age, or educational status; and (2) there was a significant difference in the participants' age, gender, and educational status with regard to their perceptions of oral and systemic health.

Materials and Methods

The present cohort study was designed as a survey and was approved by the Clinical Research Ethics Committee of İstanbul University İstanbul Faculty of Medicine (decision no: 416, date: 16.04.2013).

Subjects

A sample size of 471 was calculated based on the probable knowledge rate of 20% on oral-systemic health relation with a margin error of 5% (confidence interval of 95%) using the G*Power program (G*Power v3.1.9.2., Heinrich-Heine-Universität, Düsseldorf, Germany). Regarding the probable missing data and exclusions, the total number of the subjects was

determined as 500. The present study was conducted between April and June of 2013 at İstanbul University Faculty of Dentistry. Subjects aged between 18 and 78 were included in the study from whom applied to department of restorative dentistry clinics. Pregnants, lactating mothers and patients with emergency had excluded from the study. Written consents from participants had taken and kept in files separated for each one.

Questionnaire

21-item surveys (Appendix 1) were prepared. Surveys consisted of detailed questions to investigate the socio-demographic values of the patients such as age, gender and occupation in the first part. In the second part, there were questions on subjects' own oral habits, existing systemic diseases and daily medicaments. The last part was aimed to measure awareness of their own oral health and to understand participants' oral knowledge on caries development and the relation between oral and systemic health. All surveys were carried out as interviews by the same dentist and numbered in a sequel.

Statistical Analysis

All data with no missing answers were delivered to Microsoft Excel program at first then evaluated by SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Frequencies and percentages were used while analyzing and comparisons were evaluated by chi-square exact test. The significance was adjusted to p<0.05.

Results

Table 1 shows participants' demographic data. Among 500 patients, the average age was found to be 34.5±13.5. The number of female (50.6%) and male (49.4%) subjects were similar with no statistical difference (p>0.05).

Of the 500 subjects, 240 (48%) reported brushing their teeth once a day, 176 (35%) brushed their teeth 2 or 3 times a day, and 34 (7%) brushed only once a week. Among all participants, 34 (8%) of them brushed irregularly, and 9 (2%) of them never brushed (Figure 1). Most of the subjects (86%) did not attend routine dental recalls or use dental floss. Evaluating their toothpaste choices, subjects specified that they rely on their own experiences (35%) rather than dentists (28%).

Of the subjects, 55.4% had gingival bleeding while brushing, and 44.6% had spontaneous gingival

bleeding. To add more, 46.6% of the subjects had a toothache in the last 6 months. In the last 6 months, 24.8% of the subjects had tooth scaling.

According to the data, most of the subjects specified that inadequate tooth brushing (70.6%) was one of the main factors affecting caries development, while diet was the second most reported factor (50.2%). Participants were asked about their knowledge of factors affecting dental caries, and the majority of subjects were unaware of the effective factors other than tooth brushing (Figure 2).

Table 2 summarizes the multiple comparisons on subjects' knowledge on factors of caries development and their demographic data.

According to Table 2, participants, who determined "genetics" as a factor for caries development, were significantly different in terms of their gender, educational status and age. Age was not also a significant parameter among participants who

| Table 1. Demographic structure of the subjects | | | | | | | |
|--|-------------|--|--|--|--|--|--|
| Characteristics Number (%) | | | | | | | |
| Gender | | | | | | | |
| Male | 247 (49.4%) | | | | | | |
| Female | 253 (50.6%) | | | | | | |
| Age | | | | | | | |
| 18-30 | 229 (46%) | | | | | | |
| 31-50 | 193 (39%) | | | | | | |
| 51+ | 78 (15%) | | | | | | |
| Education level | | | | | | | |
| Primary school | 123 (25%) | | | | | | |
| Middle school | 37 (7%) | | | | | | |
| High school | 244 (49%) | | | | | | |
| University | 96 (19%) | | | | | | |



Figure 1. Toothbrushing frequency of the subjects

described "regular dental visits" as an affecting factor for caries development (p>0.05). However, they were different in terms of gender and educational status (p<0.05). Participants determined that "inadequate tooth brushing" is a factor for caries development, and they were statistically significant concerning their educational status only. Diet was found to be a factor for caries development, and it was highly significantly different among participants' gender (p<0.001). Participants who described that "lack of dental knowledge" may affect their caries development were not significantly different by any of the questioned demographic factors (p>0.05).



Figure 2. Subjects' knowledge on factors of caries development

The present survey determined that no patients were suffering from multiple sclerosis or any neurological diseases. Table 3 summarizes subjects' situation of systemic diseases and habits. Only 25% of the subjects with at least one systemic disease had their conditions under a physician's control. Of all the systemically disordered subjects, only 22.2% had regular medications according to their illnesses. To add more, subjects with systemic diseases or conditions who were visiting their physicians regularly and taking daily medicines had a statistically significant difference compared to those who were not (p<0.05).

Evaluating the awareness and knowledge on the oral symptoms of systemic diseases, a majority of the subjects (65%) were found to have halitosis as a result of systemic disease. Figure 3 shows the results of the related question.

A few ratios of the subjects (19%) declared that oral symptoms were not significant in the early diagnosis of systemic disease. 41% had the opposite answer, and 40% had no idea about the issue. In addition, 24% of the subjects specified that systemic diseases could not affect dental treatments, while 45% declared the contrary. Figure 4 summarizes subjects' answers on their awareness of the oral-systemic health relation.

| Table 2. Significance between subjects' oral knowledge on caries development and demographic data | | | | | | | | |
|---|----|---|---|--|--|--|--|--|
| Gender Age groups Educational status | | | | | | | | |
| Genetics | + | + | + | | | | | |
| Regular dental visits | + | - | + | | | | | |
| Inadequate tooth brushing | - | - | + | | | | | |
| Diet | ++ | + | - | | | | | |
| Lack of dental knowledge | - | - | - | | | | | |
| Signs refers to (+): p<0.05, (++): p<0.001, (-): p>0.05 | | | | | | | | |

| Table 3. Subjects' systemic diseases and habits | | | | | | | |
|---|---------------------|------------------------------|--|--|--|--|--|
| Diseases/habits | No. of participants | Ratio among all participants | | | | | |
| Cardiovascular diseases | 45 | 9% | | | | | |
| Thyroid disorders | 15 | 3% | | | | | |
| Respiratory system diseases | 13 | 2.6% | | | | | |
| Rheumatic diseases | 54 | 10.8% | | | | | |
| Diabetes | 53 | 10.6% | | | | | |
| Anemia | 70 | 14% | | | | | |
| Hypertension | 27 | 5.4% | | | | | |
| Tobacco and/or alcohol use | 149 | 29.8% | | | | | |

In terms of age and gender, there was no statistically significant difference in subjects' awareness of the oral-systemic health relation (p=0.113), but there was a statistically significant difference among subjects' educational status (p<0.05).

Discussion

As oral health is an inseparable part of systemic health, it is obvious that chronic problems in the oral environment could cause a systemic effect. Thus, by fulfilling oral habits, ideally with optimum knowledge on oral diseases, a healthy systemic condition can be reached. It is important for every individual of the public to consider the relation between oral and systemic health and to reach out to available health services. Using a 21-item survey, the present study assessed the oral behavior, knowledge, and perception of the 500 patients who were willing to attend a dental service. The present study showed that the knowledge on factors of dental caries changed significantly regarding participants' gender, age, and



Figure 3. Subjects' knowledge on the oral symptoms of systemic diseases



Figure 4. Subjects' awareness on the relation between oral and systemic health

educational status. Therefore, the first hypothesis is rejected.

When evaluating the oral knowledge on caries development, the most common factor leading to caries development was tooth brushing. Even though subjects knew that a lack of tooth brushing caused caries development, they did not practice proper oral habits. Thus, knowledge about the risk of a disease does not always integrate into habitual behavior. Studies evaluating this issue were mainly focused on the knowledge of periodontal diseases of diabetic patients (14-18). However, there are a few studies (18,19) evaluating patients' opinions on the risk factors of caries development. So, the present study is among the rare few investigating patients' knowledge on the factors causing dental caries.

Of the factors causing caries development, tooth brushing (70.6%) and diet (50.2%) were common answers among subjects. With a high percentage of knowledge on the effects of tooth brushing on caries development, the cause for the low ratio of tooth brushing among subjects was unclear. Furthermore, a diet consisting of refined carbohydrates and sugars had a crucial impact on bacterial nutrition and growth by increasing the acidic pH of oral cavities (20). Aside from this importance, nearly half of the subjects (49.8%) described no relation between diet and caries development. Besides, routine dental visits were important to arrest white spot lesions that could be re-mineralized and to prevent caries progression. However, routine dental visits were thought not to be related with caries development among subjects (63.8%). Moreover, dental knowledge was found to be irrelevant by most of the subjects (nearly 80%); however, with a clinical examination among the subjects, caries prevalence would have been high. Tafere et al. (18) showed statistically and significantly lower caries prevalence among subjects with better knowledge of dental caries. In the related study, subjects fulfilling oral hygiene procedures were found to have statistically lower dental caries, and this would have been assumed in the present study as well. Another novel study by Francis et al. (19) showed that oral knowledge on both the cause and prevention of dental caries had a statistically significant increase among age. Although the mentioned study was conducted among high school students aged between 16 and 18, regarding whether subjects could learn

from lessons in schools, the present study had the same result among adults as well. Having optimum oral knowledge could allow the public to improve oral habits and behaviors as well as lower the incidence of dental caries in future generations.

As the connection between oral and systemic health has been proven recently, it is not only physicians' but also dentists' responsibility to popularize the scientific data and inform patients. In addition, such responsibility is important to form proper oral habits and to be knowledgeable about oral hazards. 55.4% of all subjects had at least one systemic disease, and nearly 30% of the subjects used tobacco or alcohol. Unfortunately, only one-fourth (1/4) of the diseased subjects were under physicians' control and took regular medicines daily. It is clear from the results that subjects were neither interested in their oral health nor their systemic health. Since subjects had inadequate knowledge of the probable oral symptoms of systemic diseases, the ratio of halitosis (65%) was superior to others' symptoms such as caries (47.6%). Also, it is obvious from the results that most of the subjects had inadequate knowledge of the oral and systemic relation. Diabetes was prevalent among subjects (10.6%), and its relation between periodontal diseases was obvious; still, subjects did not relate either gingival bleeding (37.8%) or gingival recession (15.4%) as a symptom for diabetes. It should be taken into consideration that both physicians and dentists have a role in misguiding patients. In particular, physicians should direct patients with systemic diseases or habits to dentists immediately after the diagnosis or first appointment. The opposite is valid for dentists if the systemically ill patients' oral health status becomes worse. In the present study, educational status was shown to have a positive correlation with subjects' awareness of the oral and systemic health relation, similar to Shanmukappa et al.'s (17) and Tafere et al.'s (18) studies. It was clear from the results that a high amount of ratios were taken from subjects with "no idea". Subjects lacked knowledge; however, it could be concluded that consideration for the oral and systemic health relation existed among subjects. At most, pregnancy seemed to be linked with altered oral health among subjects. This part of the answers could be related to the higher educated portion of the subjects. That is why only the differences between participants' educational status

had statistical significance in the perception of the oral and systemic health relation; thus, the present study's second hypothesis is partially accepted. When the educational status is increased, the awareness of oral and systemic health is higher. In addition, when the educational status is higher, subjects thought of more factors affecting dental caries such as genetics and dental visits, apart from the common answer of tooth brushing. In a study (21) conducted among 450 practitioners, dentists described that their knowledge on the influence of systemic diseases on oral health is inadequate. On the other hand, some studies (6,22) also showed that physicians recognize the importance of oral health; however, they had a deficient perception of the effect of oral health on their systemic health. Thus, a common approach should be adopted by both physicians and dentists in order to guide systemically diseased patients.

The findings on oral behavior showed the inadequate application of oral hygiene habits such as brushing and flossing. A majority of subjects brushed their teeth once a day (48%), and only 14% flossed. Even if the recommended brushing frequency is twice a day (23), only one-third of the subjects (35%) followed the general recommendation. In accordance and in contrast to the present study, several studies have evaluated the oral habits of the population conducted in many countries. In Nigerian studies (24) with more than 7,600 responders and in South American studies (25) with more than 1,600 responders, nearly 50% practiced tooth brushing twice a day. Although only 10.5% of Nigerian responders flossed, which was similar to the ratio of the present study, there were still more brushers than flossers. In a study (26) conducted in Italy with 2,200 adults aged between 18 and 98, more than 70% of the responders brushed once a day, and this was superior to the present study's results (48%); however, it showed the same flossing ratio. It is obvious from the different studies' scores that subjects brush their teeth more than they floss. The present study detected that 9% brushed irregularly and 2% had never brushed before. A higher ratio was described in the Iranian population of 12,105 responders, with 32.5% having never brushed and 83% having never flossed (27). Although the size of respondents varied in many studies and the ratios changed with the participants' age, gender, and educational status, as well as the

country's socioeconomic level (24,25,28), the ratio of ideal oral habits was low. Despite lacking oral hygiene procedures, subjects also demonstrated challenges meeting regular dental visits. Routine dental visits are important for early diagnosis of oral problems; also, if a systemic disease such as diabetes is present, it is crucial to detect oral lesions at their early stages (29). For the ratios of one dental visit a year, studies (30) from Germany (60%), Ireland (44%), and Spain (27%) showed superior results compared to the present study's subjects (14%). Furthermore, nearly half of the subjects (46.6%) had a toothache in the last 6 months, and half had spontaneous gingival bleeding (44.6%). Without fulfilling regular oral hygiene procedures, most of the oral problems become expectable. It is obvious that not only spontaneous gingival bleeding but also probable caries that lead to toothaches could simply be prevented by regular brushing. However, subjects showed inadequate oral habits, revealed excessive oral problems, and described rare dental visits. Therefore, it was clear that subjects were only applying to emergency clinics when there was a chronic oral problem or a toothache. Among all, subjects tend to rely on their own choices when selecting toothpastes rather than the dentists' recommendations. Beginning with university clinics, a nationwide approach should be taken to generalize the significance of oral hygiene procedures. In addition, oral health promotions of universities or public clinics should be easily accessible for all patients.

Conclusion

Subjects of the present study had inadequate knowledge about both caries development and the oral and systemic health relation. In addition, it was obvious that subjects had an unfavorable interest in oral hygiene habits. There should be a mutual relationship between patients and dentists in improving patients' oral health knowledge and behaviors. Patients should learn the etiologies of not only dental diseases but also the outcomes of systemic conditions on dental tissues; also, dentists should be trained to provide oral habits education. The public should learn where to access dental information or refer to a dental specialist on routine recalls and/or daily practices. Common guidelines should be developed with medical organizations in order to inform systemically ill patients and to warn them about probable dental complications. To add more, academic institutions should educate on the value of scientific research and the oral and systemic health relation so that both medical and dental students can put these principles into practice.

Ethics

Ethics Committee Approval: The present cohort study was designed as a survey and was approved by the Clinical Research Ethics Committee of İstanbul University İstanbul Faculty of Medicine (decision no: 416, date: 16.04.2013).

Informed Consent: Written consents from participants had taken and kept in files separated for each one.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: U.E., G.O., Design: U.E., Supervision: U.E., G.O., Fundings: U.E., G.O., L.E.G., E.Y., Materials: G.O., L.E.G., Data Collection or Processing: G.O., L.E.G., Analysis or Interpretation: E.Y., Literature Search: U.E., E.Y., G.O., L.E.G., Writing: U.E., G.O., L.E.G., E.Y., Critical Review: E.Y., U.E.

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| Appendix 1: The questionnaire of oral knowledge, oral habits and perception | | | | | | | | |
|---|--|--|--|--|--|--|--|--|
| 1. Age: 2. Gender: Women Men | | | | | | | | |
| 3. Neighborhood: | | | | | | | | |
| 4. Educational status: a) Primary b) Middle school c) High school d) University/college e) None | | | | | | | | |
| 5. Do you have health insurance?a) SGKb) Retirement fundc) Private insuranced) Med-nased insurancee) None | | | | | | | | |
| 6. How many times do your brush your teeth?a) Once a dayb) 2-3 times a dayc) Once a weekd) Irregulare) None | | | | | | | | |
| 7. Do you have the habit of flossing? a) Yes b) No | | | | | | | | |
| 8. Do you follow your dental recalls? a) Yes b) No | | | | | | | | |
| 9. Did you have ever gum bleeding in the last 6 months? a) Yes b) No | | | | | | | | |
| 10. Did you have ever toothache in the last 6 months? a) Yes b) No | | | | | | | | |
| 11. Did you ever have tooth scaling in the last 6 months?a) Yesb) Noc) No idea | | | | | | | | |
| 12. What is the leading factor on your decision on choosing toothbrush and toothpaste? a) Advertisements b) My dentists opinion c) Price d) My own experience | | | | | | | | |
| 13. What is/are the factor/-s that affects caries development? a) Diet b) Toothbrushing c) Recalls d) Lack of oral knowledge e) Genetics | | | | | | | | |
| 14. Do you have one or more of the below-mentioned conditions or diseases? a) Cardiovascular diseases b) Thyroid diseases (Such as goiter) c) Pulmonary diseases (Such as bronchitis, asthma) d) Rheumatic diseases e) Diabetes (Type I or II) f) Anemia g) Multiple sclerosis | | | | | | | | |

h) Hypertension i) Neurological diseases (Such as Parkinson's, stroke) i) Epilepsia k) Chronical kidney failure I) Alcohol/Tobacco use m) Others 15. If you have any of the above-mentioned conditions/diseases, is it under control of your physician? b) No a) Yes 16. Do you use a drug/medicament regularly? a) Yes b) No 17. Which of the following /-s could be seen in individuals dealing with a systemic disease? a) Gum bleeding while brushing b) Halitosis c) Xerostomia d) Gingival hyperplasia e) Dental caries f) Teeth loss g) Gingival recession h) Osteoporosis at jaw i) Toothache j) Malocclusion 18. Do you think that the oral symptoms could play a role on the early diagnosis of systemic diseases? c) No idea a) Yes b) No 19. Do you think that systemic diseases could affect oral environment? a) Yes b) No c) No idea 20) Do you think that systemic diseases could affect your dental treatments? c) No idea a) Yes b) No 21) Do you think that any oral problem could affect your systemic health? a) Yes b) No c) No idea 22. Do you think that any oral problem could affect pregnancy? c) No idea a) Yes b) No

Which Technique Should We Select in Laparoscopic Inguinal Hernia Repairs?

Laparoskopik İnguinal Herni Onarımlarında Hangi Tekniği Seçmeliyiz?

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Keywords

Laparoscopic inguinal hernia repair, inguinal hernia, transabdominal preperitoneal repair, totally extraperitoneal repair

Anahtar Kelimeler

Laparoskopik kasık fıtığı onarımı, inguinal herni, transabdominal preperitoneal onarım, total ekstraperitoneal onarım

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Abstract

Objective: With the increasing popularity of laparoscopic surgeries, laparoscopic repairs in inguinal hernias have become more common day by day. Laparoscopic inguinal hernia repairs are most commonly performed using totally extraperitoneal (TEP) and transabdominal preperitoneal (TAPP) repair techniques. This study aimed to compare laparoscopic inguinal hernia repair results according to surgical techniques.

Materials and Methods: Data of patients who underwent closed inguinal hernia repair between July 2017 and July 2020 were retrospectively analyzed, and patients were divided into two groups: those who underwent the TAPP (group 1) and TEP (group 2) techniques. Postoperative recurrence rates of both groups, demographic data of patients, postoperative complication rates, complication types, operation duration, and postoperative hospital stay duration were evaluated; postoperative first-week, first-month, and third-month pain scores were evaluated with the visual analog scale (VAS). Data of both groups were evaluated in terms of statistical differences.

Results: A total of 113 patients underwent surgery in July 2017–July 2020, wherein 43 had TAPP (group 1) and 70 had TEP (group 2). The mean postoperative follow-up duration of patients was 10.01 ± 4.58 months. No significant difference was found in the recurrence between the groups during the follow-up (p=0.67). No significant difference was found in postoperative complications between the groups. The operation durations were longer in group 1 than in group 2 (p=0.04). No significant difference was found between the groups in terms of postoperative hospital stay duration (p=0.29). Postoperative first-week, first-month, and thirdmonth VAS scores were higher in group 1 than in group 2 (p<0.001, p=0.001, p=0.006, respectively).

Conclusion: Laparoscopic inguinal hernia repairs can be performed safely, and the TEP technique is more comfortable than TAPP for patients in the early postoperative period.

Öz

Amaç: Laparoskopik cerrahilerin popülaritesinin artması ile kasık fıtıklarında laparoskopik onarımlar gün geçtikçe yaygınlaşmıştır. Kapalı kasık fıtık onarımları en sık total ekstraperitoneal (TEP) ve transabdominal preperitoneal onarım (TAPP) teknikleri ile yapılmaktadır. Çalışmamızda laparoskopik kasık fıtığı onarım sonuçlarımızı cerrahi tekniklere göre karşılaştırmayı amaçladık.

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Gereç ve Yöntemler: 2017-2020 Temmuz tarihleri arasında kapalı kasık fitiği onarımı yapılan hastaların dosyaları retrospektif olarak incelenerek hastalar TAPP (grup 1) tekniği ve TEP (grup 2) tekniği ile opere olanlar olarak iki gruba ayrıldılar. Her iki grubun ameliyat sonrası nüks oranları, hastaların demografik verileri, postoperatif komplikasyon oranları, komplikasyon çeşitleri, ameliyat süreleri, postoperatif hastanede yatış süreleri; postoperatif 1. hafta, 1. ay ve 3. ay ağrı skorları visual analog skala (VAS) ile değerlendirildi. Her iki grubun verileri istatiksel farklılık açısından değerlendirildi.

Bulgular: 2017-2020 Temmuz tarihleri arasında 113 hasta ameliyat edildi. Bunlardan 43'ü TAPP onarımı (grup 1) ve 70'i TEP onarımı (grup 2) idi. Hastaların ameliyat sonrası takip süresi ortalama 10,01 \pm 4,58 ay olarak saptandı. Gruplar arasında takip boyunca nüks olarak anlamlı farklılık saptanmadı (p=0,67). Gruplar arasında postoperatif gerçekleşen komplikasyonlarda anlamlı farklılık bulunmadı (p=0,93). Ameliyat süreleri grup 1'de daha uzun olarak saptandı (p=0,04). Gruplar arası postoperatif hastanede kalış süresi açısından anlamlı farklılık saptanmadı (p=0,29). Postoperatif 1. hafta, 1. ay ve 3. ay VAS skorları grup 1'de daha yüksek saptandı (p<0,001, p=0,001, p=0,006).

Sonuç: Laparoskopik kasık fıtık onarımları güvenli bir şekilde yapılabilir. Hastalar için postoperatif erken dönemde TEP tekniğinin TAPP tekniğinden daha konforlu olduğunu düşünüyoruz.

Introduction

Although inguinal hernias are traditionally treated with open surgical repair, traditional methods have changed towards laparoscopic inguinal hernia repairs with the development and increase in the popularity of laparoscopic surgery in the last 20 years (1). Some studies have shown that laparoscopic inguinal hernia repairs are superior to open hernia repairs in terms of postoperative pain, recovery and morbidity (2). Today, transabdominal preperitoneal (TAPP) and totally extraperitoneal (TEP) techniques are used in laparoscopic inguinal hernia repairs (3). Although the repairs of laparoscopic inguinal hernias have been specified as guidelines by the international endohernia association, today there is no consensus about the superiority of both repair techniques (4). In our study, we aimed to reveal the difference between the two techniques by comparing TAPP and TEP in terms of hernia recurrence, postoperative pain scores, duration of operation, length of postoperative hospital stay and complication rates.

Materials and Methods

In the study, files and outpatient clinic notes of patients who underwent closed inguinal hernia repair in Aydın State Hospital General Surgery Clinic between 2017-2020 July were analyzed retrospectively. Local ethics committee approval was obtained from Aydın Adnan Menderes University Non-Invasive Procedures Committee for the study (protocol no: 2020/159, date: 03.09.2020). Consent for the surgical procedure was taken from the patients. Nevertheless, due to the retrospective nature of the study, consent for the study was not taken from the patients. The patients were classified into two groups as those who were underwent surgery by the TAPP (group 1) technique and the TEP (group 2) technique. Demographic data, hernia characteristics, and follow-up durations of the patients were examined. Postoperative recurrence rates of both groups, postoperative complication rates, types of complications, duration of operation, length of postoperative hospital stay; postoperative first week, first month and third month pain scores were evaluated with the visual analog scale (VAS). It was evaluated whether there was a statistical difference between the data of both groups.

Statistical Analysis

For data evaluation, the SPPS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical packaged program was used. The variables were stated using the mean ± standard deviation, percentage and frequency values. Kolmogorov-Smirnov test was performed to evaluate the homogeneity of the data. In the analysis of data, Student's t-test were used for the comparison of two groups. When Student's t-test did not provide preconditions, Mann-Whitney U test was used. Categorical data were analyzed by Fisher's Exact test and chi-square test. P<0.05 was considered statistically significant.

Results

Files of 113 patients who underwent closed inguinal hernia repair in 2017-2020 July were retrospectively reviewed. While TAPP repair was performed in 43 of these patients (group 1), 70 of them were performed TEP repair (group 2). The mean postoperative follow-up duration of the patients was

found to be 10.01±4.58 months. Of the operated patients, 108 (95.6%) were male and 5 (4.4%) were female. Of the cases, 35 (31%) were direct, 74 (65.5%) were indirect, 4 (3.5%) were pantaloon hernias. Of the patients, 42 (37.2%) had right, 45 (39.8%) left, 26 (23%) had bilateral inguinal hernia. Of the hernias, 35 (31%) were direct, 74 (65.5%) were indirect, 4 (3.5%) were pantaloon hernias. The mean age of the patients was calculated as 51.55±13.81 years. Operation duration was calculated as 51.66±14.33 minutes. The mean duration of follow-up of the patients was calculated as 10.01±4.58 months. Recurrence was detected in 3 (2.65%) patients during follow-up. The demographic data of the patients are shown in Table 1.

The recurrence rate was detected as 2.3% in group 1 and 2.9% in group 2 (p=0.67). When looking at the complications, 7 (16.3%) patients in group 1 and 11 (15.7%) patients in group 2 had complications (p=0.93). As complications, seroma in 2 patients, cord edema in 4 patients, scrotal ecchymosis in 1 patient were detected in group 1; and in group 2, 3 patients had seroma, 6 patients had cord edema, and

2 patients had scrotal ecchymosis. Postoperative 1^{st} week VAS scores were calculated as 2.81 ± 0.958 in group 1, and 2.11 ± 0.84 in group 2 (p<0.001). In the postoperative 1^{st} month, VAS scores were calculated as 0.98 ± 1.12 in the first group and as 0.4 ± 0.8 in the second group (p=0.001). The calculated VAS scores of the patients on the postoperative 3^{rd} month were 0.47 ± 0.85 in the first group and 0.13 ± 0.47 in the second group (p=0.006).

The mean operation duration was calculated as 54.9 ± 14.73 minutes in the patients operated with the TAPP technique, and 49.6 ± 13.8 minutes in the patients operated with the TEP technique (p=0.04). The mean length of hospital stay in patients operated with the TAPP technique was 1.19 ± 0.39 days, and 1.11 ± 0.32 days in patients operated with the TEP technique (p=0.29). Table 2 shows the comparison between the two groups.

Discussion

With the development and widespread use of laparoscopic surgery in 1990, the first minimally

| Table 1. Demographic data of the patients | | | | | | | |
|---|-----------------------------------|---------------|--|--|--|--|--|
| Parameters | Group 1 (TAPP) | Group 2 (TEP) | | | | | |
| Number of patients | 43 | 70 | | | | | |
| Age | 52.51±13.19 | 50.96±14.24 | | | | | |
| Gender | | | | | | | |
| Male, n (%) | 43 (100%) | 65 (92.9%) | | | | | |
| Female, n (%) | 0 (0%) | 5 (7.1%) | | | | | |
| n: Number of patients. TAPP: Transabdominal preperitone | eal. TEP: Totally extraperitoneal | | | | | | |

| Table 2. Detailed comparison of both groups | | | | | | | |
|---|-------------------------------|---------------------------------------|----------|--|--|--|--|
| | Group 1 (TAPP) | Group 2 (TEP) | р | | | | |
| Recurrence, n (%) | 1 (2.3%) | 2 (2.9%) | 0.67 | | | | |
| Complication, n (%) | 7 (16.3%) | 11 (15.7%) | 0.93 | | | | |
| Seroma | 2 | 3 | - | | | | |
| Cord edema | 4 | 6 | - | | | | |
| Scrotal ecchymosis | 1 | 2 | - | | | | |
| VAS 1 st week | 2.81±0.958 | 2.11±0.84 | p<0.001 | | | | |
| VAS 1 st month | 0.98±1.12 | 0.4±0.8 | 0.001 | | | | |
| VAS 3 rd month | 0.47±0.85 | 0.13±0.47 | 0.006 | | | | |
| Duration of operation (minute) | 54.9±14.73 | 49.6±13.8 | 0.04 | | | | |
| Length of hospital stay (days) | 1.19±0.39 | 1.11±0.32 | 0.29 | | | | |
| n: Number of patients, VAS: Visual analo | og scale, TAPP: Transabdomina | I preperitoneal, TEP: Totally extrape | ritoneal | | | | |

invasive inguinal hernia repair was performed in 1992 (5).

Most of the patients we operated were males. Of the 5 female patients we operated with the TEP technique, 4 had an indirect hernia, and 1 had a direct hernia. There are studies stating that inguinal hernias are more common in male gender (6). The cases were mostly left-sided, with indirect inguinal hernia as a type of hernia. In the majority of the population, unilateral hernias have the highest rate of left indirect inguinal hernia (7).

In the patients we operated, recurrence was observed at a rate of 2.3% in group 1, while a recurrence rate was 2.9% in group 2, and no significant difference was observed between the two techniques in terms of recurrence. In a study conducted by Toma et al. (8) on TEP repairs in inguinal hernia, the recurrence rate has been found to be 1.3%, and it closely resembles ours. The recurrence rate has been found to be 3.1% in Erdoğan et al.'s (9) study on repair with the TAPP technique in inguinal hernias, and it was found to be 2.3% in our study. In our study, no significant difference was found between the two techniques in terms of recurrence, and no significant difference has been found in terms of recurrence in the systematic review study performed by McCormack et al. (10). There are various studies in the literature showing that there is no difference between TEP and TAPP techniques in terms of recurrence (11,12).

Different complication rates have been reported in the literature in laparoscopic inguinal hernia repairs. Since the abdomen is entered in the TAPP technique, the surgical area is wider than the TEP technique. It has the advantage of entering the abdomen; however, there is the possibility of developing complications such as trocar site hernias, solid organ injuries, and bride ileus (13,14). In the TEP technique, it is a great advantage that not to enter the abdomen, the operation does not require general anesthesia and the complications in TAPP do not develop as a result (15,16). Nawaz et al. (11) have found in their study no difference in terms of complications between TEP and TAPP techniques. In also our study, no significant difference was found between the two techniques in terms of complications.

Postoperative pain may be more common in the TAPP technique, compared to the TEP technique, due

to the greater use of tackers for fixation purposes in mesh fixation and to close the peritoneum (17). Therefore, absorbable tackers and non-tacker adhesives have been recommended for mesh fixation to reduce postoperative pain (18). We used absorbable tacker (AbsorbaTack, Covidien) in our operations. We think that opening the peritoneum and entering the abdominal cavity in the TAPP technique may be one of the factors that increase pain in the postoperative period. In our study, postoperative 1st week VAS scores were found to be significantly higher in the TAPP group. Although there was a statistically significant increase in pain scores in the postoperative 1st and 3rd months, we think that there was no difference in terms of pain in the long-term since VAS scores between 1 and 0 are not clinically significant.

Although the duration of the operation of the TEP and TAPP techniques may differ, in our study, the mean duration of operation for TAPP was 54.9±14.73 minutes, while duration of operation in the TAPP technique has increased to 90 minutes in Pironi. et al.'s (19) study. In our study, while the duration of operation of the patients operated with the TEP technique was observed as 49.6±13.8 minutes, Hasbahceci et al. (20) in their study on TEP, the mean duration of operation has been found to be 55±22.8 minutes. Nawaz et al. (11) in their study, the operation duration of the TEP technique has been found to be shorter than the TAPP technique. In our study, the operation duration of the TEP technique was found to be shorter than the TAPP technique. We think that this difference may occur due to the extra time spent for peritoneal closure in the TAPP technique.

Although in the study conducted by Baca et al. (21), the length of postoperative hospital stay of patients who underwent TEP surgery was shorter than patients who had surgery with the TAPP technique, no difference was observed in the length of postoperative hospital stay of the patients in our study.

Conclusion

Closed inguinal hernia repair with a low complication rate can be performed safely in patients. While both laparoscopic techniques can be selected according to surgeon's experience and preference, the TEP technique can provide better comfort and shorter operation time for the patient in terms of pain in the early postoperative period compared to the TAPP technique.

Ethics

Ethics Committee Approval: The study was approved by Non-Invasive Clinical Research Ethics Committee of Aydın Adnan Menderes University Faculty of Medicine (protocol no: 2020/159, date: 03.09.2020).

Informed Consent: Consent for the surgical procedure was taken from the patients. Nevertheless, due to the retrospective nature of the study, consent for the study was not taken from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.K., Design: E.K., Supervision: E.M.Y., Fundings: E.M.Y., Materials: E.K., E.Kü., Data Collection or Processing: E.M.Y., Analysis or Interpretation: E.K., E.Kü., Literature Search: E.Kü., Writing: E.K., Critical Review: E.K., E.M.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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Assessment of Morphological Alterations of Temporomandibular Joint Articular Surfaces in Patients with Temporomandibular Dysfunction

Temporomandibular Disfonksiyonlu Hastalarda Temporomandibular Eklem Yüzeylerindeki Morfolojik Değişikliklerin Değerlendirilmesi

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Keywords

Cone-beam computed tomography, mandibular condyle, temporomandibular joint

Anahtar Kelimeler

Konik ışınlı bilgisayarlı tomografi, mandibular kondil, temporomandibular eklem

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Abstract

Objective: This study aimed to examine the distribution of condyle and articular fossa shapes in patients with temporomandibular joint dysfunction (TMD) and their relationship with each other using cone-beam computed tomography (CBCT) images.

Materials and Methods: CBCT scans of 134 patients (268 joints) with TMD were evaluated retrospectively. In the coronal and sagittal views, condyles were classified based on the following basic shapes: round, oval, flattened, and triangular. Shapes of the articular fossa were classified as oval, triangular, angled, and trapezoidal. The evaluation was made in the sagittal and coronal sections where the articular fossa and mandibular condyle were most clearly seen. Data were analyzed using the chi-square test.

Results: Sagittal-oval and coronal-flattened condyles were seen more frequently than other shapes. Identical sagittal and coronal condyles were observed in 83 joints (30.97%). In sagittal sections, the shapes of the articular fossa were oval in 128 (47.8%), angular in 68 (25.4%), trapezoid in 50 (18.7%), and triangular in 22 (8.2%) patients. The most common fossa shape was oval in each shape of the condyles in sagittal and coronal sections. No relationship was found between gender or age groups and shapes of the articular fossa and condyle in all sections. **Conclusion:** Knowledge of condyle and fossa shapes may help clinicians understand morphological bone changes in patients with TMD. CBCT can be used as an accurate diagnostic tool when three-dimensional examinations of TMJ bone surfaces are necessary.

Öz

Amaç: Çalışmanın amacı, temporomandibular eklem (TME) bozukluğu olan hastalarda kondil ve artiküler fossa şekillerinin dağılımını ve birbiriyle ilişkisini konik ışınlı bilgisayarlı tomografi (KIBT) görüntüleriyle incelemektir.

Gereç ve Yöntemler: Bu çalışmada, TME bozukluğu olan 134 hastanın (268 eklem) KIBT görüntüleri geriye dönük olarak değerlendirildi. Koronal ve sagittal kondil

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şekillerinde kullanılan sınıflandırma yuvarlak, oval, düz ve üçgen şeklindeydi. Artiküler fossa şekilleri oval, üçgen, açılı, trapezoid şeklinde sınıflandırıldı. Artiküler fossa ve mandibular kondilin en net görüldüğü sagittal ve koronal kesitlerde değerlendirme yapıldı. Veriler ki-kare testi kullanılarak değerlendirildi.

Bulgular: Sagittal kesitlerde oval ve koronal kesitlerde düz şekil diğer şekillere göre daha sık görüldü. Sadece 83 eklemde (%30,97) sagittal ve koronal kondil şeklinin aynı olduğu tespit edildi. Sagittal kesitlerde eklem fossa şekilleri 128'inde (%47,8) oval, 68'inde (%25,4) açılı, 50'sinde (%18,7) trapezoid ve 22'sinde (%8,2) üçgen şeklindeydi. Sagittal ve koronal kesitlerde her kondil şekli grubunda en yaygın fossa şekil ovaldi. Cinsiyet veya yaş grupları ile artiküler fossa ve kondil şekilleri arasında anlamlı ilişki saptanmadı. **Sonuç:** Kondil ve artiküler fossa şekillerinin bilinmesi, klinisyenlerin TME bozukluğu olan hastalardaki morfolojik kemik değişikliklerini

anlamalarına yardımcı olabilir. KIBT, TME kemik yüzeylerinin üç boyutlu muayenesi gerektiğinde doğru tanı aracı olarak kullanılabilir.

Introduction

The temporomandibular joint (TMJ) is an important and complicated joint in the human body. This joint performs speaking, chewing, and swallowing with the harmony of many soft and hard tissues. The degenerative diseases affecting bone metabolism and trauma can cause morphologic changes in mandibular condyle and articular fossa of temporal bone (1,2). Bone changes occurring in the TMJ, such as subchondral sclerosis, osteophyte formation, surface erosion, flattening can be the causes and the findings of TMJ dysfunction (3).

Temporomandibular joint dysfunction (TMD) is a multifactorial and complex disorder which is common in population. TMD defines the impaired relationship between the articular disc, articular eminence, articular fossa, and mandibular condyle, with symptoms such as joint pain and sounds, headache, restricted jaw movements, and muscle pain (4). Diagnosis of TMD is based on detailed anamnesis, clinical and radiological examination (5).

Radiographic examination is an important diagnostic tool in the evaluation of TMD which identifies bony changes, position of articular disc and spatial relationships of the condyle and the fossa (6,7). Conventional radiography techniques such as panoramic radiography, transcranialoblique radiography, Reverse Towne's radiography only provides limited sectional images of the bony components of the TMJ. These techniques provide superimpositions because of the complexity of TMJ anatomy (8,9). Cone-beam computed tomography (CBCT) technology which is using in dentistry for many years, produces high resolution images with high specificity and sensitivity in diagnosis of TMJ bone changes (10,11). The other hand, magnetic resonance imaging has great advantages that its ability to depict soft tissue changes of the TMJ (12).

Detection of abnormal morphologic changes of TMJ bone tissues is possible with the appropriate imaging method. In the present study, we examined the CBCT images of patients who were previously diagnosed as TMD by the clinical examination. The purpose of the present study was to determine the shape of mandibular condyle and articular fossa according to age, gender.

Materials and Methods

This study was approved by the Aydın Adnan Menderes University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee on Human Research (protocol no: 2020/31, date: 20.02.2020). In the present study, CBCT scans of 134 patients (268 joints) with TMJ dysfunction which performed between July 2016 and October 2019 were evaluated retrospectively. All of patients were scanned with CBCT because of TMD diagnosis and had clinical symptoms such as TMJ pain, noise during jaw movements, mouth-opening limitation, and nonharmonic movements of the joint. The presence of congenital craniofacial abnormalities, history of facial trauma, orthodontic treatment and any systemic conditions that may affect the bone tissues and CBCT images with artefacts that preventing optimal evaluation were excluded from the study.

All CBCT images were acquired by Planmeca Promax 3D (Planmeca, Helsinki, Finland) with standard TMJ mode (field of view 8x5 cm², 90 kV, 8 mA, 12 s, voxel size: 0.2 mm) and examined Romexis software v3.83. Radiological assessments were analyzed by 2 experienced dentomaxillofacial radiologists independently. Differences in interpretation of the images were solved by consensus.

The condylar shapes and fossa shapes were categorized according to Cortés et al. (13), Katsavrias (14) and Yasa and Akgül (15) previously reported

classification. The basic shapes used for classification included round, oval, flattened, and triangular for the condyles in a coronal and sagittal view (Figure 1, 2) articular fossa shapes were classified as oval, triangular, angled, trapezoidal (Figure 3). Evaluation was made in the sagittal and coronal sections where the articular fossa and mandibular condyle were most clearly seen.

Statistical Analysis

Statistical analyses were conducted with SPSS software (SPSS 22.0 for Windows; SPSS Inc., Chicago, IL, USA). Differences in condyle and fossa shapes

between the groups were evaluated by chi-square test followed by a Bonferroni post-hoc test. Values of p<0.05 were considered to indicate statistical significance.

Results

In 134 patients with TMD, 268 joints (38 males and 96 females; mean age, 41.60±16.07 years) were examined. The distribution of the condyle shapes in the coronal and sagittal sections are listed in Table 1. There was a significant statistical relationship between coronal and sagittal condyle shape



Figure 1. Four condyle shapes in a coronal section: oval (a), triangular (b), flattened (c), round (d)



Figure 2. Four condyle shapes in a sagittal section: oval (a), triangular (b), flattened (c), round (d)



Figure 3. Four fossa shapes in a sagittal section: oval (a), triangular (b), angled (c), trapezoid (d)

(p=0.001). A sagittal-oval condyle shape (p=0.000) and coronal-flattened shape (p=0.009) were seen more frequently than other shapes. The post hoc test revealed that if sagittal condyle shape is oval, triangular shape is significantly less than round shape in coronal view. If sagittal condyle shape is flattened, round shape is significantly less than flattened and triangular shape in coronal view (Table 1). It was found that identical sagittal and coronal condylar shape occurred in only 83 joints (31%).

The distribution of the articular fossa shapes in the sagittal sections was presented in Table 2. The shapes of articular fossa in sagittal sections were oval in 128 (47.8%), angled in 68 (25.4%), trapezoid in 50 (18.7%) and triangular in 22 (8.2%). There was no significant difference between the shape of condyle in sagittal or coronal sections and the shape of articular fossa (respectively p=0.954, p=0.072). The most common fossa shape was oval in each shape of the condyles in sagittal and coronal sections.

The distributions of shapes of condyle and fossa according to gender were shown in Table 2. There was no relationship between gender and shape of condyle in coronal and sagittal sections (p=0.273, p=0.412 respectively). In sagittal section, triangular articular

fossa was significantly less than oval articular fossa in both genders (p=0.004).

The patient was grouped according to the age of the subjects (18-39, 40-59, 60-81 years). There were no significant differences between sagittal condyle shapes, coronal condyle shapes sagittal fossa shapes and age groups (respectively p=0.075, p=0.062, p=0.922).

Discussion

In this study, we investigated the distribution and relationship of condyle and fossa shapes in TMD patients. Knowledge of the specific morphological changes of TMJ are necessary for accurate diagnosis supported by clinical examination. There are limited studies in the literature examining the relationship between the shapes of condyle and articular fossa in patients with TMD (2,14-19). To the best of our knowledge, this is the first study to evaluate the relationship between coronal condylar shapes and sagittal condylar shapes. Findings of the present study may help clinicians to understand morphologic bone changes in TMD and to treat their patients accurately at the same time.

| Table 1. Distribution of condyle shapes on coronal and sagittal sections | | | | | | | | |
|--|-----------|--------------|------------|------------|------------|-------------|--------|--|
| | | Coronal view | | | | | | |
| Round Oval Triangular Flattened | | | | | | | þ | |
| | Round | 12 | 10 | 4 | 5 | 31 (11.6%) | 0.123 | |
| 3 | Oval | 50 | 29 | 20 | 41 | 140 (47.8%) | 0.002* | |
| l vie | Triangle | 5 | 3 | 8 | 5 | 21 (8.2%) | 0.488 | |
| gitta | Flattened | 9 | 13 | 20 | 34 | 76 (28.4%) | 0.000* | |
| SaĘ | Total | 76 (28.4%) | 55 (20.5%) | 52 (19.4%) | 85 (31.7%) | 268 (100%) | - | |
| *Chi-square test. P<0.05 was significant | | | | | | | | |

| Table 2. Association between genders and shapes of condyle and articular fossa | | | | | | | | | | | | |
|--|------------------------|------|-----------|------------|-----------------------|------|-----------|----------------------|------|------------|--------|-----------|
| | Sagittal condyle shape | | | | Coronal condyle shape | | | Sagittal fossa shape | | | | |
| | Round | Oval | Flattened | Triangular | Round | Oval | Flattened | Triangular | Oval | Triangular | Angled | Trapezoid |
| Women | 20 | 97 | 58 | 17 | 49 | 38 | 66 | 39 | 99 | 9 | 46 | 38 |
| Men | 11 | 43 | 18 | 4 | 27 | 17 | 19 | 13 | 29 | 13 | 22 | 12 |
| Total | 31 | 140 | 76 | 21 | 76 | 55 | 85 | 52 | 128 | 22 | 68 | 50 |
| р | 0.412 0.273 0.004* | | | | | | | | | | | |
| *Chi-square test. P<0.05 was significant | | | | | | | | | | | | |

Clinical and radiological examinations are important in evaluating patients with TMD. Various radiologic methods have been used in previous studies to examine the morphologic changes of articular fossa and condyle (2,18,20,21). We examined TMJ bone surfaces with CBCT because of its superiorities in bone tissue imaging. Through the three dimensional imaging methods, CBCT has many advantages such as lower radiation dose, shorter exposure time and accessibility (22,23). So, CBCT can be used when the clinician suspects any changes in bone surfaces of TMJ which is limited in two-dimensional imaging.

Previous studies showed a higher prevalence of convex, rounded and angled condyles in patients with anterior disc displacement (17,24). In the research of Katsavrias (14), distribution of condyle shapes in coronal CBCT sections was oval in 60.4%, followed by round in 29.2%, flattened in 5.25%, triangular 5.2% of the patients with Class II Division 2 malocclusions in non-TMD population. In the same study, percentages for the fossa shapes were oval in 58.3%, triangular in 18.8%, trapezoidal in 15.6% and round in 7.3%. Cağlayan et al. (16) determined that there were differences in the mandibular condyle and fossa shapes among with and without TMJ disorder in CBCT sections. They reported the distribution of coronal condyle shapes in the TMJ disorder group were round in 45.2%, flattened in 26.0%, triangular in 5.8% and oval in 23.1% and the most common shape of condyle was oval in without TMJ disorder subjects. They also found that most common shape of articular fossa was round in both groups. In the study conducted by Yasa and Akgül (15), an oval-shaped condyle and fossa were the most common variant in both the asymptomatic group and the TMD group. Regarding the articular fossa morphology in the sagittal section, our findings were in agreement with Katsavrias (14) and Yasa and Akgül (15), but in the coronal sections, distribution of condyle morphologies were different. Our findings were compatible with Santos et al. (17) who observed a higher prevalence of flattened condyles in patient with TMD. Distribution the shapes of articular surfaces may change due to number differences in the selected patient population, genetic, age group or racial differences.

Matsumoto et al. (18) suggested that the disharmony between the condyle and fossa shape may cause anterior disc displacement. Katsavrias (14)

matched articular fossa and condylar shapes in sagittal sections and revealed that 52.1% joint had identical shapes. In the present study, we did not compare fossa and condyle shapes with each other, but the most common fossa shape was oval in all condyle shapes. In the present study, when the shape of condyle in the sagittal and coronal section was matched, it was observed that the same appearance was observed in only 31% of condyles. In patients with TMD, different shapes of condyle and articular fossa can be observed in different sections due to different of biological and functional aspects.

In the study conducted by Tassoker et al. (19), it was found that there was no relationship between coronal condyle shape and gender. In the same study, it was indicated that the frequency of the flattened and angled coronal condyle shape increased with increasing age. Similarly, Yalcin and Ararat (2) found a correlation between age and coronal condyle shapes. However, in the present study no relationship was found between the shapes of articular surfaces, genders and age groups.

Conclusion

CBCT provides a three-dimensional image of the TMJ bone tissues without distortion and magnification. Because of increased accuracy in the diagnosis of cortical bone alterations, CBCT can be used for a dignostic tool when three dimensional examinations of TMJ bone surfaces needed. Our results will be suggestive when evaluating CBCT images of patients with TMD. Limitations of the present study were the absence of the non-TMD group and the non-known of clinical symptoms because this was a retrospective study. Further studies are needed to include larger TMD and non-TMD patient groups. This methodology is very simple, and more sophisticated methods such as geometric morphometric analysis should be used for shape studies.

Ethics

Ethics Committee Approval: This study was approved by the Aydın Adnan Menderes University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee on Human Research (protocol no: 2020/31, date: 20.02.2020).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: R.S.A., Design: R.S.A., Supervision: E.K., Data Collection or Processing: R.S.A., Analysis or Interpretation: R.S.A., Literature Search: R.S.A., Writing: R.S.A., E.K., Critical Review: E.K.

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Comparison of CE-Chirp and Click Auditory Brainstem Response Methods in Patients with Unilateral Total Hearing Loss

Tek Taraflı Total İşitme Kaybı Olan Hastalarda CE-Chirp ABR ve Click ABR Yöntemlerinin Karşılaştırılması

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Keywords

CE-Chirp ABR, Click ABR, unilateral, total hearing loss

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Abstract

Objective: To compare the V. wave latencies, amplitudes, and testing times of auditory brainstem response (ABR) using Click and CE-Chirp stimuli in patients with unilateral total hearing loss (HL).

Materials and Methods: Male patients with one normal ear and a total HL in the other were tested for Click and CE-Chirp ABR, Pure Tone Audiometry (PTA), Stenger, and Tympanometry. PTA thresholds in normal hearing ears were 20 dB HL for each frequency, tympanogram resulted to type A, and Stenger was negative in total HL. Click and CE-Chirp stimuli were sent using an alternating polarity and inserting ER 3A headphones (Rate: 20.1, High Pass Filter: 100 Hz, and Low Pass Filter: 3,000 Hz). Ear with total HL tested with 100 dB and 95 dBnHL, normal hearing ear was tested with 80, 60, 40, 30, 20, and 10 dBnHL, 15 dB, and 5 dBnHL to determine the hearing level. ABR thresholds, V. wave latencies, amplitudes, and test times for each Click and CE-Chirp stimuli were compared.

Results: Results of 71 patients were analyzed. The CE-Chirp ABR wave V amplitudes were higher at all levels except 80 dBnHL. Click ABR wave V latencies at 80 and 60 dBnHL levels were longer (p=0.00). CE-Chirp ABR wave V latencies at 40 dBnHL and below were longer (p=0.00). CE-Chirp ABR thresholds (12.81 dBnHL) were closer to 2-4 kHz behavioral threshold averages (10.45 dBnHL) than Click ABR thresholds (14.64 dBnHL). CE-Chirp ABR test time was shorter (14.57 \pm 3.83 vs. 17.91 \pm 3.94 min, p=0.00).

Conclusion: The CE-Chirp stimulus was used to evaluate the normal hearing ear in patients with unilateral total HL, which shortens the test time and provides closer results to behavioral thresholds. CE-Chirp ABR method is more advantageous than the Click ABR method to evaluate patients with unilateral total HL.

Öz

Amaç: Tek taraflı total işitme kaybı olan hastalarda Click ve CE-Chirp uyaranları ile elde edilen işitsel beyin sapı yanıtı (ABR) eşiklerinin V. dalga latans ve amplitüdlerini ve test zamanlarını karşılaştırmaktır.

Gereç ve Yöntemler: Bir kulağı total işitme kayıplı, diğer kulağı normal işiten erkek hastalara Click ve CE-Chirp uyaranlar kullanılarak sedasyon altında ABR testi

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yapıldı. Pure Tone Odiyometri (PTA), Stenger testi ve Timpanometri testleri uygulandı. Normal işiten kulaklarında PTA eşikleri her frekans için ≤20 dB HL, timpanogram sonucu tip A ve total işitme kayıplı kulaklarında Stenger negatif olan kişiler dahil edildi. Click ve CE-Chirp uyaranlar alternating polarite ve insert ER 3A kulaklıklar ile gönderildi. Rate: 20,1, Yüksek Geçiren Filtre (HPF): 100 Hz, Alçak Geçiren Filtre (LPF): 3.000 Hz olarak ayarlandı. Total işitme kayıplı kulaklar Click ve CE-Chirp uyaran kullanılarak 100 dB ve 95 dB ses şiddetlerinde ABR testi uygulandı. Normal işiten kulaklara 80, 60, 40, 30, 20, 10 dB ve eşik belirlemek için gerektiğinde 15 dB, 5 dB düzeyinde sesler gönderildi. Click ve CE-Chirp uyaran ile gerçekleştirilen ABR eşikleri, dalga V latansları, dalga V amplitüdleri ve test süreleri karşılaştırıldı.

Bulgular: Yetmiş bir hastanın sonuçları incelendi. 80 dB nHL dışındaki bütün düzeylerde CE-Chirp ABR dalga V amplitüdleri Click ABR dalga amplitüdlerinden daha büyüktü. 80 ve 60 dB nHL düzeylerinde Click ABR dalga V latansları CE-Chirp ABR dalga latanslarından uzun bulunurken (p=0,00), 40 dB nHL ve altındaki düzeylerde CE-Chirp ABR dalga V latansları Click ABR daha uzundu (p=0,00). CE-Chirp ABR eşikleri (12,81 dB nHL) Click ABR eşiklerine (14,64 dB nHL) göre 2-4 KHz davranışsal eşik ortalamalarına (10,45 dB nHL) daha yakındı. CE-Chirp ABR test süresi Click ABR test süresinden daha kısaydı (14,57±3,83 vs. 17,91±3,94 dakika, p=0,00).

Sonuç: Unilateral total işitme kaybında CE-Chirp uyaran kullanımının ABR test süresini kısalttığı ve normal işiten kulaklarda davranışsal işitme eşiklerine daha yakın cevaplar sağladığı gözlenmiştir. Unilateral total işitme kayıplı hastaların değerlendirilmesinde CE-Chirp ABR yöntemi Click ABR yönteminden daha avantajlıdır.

Introduction

Brainstem auditory-evoked potentials (AEPs) are bioelectrical potentials that arise from specific neural activities in the auditory pathway from the cochlea to the auditory cortex after the presentation of an auditory stimulus (1). Although this electrical activity takes approximately 0.5 seconds with low severity, it can be recorded in case of voltage fluctuations using electrodes placed on the skin surface (1,2). Auditory brainstem response (ABR) is defined as AEPs that occurs in the process between 2-12 msec after auditory stimulation in healthy individuals (2). ABR results are recorded based on Click, tonal and Chirp techniques. In the Click ABR method, the sound wave reaches its peak from the basal region of the cochlea in a longer time. The low frequency region of the originated response emerges msec after the high-frequency region (3). Basal cells are not stimulated ubiquitously. Thus, nerve cells cannot occur simultaneously by depolarization. This situation is clarified as cochlear travel delay or cochlear delay (waves of sound circulation time in the cochlea) (3,4). Chirp record is a newly defined stimulus for ABR evaluation (5). Chirp stimulus can be broad band Click-stimulus derivative CE-Chirp or narrow as frequency-specific tone-band derivative narrow-band CE (NB-CE) Chirp. In recent years, there is also a newly developed level specific (LS) Chirp stimulus (6). Frequency spectrums of Click and CE-Chirp stimuli are the same. CE-Chirp is a stimulus developed to assess ABRs. This stimulus can provide synchronous stimulation in the cochlea (5,6). The difference of the CE-Chirp stimulus from the Click stimulus is the occurrence of delivery of low,

medium and high-frequency components to stimulate all frequency regions in the cochlea simultaneously basal cells can achieve different frequency targets using CE-Chirp stimulus (7). Larger amplitude ABR waves are obtained by simultaneous depolarization in all frequency regions of the cochlea by CE-Chirp stimulus (1,2).

This study was designed to compare the ABR test results obtained with CE-Chirp and Click stimuli in patients with unilateral total hearing loss.

Materials and Methods

This study was a cross-sectional analytical research. Ethical approval was obtained with the decision of Gülhane Military Medical Academy Ethics Committee (decision no: 50687469-1491-139-14/1648.4-407, date: 25.02.2014) for this study. This study was conducted in accordance with the Helsinki Declaration. Seventy-one men (18-25 years old) with one ear with total hearing loss and the other ear with normal hearing participated in the study. All individuals participating in the study were informed by experts and their verbal and written consents were obtained. According to the results of Pure Tone Audiometry (PTA), Stenger test and tympanometry tests, male patients with total hearing loss in one ear and hearing the other ear normally were included in the study. Among these patients, patients between the ages of 19-25 and PTA thresholds for normal hearing ears with ≤20 dB HL for each frequency were included in the study. Patients who were diagnosed with mental retardation, having psychiatric disease, and getting out of sleep were excluded from this study.

In order for the patients to be included in the study, their normal hearing ears; for each frequency 20 dB HL PTA thresholds, type A tympanogram, negative Stenger test result were required. TABR thresholds, wave V latencies and wave V amplitude data were analyzed in patients' normal hearing ears. The time taken to obtain ABR responses via CE-Chirp and Click stimulus were also compared.

PTA tests were performed using the Interacoustics model AC40 (calibrated as per ANSI S3.6, 1996) (Interacoustics AS, Assens, Denmark) as the Pure Tone Audiometer device in the soundproof cabinet. PTA Airway thresholds (between 250-8,000 Hz), bone path thresholds (between 500-4,000 Hz) were tested. Headphones TDH 39 (Telephonics Co. Farmingdale, NY, USA) were used for airway transmission and vibrator RadioEar B-71 (RadioEar Co. Middelfart, Denmark) were used for bone conduction. Then, these patients underwent sedation and ABR tests were performed with Click stimulus and CE-Chirp stimulus. The sedation of the patients was provided by the relevant anesthesia team. CMS-60 model pulse oximeter device was used to control the pulse and oxygenation of the patient after sedation. In order to provide oxygen to the patient, 10 liters, 150 Bar, 1.5 m³ medical oxygen cylinder was kept in the room.

Click ABR and CE-Chirp ABR tests were applied under the sedation to patients who conformed circumstances stated above. Interacoustic Eclips Ep 15 ABR system (Interacoustics, Middelfart, Denmark) was used for ABR testing and recording. The stimuli were calibrated to ISO 389-6 (2007) for the Click and to manufacturer's data for the Chirps. In ABR test protocol, electrodes with the positive line were placed on the upper forehead area, electrodes with the neutralized line were placed on the bottom side of the forehead, while one negative electrode was settled on to the mastoid process area on the left and other one was settled on to the mastiod process area on the right. The positive (active) electro was placed in the midline upper part (Fz) of the forehead, the ground electrode in the midline (Fpz) of the forehead, the reference electrodes were placed in the right (M2) and left (M1) mastoid areas. Reference electrodes were placed on the right (M2) and left (MI) mastoid areas. Care was taken to ensure that the electrode-skin impedances are below 3 k Ω and that the cables do not overlap. Click and CE-Chirp stimuli

were sent via the insert ER-3A (Etymotic Research) headphones with alternating polarity, rate: 20.1. High Pass Filter: 100 Hz, Low Pass Filter (LPF): 3,000 Hz and artefact exclusion level were set to 40 nV in the measurements. The tests were started by sending monaural Click stimulus to the ears with total hearing loss. Ears with total hearing loss were tested at 100 dB and 95 dB. While testing ears with total hearing loss, a mask sound was sent to normal hearing ears. Normal hearing ears of the patients were tested at levels such as 80, 60, 40, 30, 20, 10 dB and, if necessary, 15 dB, 5 dB to determine the threshold. After performing ABR test using Click stimulus, ABR was performed using CE-Chirp stimulus with the same test technique. ABR wave V amplitudes (peak to following trough) and their latencies were determined.

The preparation stage of the patients for the test was not included in the test period. When the patients were asleep for the test, the tests were started and the test times were recorded.

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 program (IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp, USA). Click ABR and CE-Chirp ABR for dependent variables in comparing the differences between wave latency findings; Paired t-test) between the means of paired data averages was chosen as the method. Kolmogorov-Smirnov test was used to test normality assumption. Click ABR and CE-Chirp ABR test time comparison (Paired t-test) method was used. ANOVA "One-Way Analysis of Variance" was used to control the proximity between the Click ABR threshold, the CE-Chirp ABR threshold and the PTA 2-4 KHz thresholds, and the average of the 2-4 KHz threshold, and the Tukey test was used to control the factor that caused the difference. Tukey test was applied to control the factor that caused all the difference with a significance level of 95% or α=0.05.

Results

In this study, the data obtained from 71 male patients between the ages of 19-25 who had a mean age of 28.6 were evaluated. Twenty-eight of the patients had right (39.4%) and 43 (60.6%) of the patients left ears had total hearing loss. ABR waves were not observed with both types of stimuli in ears with total hearing loss. Pure sound tonal

audiometry thresholds of normal hearing ears are shown in Table 1. The differences of the thresholds were examined using One-Way ANOVA [Tukey t-test (phostoc)] method in the normal hearing ears. As a result, PTA was determined as 2-4 KHz threshold average < CE-Chirp ABR threshold < Click threshold. According to the CE-Chirp ABR thresholds, PTA was found closer to the 2-4 KHz threshold averages compared to the Click ABR thresholds (Figure 1). One-Way ANOVA (Tukey t-test method) was used to examine the differences of the thresholds in the normal hearing ears of the patients. Click ABR thresholds was



Figure 1. Comparison of Click ABR and CE-Chirp ABR avarage thresholds in terms of proximity to the 2-4 KHz pure tone audiometry avarage threshold in normal hearing ears of patients

seen to be different from the behavioral thresholds than the PTA thresholds. Results closer to the 4 KHz thresholds were found compared to the 2 KHz and 2-4 KHz threshold averages (Figure 2). It was also investigated to which frequency region the CE-Chirp ABR thresholds were closer than the behavioral thresholds. Thus, CE-Chirp ABR Threshold PTA was found similar and close to the 4 KHz threshold. CE-Chirp ABR thresholds were found close to the 2-4 KHz threshold average after 4 KHz and the latest 2 KHz PTA thresholds. We should note that CE-Chirp ABR thresholds are very close to similar to behavioral thresholds to 4 KHz thresholds (Figure 3, Table 2). According to the results obtained by comparison



Figure 2. Click ABR thresholds and PTA thresholds of patients' normally hearing ears

ABR: Auditory brainstem response, PTA: Pure Tone Audiometry

| Table 1. Average values of pure tonal audiometry test results of normal hearing ears of patients | | | | | | | | | |
|--|---|------|------|------|------|------|------|--|--|
| | 250 Hz 500 Hz 1,000 Hz 2,000 Hz 4,000 Hz 8,000 Hz | | | | | | | | |
| | Air path (dB) | 14.3 | 12.3 | 10.9 | 8.7 | 11.4 | 13.5 | | |
| Right | Bone path (dB) | 7.8 | 7.4 | 6.3 | 6.3 | 7.1 | 6.4 | | |
| | Air path (dB) | 17 | 14.5 | 13.2 | 10.5 | 11.6 | 13.9 | | |
| Left | Bone path (dB) | 11.3 | 9.5 | 8.2 | 8.4 | 7.9 | 7.9 | | |

| Table 2. The relationship between CE-Chirp ABR thresholds and behavior thresholds of patients' normal hearing ears | | | | | | | |
|--|--------------------|----------------|----------------|--|--|--|--|
| Test | Number of patients | 1 | 2 | | | | |
| Pure Tone Audiometry 2 KHz threshold average | 71 | 9,6479 dB nHL | - | | | | |
| Pure Tone Audiometry 2-4 KHz threshold average | 71 | 10,4577 dB nHL | - | | | | |
| Pure Tone Audiometry 4 KHz threshold average | 71 | 11,2676 dB nHL | 11,2676 dB nHL | | | | |
| CE-Chirp ABR threshold | 71 | | 12,8169 dB nHL | | | | |
| | - | 0.125 | 0.153 | | | | |
| ABR: Auditory brainstem response | | | | | | | |

ABR: Auditory brainstem response, PTA: Pure Tone Audiometry

statistical tests, wave V latencies were found to be longer at 80 dB nHL and 60 dB nHL than CE-Chirp ABR method with Click ABR method (p=0.00). Contrary to high intensities at 40 dB nHL, CE-Chirp wave V latencies were shorter than Click ABR wave V latencies (p=0.00) (Figure 4). At 80 dB nHL, Click ABR wave V amplitudes were larger than CE-Chirp ABR wave V amplitudes, while at lower levels CE-Chirp ABR wave V amplitudes were recorded as larger than Click ABR wave V amplitudes (Figure 5). The CE-Chirp ABR test time was found to be shorter than the Click ABR test time [(14.57±3.83 vs. 17.91±3.94) minutes, p=0.00]. The preparation stage of the patients for testing was not included in the test time. The test was started when the patients went to sleep required for the test, and from this moment on, the test times were recorded.



Figure 3. CE-Chirp ABR thresholds and PTA thresholds of patients' normally hearing ears



ABR: Auditory brainstem response, PTA: Pure Tone aAudiometry

Figure 4. Comparison of Click ABR and CE-Chirp ABR wave V latencies of normal hearing ears of patients

ABR: Auditory brainstem response, PTA: Pure Tone Audiometry

Discussion

In our study, ABR waves were not observed with both types of stimuli for the ears of patients in total hearing loss. In patients' normal hearing ears, CE-Chirp ABR thresholds (12.81 dB nHL) were found closer to the average of 2-4 KHz behavioral thresholds (10.45 dB nHL) than the Click ABR thresholds (14.64 dB nHL) (Figure 1). Example Click ABR and CE-Chirp ABR images demonstrate that the CE-Chirp ABR threshold is determined 5 dB lower than the Click ABR threshold. Prigge et al. (6) reported that individuals with normal hearing had more reliable feedbacks than CE-Chirp stimulus and Click stimulus, and CE-Chirp stimulus was the ideal stimulus regarding threshold estimation. In our study, the closeness of CE-Chirp ABR thresholds and Click ABR thresholds to behavioral threshold averages of 2 KHz, 4kHz, 2-4 kHz were also examined. It is noteworthy that CE-Chirp ABR thresholds are very close to similarly to behavioral thresholds to 4 kHz thresholds.

In 30-35 dB nHL, result of "passed" in hearing screening was obtained with CE-Chirp ABR more than CE-Chirp stimulus results by comparison of 40 newborns with a risk of hearing loss and no risk of hearing loss based on Almeida et al. (8) findings. In their study, Cebulla et al. (9) investigated the waveform morphology, latency, and amplitude values in newborns and compare them with those evoked by the Click. Their findings showed that regardless of the type of stimulus in 96 newborns at 60 dB nHL, wave V was present in all newborns, at 40 dB nHL; wave V. was present as 95% with Click ABR, while Chirp ABR was determined as 100% (9). Khorsand et al. (10)



Figure 5. Comparison of Click ABR and CE-Chirp ABR wave V amplitude sizes of the patients' normal hearing ears

ABR: Auditory brainstem response

studied on the CE-Chirp and Click ABR comparison and they repoerted that thresholds of V. wave in 15 individuals with no hearing impairment between the ages of 20-30 and CE-Chirp ABR wave V thresholds were obtained approximately 5 dB better than the Click ABR wave V thresholds (10).

In our study, CE-Chirp ABR wave V amplitudes were found to be larger in all ears except normal 80 dB nHL than Click ABR wave V amplitudes demonstrated in Figure 5. Consistent with our findings, Khorsand Sabet et al.'s research showed that in 15 individuals with normal hearing had bigger amplitudes than Click ABR wave V amplitudes than CE-Chirp ABR at 20, 40, 60 dB sound intensity. Click ABR wave V had bigger amplitudes than that of CE-Chirp ABR at 80 dB nHL (10). Similarly, a study was conducted by Rodrigues and Lewis (5) conducted with 12 adults with normal hearing, their findings showed that higher levels of amplitude than CE-Chirp ABR and Click ABR were obtained in all levels (60, 40, 30, 20, 10 dB nHL) except 80 dB nHL.

Compatible with our findings, in their study, Stuart and Cobb (11). In their study in which they compared the results of ABR tests with CE-Chirp and Click stimuli in 23 newborns at 30 dB nHL, their findings showed that larger wave V amplitudes were obtained with CE-Chirp stimulus. There are some other studies indicating that the deficiency in normal hearing ears at 80 dB nHL with CE-Chirp stimulus to provide lower amplitude responses than Click stimulus and can be eliminated by LS Chirp stimulus. Elberling et al. (12) studied to compare ABR test results obtained via LS Chirp, classical CE-Chirp and Click stimulus in normal hearing individuals. They reported bigger amplitudes in LS Chirp stimulus than both CE-Chirp ABR and Click ABR at 80 dB nHL (12).

Cargnelutti et al. (13) obtained larger wave V amplitudes compared to LS stimulus and Click stimulus by performing a comparative study with LS CE-Chirp ABR and Click ABR results at 85 dB nHL in 30 individuals with normal hearing. Since our research was conducted using sedation when the patient went to rest required for the test, the tests were started and the test times were recorded from this moment. In this respect, both ABR methods were applied equally and simultaneously in our study, which makes our research advantageous regarding comparing ABR test times performed with both stimulus types. In our study, CE-Chirp ABR test time was shorter than Click ABR test time [(14.57±3.83 vs. 17.91±3.94) minutes, p=0.00].

Inconsistent with our findings, Almeida et al.'s (8) findings showed application time of CE-Chirp ABR test at 30-35 dB nHL was shorter than that of Click ABR test and results' potentials were compared with Click stimulus and Chirp stimulus in 96 newborns (8). Greater amplitude responses were obtained with Chirp ABR, and more reliable test results besides shorter test time were reported (9). It has been shown to be five minutes faster (14).

In a study on the use of CE-Chirp stimulus for monitoring during surgery which was conducted by Di Scipio and Mastronardi (15). Their findings showed that the use of Chirp ABR during surgery provides a rapid response with larger wave amplitudes and may also provide faster feedback to the surgeon who performs the surgery (15).

There are also studies showing that the Chirp stimulus has areas of use other than the ABR test. Chertoff et al. (16) achieved larger N1 wave amplitudes in the Combined Action Potentials performed with Chirp stimuli in 16 adults with normal patients.

NB-CE Chirp ASSR thresholds and Tone Burst ABR thresholds for closeness to behavioral thresholds in children with normal and hearing loss patients were compared in Venail et al.'s (17) studies. It has been reported that there is a high degree of correlation between NB-CE Chirp ASSR thresholds and 0.5, 1, 2, 4 KHz behavioral thresholds (18). These results suggest that the clinical use of Chirp stimulus may also become widespread in other electrophysiological audiology test applications.

Conclusion

CE-Chirp ABR thresholds were found closer to PTA thresholds than Click ABR thresholds in normal hearing ears of patients with unilateral total hearing loss. It has also been found that ABR can be performed in a shorter time with the CE-Chirp stimulus.

The findings obtained in this study suggest that the use of CE-Chirp stimulus in patients with unilateral total hearing loss shortened the time of ABR testing and provided closer responses to behavioral thresholds (PTA thresholds) than Click ABR thresholds in normal hearing ears of patients with unilateral total hearing loss. The results of this study; supports that the use of CE-Chirp stimulus may be more appropriate compared to Click stimulus when performing ABR test in patients with unilateral total hearing loss.

Ethics

Ethics Committee Approval: Ethical approval was obtained with the decision of Gülhane Military Medical Academy Ethics Committee (decision no: 50687469-1491-139-14/1648.4-407, date: 25.02.2014) for this study.

Informed Consent: All individuals participating in the study were informed by experts and their verbal and written consents were obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.C., M.F.Ö., Design: S.C., M.Ş., M.F.Ö., Supervision: M.F.Ö., M.Ş., Fundings: S.C., M.F.Ö., Materials: S.C., M.Ş., Data Collection or Processing: M.Ş., S.C., M.F.Ö., Analysis or Interpretation: S.C., M.Ş., M.F.Ö., Literature Search: M.Ş., S.C., M.F.Ö., Writing: S.C., M.Ş., Critical Review: M.Ş., M.F.Ö., S.C.

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Measurement of Oncostatin M, Leukemia Inhibitory Factor, and Interleukin-11 Levels in Serum, Saliva, and Gingival Crevicular Fluid of Patients with Periodontal Diseases

Periodontal Hastalıklı Bireylerde Serum, Tükürük ve Diş Eti Oluğu Sıvısında Onkostatin M, Lösemi İnhibitör Faktör ve İnterlökin-11 Seviyelerinin İncelenmesi

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Keywords

Chronic periodontitis, interleukin-11, leukemia inhibitory factor, oncostatin M, periodontal therapy

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Abstract

Objective: This study aimed to determine oncostatin M (OSM), interleukin-11 (IL-11), and leukemia inhibitory factor (LIF) levels in gingival crevicular fluid (GCF), saliva, and serum in periodontally healthy individuals and those with gingivitis (G) and chronic periodontitis (CP) before and after periodontal treatment and to evaluate the relationship between these cytokine levels and clinical periodontal parameters.

Materials and Methods: This study involved 24 patients with healthy (H) periodontal tissues, 24 patients with G, and 24 patients with CP. Initially, GCF, saliva, and serum samples were collected, and clinical periodontal measurements, including the plaque index, gingival index, probing depth, and clinical attachment levels, were recorded. At 8 weeks after the initial periodontal treatment, the abovementioned parameters were recorded in the G and CP groups. Cytokine levels were determined using enzyme-linked immunosorbent assay.

Results: OSM levels in the GCF, saliva, and serum were significantly higher in the CP group (p<0.05) than in other groups. LIF levels in GCF exhibited a significant increase (p<0.05) in the CP group; however, no significant difference was found in the serum and saliva LIF levels among groups (p>0.05). IL-11 levels were significantly higher in the CP group (p<0.05) than in other groups, but no significant difference was noted in the serum IL-11 levels among the groups (p>0.05). Similarly, saliva IL-11 levels were significantly higher in the CP group (p<0.05), that in the CP group than in the H group (p<0.05), but they did not show significant difference between the CP and G groups (p>0.05). Comparative analysis of GCF, saliva OSM, and IL-11 levels in the G and CP groups before and after initial periodontal therapy revealed that they are significantly lower in both groups after therapy (p<0.05).

Conclusion: Levels of OSM, LIF, and IL-11 are higher in the G and CP groups, which indicate periodontal tissue destruction. Decreases in IL-11, OSM, and LIF levels after treatment support the idea that initial periodontal therapy can inhibit periodontal tissue destruction.

Öz

Amaç: Bu çalışmanın amacı periodontal açıdan sağlıklı, gingivitisli ve kronik periodontitisli bireylerde tedavi öncesi ve sonrasında diş eti oluğu sıvısı (DOS), serum ve tükürükte onkostatin M (OSM), lösemi inhibitör faktör (LIF) ve interlökin-11 (IL-11) seviyelerini tespit etmek ve klinik periodontal parametreler ile adı geçen bu sitokin seviyeleri arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Bu çalışmaya 24 periodontal olarak sağlıklı, 24 gingivitisli (G) ve 24 kronik periodontitisli (CP) birey dahil edildi. Başlangıçta tüm gruplardan DOS, serum ve tükürük örnekleri alındı ve plak indeksi (Pİ), gingival indeks (Gİ), sondalanabilir cep derinliği (SCD) ve klinik ataşman kaybı (KAK) değerlerini içeren klinik periodontal ölçümler kaydedildi. G ve CP gruplarında başlangıç periodontal tedaviden 8 hafta sonra veriler tekrar kaydedildi. Sitokin düzeyleri enzime bağlı immünosorbent testi metoduyla saptandı. **Bulgular:** DOS, serum ve tükürük OSM seviyeleri CP grubunda diğer gruplara göre anlamlı derecede yüksek bulundu (p<0,05). DOS LIF seviyeleri CP grubunda diğer gruplara göre anlamlı derecede yüksek bulunurken (p<0,05), serum ve tükürük LIF seviyeleri gruplar arasında farklılık göstermedi (p>0,05). DOS IL-11 seviyeleri CP grubunda diğer gruplara kıyasla anlamlı derecede yüksek bulundu (p<0,05). Serum IL-11 seviyeleri gruplar arasında farklılık göstermedi (p>0,05). Tükürük IL-11 seviyeleri CP grubunda H grubuna göre anlamlı derecede yüksek bulunurken (p<0,05), G grubu ile fark saptanmadı (p>0,05). G ve CP gruplarında başlangıç periodontal tedavi öncesi ile karşılaştırıldığında, tedavi sonrası DOS ve tükürük OSM ve IL-11 seviyelerinin istatistiksel olarak anlamlı derecede düşük olduğu bulundu (p<0,05).

Sonuç: OSM, LIF ve IL-11 seviyelerinin G ve CP gruplarında yüksek bulunması periodontal doku yıkımının mevcudiyetini göstermektedir. Tedavi sonrası OSM, LIF ve IL-11 seviyelerindeki azalma periodontal başlangıç tedavisinin periodontal doku yıkımını engelleyebileceğini desteklemektedir.

Introduction

Periodontitis, which is the most common form of periodontal disease, is defined by alveolar bone and periodontal attachment damage and refers to an inflammation spreading from the gingival edge to the periodontal supporting tissues. The primary etiologic agent for periodontitis is dental plaque bacteria. However, in explaining the formation of periodontal disease, it has been stated that only addressing the presence of bacteria is not sufficient; besides that, interactions between bacteria and host defense systems have also contributed to the development and progression of the disease. When cells of the host defense systems encounter microbial dental plaque and bacteria products, both tissue destructive and protective mechanisms are activated simultaneously. Periodontal tissue destruction mainly occurs in the absence of protective mechanisms (1).

The synthesis and release of pro-inflammatory and immuno-secretory cytokines resulting from microorganisms' interaction with host tissue cells play an essential role in periodontal disease (2). Those are also responsible for many pathological tissue changes, from connective tissue destruction to bone loss. Some cytokines are crucial in diagnosing periodontal destruction and determining its progression (3). Oncostatin M (OSM), an interleukin-6 (IL-6) family member, belongs to the glycoprotein (gp)130 cytokine receptor subunit. Gp130 is a common receptor subunit for the IL-6 family of cytokines, including primarily IL-6, OSM, leukemia inhibitory factor (LIF), and IL-11, and capable of intracellular signaling required for a wide range of cellular action (4).

Gp130 cytokines are synthesized by immune and non-immune cells and affect hematopoietic, immunological, and inflammatory cellular communications (5). Their common feature is that they use the gp130 molecule as a signaling molecule to interact with receptor complexes on the cell surface. Thus, IL-6, OSM, LIF, and IL-11 induce responses caused by receptor complexes dependent on gp130 and the biological responses associated with them (6).

It is a known fact that bone metabolism depends on the balance between osteoblastic and osteoclastic activities. Previous studies on gp130 cytokines have reported that these cytokines play a role in both osteoblastic and osteoclastic activities, affecting bone metabolism (4). OSM can cause bone resorption by acting through autocrine IL-6 and paracrine receptor activator of NF-kB ligand regulation on osteoblasts and osteoclasts. It can also upregulate the production of matrix metalloproteinase (MMP) or increase the production of IL-6 by acting synergistically with IL-6 and tumor necrosis factor-alpha. In this way, it can lead to alveolar bone resorption in periodontitis (7). It has also been described that there is a positive correlation between the severity of periodontal disease and the gingival crevicular fluid (GCF) OSM level (8).

LIF, another gp130 cytokine, has functions similar to OSM. In humans, information about LIF and OSM cycle in skeletal tissue is limited (9). LIF and OSM have been shown to play roles in bone remodeling and the regulation of bone cell functions in mouse calvarial bone cultures (10). Richards et al. (11), too, demonstrated that OSM and LIF have a critical potential role in regulating osteoclast formation and osteoblast activation in mouse bone marrow and calvaria cells.

IL-11 has been evaluated as a possible molecule for therapeutic modulation of host response in treating periodontal disease (12). By showing antiinflammatory effect of IL-11 for the inhibition of some pro-inflammatory cytokines; it has been shown to stimulate bone resorption by increasing osteoclast formation and osteoblast mediated osteoid degradation (13). This cytokine also regulates inflammation by stimulating MMP-1 tissue inhibitor in synoviocytes and chondrocytes, similar to IL-6, too (14).

While clinical measurements can provide important information about periodontal disease's severity, they cannot give necessary information about the disease's activation. Therefore, GCF, blood, and saliva samples should be analyzed together to evaluate periodontal disease activity accurately (15).

This study's hypothesis is to demonstrate the detectability of OSM, LIF, and IL-11 in GCF, as well as in serum and saliva, and the preventability of tissue destruction by changes in the levels of these cytokines after nonsurgical periodontal therapy.

The aim of our study is to detect OSM LIF and IL-11 levels in GCF serum and saliva in individuals with periodontally healthy gingivitis (G) and chronic periodontitis (CP) before and after periodontal treatment and to investigate the relationship between clinical periodontal parameters and the levels of these cytokines.

Materials and Methods

Study Population

Systemically healthy 72 individuals, regardless of gender, applied to Atatürk University Faculty of Dentistry Department of Periodontology from 2014 March to 2014 August were enrolled in the study and were defined as healthy, G, and CP individuals based on clinical examination and radiographic analysis. This study was performed after Atatürk University Faculty of Dentistry Ethics Committee (decision no: 22/2014, date: 01.08.2014) approval was obtained. The research was conducted under the Helsinki Declaration of 1975 (revised in 2000). Informed consent form was given to each individual. Systemic and dental anamnesis were provided from all participants. Patients with any systemic disease and condition, those taking any medication, those with acute complaints, those who have undergone periodontal treatment within the past six months, smokers, and patients with caries and/or restoration in teeth to be taken GCF sample were excluded. Patients were added if they had \geq 16 teeth.

The patients' selection was made according to the diagnostic criteria proposed by the International Symposium on Classification of Periodontal Diseases and Conditions 1999 (16). Study participants were divided into three groups, as outlined below.

Healthy group (group H) (n=24) included individuals with probing depth (PD) \leq 3 mm, no sites with attachment loss, and no radiographic evidence of alveolar bone resorption. They exhibited no sign of inflammation [gingival index (GI=0)]. G group (n=24) had varying degrees of gingival inflammation (GI \geq 1), PD \leq 3 mm with no clinical attachment loss (CAL) or with no alveolar bone destruction. The CP group (n=24) was defined as those who were with PD \geq 4 mm, CAL \geq 2 mm, and who had bone loss affecting >30% of the existing teeth on clinical and radiographic examination.

Clinical Assessment

The clinical evaluation was performed by measurements of plaque index (PI), GI, PD, and CAL. All these measurements were evaluated at six areas for each tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual) with a manual periodontal probe (Hu-Friedy) by a single calibrated examiner (T.A.). Calibration of intra-examiner was provided by the evaluation of 10 participants with CP. All patients were measured the PD at 6 areas of each tooth in the maxilla every 3 days by the examiner for 3 times prior to study initiation. PD measurements were evaluated and the reproducibilities of intra-examiner in terms of the interclass correlation coefficient was 0.95.

Collection of Saliva, Gingival Crevicular Fluid and Serum Samples

Saliva, serum, and GCF sampling were applied in the morning hours 2 days after the clinical periodontal measurements. Patients were advised to brush their teeth, not drink anything, or not eat one hour before sampling. All saliva samples were obtained using the unstimulated saliva collection procedure. By giving polypropylene tubes to each patient, about 2 mL of a saliva sample were taken directly in the tube, and by closing the lid of the tubes immediately, it was centrifuged (Nüve NF 800 R, Ankara, Turkey) at 1000 rpm for 10 minutes at 4 °C to remove cellular elements and plaque. Then, it was immediately frozen and stored at -80 °C until analyses.

In whole groups, GCF samples were collected from the buccal sides of mesial or distal aspects of two single-root teeth by the same periodontist (T.A.). GCF was collected from areas that showed no clinical signs of inflammation in group H. In group G, tooth areas showing GI >1, but no CAL was chosen for GCF sampling. In group CP, GCF was accumulated from sites with the highest probing depth and radiographic confirmation of alveolar bone loss showing GI>1. At selected sites for GCF sampling, the supragingival plaque was removed with a sterile curette, isolated with sterile cotton rolls, and the teeth were lightly air dried. Paper strips (Periopaper[™] Oraflow Inc. Plainview, NY, USA) were placed carefully into the gingival sulcus and were left in position for 30 seconds. Strips contaminated with blood or saliva were rejected. GCF volume of the per strip was measured with a calibrated electronic device (Periotron 8000, Oraflow). The strips were then transferred to sterile polypropylene tubes containing 300 µl of phosphate buffered saline, frozen and stored at -80 °C until analysis.

From all study participants, at baseline and after nonsurgical periodontal treatment, 6 mL of venous blood was collected from the anterocubital vein using the standard venipuncture method. Serum was isolated by centrifugation at 3000 rpm for 5 minutes at 4 °C and then stored at -80 °C until analyses.

Nonsurgical Periodontal Treatment

After baseline serum, GCF and saliva sampling, ultrasonic scaling therapy was performed in group G and group CP. Oral hygiene education, including the use of toothbrushes and dental floss and/or interproximal brushes, was given to them. One week later, non-surgical periodontal treatment consisting of SRP (quadrant to quadrant) using manuel curettes and scalers was applied to the CP group under local anesthesia. No antibiotics or any medications were prescribed during the treatment. Periodontal therapy was applied by the same researcher (T.A.). Clinical periodontal measurements and GCF, serum and saliva samples were repeated eight weeks after periodontal therapy in group G and group CP.

Measurements of Biochemical Mediators

Enzyme-linked immunosorbent kits assay measured GCF, serum and saliva IL-11 (Ray Bio, Norcross, GA.), LIF (eBioscience, Bender Medsystems, Vienna, Austria.), and OSM (Ray Bio, Norcross, GA.) levels. Analyses were performed according to the manufacturer's instructions and using 96-well plates pre-coated with appropriate antibodies. The lower detection verges for IL-11, OSM, and LIF assays were 3.0, 1.0, and 0.3 pg/mL, respectively. The optical densities were read at 450 nm. Results were computed using the standard curves composed in each assay. Concentrations of the cytokines were described as pg/mL.

Statistical Analysis

The minimum sample size was performed based on a previous study (42) regarding the GCF levels of the OSM type cytokines and admitting a power of 80% and p=0.05 in study groups. It was determined that the appropriate sample size should be a minimum of 22 for each group. The data were evaluated using the SPSS for Windows 18.0 (SPSS Inc., Chicago, USA) software program. The significance level was considered as p<0.05 in statistical analysis. The arithmetic values given according to the groups were indicated by mean ± standard deviation. Whether distribution was normal and homogeneity of variances were controlled by the Kolmogorov-Smirnov test and Levene test, separately. After the normality and homogeneity assumptions were provided, One-Way ANOVA and post-hoc Duncan multiple comparison tests were used to compare independent groups, whereas the Paired Samples t-test compared dependent groups. Pearson's correlation test was employed to evaluate the correlations of laboratory and clinical parameters with each other.

Results

Clinical Findings

Demographics are presented in Table 1. All clinical periodontal values were significantly higher in group CP compared with groups H and G. GI, PI, and PD scores were significantly higher in group G compared with group H (p<0.05). Average GCF volume varied significantly between groups (p<0.05). Clinical parameters and GCF volume are presented in Table 2.

GCF volumes and the mean values of clinical periodontal parameters, at baseline and after nonsurgical periodontal treatment in group G and group CP, are given in Table 3. GCF volume and all clinical parameters, except CAL, decreased statistically significantly after SRP in group G (p<0.05). Likewise, after SRP, GCF volume and all clinical parameters decreased statistically in patients with CP (p<0.05).

| Table 1. Demographic data of the groups in our study | | | | | |
|--|----|------------|--------|------|--|
| | | | Gender | | |
| | | Age | Female | Male | |
| Group H | 24 | 30.86±1.7 | 12 | 12 | |
| Group G | 24 | 34.14±7.15 | 11 | 13 | |
| Group CP | 24 | 37.24±7.86 | 10 | 14 | |
| G: Gingivitis, CP: Chronic periodontitis, H: Healthy | | | | | |

Laboratory Findings

Laboratory findings are presented in Table 4. GCF and salivary OSM levels of group G were significantly higher than group H (p<0.05). Compared to group G, GCF and serum OSM levels of group CP were significantly higher (p<0.05). It was also remarkable that GCF, serum, and saliva OSM levels of group CP were significantly higher than group H (p<0.05).

There were significantly higher GCF LIF levels of group CP than group H (p<0.05). LIF levels in serum and saliva did not differ significantly between the groups (p>0.05).

Group CP had significantly higher levels of GCF IL-11 than group G (p<0.05). Compared with group CP, group H had lower levels of GCF and saliva IL-11 (p<0.05). There were no significant differences in serum IL-11 levels between the study groups (p>0.05).

Before and after periodontal therapy, mean values of GCF, serum and saliva OSM, IL-11 and LIF levels in group G and group CP and comparison of these values between groups are presented in Table 5.

Group G results showed statistically significant decreases in both GCF and saliva OSM, LIF and IL-11 levels after periodontal treatment compared to baseline (p<0.05).

In group CP, GCF and saliva OSM and IL-11 levels were significantly reduced after nonsurgical periodontal treatment (p<0.05). Similarly, serum

| Table 2. Comparison of clinical parameters and GCF volume between groups H, G and CP | | | | | | |
|--|------------------------|------------------------|------------------------|------------------------|------------------------|--|
| Groups | PI | GI | CAL (mm) | PD (mm) | GCF volume | |
| Н | 1.39±0.38 | 0±0.00 | 0±0.00 | 1.62±0.17 | 0.03±0.01 | |
| G | 2.52±0.28 ⁺ | 2.0±0.23 ⁺ | 0±0.00 | $2.63\pm0.51^{+}$ | 0.13±0.05 ⁺ | |
| СР | 3.82±0.63 [‡] | 2.28±0.35 [‡] | 5.70±1.23 [‡] | 6.50±1.84 [‡] | 0.38±0.07 [‡] | |

[†]Significant difference from the H group, [‡]Significant difference from the H and G groups, PI: Plaque index, GI: Gingival index, CAL: Clinical attachment loss, PD: Probing depth, GCF: Gingival crevicular fluid, G: Gingivitis, CP: Chronic periodontitis, H: Healthy

| Table 3. Comparison of clinical parameters and GCF volume before and after periodontal therapy in groups G and CP | | | | | | |
|---|------------------------|------------------------|------------------------|------------------------|------------------------|--|
| | | a | CAL (mm) | DD (mm) | GCF | |
| | | | | | Volume (µl) | |
| Group G | 2.52±0.28 | 2.00±0.23 | 0.00±0.00 | 2.63±0.51 | 0.13±0.05 | |
| After therapy | 1.13±0.56 ⁺ | 0.38±0.40 ⁺ | 0.00±0.00 | 2.01±1.51 ⁺ | 0.03±0.01 ⁺ | |
| Group CP | 3.82±0.63 | 2.28±0.35 | 5.70±1.23 | 6.50±1.84 | 0.38±0.07 | |
| After therapy | 1.17±0.52 [‡] | 0.42±0.48 [‡] | 2.42±1.76 [‡] | 3.62±1.71 [‡] | 0.07±0.01 [‡] | |
| [†] Significant difference from the G group, [‡] Significant difference from the CP group. CP: Chronic periodontitis, G: Gingivitis, PI: Plaque index, GI: Gingival | | | | | | |

index, CAL: Clinical attachment loss, PD: Probing depth, GCF: Gingival crevicular fluid

OSM levels were significantly lower after periodontal treatment (p<0.05).

Correlations

Correlations are presented in Table 6. There was no statistically significant correlation between the terms of clinical parameters and laboratory parameters in group H. In group G, there was a significant and positive correlation between PI and GCF IL-11 levels and between CAL and saliva LIF levels.

In group CP, there was a positive significant correlation between PI and GCF OSM; also, the saliva OSM level was correlated with CAL. The PI level was

 Table 4. Average values of GCF, serum and saliva OSM, LIF and IL-11 levels in groups H, G and CP and statistical comparison of these values between groups

| | GCF (pg/mL) | Serum (pg/mL) | Saliva (pg/mL) | | | |
|--|---------------------------|--------------------------|--------------------------|--|--|--|
| OSM | | | | | | |
| Group H | 9.61±4.30 | 8.33±5.63 | 26.60±19.41 | | | |
| Group G | 64.30±46.70 ⁺ | 10.28±5.54 | 82.18±42.93 ⁺ | | | |
| Group CP | 253.60±97.41 [‡] | 72.51±38.67 [‡] | 86.54±32.33 [‡] | | | |
| LIF | LIF | | | | | |
| Group H | 8.78±0.82 | 9.04±2.29 | 10.13±3.51 | | | |
| Group G | 8.89±1.60 | 9.50±2.68 | 10.53±5.26 | | | |
| Group CP | 13.20±4.07 [‡] | 10.21±4.44 | 11.33±5.90 | | | |
| IL-11 | | | | | | |
| Group H | 32.81±16.07 | 34.34±24.80 | 32.51±14.27 | | | |
| Group G | 40.41±15.62 | 35.73±21.10 | 61.84±24.53 | | | |
| Group CP | 109.30±41.17 [‡] | 43.07±32.10 | 84.68±32.34 ⁺ | | | |
| Significant difference from U group Significant difference from U and C groups C. Cincipitis CD: Chronic periodentitis U. U. Halthy, CCC, Cincipal | | | | | | |

[†]Significant difference from H group, [‡]Significant difference from H and G groups. G: Gingivitis, CP: Chronic periodontitis, H: Healthy, GCF: Gingival crevicular fluid, OSM: Oncostatin M, LIF: Leukemia inhibitory factor, IL-11: Interleukin-11

Table 5. Comparison levels of GCF, serum and saliva OSM, LIF and IL-11 and the statistical comparison of these values between groups before and after periodontal therapy in groups G and CP

| | GCF (pg/mL) | Serum (pg/mL) | Saliva (pg/mL) | | | |
|---|--------------------------|-------------------------|--------------------------|--|--|--|
| OSM | | | | | | |
| Group G | 64.30±46.70 | 10.28±5.54 | 82.18±42.93 | | | |
| After therapy | 16.64±5.05 ⁺ | 9.73±6.44 | 48.18±14.96 ⁺ | | | |
| Group CP | 253.60±97.41 | 72.51±38.67 | 86.54±32.33 | | | |
| After therapy | 21.64±9.05 [‡] | 28.77±9.46 [‡] | 52.28±12.97 [‡] | | | |
| LIF | | | | | | |
| Group G | 8.89±1.60 | 9.50±2.68 | 10.53±5.26 | | | |
| After therapy | 5.42±3.16 ⁺ | 8.96±3.43 | 6.06±2.52 ⁺ | | | |
| Group CP | 13.20±4.07 | 10.21±4.44 | 11.33±5.90 | | | |
| After therapy | 8.42±3.10 ⁺ | 10.04±4.34 | 10.20±4.63 | | | |
| IL-11 | | | | | | |
| Group G | 40.41±15.62 | 35.73±21.10 | 61.84±24.53 | | | |
| After therapy | 24.42±12.36 ⁺ | 34.56±18.66 | 32.12±14.58 ⁺ | | | |
| Group CP | 109.30±41.17 | 43.07±32.10 | 84.68±52.34 | | | |
| After therapy | 54.62±10.40 [‡] | 39.24±22.61 | 40.16±17.59 [‡] | | | |
| [†] Significant difference from group G, [‡] Significant difference from group CP. G: Gingivitis, CP: Chronic periodontitis, H: Healthy, GCF: Gingival crevicular fluid, OSM: Oncostatin M, UE: Laukemia inhibitory factor, II-11: Interlaukin-11 | | | | | | |

| Table 6. Significant correlations of clinical and laboratory parameters | | | | |
|--|-----------------|--------|-------|--|
| | | r | р | |
| Crown C | PI-GCF IL-11 | 0.534 | 0.03 | |
| Group G | CAL-Saliva LIF | 0.450 | 0.02 | |
| | PI-GCF OSM | 0.468 | 0.03 | |
| Crown CD | PI-Saliva LIF | -0.487 | 0.03 | |
| Group CP | PI-Saliva IL-11 | -0.445 | 0.05 | |
| | CAL-Saliva OSM | 0.472 | 0.03 | |
| Group CP | | | | |
| | PI-Saliva OSM | -0.680 | 0.002 | |
| After therapy | GI-Saliva OSM | -0.514 | 0.02 | |
| *r, Pearson's correlation coefficient. CP: Chronic periodontitis, GCF: Gingival crevicular fluid, LIF: Leukemia inhibitory factor, IL-11: Interleukin-11, OSM: | | | | |

determined to be negatively correlated with saliva LIF, IL-11, and OSM levels. In group CP, a statistically significant negative correlation existed between saliva OSM and GI.

Discussion

The interaction between the pathogenic bacteria in the microbial dental plaque and the host response mechanism causes periodontal destruction. The host response stimulated by bacteria protects periodontal tissues, which are also destroyed simultaneously. Recent studies have focused on indirect mechanisms that play a role in periodontal diseases (17-19).

PI, GI, PD, and CAL measurements and radiographic techniques, which are used to evaluate periodontal tissue destruction and periodontal treatment success, are the most important parameters in determining the intensity of the disease and the level of success achieved with treatment. This study revealed that participants with periodontal disease had higher PI, GI, PD and CAL parameters than healthy participants. Our study findings are in line with the results of many studies conducted to date (20-23).

Afacan et al. (24), in their study, reported that there was a positive correlation between periodontal inflammation and GCF volume. Some researchers have also demonstrated that the GCF volume decreases after periodontal therapy (25,26). GCF volume showed a statistically significant decrease in our study, too, eight weeks after nonsurgical periodontal therapy.

In periodontal diseases, inflammatory changes caused by bacterial biofilm lead to changes in biochemical marker levels in various body fluids such as GCF, serum, and saliva (27). It has been known that measuring these biochemical markers' levels in these fluids provides diagnostic, therapeutic, and prognostic benefits by contributing to clinical index systems in various diseases (27,28). Our study investigated the presence and levels of inflammatory cytokines such as OSM, LIF, and IL-11 in saliva for the first time. Previous studies have examined them in GCF and serum, but not in saliva.

Many cytokines found in GCF, mainly proinflammatory and inflammatory cytokines, have been shown as diagnostic or prognosis markers in periodontal destruction (29). A variety of cytokines from the IL-6 family are involved in this inflammatory process and stimulate various cellular responses (30). In the current study, GCF, serum, and saliva OSM levels were higher in participants with periodontal disease than in healthy subjects.

Various studies in the literature have addressed that OSM can be thought of as an inflammatory biomarker in periodontal diseases, and this cytokine may play a role in alveolar bone resorption (31,32). In addition, it is thought that the reason for the increase in serum OSM level in CP patients may be the spread from diseased periodontal tissues or GCF to the systemic circulation or the systemic inflammatory response that develops against periodontal disease (31). The present study is the first study to show OSM's presence in saliva in periodontally healthy and sick individuals. High OSM levels in participants with periodontal disease in our study support the view that this cytokinin can be considered an inflammatory biomarker in periodontal diseases. In their study on healthy individuals with periodontal disease, Becerik et al. (33) reported that there was no difference in GCF OSM levels in the comparison between the groups. Naemura and Radka (34) could not detect plasma and serum OSM levels in healthy individuals in a study they conducted. They reported the reason for this as the difference in the role of OSM on soft and hard tissue destruction in the periodontium (32). These results are not compatible with the results of our study. It can be said that the reason for this incompatibility is due to material and method differences in related studies.

While the presence of LIF in GCF, serum, and saliva was determined in all our study participants, GCF LIF level was found to be higher in those with periodontal disease than healthy subjects. Sakai et al. (35) indicated LIF in gingival tissue samples in 6 out of 7 patients with CP and 4 out of 7 periodontally healthy individuals. Palmqvist et al. (36) confirmed the presence of LIF in human gingival fibroblasts in their in vitro study. In an animal study, LIF was shown to stimulate osteoclast formation (10). Our study is the first study investigating the presence and levels of serum and saliva LIF as far as we know. Previous studies suggest that high LIF levels in individuals with periodontal disease can play a role in active tissue destruction and be considered an inflammatory biomarker. Becerik et al. (33) stated that the GCF LIF level was higher in healthy individuals than in periodontal disease subjects. They also reported that this result might be due to the LIF's regulatory role in alveolar bone metabolism and protective role in the host response to infection.

It has been shown that IL-11 is an important member of the cytokine group that controls osteoclast development and has different properties compared to other cytokines. IL-11 plays a crucial role in osteoclast formation (37). It has been reported that IL-11 increases bone resorption and stimulates osteoclast-mediated mineral mobilization by a mechanism dependent on prostaglandin E2 synthesis, and also causes bone matrix damage in mice (38,39). Becerik et al. (33) suggested that GCF IL-11 levels were lower in healthy persons than in persons with CP, and they showed a positive correlation with pocket depth and clinical attachment level. Similarly, in the current study, GCF IL-11 levels were lower in healthy persons than in CP patients. Based on our study results, we think that IL-11 can play a crucial role in active tissue destruction and alveolar bone resorption throughout the periodontal disease process.

Similar to our study results, in their studies on individuals with CP, Johnson et al. (40) reported that IL-11 concentration was higher in areas with less pocket depth and this concentration decreased in parallel with the increase in pocket depth, and the lowest IL-11 concentrations were in healthy gingival tissue. Unlike our findings, other studies demonstrating lower GCF IL-11 levels in individuals with CP than healthy subjects are also available. Guided by all these study data, it has been suggested that IL-11 may have a protective and anti-inflammatory effect in the pathogenesis of periodontal diseases, and play a key role in preventing progressive inflammation that can cause periodontal tissue destruction. It has also been stated that low IL-11 levels in CP patients with high pocket depth may be due to the decreased protective effect of IL-11 on periodontal lesions or the episodic characteristic of periodontal disease (12,41). The present study, at the same time, is of great importance in terms of being the first study to show the presence of IL-11 in saliva and serum. We believe that differences in all study results in the literature may have originated from genetic variations that disrupt the inflammatory mechanism and individual differences in immune response and severity of the clinically observed inflammation.

Our study revealed a significant decrease in serum and saliva OSM, LIF, and IL-11 levels in group G and group CP after nonsurgical periodontal therapy. Likewise, Thorat et al. reported decreased GCF and serum OSM levels in CP patients after nonsurgical periodontal treatment (32,42). In their study carried out with 60 individuals, Pradeep et al. (31) found that serum OSM levels decreased after initial periodontal treatment in individuals with CP.

Recent study has only evaluated OSM, IL-11, and LIF levels; but chronic inflammatory diseases like periodontitis also include other cytokines. Therefore, further work will be beneficial to investigate the relationship between these three cytokines and others. Within the limitations of this study; we have shown that IL-11, LIF and OSM may play a role as inflammatory biomarkers in the pathogenesis of periodontal disease. Additional researches may reveal the roles of IL-11, LIF and OSM in the pathogenesis of CP and the relation with systemic conditions such as atherosclerosis, rheumatoid arthritis, and diabetes.

Conclusion

With the present study, it was introduced that there was a close relationship between periodontal clinical and biochemical parameters and that clinical improvement affected biochemical parameters. Besides, the reduction in GCF volume due to treatment was reflected in clinical and biochemical parameters. The mechanisms that enable pro-inflammatory cytokines involved in the pathogenesis of periodontal disease to activate collagen degradation and loss of attachment and bone destruction are still not fully clarified. For illuminating all these processes, which will enable rapid diagnosis of the disease and increase the effectiveness of the treatment to be applied, further and comprehensive studies are needed.

Ethics

Ethics Committee Approval: This study was performed after Atatürk University Faculty of Dentistry Ethics Committee (decision no: 22/2014, date: 01.08.2014) approval was obtained.

Informed Consent: Informed consent form was given to each individual.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.D., T.A., Design: A.D., T.A., Supervision: A.D., T.A., Materials: T.A., Data Collection or Processing: T.A., Analysis or Interpretation: T.A., Literature Search: T.A., Writing: T.A., Critical Review: A.D., T.A.

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Pain and Anxiety in Cataract Surgery: Comparison Between the First and Second Eye Surgeries

Katarakt Cerrahisinde Ağrı ve Anksiyete: Birinci Göz ve İkinci Göz Cerrahisi Arasında Karşılaştırma

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Keywords

Topical anesthesia, bilateral cataract surgery, perioperative process, pain, anxiety

Anahtar Kelimeler

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Abstract

Objective: This study aimed to determine and compare the pain and anxiety levels in the perioperative period of patients undergoing cataract surgery on both eyes. **Materials and Methods:** The study used a descriptive design to assess 60 patients who had undergone cataract surgery on both eyes. The visual analog scale (VAS) and the State-Trait Anxiety Inventory were used to evaluate the subjective parameters of patients in the surgical process. Objective measurements in the perioperative process were recorded in the physiological parameters form.

Results: The state anxiety levels of patients in the preoperative period of the first eye surgery were found to be higher compared with that of the second eye surgery (p=0.003). In addition, patients were determined to have more severe anxiety in the preoperative period of the first eye surgery (VAS: 4.510) and before (VAS: 4.483) and during the perioperative period (VAS: 4.150) of the second eye surgery. Patients had a higher pain score and a higher state of anxiety after clinic admission in the postoperative period of the second eye surgery compared with that of the first eye surgery (p<0.05). The diastolic blood pressure value before the operation and the pulse and respiratory rate during the operation were higher in the first eye surgery than in the second eye surgery (p=0.038; p=0.000; p=0.000, respectively).

Conclusion: The results of the subjective and objective measurements revealed that the anxiety experienced in the first cataract surgery made the perceived anxiety and sensation of pain more sensitive in the second eye surgery.

Öz

Amaç: Bu çalışma her iki gözde katarakt ameliyatı geçiren hastaların perioperatif dönemdeki ağrı ve anksiyete düzeylerini belirlemek ve karşılaştırmak amacıyla yapıldı.

Gereç ve Yöntemler: Tanımlayıcı nitelikte olan çalışmanın örneklemini, her iki göze katarakt cerrahisi uygulanan 60 hasta oluşturdu. Vizuel analog skala (VAS) ve Durumluk Sürekli Kaygı Envanteri, hastaların cerrahi süreçteki subjektif parametrelerini değerlendirmek için kullanıldı. Perioperatif süreçte değerlendirilen objektif ölçümler ise fizyolojik parametre formuna kaydedildi.

Bulgular: Ameliyat öncesi dönemde hastaların durumluk kaygı düzeyleri ikinci göz cerrahisine göre daha yüksek bulundu (p=0,003). Ayrıca hastaların ilk göz cerrahisi

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ameliyat öncesi dönemde (VAS: 4,510) ve ikinci göz cerrahisi ameliyat öncesi (VAS: 4,483) ve ameliyat esnasında (VAS: 4,150) daha şiddetli anksiyeteye sahip oldukları belirlendi. İkinci göz cerrahisi ameliyat sonrası dönemde, hastaların ilk göz cerrahisine göre ağrı düzeyleri ve kliniğe alındıktan sonra durumluk anksiyete düzeyleri daha yüksekti (p<0,05). İlk göz cerrahisinde ameliyat öncesi ölçülen diyastolik kan basıncı değeri ve ameliyat sırasında ölçülen nabız ve solunum hızı ikinci göz cerrahisinde ölçülen değerlerden daha yüksekti (sırasıyla p=0,038; p=0,000; p=0,000).

Sonuç: Bu çalışmada; subjektif ve objektif ölçümlerin sonuçları, ilk katarakt cerrahisinde yaşanan kaygının, ikinci göz cerrahisinde algılanan kaygı ve ağrı hissini daha duyarlı hale getirdiğini ortaya koymuştur.

Introduction

Cataract surgery is the most frequently performed surgery in the world, and with the developing technology today, the operation time is quite short. The surgical procedure is often performed under local anesthesia (1,2). During the surgical procedure, topical anesthesia is preferred to ensure the comfort of the surgeon and to speed up the recovery time of the patient (3).

Topical anesthesia is a method that can be applied fast in cataract surgery, and it is known to reduce the risk of complications in the patient (4). However, studies report that, besides this positive feature of topical anesthesia, it causes pain ranging between 34% and 90% both during and after surgery (4-6). Patients are awake so that they can follow the surgeon's directives during the operation and this may cause anxiety (7), and also lead to negative consequences in physiological parameters such as hypertension or tachycardia (8).

Since the prospect of feeling pain and loss of visual function is a fearful condition, patients may be highly anxious before surgery (9). Patients can move due to anxiety and pain during the operation and lose their visual function due to complications such as hemorrhage or postoperative glaucoma. Therefore, evaluating and controlling pain and anxiety during the operation is important in terms of ensuring patient comfort and prognosis of the surgery (10). In cataract surgery, the management of pain and anxiety does not only reduce the anxiety of patients but also increases patient collaboration during surgery (8).

Studies in the literature report that, in the evaluation of subjective symptoms of patients with bilateral cataracts, there are differences between the first and second eye surgery (8,11-15). Pain, which is among these symptoms in cataract surgery, has been studied quite widely (1,3,6,8,11-18). However, there

are fewer studies on cataract surgery where pain and anxiety are evaluated together (8,12,15,19).

In studies comparing pain and anxiety between the two eye surgeries (8,12,15,19), anxiety was evaluated before the surgery and pain during or after surgery. In a study evaluating pain and anxiety in patients undergoing cataract surgery in both eyes, the results of pain and anxiety between the first and second eye surgery of different patients were compared (8). In the study of Yu et al. (15), objective measurements such as physiological parameters were not included in the data. In these studies in the literature of the last decade (8,12,15,19), pain and anxiety level assessment included different phases of cataract surgery.

When the study results were examined, anxiety levels of the patients were determined to be lower before the second eye surgery, whereas the severity of the pain was higher during the surgery (8,12,15). While some researchers examining the increased pain during the second eye surgery stated that anxiety was the underlying cause of the increased pain in the second eye surgery (20), there are also different study results suggesting that it depended on patient's perception (14,21).

Due to differences in previous study methods, measurement times, and findings, it is necessary to carry out studies to strengthen the level of evidence by evaluating the pain and anxiety of patients undergoing cataract surgery in the perioperative process. According to the review of the literature, no studies evaluating the pain and anxiety together in patients undergoing cataract surgery on both eyes during the entire surgical process were found. Therefore, the present study is considered to be original.

This study was carried out to determine and compare the pain and anxiety levels in the perioperative period of patients undergoing cataract surgery on both eyes.

Materials and Methods

Setting

The study was carried out in the ophthalmology and surgery clinic and operating room of a state hospital between October 2018 and July 2019. Operations for ophthalmology are conducted according to daily surgery procedures, and the eye surgery process is managed with 5 specialist doctors in 5 polyclinics.

Sample

The universe of the study consisted of 128 patients who underwent bilateral phacoemulsification surgery due to cataract and who presented to the ophthalmology surgery outpatient clinic. The following patients were excluded from the study: 4 patients who were administered a preliminary application, 9 patients who had had surgery due to non-cataract eye disease previously, 17 patients who gave up the second eye surgery, 28 patients who were reluctant to collaborate, 4 patients who preferred a different doctor for the second eye surgery, 1 patient who developed complications during surgery, and 5 patients who were not eligible for topical anesthesia. Accordingly, the study was completed with 60 patients. The sample size of the study was calculated on the G* Power 3.1.9.2 software package by accepting a 1 unit increase in visual analogue scale (VAS) pain severity between the first eye and the second eye surgery as significant (8). As a result of post-hoc power analysis, the study was determined to have 99% power with 1% type 1 error.

Inclusion and Exclusion Criteria

The inclusion criteria included patients who were aged over 18, who could communicate verbally, who underwent bilateral phacoemulsification surgery, whose both eye operations were carried out by the same surgeon, who were administered a surgical procedure under topical anesthesia, and who did not have any non-cataract eye diseases such as ocular surgery, glaucoma, uveitis, and keratoconus, and a psychiatric diagnosis.

On the other hand, the exclusion criteria included patients who were not eligible for collaboration, whose second eye surgery was performed by a different surgeon, who refused to have second eye surgery, who developed postoperative complications, and for whom topical anesthesia was not adequate during surgery and different intraocular anesthesia was preferred.

Measurements

A patient information form, which was made up of two sections, was used to collect information about the patients. The first section of the form included a total of 15 questions to determine the socio-demographic characteristics of the participants such as age, gender, educational status, income level, and place of residence, and the properties of surgical procedures such as the duration of surgery in the operating theater and the duration between the two operations. On the other hand, the second section of the form consisted of two questions evaluating the difference between the pain and anxiety levels experienced by patients in both eye operations.

To determine the State-Trait Anxiety Inventory-State (STAI-S) and STAI-Trait (STAI-T) anxiety levels of the patients, a 4-point Likert-type Spielberg State-Trait Anxiety scale consisting of two parts, each of which contained 20 questions, was used. The scale was developed by Spielberger et al. (22). It was adapted to Turkish society by Öner and Le Compte (23). Each item on the scale is responded using one of the four options including "not at all", "somewhat", "much", and "fully" to determine the intensity of behavior and emotions. The total score obtained from the scale consisting of two parts varies between 20 and 80. High scores indicate a high level of anxiety and low scores indicate a low level of anxiety. In this study, Cronbach's α was found to be 0.83 for STAI-S and 0.85 for STAI-T.

To evaluate patients' pain and anxiety levels, we used the VAS, a 10 cm-long horizontal line, which was developed by Cline et al. (24) and adapted to Turkish by Eti-Aslan (25). For the anxiety, the left side of the scale reads "no anxiety" and the right side reads "extreme anxiety". On the VAS pain scale, on the other hand, one end of the line reads "no pain" and the other end reads "unbearable pain". Values range from 0 to 10, and high values indicate increased anxiety and pain.

Also, a form for physiological parameters, which was developed by the researcher, was used to collect data about objective measurements of patients including systolic and diastolic blood pressure value, pulse and respiratory rate, and oxygen saturation value.

The Procedure

The data were collected by the researcher. At the outset, the forms were piloted to 4 patients to assess the applicability of the forms. These patients were not included in the sample group.

The purpose of the study was explained to the patients who presented to the ophthalmology and surgery outpatient clinic for cataract, who were planned to undergo phacoemulsification surgery on both eyes, and who met the study criteria. The contact information and written consent of the patients were obtained.

Data on pain, anxiety, and physiological parameters were collected in a five-stage process in both eye surgeries. The first stage started with the hospitalization of the patient. Patients who came to the clinic were assessed for anxiety levels with STAI-S and STAI-T, the severity of anxiety with VAS, and physiological parameters. To achieve the full dilation of the pupils, the eye was administered medication by nurses at the clinic 30 minutes before the surgery. The patients were delivered to the operating room nurses by the clinical nurses for the surgical intervention, and the second phase of the data collection process was initiated. In the second stage, the anxiety and physiological parameters of the patients were assessed with VAS just before the operation. Then, patients were taken to the operating room for phacoemulsification surgery and monitored.

Phacoemulsification is known as closed system cataract surgery, which allows the lens material to be broken up and removed by ultrasound. It has superior advantages compared to other cataract surgeries in terms of short operation time, small incision area, less astigmatism, less inflammation and rapid recovery after the operation (26).

The operating theatre and all procedures performed using surgical equipment and instruments were used in all patients and both eye surgeries without making any change. The conjunctival area was washed with povidone-iodine (0.02%) 5 minutes before surgery. With the administration of 5% proparacaine, topical anesthesia application involved 3 stages, including 5 minutes before the operation, 1 minute before the operation, and after placing the retractor. The patients were not administered oral and intravenous sedative or analgesic medication. All procedures were applied to the patients by the same surgeon in both eye surgeries.

The VAS scale used in the third stage to determine the pain and anxiety of the patients during surgery was evaluated after the phacoemulsification process was completed after the corneal incision and the lens was placed and the viscoelastic aspiration of the intraocular residues was done. At the same time, physiological parameters were followed on the monitor and recorded on the related form. Immediately after the operation was completed, the patient was taken to the follow-up room, and then the fourth stage process involving pain, anxiety, and physiological parameter evaluations was performed.

The fifth stage started approximately one hour later when the patient was taken to the clinical room. At this stage, the STAI-S, VAS and physiological parameters evaluation form was re-administered to the patients. After the completion of both eye surgeries, patients were asked to evaluate the difference between pain and anxiety they experienced in both eye surgeries with the following possible answers: "I had more pain in the first eye surgery"; "I had more anxiety in the first eye surgery"; "I had more pain in the second eye surgery"; "I had more anxiety in the second eye surgery"; "I had the same anxiety in both eye surgeries"; "I had the same pain in both eye surgeries". The responses given by the patients were recorded in the second part of the patient information form, and the evaluation steps for pain and anxiety were completed.

Collection in of 1st and 2nd eye surgery data was conducted between 08:00 and 16:00, according to the time when the patients were taken to the surgery. For each eye surgery, the data collection process consisting of the stages such as obtaining written permission from the patient, administration of the preoperative, perioperative, and postoperative measurement tools took approximately 60 minutes. Approximately 120 minutes was allocated for data collection in both eye surgeries for each patient.

Statistical Analysis

Data were analyzed using the Statistical IBM SPSS Statistics 22 (IBM SPSS; Turkey). The suitability of the variables to normal distribution was evaluated by the Shapiro-Wilks test. Categorical measurements were calculated as numbers and percentages, while numerical measurements were calculated as mean, standard deviation, and frequency values. The paired sample t-test was employed to compare the results of the first and the second surgical interventions, the repeated measures ANOVA was used to evaluate the measurements obtained during interventions, and Bonferroni test was used to determine which measurement caused the difference in the group. In all statistical analyses, significance level was accepted as p<0.05.

Ethical Considerations

At the outset, the Ethics Committee approval (decision no: 2018/10, date: 10.09.2018) of Nevşehir Hacı Bektaş Veli University, institutional permission of the state hospital where the data were collected (issue 55831188-604.02), and the written consent of the participants were obtained. The data were collected and securely stored by the researchers as required.

Results

Patient Characteristics

The mean age of the patients was 65.65 ± 6.51 years, 60.0% were female, 70.0% were literate or primary school graduates, 93.3% were married, and 55.0% were housewives. Also, 70% of the patients were determined to perceive their income and expenses as equal, 36.7% lived in a village/town, and 50.0% lived with their spouses. Besides, 66.7% of the patients had a chronic disease, and 80.0% had undergone an operation before (Table 1). The duration of patients' cataract complaints was 20.22±34.67 months, and the mean time between the two surgeries was 28.77±26.45 days. There was no statistically significant difference between the operating-room duration of the patients' 1st and 2nd surgeries (p>0.05) (Table 2).

Comparison of Subjective Anxiety

The within-group and between-group comparisons of the severity of anxiety levels were made (Table 3). When the means of STAI-T and VAS-anxiety scores were compared between the groups, there was no statistically significant difference between the 1^{st} and 2^{nd} eye surgeries (p>0.05). In the 2^{nd} eye surgery, the STAI-S anxiety score measured before going to the operating room was found to be lower than the 1^{st} eye surgery (p<0.05). When comparing the within-group mean scores of STAI-S anxiety, the anxiety scores

| | x | SD | |
|---------------------|---------------------------------|------|------|
| Age (49-82) | 65.65 | 6.51 | |
| | | n | % |
| | Female | 36 | 60.0 |
| Gender | Male | 24 | 40.0 |
| | Illiterate | 7 | 11.7 |
| | Literate or primary school | 42 | 70.0 |
| Education | Secondary school | 4 | 6.7 |
| | High school | 5 | 8.3 |
| | University and higher education | 2 | 3.3 |
| | Married | 56 | 93.3 |
| Marital status | Single | 4 | 6.7 |
| Occupation | Retired | 25 | 41.7 |
| | Housewife | 33 | 55.0 |
| | Worker | 1 | 1.7 |
| | Other | 1 | 1.7 |
| | Income less than expenses | 17 | 28.3 |
| Income status | Income equal to expenses | 42 | 70.0 |
| | Incomes more than expenses | 1 | 1.7 |
| | City | 21 | 35.0 |
| Place of residence | District | 17 | 28.3 |
| | Village/town | 22 | 36.7 |
| | Alone | 5 | 8.3 |
| De evel e l'éclere | With spouse | 30 | 50.0 |
| together at home | With children | 6 | 10.0 |
| | With spouse and children | 19 | 31.7 |
| Presence of chronic | Yes | 40 | 66.7 |
| disease | No | 20 | 33.3 |
| | HT | 28 | 70 |
| | DM | 18 | 45 |
| *Type of chronic | COPD | 8 | 20 |
| uisease | HF | 10 | 25 |
| | **Othor | 2 | 7 5 |

measured in the clinic after the operation in the 2^{nd} eye surgery were higher than the mean scores measured before going to the operating theater (p<0.05). In the within-group evaluation of VAS anxiety mean scores, the difference between the 1^{st} and 2^{nd} eye surgery within-group anxiety mean scores was found to be statistically significant (p<0.05). In further analyses conducted to determine which measurement caused this difference, it was determined to stem from the high anxiety scores measured before the operation in

| Table 2. Surgical procedure characteristics of the sample | | | | | |
|---|-------|-------|------|--|--|
| | | n | % | | |
| Status of undergoing an | Yes | 48 | 80.0 | | |
| operation before | No | 12 | 20.0 | | |
| | x SD | | | | |
| Duration of cataract complaint (moon) | 20.22 | 34.67 | | | |
| Period between two cataract surgeries (day) | 28.77 | 26.45 | | | |
| Time spent in operating room (minute) | | | | | |
| First surgery | 21.97 | 10.72 | | | |
| Second surgery | 21.32 | 7.06 | | | |
| SD: Standard deviation | | | | | |

VAS: Visual analog scale

the 1^{st} eye surgery and those measured before and during the operation in the 2^{nd} eye surgery (Table 3).

Comparison of Perceived Subjective Pain

The within-group and between-group comparisons of the severity of pain levels were conducted (Table 4). In the between-group evaluation of patients' VAS pain severity, the pain score measured after the operation was higher in the 2^{nd} eye surgery compared to the 1^{st} eye surgery (p<0.05). In the within-group evaluation, in the 2^{nd} eye surgery, the within-group difference between the mean scores of pain was found statistically significant (p<0.05). In further analyses to determine which measurement caused this difference, it was determined to come from the high pain scores measured soon after the surgery (Table 4).

Comparison of Objective Measures

The within-group and between-group comparisons regarding the physiological parameters of the patients were conducted (Table 5). In the withingroup and between-group comparisons, there was no statistically significant difference between systolic blood pressure and oxygen saturation values in the 1st and 2nd eye surgery (p>0.05). The diastolic blood pressure value measured before the operation and

| A | First eye surgery | | Second ey | Second eye surgery | | |
|------------------------------------|-------------------|-------|-----------|--------------------|----------|--|
| Anxiety | x | SD | x | SD | -p-value | |
| VAS-anxiety | | | | | | |
| Before going to the operating room | 3.350 | 2.070 | 3.150 | 0.231 | p=0.388 | |
| Before surgery | 4.510 | 2.120 | 4.483 | 0.282 | p=0.844 | |
| During surgery | 3.780 | 1.960 | 4.150 | 0.283 | p=0.211 | |
| Immediately after surgery | 2.600 | 1.580 | 2.933 | 0.258 | p=0.374 | |
| After taken to the clinic | 2.010 | 1.290 | 2.317 | 0.216 | p=0.425 | |
| ²p-value | p=0.000 | | p=0.000 | p=0.000 | | |
| STAI-State | | | | | | |
| Before going to the operating room | 37.40 | 5.53 | 35.85 | 5.47 | p=0.003 | |
| After taken to the clinic | 37.16 | 5.10 | 37.83 | 6.81 | P=0.834 | |
| ²p-value | p=0.777 | | p=0.007 | p=0.007 | | |
| STAI-Trait | | | | | | |
| Before going to the operating room | 49.31 | 6.12 | 50.11 | 5.86 | p=0.078 | |

Table 3. Comparison of intergroup and intragroup VAS-Anxiety, STAI-S and STAI-T mean scores according to the first and second eye surgery

| Table 4. Comparison of intergroup and intragroup VAS-pain mean scores according to the first and second eye surgeries | | | | | | |
|---|-------------------|------|--------------------|------|---------|--|
| Dein | First eye surgery | | Second eye surgery | | 1 | |
| Pain | x | SD | x | SD | p-value | |
| During surgery | 2.86 | 1.39 | 3.35 | 2.07 | p=0.580 | |
| Immediately after surgery | 3.86 | 1.70 | 4.51 | 2.12 | p=0.010 | |
| After taken to the clinic | 3.55 | 1.66 | 3.78 | 1.96 | p=0.265 | |
| ²p-value | p=0.077 | | p=0.002 | | | |
| *Column significance values are for intergroup and row significance values are for intragroup. ¹ Paired sample t-test, ² Related Sample One-Way Analysis of Variance, Bonferroni test, n<0.05, SD: Standard deviation, VAS: Visual analog scale | | | | | | |

the pulse and respiratory rate measured during the operation in the 1^{st} eye surgery were higher than those measured in the 2^{nd} eye surgery (p<0.05). In the within-group evaluation, the diastolic blood pressure value during the 1^{st} eye surgery was higher than all other measurements (p<0.05) (Table 5).

Patients' Perception of Anxiety and Pain

When patients were asked to compare the pain and anxiety levels they felt in 1st and 2nd eye surgery, 51.7% stated that they experienced more pain in the second eye surgery and 38.3% experienced an equal level of anxiety in both eye operations.

Discussion

High levels of anxiety in the surgical process can cause an increase in pain sensitivity and negatively affect physiological parameters such as blood pressure and heart rate (27). In this context, the study sought answers to the questions relating to the difference between pain and anxiety levels and physiological parameters of patients who underwent phacoemulsification procedure on both eyes at different times, and how these variables changed through the stages of measurement.

The first important finding of this study was that patients had higher state anxiety levels before the first eye surgery compared to the second eye surgery. This finding was similar to that of Nijkamp et al. (28). Researchers explained this finding saying that the cataract surgery was not performed by the same person and in the same way. It would be a mistake to make the same comment for the present study. In the present study, all patients were operated by the same surgical team and two eye surgeries of the same patients were compared. Therefore, the state anxiety only by the surgical team and the surgical procedure. Some studies report that the age and education level of the patients should be taken into consideration especially when informing patients regarding the surgery. Low education levels with advanced age may increase anxiety by decreasing the permanence and comprehensibility of the information provided (28). Considering that the patients participating in this study were at an advanced age and that the majority of them had a primary level of education, the results were not so surprising. Also, the patients were informed by the physician in the outpatient clinic in the hospital where the study was conducted. These results suggest that the preoperative patient training should be done by taking patient characteristics into account and by allocating sufficient time to patients. Besides, nurses should take an active role in the preoperative training process of cataract surgery.

levels of the patients were observed to be not affected

The second important finding of this study was the high preoperative and perioperative anxiety perceptions of the patients in the second eye surgery and the high postoperative state-trait anxiety levels after they were taken to the clinic. Ramirez et al. (19) determined that the source of anxiety in the preoperative period was related to the surgery itself and the fear of losing eyesight and that the fear of the surgery continued in the postoperative period, causing anxiety. This finding is important in terms of showing that patients need psychological support for fear and anxiety management in second eye surgery. In a randomized controlled study on patients undergoing cataract surgery conducted by Haripriya et al. (29), the determination of the fact that patients who received counseling during the

| | | | First eye surger | First eye surgery | | Second eye surgery | |
|--------|---|------------------------------------|------------------|-------------------|---------|--------------------|----------------------|
| Measu | irement st | eps | x | SD | x | SD | ¹ p-value |
| | sure | Before going to the operating room | 123.00 | 14.53 | 122.583 | 1.468 | p=0.66 |
| | pres | Before the surgery | 151.53 | 21.31 | 148.467 | 2.961 | p=0.25 |
| | pool | During the surgery | 150.52 | 23.15 | 148.500 | 2.604 | p=0.277 |
| | c blo | Immediately after the surgery | 146.42 | 22.28 | 146.417 | 2.641 | p=0.952 |
| | tolic | After taken to the clinic | 125.58 | 11.72 | 126.417 | 1.513 | p=0.529 |
| | Sys | ²p-value | p=0.992 | | p=0.215 | | |
| | | Before going to the operating room | 74.25 | 8.77 | 74.883 | 1.264 | p=0.611 |
| | _ | Before the surgery | 81.53 | 12.60 | 80.983 | 1.322 | p=0.038 |
| | pool | During the surgery | 85.73 | 12.87 | 83.150 | 1.293 | p=0.064 |
| meters | ic bl re | Immediately after the surgery | 81.95 | 12.09 | 83.000 | 1.228 | p=0.668 |
| | istol | After taken to the clinic | 75.21 | 7.13 | 75.517 | 0.821 | p=0.914 |
| | Dia | ²p-value | p=0.026 | p=0.026 | | | |
| | | Before going to the operating room | 75.767 | 1.31 | 77.667 | 1.402 | p=0.121 |
| oara | | Before the surgery | 78.317 | 1.60 | 78.300 | 1.731 | p=0.074 |
| cal | | During the surgery | 77.333 | 1.74 | 76.550 | 1.591 | p=0.000 |
| logi | ate | Immediately after the surgery | 76.450 | 1.52 | 76.233 | 1.428 | p=0.966 |
| iysic | lse r | After taken to the clinic | 75.533 | 1.32 | 76.083 | 1.030 | p=0.354 |
| Ч | Pu | ²p-value | p=0.350 | | p=0.101 | | |
| | | Before going to the operating room | 23.400 | 0.209 | 23.067 | 0.220 | p=0.251 |
| | e | Before the surgery | 23.933 | 0.346 | 23.533 | 0.313 | p=0.330 |
| | y rat | During the surgery | 24.000 | 0.389 | 23.600 | 0.414 | |
| | ator | Immediately after the surgery | 23.733 | 0.295 | 23.000 | 0.275 | p=0.094 |
| | spira | After taken to the clinic | 23.600 | 0.227 | 23.333 | 0.216 | p=0.405 |
| | Re | ²p-value | p=0.763 | - <u>-</u> | p=0.928 | | |
| | | Before going to the operating room | 95.25 | 0.26 | 95.433 | 0.243 | p=0.565 |
| | c | Before the surgery | 95.16 | 0.34 | 95.283 | 0.317 | p=0.779 |
| | atio | During the surgery | 95.65 | 0.29 | 95.717 | 0.264 | p=0.592 |
| | atur | Immediately after the surgery | 95.91 | 0.27 | 95.933 | 0.211 | p=0.850 |
| | 0 ² s: | After taken to the clinic | 95.25 | 0.24 | 94.917 | 0.216 | p=0.093 |
| | Sp(| ²p-value | p=0.700 | | p=0.604 | | |
| *Sn0 · | *SpQ : Oxygen saturation, SD: Standard deviation, ¹ Paired sample t-test, ² Related sample One-Way Analysis of Variance, Bonferroni | | | | | | |

Table 5. Comparison of intergroup and intragroup systolic and diastolic blood pressure, pulse, respiration and oxygen saturation mean values according to the first and second eye surgery

*SpO₂: Oxygen saturation, SD: Standard deviation, ¹Paired sample t-test, ²Related sample One-Way Analysis of Variance, Bonferroni test. p<0.05

surgical process experienced less fear than those who did not experience it showed the effect of counseling on psychological factors. However, during second eye surgery, subjective sensations such as photosensitivity, the sensation of swelling in the eyes, and pain were reported to increase (15). Therefore, the level of anxiety felt during the second eye surgery may increase with other subjective sensations.

The third important finding of this study was that the pain score measured immediately after the end of the surgery was higher in the 2nd eye surgery compared to the 1st one. Regarding the within-group evaluation, the pain scores measured in the 2nd eye surgery immediately after the operation were higher. Studies showed that many patients who underwent cataract surgery with topical anesthesia felt more pain during the second eye surgery compared to the first one (8,13-15). Zhu et al. (30), on the other hand, explained the increased pain level in the second eye by handling the issue on a physiological dimension. In their study, they reported that the concentration of MCP-1, pain-related inflammatory cytokines in the first eye, increased during the second eye surgery, causing higher levels of pain. It was also emphasized that adding an anti-inflammatory drug to the treatment plan to prevent macular edema in patients after the first eye surgery would be effective in reducing pain (31). In the present study, considering that an antiinflammatory drug was added to the treatment plan after the first eye surgery by the surgeon performing the operation, the necessary measures were thought to be taken to avoid a physiological effect on the pain during surgery. At the same time, the results show that the provision of information by nurses about the prescribed drugs in the discharge training content of patients undergoing cataract surgery is very valuable. In the study, although there was no pain during the second eye surgery, increased pain was observed immediately after the operation. In a study in which Porela-Tiihonen et al. (5) evaluated postoperative pain after cataract surgery, approximately one-third of the patients reported pain symptoms in the early postoperative period, and the majority of these patients (79%) were determined to leave the hospital with pain symptoms. Especially in patients with high anxiety, pain sensitivity was reported to increase and the patients were found to tend to exaggerate pain (20). In this study, too, high postoperative state anxiety scores, as well as high postoperative pain scores, suggest that psychosocial factors other than physiological events play a role in explaining the source of pain. This finding also suggests that patients may have difficulties with home care after the first eye surgery (use of anti-inflammatory drugs, eye care, etc.) and that the increased pain level after

the second eye surgery may be related to patients' concerns about postoperative care. Therefore, it should be remembered that there is a possibility that high anxiety and inadequate social support for eye care may lead to an increase in the level of pain. However, it should not be forgotten that pain may be a serious complication indicator. For this reason, the surgical team must well identify the pathologies represented by these different causes of pain (1). At this stage, physiological parameter data can be used to objectively evaluate the change in the severity of pain.

The fourth important finding of this study was that the diastolic blood pressure value measured before the operation and the pulse and respiration rates of patients measured during the surgery were higher in the 1st eye surgery than those of the 2nd eye surgery. In the within-group evaluation, the value of diastolic blood pressure during the 1st eye surgery was higher than all other measurements. In the study of Jiang et al. (8) on cataract surgery patients, there was no change in physiological parameter measurements during both eye surgery operations. In the same study, when they examined the correlation between subjective measurements such as anxiety and pain and objective measurements such as physiological parameters, the blood pressure and pulse rate were found to vary according to the level of anxiety in the second preoperative period, and the number of diastolic blood pressure and pulse rate of the patients were determined to increase as pain severity increased. The researchers stated that monitoring the perioperative blood pressure and pulse rate values may help determine painful patients during surgery (8). In this study, considering the high anxiety and postoperative pain of the patients during the second eye surgery, physiological parameters are expected to increase as reported by studies in the literature. However, despite the high pain and anxiety, the pulse rate and diastolic blood pressure were observed to decrease in patients in the second eye surgery. Therefore, objective data suggest that patients' pain and anxiety levels may be lower than reported and these subjective measurements may vary according to the patient's perception. Indeed, while some researchers examining the possible causes of increased pain during the second eye surgery said anxiety was the underlying cause of pain in the second eye surgery (20), some studies suggested that this depended on the perception of the patient (8,14,21). In this study, when the patients were asked to compare their perception of pain and anxiety they felt in two eye surgeries, the results were not much different from those reported in the surgical process. The patients stated that second eye surgery was a more painful experience, but that they experienced a similar level of anxiety in both eye surgeries. Because pain has many physical, emotional, perceptual, and psychosocial dimensions and there is the possibility that they may affect the patient with all these aspects in the surgical process, the results show that other factors affecting patients' perception of anxiety and pain should be evaluated comprehensively.

Conclusion

The state anxiety levels of the patients were higher in the first eye surgery compared to the second eye surgery. Although patients indicated high levels of anxiety during the second eye surgery, diastolic blood pressure, respiration and pulse values, which were among the physiological parameters, indicated more intensive anxiety findings in the first eye surgery. Patients had higher pain scores soon after the second eye surgery and higher state-anxiety scores after they were taken to the clinic. In conclusion, the results of subjective (pain and anxiety) and objective (blood pressure and heart rate) measurements in this study showed that the anxiety experienced in the first eye cataract surgery made the perceived anxiety and sensation of pain more sensitive in the second eye surgery.

This study was carried out in January 2020 in Nevsehir Haci Bektas, Veli University Health Sciences Faculty Institute of Nursing Department has been produced from the master thesis entitled "Pain and Anxiety During Cataract Surgery: A Comparison Between The First and Second Eye Surgeries".

Ethics

Ethics Committee Approval: This study was conducted with an approval from the Nevşehir Hacı Bektaş Veli University Ethics Committee (decision no: 2018/10, date: 10.09.2018).

Informed Consent: The written consent of the participants was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.K.Ç., C.A.A., F.İ., Design: F.İ., G.K.Ç., C.A.A., Supervision: F.İ., G.K.Ç., C.A.A., Fundings: C.A.A., G.K.Ç., Materials: F.İ., G.K.Ç., C.A.A., Data Collection or Processing: C.A.A., G.K.Ç., Analysis or Interpretation: F.İ., G.K.Ç., C.A.A., Literature Search: C.A.A., G.K.Ç., Writing: G.K.Ç., C.A.A., Critical Review: F.İ., C.A.A., G.K.Ç.

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Is Manual Segmentation the Real Gold Standard for Tooth Segmentation? A Preliminary *in vivo* Study Using Conebeam Computed Tomography Images

Manuel Segmentasyon, Diş Segmentasyonu için Gerçek Altın Standart mı? Konik Işınlı Bilgisayarlı Tomografi Görüntüleri Üzerinde Bir Ön in vivo Çalışma

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Keywords

Cone-beam computed tomography, image analysis, segmentation, impacted tooth

Anahtar Kelimeler

Konik ışınlı bilgisayarlı tomografi, görüntü analizi, bölütleme, gömülü diş

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Abstract

Objective: This study aimed to assess whether manual segmentation is an accurate method in tooth volume measurement and to compare the outcomes of manual, automatic, and semiautomatic segmentations on cone-beam computed tomography (CBCT) images by comparing each system with the water displacement method, which is the gold standard.

Materials and Methods: CBCT images of 10 maxillary impacted teeth were used in this preliminary *in vivo* study. Following the acquisition of CBCT scans, manual, automatic, and semiautomatic segmentations were completed by the same operator. After surgical removal, the volumes of all impacted teeth were measured with the water displacement method, which was used as the gold standard. The volume of each segmented image was measured in mm³ using the 3D-Doctor software. The established volumes of each segmented image were compared with those of the gold standard using the 95% confidence interval bootstrap percentiles. Intraobserver reliability was determined using the intraclass correlation coefficient.

Results: All segmentation methods revealed significantly different volume values both from the gold standard and from each other (p=0.000). The semiautomatic segmentation demonstrated comparable performance with the manual method, and both systems provided comparable volumes with the gold standard than did the automatic method. Excellent intra-observer intraclass correlations were found for all protocols.

Conclusion: The actual volumes of the specimen were not obtained by manual, semiautomatic, and automatic segmentations. Semiautomatic segmentation demonstrated comparable performance to the manual method, whereas automatic segmentation yielded the poorest values. The automatic and semiautomatic segmentations may be improved by the development and utilization of novel or hybrid segmentation algorithms for a faster process and more accurate results.

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Öz

Amaç: Manuel segmentasyonun (bölütleme) diş hacmini ölçmek için doğru bir yöntem olup olmadığını değerlendirmek ve konik ışınlı bilgisayarlı tomografi (CBCT) görüntülerinde manuel, otomatik ve yarı otomatik segmentasyon sonuçlarının her birini altın standart olarak kabul edilen su deplasman yöntemi ile karşılaştırmaktır.

Gereç ve Yöntemler: Bu ön *in vivo* çalışmada maksiller gömülü 10 dişin CBCT görüntüleri kullanılmıştır. CBCT taramalarının alınmasının ardından manuel, otomatik ve yarı otomatik segmentasyon aynı operatör tarafından tamamlanmıştır. Cerrahi olarak çıkarıldıktan sonra tüm gömülü dişlerin hacimleri altın standart olarak kullanılan su deplasman yöntemi ile ölçülmüştür. Her bölütlenmiş görüntünün hacmi, 3D-Doctor yazılımı kullanılarak mm³ cinsinden ölçülmüştür. Tüm bölütlenmiş görüntülerin belirlenen hacimleri, %95 güven aralığı bootstrap yüzdelikleri kullanılarak altın standartlarla karşılaştırılmıştır. Gözlemci içi güvenilirlik, sınıf içi korelasyon katsayısı kullanılarak belirlenmiştir.

Bulgular: Tüm segmentasyon yöntemleri hem altın standarttan hem de birbirinden önemli ölçüde farklı hacim değerleri ortaya çıkarmıştır (p=0,000). Yarı otomatik bölütleme, manuel yönteme benzer performans ortaya koymuş ve her iki sistem de otomatik yönteme göre altın standartla karşılaştırılabilir hacimler sağlamıştır. Tüm protokoller için mükemmel gözlemci içi sınıf içi korelasyonlar bulunmuştur.

Sonuç: Manuel, yarı otomatik ve otomatik segmentasyonla elde edilen sonuçlar numunelerin gerçek hacimlerinden farklı bulunmuştur. Yarı otomatik segmentasyon, manuel yönteme benzer performans sağlarken, otomatik segmentasyon altın standarda en uzak sonuçları sunmuştur. Otomatik ve yarı otomatik bölütleme, daha hızlı işlem ve daha doğru sonuçlar için yeni veya hibrit bölümleme algoritmalarının geliştirilmesi ve kullanılmasıyla iyileştirilebilir.

Introduction

During the last decades, diagnostic imaging technologies have greatly increased the knowledge of normal and diseased in many fields of medical research and clinical practice. The growing number of the imaging modalities have necessitated the use of computers to facilitate data processing and analysis (1). One of those analysis modalities is image segmentation which is defined as the partitioning of an image into non-overlapping, constituent regions that are homogeneous with respect to some characteristics such as intensity or texture (2).

Segmentation can be accomplished using manual. automatic and semi-automatic methods. The most general approach to segmentation is the manual method, where the user outlines the structures slice by slice. Manual segmentation is often used as a reference for comparison with other segmentation methods (3-5), however it is subjective, userdependent, tedious and time-consuming. On the other hand, automated segmentation is a fast, easy and operator independent method (6). Unfortunately, because of the presence of inaccuracies with respect to the delineation of the borders of the image to be segmented that often requires the operators' manual intervention and guidance, this method may not be considered appropriate especially for complex medical images (7). To overcome these problems, a lot of work has been invested in semi-automatic

segmentation methods (8). In semi-automatic segmentation, the components of both the automatic and manual segmentation are included. Thus, not only the advantages but also the disadvantages of both modalities are transferred, as well. This matter has raised concerns about the accuracy and utility of semi-automatic segmentation (3,4,9).

The segmentation accuracy on conventional medical computerized tomography (CT) images have been studied extensively (7,10,11). Considering the fact that conventional medical CT protocols are generally associated with relatively high radiation dose levels, cone beam computerized tomography (CBCT) has gained popularity in daily dental practice for 3D imaging of the maxillofacial and dentoalveolar structures, due to its high resolution for hard tissues and relatively low radiation exposure (10). Accurate segmentation of regions of interest by using computer algorithms is becoming increasingly important in assisting dentomaxillofacial diagnosis, treatment planning and outcome evaluation (6,12-14). On CBCT images, segmentation has been utilized to assess the tongue volume which is an important contributor to the etiology of dental malocclusions.dentofacial deformities (15) and sleep apnea disorders (16). Segmentation becomes even more imperative to avoid post-operative complications prior to dental implant placement, third molar surgical removal and other craniofacial or orthognathic surgical operations, and also to accurately diagnose numerous vascular

and neurogenic pathologies associated with the mandibular nerve (17,18). Segmentation is also exploited for establishment of morphological changes within the temporomandibular joint to provide about functional/pathological data alterations of the mandibular complex (19,20). Additionally, for detection of the volume of neoplastic or nonneoplastic osteolytic lesions of the jaws, automatic segmentation on CBCT images can provide promising results (17,21). In orthodontics, development of the external root resorption can be observed by calculation of the volume of the tooth (4). Similarly, segmentation has been employed in the evaluation of lesion healing after endodontic surgery (13), in 3D analyses of root canal anatomy (6,22,23), and even in age estimation in forensic dentistry (24). However, CBCT images have relatively poor quality due to limited radiation exposure and low signal to noise ratio (25,26), which makes the segmentation more challenging than that in CT, especially for the tooth structures. Higher image noise, lower image contrast between the tooth root and the alveolar bone and close proximity of adjacent tooth structures are the reasons that complicate the tooth segmentation on CBCT images (27).

There are studies in dental literature evaluating the accuracy of segmentation of tooth structures by using different CBCT machines and/or 3D printing technologies (4,5,7,26,28-30). However; in most of those investigations, manual segmentation method (5,7,29) or micro-CT (4,30) have been employed as the gold standard.

To the authors' knowledge, there is no published data assessing the accuracy of the manual segmentation by comparing the volume measurements of segmented and the actual anatomical tooth using *in vivo* CBCT images. Likewise, there is no research comparing the accuracy of manual, semi-automatic and automatic tooth segmentation by using the real anatomical tooth measurements as the gold standard. Additionally, the tooth anatomical structure is unique since it has different contrast values at the crown and root, and thus, it is usually considered as a major constraint in such study designs (3). Due to this complexity, only few studies have used multi rooted teeth for age estimation in dental forensics (31,32).

In the literature, different segmentation methods are evaluated both in *ex vivo* or *in vivo* studies.

The anatomic location of the object that would be segmented is a very important parameter (3,33) since the outlines of that particular object has to be clearly delineated both manually and automatically. However, easily outlined *in vivo* hard tissues such as temporomandibular joint and impacted third molars have been utilized in many papers (19,34,35). Considering that the preferred segmentation method has to be as accurate as possible even in very complicated *in vivo* cases and the most complex tooth-root anatomical structure has been observed in the cases of impacted teeth (36), the accuracy of different segmentation needs to be assessed on impacted teeth.

Therefore, the aim of this study was to assess whether manual segmentation is an accurate method of volume measurement in impacted maxillary teeth by comparing the outcomes of manual, automatic and semi-automatic segmentation methods on CBCT images with water displacement method, which is accepted as the gold standard.

Materials and Methods

Study Sample

A total of 10 individuals referred to the Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Ege University for CBCT evaluation in order to assess the positions and relationships of impacted maxillary teeth with adjacent roots or other anatomic structures before surgery were included in the present pilot study. The study protocol was approved by the Ethics Committee of the Medical Faculty of Ege University (approval #16-12/11, 01.03.2017) and was conducted according to the Declaration of Helsinki on experimentation involving humans.

Radiographic Technique

CBCT examinations were performed using the Kodak 9000 3D (Kodak Carestream Health, Trophy, France) system and the imaging parameters were 10 mA and 70 kVp with 2.5 mm Al equivalent filtration. CBCT acquisition of each patient was completed after a single 360° rotation with 10.8 s scan time, and a volume with a spatial resolution of 76 μ m (isotropic voxel) was reconstructed. All images were taken by the same operator and the DICOM files of the CBCT images were saved to a portable hard disk.

Surgical Procedure

Before surgery, patients were informed about possible complications of removal of the impacted tooth and their written informed consents were obtained. All impacted teeth were extracted by the same surgeon using standard surgery protocol for impacted tooth removal under local anaesthesia (2% articaine and epinephrine 1:1000.000), with similar surgical instruments.

Segmentation

CBCT images of 10 impacted teeth were used in this preliminary *in vivo* study. Manual, semi-automatic and automatic segmentation and reconstruction procedures are shown in Figure 1. Semiautomatic and automatic segmentation of DICOM images were performed by using the thresholding method. Firstly, DICOM images were imported in 3D-doctor (Able Software Corp, MA, USA) and the voxel heights of the images were calibrated. Then the region of interest



Figure 1. Protocol of segmentation and reconstruction procedures

(ROI) was determined while it was ensured that the tooth which to be segmented was left in the ROI in all sections. The images were segmented with the determined threshold, reconstructed in 3D-doctor and their volumes were measured. In semi-automatic segmentation, this procedure was performed by manual editing of the images before reconstruction (Figure 1).

Thresholding Method

Thresholding method is one of the basic and most important methods in the processing of medical images. This method is essentially a segmentation method for separating objects from the background by using a threshold T-value that is determined in the histogram showing the gray level distributions of the image, and the pixels in the image are compared to that threshold.

For a given image f (i, j) for any (i, j) pixel in the image, threshold image g (i, j) (37);

$$g(i,j) = \begin{cases} 1, iff(i,j) > T \\ 0, iff(i,j) \le T \end{cases}$$

In order to establish the optimum threshold value in automatic and semi-automatic segmentation of teeth, bisection search which is a root-finding method that can be used for one dimensional global optimization problems (38) deemed appropriate. The determination of the optimum threshold can be formulated as a minimization problem of histogram curve of the image and can be estimated by finding the local minima between the peaks points corresponding to the teeth and the background in the histogram. In this method, the optimum threshold value must be the largest threshold value that prevents over segmentation while maintaining the shape and size of the segmented teeth in the previous slice (39). On each slice of CBCT images of 10 teeth, manual (Figure 2a), semi-automatic (Figure 2b) and automatic (Figure 2c) segmentation were performed.

The manual and semi-automatic segmentation were repeated three times by the same operator. In each segmentation, the time required from the start to the end of segmentation was also recorded.

Reconstruction of Segmented Images and Volume Measurements

After completion of manual, semi-automatic and automatic segmentation for 10 teeth, segmented

section images were reconstructed in 3D-doctor software (Figure 3) to create 3D models and the radiographic volumes of the teeth were measured from these models.

Physical Volume Measurements of the Teeth (Gold Standard)

The physical volumes of the operated teeth were measured with the Precisa XB 220A analytical balance using the water displacement method (Archimedes principle). A 10 mL cylinder with 0.1 mL gradations was filled with room temperature water up to the 9 mL mark and the tooth was dipped completely into the cylinder. After immersion, the water level was recorded. Using the pre and post immersion readings, the volume of each tooth was measured. The procedure was repeated three times to reduce measurement errors and the mean of three measurements was used as the physical volume of

the tooth, that is the gold standard for that particular tooth.

Statistical Analysis

The comparisons between the gold standards and the radiographic volumes obtained with manual, semi-automatic and automatic segmentation were performed using repeated analyses of variance. In order to assess the significance of the differences in post hoc comparisons of ANOVA analysis, bootstrapping sampling method was used. With the intention of deriving less biased standard errors, a total of 1.000 bootstraps were created from the data set. The bias, standard error and the upper and lower levels of 95% confidence interval were established. In order to assess the intraobserver agreement, the measurements were performed twice with an interval of three months and the reliability of the observer was assessed with intraclass correlation coefficient (ICC).



Figure 2. Images specimens of a) manuel, b) semi-automatic and c) automatic segmented image of same slices



Figure 3. Reconstructed 3D geometry specimen

The data were analyzed with SPSS version 15.0 (SPSS, Chicago, Illinois, USA). In all tests, p was set as 0.05.

Results

The mean radiographic volume measurements for manual, semi-automatic and automatic segmentation and the gold standards are presented in Table 1. ANOVA analysis revealed that the differences between the gold standard and the mean volume measurements obtained with manual, semi-automatic and automatic segmentation were statistically significant in all samples (p=0.000).

The segmentation method which presented the closest values to the gold standard measurements was revealed with the post hoc bootstrap analysis (Table 2). Among 10 samples, semiautomatic method values were similar to the gold standard in 5 samples (sample #1,5,6,7 and 10), whereas manual method revealed lower differences in samples 2,3,4,8 and 9.

In the present study, the ICC was 0.999 (95% confidence interval ranged between 0.996 and 1.000) and the observer's level of reliability was considered as "excellent" (p<0.05) (ICC<0.5: poor reliability, ICC=0.5-0.75: moderate reliability, ICC=0.75-0.9: good reliability, ICC>0.90: excellent reliability).

Regarding the time required for segmentation process, the automatic segmentation lasted less than average 1 second per slice, while the manual segmentation took approximately 22 seconds per slice and the semi-automatic segmentation lasted on average 10 seconds per slice. The differences were statistically significant (p=0.000).

Discussion

Segmentation using a global threshold based method on image intensity values is common in medical modeling (33,40-42). However, it has limitations in dental modeling both because of the variability of the density of the structures within the maxillofacial region and the technical capabilities of the devices and algorithms used in dental imaging (13,33). The density of tooth is heterogeneous from crown to apex and this natural feature leads to less clear difference between the root and the alveolar bone as the contrast between the root and bone decreases. This, consequently, impedes segmentation of the tooth from alveolar bone (3). In the present study, the segmentation was performed on impacted maxillary teeth, which makes this procedure especially arduous because of the close proximity of the impacted teeth to the roots and apices of the adjacent teeth and other anatomical structures. Besides, due to the strong noise, low contrast of tooth roots and sockets, and intensity inhomogeneity in CBCT images, accurate segmentation of tooth regions suffers from great challenges. Similar considerations were presented for automatic segmentation of mandibular condyle using CBCT images (19). Low bone density of the condylar bone but high density of the petrous temporal bone, presence of adjacent anatomical structures, the conical shape of the CBCT beam, and low contrast resolution of the CBCT data have been stressed as the confounding factors (19). Thus, segmentation of tooth from CBCT images to reveal the root anatomy and supporting bone requires a more comprehensive model compared with medical CT images. Recently,

| Table 1. Volumes in mm ³ of 3D geometries of reconstructed images and physical volume measurements of each tooth | | | | | | |
|---|--------|----------------|-----------|---------------|--|--|
| Sample # | Manual | Semi-automatic | Automatic | Gold standard | | |
| 1 | 185.79 | 197.09 | 173.55 | 207.45 | | |
| 2 | 184.10 | 182.59 | 181.61 | 195.06 | | |
| 3 | 391.76 | 405.53 | 414.13 | 396.79 | | |
| 4 | 244.66 | 236.17 | 240.43 | 264.68 | | |
| 5 | 232.43 | 240.16 | 236.91 | 253.36 | | |
| 6 | 163.82 | 163.24 | 169.34 | 162.22 | | |
| 7 | 325.19 | 326.99 | 321.94 | 347.01 | | |
| 8 | 304.46 | 289.17 | 283.55 | 343.63 | | |
| 9 | 151.86 | 147.14 | 119.86 | 198.49 | | |
| 10 | 308.68 | 312.74 | 308.4 | 366.48 | | |

| Table 2. Bootstrap analysis results of three segmentation methods | | | | | | | |
|---|-----------|------------------|------------------|----------------|-----------------------------|--------|--|
| | | | Bootstrap multip | le comparisons | | | |
| | | | | | BCa 95% confidence interval | | |
| Sample | Method | Mean difference* | Bias | Standard error | Lower | Upper | |
| 1 | Manual | 21.65 | -0.05 | 1.99 | 16.88 | 24.56 | |
| | Semi-auto | 10.36 | -0.04 | 0.45 | 9.48 | 11.24 | |
| | Auto | 33.9 | -0.03 | 0.37 | 33.24 | 34.8 | |
| 2 | Manual | 10.95 | 0.05 | 0.41 | 10.01 | 11.68 | |
| | Semi-auto | 12.45 | 0.01 | 0.2 | 12.07 | 12.83 | |
| | Auto | 13.45 | 0.02 | 0.17 | 13.01 | 13.71 | |
| 3 | Manual | 5.02 | -0.12 | 1.14 | 2.98 | 7.36 | |
| | Semi-auto | -8.73 | -0.11 | 0.98 | -10.21 | -6.59 | |
| | Auto | -17.33 | 0.14 | 0.95 | -18.51 | -14.96 | |
| 4 | Manual | 20.02 | 0.09 | 1.76 | 15.99 | 23.12 | |
| | Semi-auto | 28.51 | 0.01 | 1.72 | 25.06 | 31.59 | |
| | Auto | 24.25 | -0.01 | 1.34 | 21.21 | 26.17 | |
| 5 | Manual | 20.93 | -0.03 | 1.04 | 18.51 | 22.4 | |
| | Semi-auto | 13.2 | -0.02 | 1.01 | 10.83 | 14.44 | |
| | Auto | 16.45 | -0.02 | 1.01 | 14.11 | 17.62 | |
| 6 | Manual | -1.6 | -0.05 | 0.66 | -2.62 | -0.15 | |
| | Semi-auto | -1.02 | -0.08 | 0.64 | -1.87 | 0.49 | |
| | Auto | -7.12 | -0.07 | 0.63 | -7.91 | -5.55 | |
| 7 | Manual | 21.81 | 0.1 | 2.73 | 16.36 | 27.19 | |
| | Semi-auto | 20.01 | 0.09 | 2.71 | 14.57 | 25.29 | |
| | Auto | 25.05 | 0.08 | 2.7 | 19.67 | 30.31 | |
| 8 | Manual | 39.17 | -0.19 | 3.98 | 31.3 | 47.3 | |
| | Semi-auto | 54.46 | -0.12 | 3.89 | 47.01 | 62.32 | |
| | Auto | 60.08 | -0.11 | 3.88 | 52.65 | 67.91 | |
| 9 | Manual | 46.62 | 0.01 | 2.07 | 42.03 | 49.98 | |
| | Semi-auto | 51.34 | 0.01 | 2.06 | 46.79 | 54.64 | |
| | Auto | 78.62 | 0.07 | 2.06 | 74.08 | 81.9 | |
| 10 | Manual | 57.79 | -0.02 | 1.84 | 54.38 | 61.24 | |
| | Semi-auto | 53.74 | 0.13 | 1.06 | 51.56 | 55.37 | |
| | Auto | 58.07 | 0.12 | 1.02 | 55.53 | 59.39 | |

several segmentation methods and processing algorithms are being actively developed to overcome these problems. Some have proposed to segment the crown and the root separately with two level set approaches (3,4,12,28) and others have proposed improved hybrid active contour model to accurately distinguish tooth structure from its surroundings (9,39). However, in most of these studies, segmentation accuracy was tested by methods that could only be implemented under *in vitro* conditions (9,12,28,39). Performing the experiments under *in vitro* settings does not accurately mimic clinical environments, and therefore, they do not represent the real efficacy and accuracy of segmentation methods. Only a few studies have tried to determine the accuracy of volumetric analysis of teeth on *in vivo* images using CBCT (3,4,33). In 2010, Liu et al. (3) evaluated the validity of *in vivo* tooth volume determinations using two different

CBCT machines with different exposure settings. The authors used water displacement method as the gold standard to assess and compare the CBCT and actual volume values of 24 premolar teeth. They found that there was a significant difference between the physical volume measurements of the extracted teeth and CBCT measurements (p<0.05). However, the accuracy of only one segmentation method (semi-automated with manual intervention) was evaluated in that study. Besides, using two observers and two different CBCT machines on segmentation procedure showed statistically different tendencies with the CBCT volumetric measurements. In another study by Wang et al. (4), 27 premolars were scanned with CBCT before extraction and with micro-CT after extraction (micro-CT was used as a reference system for comparison). The authors utilized an individual segmentation threshold and revealed comparable results with CBCT and micro-CT. Recently, the accuracy of tooth segmentation was evaluated using four different windowing protocols for manual method by comparing the volumes obtained from CBCT segmentations. Laser scanning method was employed as the gold standard and the results revealed that only one windowing protocol showed significantly closer volumes to the gold standard (33). Most of these studies evaluating the accuracy of different segmentation procedures have used manual segmentation as the gold standard (5,7,29). However, to the authors knowledge, there is no study in the literature that used in vivo CBCT images to evaluate the accuracy of manual segmentation by using the physical tooth volume as the gold standard and to compare three different tooth segmentation procedures. The present study revealed that even though manual segmentation method requires meticulous delineation of the structures which are to be segmented, it provides significantly different volumetric values from the actual volume of the specimen and cannot be considered as the gold standard. So, in clinical applications of segmentation, especially prior to surgical operations in complicated cases, the reliability of the manual segmentation shall be questioned.

Image segmentation-based volume assessment is presented as an accurate method that provides comparative analysis of jaw lesions (17). However, the results of the present study showed that mean

radiographic volume measurements for manual, semi-automatic and automatic segmentation were significantly lower than the gold standard values. It's stated that using a uniform threshold for tooth segmentation could result in data loss because of the variable density values of teeth and surrounding tissues among different individuals (3). Additionally, the threshold level needed to be adjusted since the anatomy and density of a tooth is heterogeneous from the crown to the apex. A tooth crown is easier to segment due to its mineralized enamel which presents a distinct contrast with the adjacent air. On the contrary, there is a less clear difference between the root tissue and the surrounding alveolar bone. These anatomical characteristics cause heterogeneity of the tissue density which results with significantly different densities from crown to apex on the image, leading to more complicated segmentation process (12). Our lower mean radiographic volume measurements for manual, semi-automatic and automatic segmentation than the gold standard values may be the outcome of this above-mentioned data loss due to the uniform threshold level. Due to these findings, application of different threshold values to the crown and root of the tooth rather than using a single and standard threshold may be suggested for automatic and semiautomatic segmentation.

The other parameters that could influence the qualitative and quantitative aspects of segmentation procedure were the maxillary or mandibular location of the tooth (3), and the position of the tooth within the alveolar arch (33). Previous studies revealed that mandibles show a better CBCT image quality than maxillae since it has greater contrast between the dental alveolus and the surrounding cortex (43). Most of tooth segmentation studies concluded that segmentation procedure becomes more difficult when the roots are closer to the cortical bone or in close contact with adjacent teeth (3,33). In the present study, the impacted teeth were not at their original positions within the dental arch and were located mostly close to the adjacent teeth and cortical bone. Additionally, all of our cases were the maxillary impacted teeth, and since maxillae have poorer image quality, this was probably the most prominent cause of the challenges in delineation of anatomic structures. These parameters may be other possible reasons of lower radiographic volume measurement values as compared with the gold standard. Considering the literature, the cases utilized in the present were the most complicated and challenging ones for *in vivo* segmentation procedure.

potential indications Despite for dental segmentation, enrollment of the observers is still considered as the major pitfall of the technique. Using more than one observer has resulted with varying radiographic volume measurements obtained with CBCT images and gold standard, and statistically significant difference between the observers was attributed as the cause of this outcome (3). Both for manual and semi-automatic segmentation procedures, human eve is required to delineate the structures of interest from the adjacent areas (29) and this may be the origin of subjectivity of the observers. Additionally, the experience and the knowledge of the observer regarding the dental anatomy contribute to the overall performance and consequently, the accuracy of the segmentation process (33). Another problem is the time spent during segmentation procedures. Elongated procedure time especially during the manual segmentation process may cause tiredness of the observers, and influence the reliability of the observer/method (7,44). This was also observed in the present study, and manual segmentation required more time than the semiautomatic and automatic segmentation procedures.

A major limitation of the present pilot study is the small number of sample size. The integrity of the tooth material was vital to measure the actual tooth volume, which was the gold standard. Unfortunately, it was difficult to remove the impacted maxillary teeth as intact structures during surgical operations, and this was the main reason of low sample size. At this point, in order to help to diminish the time spent and subjective aspects of the segmentation procedure, further studies are required with a larger sample size to investigate the development and performance of new or hybrid algorithms on semi-automatic segmentation.

Conclusion

For the first time in the literature, the present study has evaluated the accuracy of manual, semiautomatic and automatic segmentation methods by comparing the radiographic volumetric values of the teeth obtained on in vivo CBCT images and the physical teeth volumes. Even though in vivo conditions complicated the segmentation of the teeth, we observed that radiographic volume values that were acquired with manual segmentation were significantly different than the physical volumes of the teeth. Our results revealed that automatic segmentation yielded the poorest values whereas semi-automatic segmentation was as accurate as manual segmentation procedure. The automatic and semi-automatic segmentation methods may be improved by development and utilization of novel or hybrid segmentation algorithms for more accurate results, that is imperative especially for treatment planning of surgical operations which may possess significant postoperative complications.

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Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of the Medical Faculty of Ege University (approval #16-12/11, 01.03.2017) and was conducted according to the Declaration of Helsinki on experimentation involving humans.

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: P.G., E.Ş., S.S., F.G., Design: P.G., E.Ş., S.S., Supervision: P.G., F.G., E.Ş., Fundings: B.O.G., P.G., E.Ş., Materials: U.T., Data Collection or Processing: R.I.T., Analysis or Interpretation: S.S., H.B., Literature Search: A.B., E.Ş., Writing: E.Ş., P.G., S.S., Critical Review: P.G., E.Ş., A.B., S.S., B.O.G.

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Therapeutic Plasma Exchange and Conservative Treatment Comparison in Patients with Hypertriglyceridemiainduced Acute Pancreatitis

Hipertrigliseridemi İlişkili Akut Pankreatit Hastalarında Terapötik Plazma Değişimi ve Konservatif Tedavinin Karşılaştırılması

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Keywords

Conservative treatment, hypertriglyceridemiainduced acute pancreatitis, therapeutic plasma exchange

Anahtar Kelimeler

Konservatif tedavi, hipertrigliseridemi ilişkili akut pankreatit, terapötik plazma değişimi

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Abstract

Objective: Hypertriglyceridemia is the third most common cause of acute pancreatitis. Immediate triglyceride level lowering is beneficial in patients with severe hypertriglyceridemia [triglyceride (TG) >1,000 mg/dL]. This study aimed to compare the severity of acute pancreatitis, in-hospital mortality, and local and systemic complications, as well as hospitalization duration between patients with hypertriglyceridemia-induced acute pancreatitis treated with conservative treatment only and with therapeutic plasma exchange (TPE) in addition to conservative treatment.

Materials and Methods: A total of 120 patients diagnosed with hypertriglyceridemia-induced acute pancreatitis treated with TPE in addition to conservative treatment (group 1) or conservative treatment only (group 2) participated in the study.

Results: Group 1 consisted of 38 patients (9 females and 29 males) and group 2 had 82 patients (29 females and 53 males). No difference was found between the two groups regarding patient characteristics. The TG levels in group 1 decreased by 56.8% in one treatment session. The rate of patients with moderately severe acute pancreatitis + severe acute pancreatitis in group 1 was 36.8%, whereas 59.8% in group 2 (p=0.029). The local complication rate was 34.2% and 57.3% in group 1 and group 2, respectively (p=0.031). No significant difference was found between the groups regarding organ failure, systemic complication, hospitalization duration, and in-hospital mortality rates.

Conclusion: Our study revealed that TPE treatment is effective in reducing local complications (especially pancreatic pseudocyst).

Öz

Amaç: Hipertrigliseridemi akut pankreatitin en sık 3 nedeninden biridir. Ciddi hipertrigliseridemisi olan hastalarda [trigliserid (TG) >1.000 mg/dL] TG düzeyinin hemen düşürülmesi faydalı olabilir. Çalışmamızda hipertrigliseridemi ilişkili akut

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pankreatit hastalarına uygulanan konservatif tedavi ile konservatif + terapötik plazma değişimi tedavilerini mortalite, hastane yatış süresi ve lokal-sistemik komplikasyonları baz alarak karşılaştırdık.

Gereç ve Yöntemler: Hipertrigliseridemi ilişkili akut pankreatit tanısı olup konservatif tedavi + terapötik plazma değişimi tedavisi alanlar (grup 1) ve sadece konservatif tedavi alan (grup 2) toplam 120 hasta çalışmaya alınmıştır.

Bulgular: Grup 1'de 38 (9 kadın, 29 erkek), grup 2'de 82 (29 kadın, 53 erkek) hasta mevcuttu. İki grup arasında hasta özellikleri açısından fark yoktu. Grup 1'de bir seans tedavi sonrası TG düzeyi %56,8 azaldı. Grup 1 hastalarının %36,8'i orta + ciddi düzeyde pankreatit iken, grup 2 hastalarında bu oran %59,8 idi (p=0,029). Lokal komplikasyon oranları grup 1 ve grup 2 hastalarda sırası ile %34,2 ve %57,3 idi (p=0,031). Gruplar arasında organ yetmezliği, sistemik komplikasyonlar, hastane yatış süresi ve hastane içi mortalite açısından fark yoktu.

Sonuç: Çalışmamızda, terapötik plazma değişimi tedavisi lokal komplikasyonları (özellikle pankreatik psödokist) azaltmada etkili olarak bulunmuştur.

Introduction

Acute pancreatitis (AP) is a common disorder having high morbidity and mortality. Although the majority of patients have a mild clinical course, the mortality rate may reach 30% in patients with severe pancreatitis (1). Hypertriglyceridemia (HTG) is the third most common cause of AP following gallstones and alcohol; it is responsible for 1-10% of AP cases (2). HTG may be primary, or it may develop secondary to alcohol abuse, diabetes mellitus (DM), pregnancy, obesity, hypothyroidism, nephrotic syndrome, or various medications such as β -blockers, oral retinoids. It is believed that AP risk is elevated in patients with triglyceride (TG) level above 1,000 mg (3). HTG has been reported to be more related to mortality, severe pancreatitis, complications, and recurrence, compared to other AP etiologies (4-6). Therefore, it is important to assess the severity and prognosis of patients with hypertriglyceridemia-induced acute pancreatitis (HTG-AP) in the early period; this helps in both individualizing the treatment and improving the prognosis of the disease. The Balthazar score plays an important role in determining the severity of AP and has been in use for over three decades (7,8).

The treatment principles in AP are fasting, lowcalorie infusions (in theacute phase), using anti-lipid agents (fenofibrate, gemfibrozil, niacin, omega-3 fatty acids), low-molecular-weight heparin (LMWH), and insulin. Non-pharmacological treatment methods such as therapeutic plasma exchange (TPE) have started to be used recently.

In our study, we aimed to compare our conservatively treated HTG-AP patients to our HTG-AP patients in whom TPE was added to the conservative treatment method, regarding AP severity, duration of hospitalization, in-hospital mortality, organ failure,

and local/systemic complication rates, based on the revised Atlanta classification.

Materials and Methods

Study Population

A total of 120 patients (38 females and 82 males, mean age of 41.1±8) diagnosed as HTG-AP and treated with conservative method only or with TPE added to conservative treatment in the gastroenterology departments of the three different university hospitals were enrolled in this study. While TPE + conservative treatment was performed in one university hospital, only conservative treatment was administered in the other two university hospitals. All patient data were retrospectively obtained from the electronic medical records. The diagnosis of HTG-AP was made based on TG levels above 1,000 mg/dL and the presence of at least two of the three diagnostic criteria for AP (abdominal pain, more than 3-fold increased serum lipase level, and characteristic imaging findings). We did not perform the genetic analysis to determine the type of hyperlipidemia in our patients.

Patient data were recorded including age, gender, alcohol consumption, the presence of diabetes mellitus, previous AP exacerbations and related therapeutic apheresis, together with previous medical treatment for hyperlipidemia. Also, values of fasting blood glucose, blood urea nitrogen, creatinine, calcium (Ca), alanine aminotransferase, lactic dehydrogenase, amylase, lipase, TG, C-reactive protein (CRP), leukocyte, hematocrit were collected for each patient. The reduction in TG was calculated using the values at admission and the day after TPE. Contrast-enhanced CT scans of the abdomen were performed within the three days following admission in all patients. The Balthazar score was confirmed by two independent radiologists. Clinical course was reevaluated after 24, 48 and 72 h. Local complication was re-evaluated after 48-72 h and 4 weeks. The severity of pancreatitis was determined taking into account the overall course of the patient after discharge. According to the 2012 revision of the Atlanta classification and the definitions by international consensus, the severity of AP was categorized in three groups as mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). MAP lacks organ failure, local or systemic complications, and exacerbation of coexisting disease. The MSAP manifests transient organ failure (≤48 hours), local complications, and/or exacerbation of coexisting disease. SAP is defined by persistent organ failure (≥48 hours). Organ failure involves pulmonary failure, defined as an arterial PO₂<mmHg on room air or the requirement for mechanical ventilation. Cardiovascular failure is defined as the development of shock (systolic pressure <90 mmHg) that persists following fluid resuscitation. Renal failure is defined as a serum creatinine level >2 mg/dL after rehydration or the need for hemodialysis in patients without preexisting renal disease. Local complications are acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, walled-off necrosis, and necrosis. The systemic complication was defined as an exacerbation of preexisting comorbidity, precipitated by AP (9). The patients were divided into two groups as treated with TPE in addition to the conservative treatment (group 1) and treated with conservative treatment only (group 2). In-hospital mortality, organ failure, duration of hospitalization, local and systemic complication rates were compared between the two groups.

The study's ethics committee approval was obtained from the Adnan Menderes University Non-Invasive Clinical Research Ethics Committee that the study was conducted (protocol no: 2017/1253, date: 26.10.2017).

Conservative Treatment

Intravenous hydration and pain management were administered in addition to the discontinuation of oral feeding. LMWH was used for thrombosis prophylaxis. Insulin was administered when glucose level was >150 mg/dL.

Plasma Exchange Procedures

A haemonetics MCS + (Haemonetics Corp. Braintree, USA) was used in all TPE procedures. Vascular access was obtained with a double-or singlelumen catheter usually placed in the femoral vein; peripheral veins were used for the return of blood in some cases. A central venous catheter was used in cases with the inappropriate vasculature. During each TPE session, one (rarely up to two) estimated plasma volume was exchanged and replaced with a bicarbonate-based electrolyte solution with 30 g/L albumin added. Anticoagulation during TPE was achieved with unfractionated heparin or trisodium citrate (either 4% or 15% solution; the protocol included intravenous Ca substitution).

Statistical Analysis

The data were analyzed by using Statistical Package for Social Sciences version 17.0 (SPPP, Inc.; Chicago, IL, USA). The descriptive statistics of categorical variables were recorded as number (%), and the chi-square test was used for intergroup comparison. The conformity of continuous variables to anormal distribution was assessed by the Kolmogorov-Smirnov test. Since age had a normal distribution, its descriptive statistical results were shown as mean + standard deviation, and the t-test in independent groups was used for the comparison of the two groups. Since the other continuous variables were not normally distributed, their descriptive statistical results were shown as median (25-75%), and the Mann-Whitney U test was used for intergroup comparison of these variables. The chi-square automatic interaction detector analysis was used to determine the factors effective in identifying the presence of local complications. P<0.05 was considered as statistically significant.

Results

A total of 120 patients were included in the study between January 2007-January 2019. Group 1 included 38 patients (9 females and 29 males, mean age of 40.3 \pm 7), and group 2 included 82 patients (29 females and 53 males, mean age of 41.6 \pm 10.7). The patient characteristics were summarized in Table 1. No significant difference was found between the groups regarding age and gender. There were 17 DM patients in group 1 (44.7%), whereas DM was present in 33 patients in group 2 (40.2%) (p=0.800); insulin

infusion was administered in all of these patients. LMWH was administered in all patients in doses of venous thromboembolism. The time between the initiation of abdominal pain or hospital admission and plasma exchange procedure was 10±4 (range 4-24) hours in average.

TPE was well-tolerated. Vomiting in six patients, palpitation and tachycardia in four patients, asymptomatic hypotension in three patients, occurred. Two cases had hypervolemia which was successfully treated with IV furosemide. Hemolysis was not detected in any of the patients. Occlusion of the catheter was seen in one patient. TPE was discontinued in none of these patients.

When the patients were evaluated according to the revised Atlanta classification, 24 MAP (63.2%), 11 MSAP (28.9%) and 3 SAP (7.9%) patients were found in group 1 and 33 MAP (40.2%), 39 MSAP (47.6%) and 10 SAP (12.2%) were found in group 2. When the patients were redistributed as MAP and MSAP+SAP, the ratio of MSAP+SAP was 36.8 in group 1, whereas it was 59.8% in group 2 (p=0.029).

There was no significant difference between the groups regarding organ failure (pulmonary failure, renal failure, and cardiovascular failure) (p=0.680) (Table 2). The local complications were summarized in Table 2.

Systemic complicationswere observed in two (5.3%) patients in group 1 and five patients (6.1%) in group 2 (p=0.610). The mean duration of hospitalization was found as 6 (4-8) days in group 1 and 5 (3.75-8) days in group 2. The in-hospital mortality rate was found as 2.6% in group 1 and 2.4% in group 2. The overall in-hospital mortality rate, covering all patients, was 2.5%.

There was no difference between groups regarding the initial TG level (p=0.078). The pre- and post-TPE levels of TG were found as 1,579 (1,406-3,323) mg/ dL and 682 (454-1,107) mg/dL, respectively (Table 3). The TG level was found to be reduced by 56.8% following one TPE session. The average time between the onset of abdominal pain or the admission to the hospital and the plasma exchange procedure was 11±3.9 (range 4-24) hours.

No significant relationships were determined between the initial TG or CRP levels and local/systemic complications and the in-hospital mortality rate.

Discussion

HTG has become one of the significant causes of AP due to changes in living conditions and lifestyle. The demographic characteristics of patients can be listed as young, male, with secondary factors such as DM and alcohol abuse, and frequently, the previous

| Table 1. Characteristics of patients | | | | | | |
|---|-----------------------|-----------------------|-------|--|--|--|
| | Group 1, n=38 | Group 2, n=82 | p | | | |
| Age (year) | 40.3±7 | 41.6±10.7 | 0.497 | | | |
| Male gender (%) | 76.3 | 64.6 | 0.285 | | | |
| Leukocyte (mm ³) | 13.250 (9.500-17.815) | 11,300 (8,800-14,500) | 0.059 | | | |
| Htc (%) | 44.3 (38.4-45.8) | 41.5 (36-44) | 0.051 | | | |
| LDH (U/L) | 199 (161-281) | 256 (201-295) | 0.067 | | | |
| Ca (mg/dL) | 9.2 (8.7-9.5) | 8.9 (8.3-9.3) | 0.052 | | | |
| Glucose (mg/dL) | 124 (100-240) | 153 (106-276) | 0.578 | | | |
| Amylase (U/L) | 212 (70-528) | 253 (103-725) | 0.226 | | | |
| Initial triglyceride (mg/dL) | 1579 (1.406-3.323) | 1,350 (1,104-1,751) | 0.078 | | | |
| Known HTG story (%) | 15 (39.5%) | 33 (40.2%) | 1.000 | | | |
| Known pancreatitis story (%) | 11 (28.9%) | 24 (29.3%) | 1.000 | | | |
| Alcohol abuse (%) | 6 (15.8%) | 11(13.4%) | 0.950 | | | |
| DM (%) | 17 (44.7%) | 39 (40.2%) | 0.800 | | | |
| Pregnancy (%) | 3 (7.9%) | 1 (1.2%) | 0.250 | | | |
| Htc: Hematocrit, LDH: Lactic dehydrogenase, Ca: Calcium, DM: Diabetes mellitus, HTG: Hypertriglyceridemia | | | | | | |
history of pancreatitis (10). In our study, also, the patients were young (mean age 41.1 ± 8), mostly male (68.3% male), with a previous history of pancreatitis (29.6%), DM (46.7%), and alcohol abuse (14.2%).

The probable mechanism of HTG-AP is hydrolysis of plasma TG into free fatty acids by pancreatic lipase, which are toxic to pancreatic endothelium and acinar cells (4). Conservative treatment (fasting, lipidlowering drugs, intravenous hydration) is not strong enough in reducing excessively elevated TG levels in patients with HTG-AP (11). In contrast, plasmapheresis might remove excessive lipid from serum in about two hours. Although the benefit of plasmapheresis is considered to be due to the rapid reduction of TG levels, removing significantly increased proteases from the blood and replacing the depleted protease inhibitors might also be augmenting the treatment process (12). Since its first description by Betteridge et al. (13) in 1978, numerous case reports (12) and case series (14) have been published about the use of plasmapheresis in the treatment of patients with HTG-AP. There is no randomized controlled study demonstrating the superiority of plasmapheresis against conservative treatment. However, it is recommended as a category III indication in the recent guideline (disorder for which the optimum role of apheresis therapy is not established, the individualized decision is necessary) in acute hypertriglyceridemic pancreatitis (15).

While reduction of TG level is achieved at the first or the second day of plasmapheresis, it is achieved in the following days of conservative treatment, and usually, it does not show a linear course. The clinical data about the effectivity of apheresis are limited by relief of clinical symptoms such as abdominal pain, nausea, vomiting, and laboratory findings such as triglyceride level. There are few studies about the effects of apheresis on the severity of AP. Yeh et al. (16) and Lennertz et al. (17) reported that they had achieved improvements in TG levels up to 70% and in clinical status and laboratory findings of their patients. In our study also, we achieved a 56.8% reductionof TG levels in TPE group after one TPE session.

The computed tomography severity index (CTSI) is a widely used clinical imaging scoring system in patients with AP which is positively correlated with mortality and development of complications (7,8). CTSI can show volume, size, and contour of the pancreas, together with surrounding tissue lesions. It can also guide in diagnosis and staging of AP by showing pancreas necrosis and fluid collection. In one study, it was shown that CTSI could predict the prognosis of AP correctly 48-72 hours after admission

| Table 2. Patients outcomes | | | |
|---|--------------------|---------------|-------|
| | Group 1, n=38 | Group 2, n=82 | p |
| Local complication (%) | 13 (34.2%) | 47 (57.3%) | 0.031 |
| APFC (%) | 10 (26.3%) | 31 (37.8%) | 0.249 |
| Pancreatic pseudocyst (%) | 0 (0%) | 9 (10.9%) | 0.023 |
| Walled-off necrosis + necrosis (%) | 2+1 (7.9%) | 1+6 (8.6%) | 0.732 |
| Systemic complication (%) | 2 (5.3%) | 5 (6.1%) | 0.610 |
| Median hospital stay (day) | 6 (4-8) | 5 (3.75-8) | 0.345 |
| CRP>150 (%) | 9 (23.7%) | 8 (9.8%) | 0.145 |
| Balthazar score D and E (%) | 13 (34.2%) | 47 (57.3%) | 0.031 |
| Pulmonary failure | 2 (5.3%) | 6 (7.3%) | |
| Renal failure | 2 (5.3%) | 5 (6.1%) | 0.680 |
| Cardiovascular failure | 1 (2.6%) | 4 (4.9%) | |
| In-hospital mortality (%) | 1 (2.6%) | 2 (2.4%) | 0.820 |
| APFC: Acute peripancreatic fluid collection, CRP: | C-reactive protein | | |

| Table 3. Comparison of serum trygliceride, before and after therapeutic plasma exchange treatment in each patient | | | | | |
|---|---------------------|-----------------|--------|--|--|
| Before After p | | | | | |
| Triglyceride (mg/dL) | 1,579 (1.406-3.323) | 682 (454-1,107) | <0.001 | | |

to the hospital (18). CTSI scoring system has a superior performance in predicting local complications in patients with HTG-AP (19,20). Lloret Linares et al. (21) reported that severe pancreatitis (need for intensive care, CRP>150 mg/dL or Balthazar score >C) had been observed in 71.5% of patients. However, no relationship was observed between TG levels and the disease severity. In our study, the rate of patients with CRP>150 mg/dL or Balthazar score >C was found as 55.8%. No significant associations of initial TG level and CRP levels with in-hospital mortality and local/ systemic complication rates were observed.

The use of plasmapheresis is limited due to its high cost in addition to its unavailability in every hospital. Thus, many healthcare centers offer only conservative treatment for their patients with HTG-AP. Due to the lack of randomized controlled studies, it is not certain whether plasmapheresis improves mortality and morbidity in patients with HTG-AP or not. Gubensek et al. (14) reported that there was no relationship between initial TG levels and severity of the disease, mortality rates and hospital staying period. Plasma exchange, performed for once or twice, resulted in the reduction of TG faster than expected. Plasma exchange was found to be related to the low complication rate. The in-hospital mortality rate was found to be low (5%), and the delay in plasma exchange therapy had not affected the hospital mortality. In a study of Nakhoda et al. (22), it was reported that, although TG levels were found to be reduced rapidly, there was no significant difference between pre- and post-TPE evaluated Acute Physiology and Chronic Health Evalation II (APACHE scores).

In a retrospective study of Chen et al. (23) in which HTG-AP patients were divided into two groups as non-plasmapheresis (group 1) and plasmapheresis (group 2), TG levels were found to be 65.8% reduced in plasmapheresis group. There was no significant difference between the two groups and also the patients with severe pancreatitis (defined by Ranson's score >3) regarding total mortality, systemic and local complication rates. In the study of He WH et al. comparing HTG-AP patients treated with highvolume hemofiltration (HVHF) or LMWH + insulin, LMWH+insulin treatment was found to be superior in reducing TG levels, whereas no significant differences were found in terms of local pancreatic complications (p>0.05), need for surgical intervention (p=0.49), mortality rate (p=0.49), and duration of hospitalization (p=0.144) (24). Wang et al. (25) conducted a study on 144 HTG-AP patients treated with conservative treatment, and 91 (63.1%) of patients were classified as MSAP and SAP. APFC, acute necrotic collections, and pseudocyst were observed in 66 (45.8%), 13 (9%) and 5 (3.5%) of their patients as local complications, respectively. Systemic complications developed in 6 (4.2%) patients, whereas mortality was observed in 8 (5.5%) patients. MSAP and SAP, together with local complications and mortality were found to be related to elevation of TG level.

In our retrospective study, we divided our patients according to the revised Atlanta Classification. MAP and MSAP+SAP rates were 63.2% and 36.8% in group 1, whereas these rates were 40.2% and 59.8% in group 2, respectively (p=0.029). Local complication rate was 34.2% in group 1 and 57.3% in group 2 (p=0.031). The occurrence of APFC and walled-off necrosis+necrosis were found to be similar in two groups. Pancreatic pseudocyst was not observed in group 1, whereas it was observed in 9 (10.9%) patients in group 2 (p=0.023) (Table 2). Total in-hospital mortality rate was found to be 2.5%. There were no statistically significant differences between the groups regarding organ failure, systemic complication, duration of hospitalization, and in-hospital mortality rates. However, it was observed that TPE treatment led to the significant reduction of AP severity and local complication rate since TPE is consistently helpful during the acute inflammatory phase.

The limitation of our study was its retrospective design. Also add to the limitations of the study, that due to its design (3 different hospitals) the effect of other differences in treatment practices or patient characteristics on outcome cannot be excluded. The distinguishing feature of our study is that it is the first study comparing HTG-AP patients having TPE with those having conservative treatment in terms of mortality, length of hospitalization, disease severity, local and systemic complications, in accordance with the revised Atlanta classification.

Conclusion

Plasmapheresis is an effective and useful method in reducing the excessively high TG levels in patients with HTG-AP. However, the use of plasmapheresis is limited to specific centers since it is a quite expensive treatment option. Apheresis should be continued until the TG level is reduced below 500-1,000 mg/dL. TPE may be effective in reducing local complications (especially pancreatic pseudocyst) but has no effect on organ failure and hospitalization duration; and optimal timing or how to select appropriate patients for this modality remains to be elucidated in further studies.

Ethics

Ethics Committee Approval: The study's ethics committee approval was obtained from the Adnan Menderes University Non-Invasive Clinical Research Ethics Committee that the study was conducted (protocol no: 2017/1253, date: 26.10.2017).

Informed Consent: All patient data were retrospectively obtained from the electronic medical records

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.K., İ.Y., M.Ç., Design: İ.T., A.C., S.V., Fundings: M.H.Y., Data Collection or Processing: A.K., S.V., M.Ç., İ.Y., A.C., Analysis or Interpretation: M.T., Literature Search: İ.T., A.K., Writing: A.K., İ.T., Critical Review: A.K., M.H.Y.

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Effects of Paracetamol and Tenoxicam on Postoperative Pain and Need for Rescue Analgesia in Root Canal Treatments Performed Under General Anesthesia: A Retrospective Study

Genel Anestezi Altında Tamamlanan Kök Kanal Tedavilerinde Parasetamol ve Tenoksikamın Postoperatif Ağrı Düzeyi ve Kurtarma Analjezisi Gereksinimi Üzerine Etkisinin Değerlendirilmesi: Retrospektif Bir Araştırma

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Keywords

General anesthesia, root canal treatment, paracetamol, postoperative pain, tenoxicam

Anahtar Kelimeler

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Abstract

Objective: This study aimed to investigate the effects of parenterally administered paracetamol and tenoxicam on early postoperative pain regarding analgesia in healthy adults who had completed root canal treatments (RCTs) in a single visit under standard general anesthesia protocols.

Materials and Methods: In this retrospective study, the data of 83 adult patients who underwent RCTs under general anesthesia in a single visit due to severe nausea reflex and/or anxiety were analyzed. Patients were divided into two groups according to the intravenous administration of 15 mg/kg paracetamol (P group) or 0.5 mg/kg tenoxicam (T group) 30 min before the end of general anesthesia to meet their analgesia requirements. Thereafter, early postoperative period visual analog scale (VAS) scores were recorded at the 5th minute after the patients were taken to the recovery room and at the subsequent 2nd hour. After 2 h, rescue analgesia was given to patients with VAS scores >4 in both groups and recorded. Data were analyzed statistically.

Results: A total of 68 patients who met the inclusion criteria were evaluated. Regarding postoperative pain values, the average VAS score was significantly lower in the T group at both the 5th minute and 2nd hour than in the P group. In both groups, the mean VAS scores were decreased by the same amount over time, and the differences between the groups were not significant (p=0.452). Moreover, no significant difference was found between the two groups in terms of the need for rescue analgesia (p=0.571).

Conclusion: Tenoxicam, administered parenterally, provides more effective analgesia for postoperative pain management compared with paracetamol when it is used in RCTs under general anesthesia.

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Öz

Amaç: Bu çalışmanın amacı, standart genel anestezi protokolleri altında tek seansta kök kanal tedavileri tamamlanan sağlıklı erişkinlerde analjezi amacı ile parenteral uygulanan parasetamol ve tenoksikamın erken dönem postoperatif ağrı üzerine etkinliklerinin araştırılmasıdır.

Gereç ve Yöntemler: Bu retrospektif araştırmada, şiddetli bulantı refleksi ve/veya anksiyete sebebiyle genel anestezi altında kök kanal tedavileri tek seansta gerçekleştirilen 83 yetişkin hastanın verileri incelenmiştir. Hastalar, analjezi gereksinimlerinin sağlanması için genel anestezi sonlanmadan 30 dakika önce 15 mg/kg parasetamol (grup P) veya 0,5 mg/kg tenoksikamın (grup T) intravenöz olarak uygulanmasına göre iki gruba ayrılmıştır. Sonrasında, hastaların derlenme odasına alındıktan sonra 5. dakikadaki ve takip eden 2. saatteki erken postoperatif dönem vizüel analog skala (VAS) ölçümleri kayıt edilmiştir. Her iki grupta da 2 saat sonunda VAS skorları 4 üzerinde olan hastalara kurtarma analjezisi uygulanmış ve kayıt edilmiştir. Veriler istatistiksel olarak analiz edilmiştir.

Bulgular: Dahil edilme kriterlerini karşılayan toplam 68 hasta değerlendirmeye alınmıştır. Postoperatif ağrı değerleri açısından hem 5. dakikada hem de 2. saatte grup T'de grup P'ye göre istatistiksel olarak anlamlı olarak daha düşük VAS skor ortalamaları gözlenmiştir. Her iki grupta da VAS skor ortalamaları zamanla aynı ölçüde azaltmıştır ve gruplar arası fark istatistiksel olarak anlamlı değildir (p=0,452). Ayrıca, kurtarma analjezi ihtiyacı bakımından da iki grup arasında anlamlı fark görülmemiştir (p=0,571).

Sonuç: Genel anestezi altında uygulanacak kök kanal tedavilerinde postoperatif ağrı yönetimi açısından parenteral olarak uygulanan tenoksikam, parasetamole kıyasla daha etkin analjezi sağlamaktadır.

Introduction

Dental anxiety is defined as an undescribable state of intense unease that develops due to fear and anxiety related to dental treatment (1). Today, despite the use of effective local anesthetic and analgesic drugs, many patients still have anxiety problems related to dental treatments (2,3). In the treatment of dental anxiety, general anesthesia procedures are used when psychological approaches are not sufficient (4). General anesthesia is described as a situation in which a patient is rendered unconscious, completely or partially loses his protective reflexes, no responses to physical and verbal stimuli, airway patency cannot be achieved, and is connected to a respiratory support unit (1). Pain is the most common complication observed after operations performed under general anesthesia (5). Pharmacological, surgical and non-pharmacological methods are used in the management of postoperative pain (6). In pharmacological applications, drugs are precribed upon the request of a doctor and administered using different methods. The purpose of this method is the maximum relieve of pain with no or minimal side effects. Pain control with pharmacological methods aims to reduce the patient's pain in the postoperative period with narcotic and non-narcotic analgesics applied in the peroperative period. These protocols are determined by considering the type of surgery and individual characteristics and according to the expected pain intensity (6). In addition, it has been reported that effective management of postoperative

pain after surgery ensures shortened recovery time and decreased duration of hospital stay (7). At the same time, effective analgesia provided to patients can prevent many complications that may develop (8,9).

Restorations, endodontic treatments, periodontal and surgical procedures are performed under general anesthesia for children and adults with mental illness, anxiety problems, psychological disorders and severe nauseareflexes(10-12). Although root canal treatments (RCTs) under general anesthesia is technically difficult and time consuming, it is indicated for teeth that can remain functional (10). Postoperative pain after RCT is one of the most common complications (13,14) and its incidence has been reported between 3 to 58% (14). Although the main purpose of endodontic treatment is to produce appropriate biological results, it should be ensured that the patient does not feel pain during and after the treatment (14). Postoperative pain is as a result of many factors and its causes are divided into preoperative and procedural factors. Several factors such as the gender and age of the patient, the presence of systemic disease, the presence of preoperative pain, the condition of the pulp, the number of visits, and the use of intra-canal medication can affect postoperative pain (15). The management of postoperative pain after RCT is multifactorial and includes the combination of a good endodontic procedure and appropriate use of analgesics. Most of the drugs used to manage postendodontic pain consist of non-narcotic analgesics including paracetamol,

non-steroidal anti-inflammatory drugs (NSAIDs) and narcotic analgesics (16).

Paracetamol is an analgesic agent that is thought to have an effect on the central nervous system through central cyclooxygenase (COX) inhibition and is thought to have a significant effect on platelet aggregation (17). On the other hand, tenoxicam is a NSAID that can be used reliably with minimal hematological side effects, has a long half-life and sufficient analgesic effect. Due to the low incidence of side effects, these two analgesic drugs are agents used in outpatient surgical procedures (18).

RCTs completed under general anesthesia are performed in single visit. There are few studies evaluating postoperative pain in dental procedures completed under general anesthesia (19,20). However, management of early postoperative pain in endodontic treatments performed under general anesthesia has never previously been investigated in the literature. Therefore, the aim of this study was to investigate the effects of parenterally administered paracetamol and tenoxicam on early postoperative pain in healthy adults under standard general anesthesia protocols for analgesia. The null hypotheses of the present study are as follows;

1. There was no difference between the paracetamol and tenoxicam groups in healthy adults undergoing RCTs under general anesthesia on early postoperative pain.

2. There was no difference between the groups in terms of the need for rescue analgesia after the administration of paracetamol and tenoxicam.

Materials and Methods

This study was conducted with an approval from the Non-Invasive Clinical Research Ethics Committee (protocol no: 2020/75, date: 02.07.2020) of the Faculty of Medicine Aydın Adnan Menderes University. This retrospective study was carried out by scanning the files of 83 adult patients between the ages of 18-60 who were referred to Faculty of Dentistry, Aydın Adnan Menderes University, during a threeyear period between January 2016 and December 2018. Patients were only limited to have performed endodontic and restorative treatments under general anesthesia. Inclusion and exclusion criteria are presented in Table 1. Before the general anesthesia consents forms stating that the patients data can bu used in the scientific research were signed by the patients.

Preoperative Evaluation

Routine hemogram, blood glucose, liver enzymes, kidney function tests, blood electrolyte values, coagulation markers were evaluated for all patients to be treated in the operating room. Patients who had no issues in physical examination and blood tests were approved for procedures under general anesthesia. Each patient was made to observe at least an 8 hours fasting period prior to the operation. IV vascular access was established for patients on the day of operation. Routine vital signs of the patients and preoperative period anxiety levels were recorded according to Beck Anxiety scale. Beck Anxiety scale is an index with questions scaling up to 63 points. Patients' anxiety levels were determined as; 0-7 points: no anxiety, 8-15 points: mild anxiety, 16-25 points: moderate anxiety, 26-63 points: severe anxiety.

After determining the anxiety levels of the patients, midazolam at a dose 0.04-0.05 mg/kg (maximum dose not exceeding 4 mg) was administered as IV 15 minutes before the surgery for premedication, All preoperative practices are routine clinical procedures specified in the files.

General Anesthesia Procedure

A routine general anesthesia protocol was applied to all patients who came to the General Anesthesia Unit. All patients were preoxygenated with a face mask after their monitorization. The same anesthesiologist (Ö.Ö.) with 10 years of clinical experience performed all of the procedures. Fentanyl 1-2 µg.kg⁻¹IV, propofol 2-2.5 mg.kg⁻¹ IV and rocuronium 0.5-0.6 µg.kg⁻¹ IV were administered for induction. One minute after unconsciousness and respiratory suppression, nasal intubation was performed with a flexible spiral tube. In the maintenance of anesthesia, 1.5-2% sevoflurane was used in a mixture of N₂O 1.0 L/min, O, 1.0 L/min. Rocuronium 0.15-0.2 mg.kg⁻¹ IV bolus was administered as an additional muscle relaxant. Metoclopramide 0.2 mg.kg⁻¹ IV was administered to each patient as an antiemetic before the end of general anesthesia. All intraoperative practices are routine procedures specified in the files.

Endodontic Treatment Procedure

All endodontic treatment procedures in this study were performed in a single session under general

anesthesia by endodontists with at least 5 years of experience. Root canal lengths were determined with the help of an endodontic apex finder (VDW, München, Germany) after opening the entrance cavity under rubberdam isolation. All canals were preformed with K-type hand files (DiaDent, Cheongju, Korea). The root canals were then shaped by applying the recommended file sequence with the Protaper Next rotary file system (ProTaper Next; Dentsply Sirona, Ballaigues, Switzerland) at the torque and speeds recommended by the manufacturer. Between each file, 2 mL of irrigation with 2.5% NaOCl was made, and in total, each channel was irrigated with at least 12 mL of NaOCI. For final irrigation, 2 mL of 17% EDTA, 2 mL of 2.5% NaOCl and 2 mL of distilled water was applied to each root canal, respectively. The root canals were then dried with sterile paper cones and filled with epoxy resin-containing root canal sealer (AH Plus; Dentsply DeTrey, Konstanz, Germany) and Gutta-percha cones (Dentsply Sirona) using a single cone technique. Teeth whose RCTs were completed were permanently restored using a single-stage selfadhesive (Tokuyama Bond Force, Tokuyama Dental, Tokyo, Japan) and light-cured composite restoration material (Clearfil Majesty, Kuraray, Tokyo, Japan).

Analgesia Dose

As a routine analgesia protocol, 15 mg/kg paracetamol or tenoxicam 0.5 mg/kg was administered intravenously 30 minutes before the end of general anesthesia to patients who underwent dental treatments under general anesthesia in our operating

room. The choice of tenoxicam or paracetamol was made according to the availability of the drugs in the hospital pharmacy during the study period. In the recovery unit, the postoperative pain levels of the patients were routinely assessed using a 10 cm visual analog scale (VAS) (beginning from -0- "no pain", to the other end -10- "unbearable pain"). In addition, the patients were followed in terms of other expected side effects and their data were recorded in the patient files (nausea, vomiting, gastric burning and/or pain, rash, allergic reaction, bleeding). Patients with VAS> 4 are given 0.5 mg/kg tramadol as rescue analgesia as mentioned in the studies of Niemi-Murola et al. (21) and Gupta et al. (22). These informations were recorded in the patient files.

Patients treated with paracetamol were sorted into group P and patients given tenoxicam in group T. Early postoperative VAS measurements were recorded at the 5th minute and subsequently at 2nd hour after the patients in both groups were taken to the recovery room. The patients' initial anxiety levels, demographic data, number of teeth treated with RCT, duration of general anesthesia, postoperative pain VAS values and rescue analgesia requirements were statistically evaluated.

Statistical Analysis

IBM SPSS version 25.0 (IBM, New York, NY, USA) package program was used for the analysis of the data obtained in this study. Shapiro-Wilk test, kurtosis-skewness values and histogram graphics were used to test the compliance of the data of the study to normal

| Table 1. Inclusion and/or exclusion criteria of patients | |
|--|---|
| Inclusion criteria | Exclusion criteria |
| Patients between the ages of 18-60 and who were physically and/or mentally healthy Patients who consented to the use of their data in research | Patients who did not consent to and/or from whom consent was not obtain for the use of their data in research |
| Patient in the I-II group of the ASA (American Society of Anesthesiologists) | Mentally unhealthy and ASA III-IV group patients |
| Patients undergoing a routine general anesthetic procedure | Patients undergoing treatments other than routine general anesthesia procedures |
| Patients who have completed at least one root canal treatment in a single visit during general anesthesia | Patients who have undergone surgical, periodontal and/or prosthetic procedures together with endodontic procedures during general anesthesia. |
| | Patients allergic to paracetomal Patients allergic to non-steroidal anti-inflammatory agents and/or have a history of asthma |
| | Patients who had pain in the preoperative period and/or used painkillers at least 3 days before the operation |

distribution. Descriptive statistics were used to analyze demographic data. Repeated measures ANOVA test was used to evaluate VAS scores according to groups and measurement times. At the end of the 2nd hour, whether there was a difference between NSAIDs in terms of the number of patients with a VAS score of 4 and above was examined by Fisher's Exact chi-square test.

Results

In the specified time range, 11 out of 83 adult patients who underwent RCT under general anesthesia were excluded from the study because they did not meet the inclusion criteria. Of the



Figure 1. Flow chart of the participants

remaining 72 patients, 32 were sorted into group P, 40 patients in group T. Three patients from group P and 1 patient from group T were excluded from the study due to missing data in their files. As a result, the data of 29 patients in group P and 39 patients in group T (68 patients in total) were analyzed (Figure 1). Demographic variables and clinical characteristics of the patients are as shown in Table 2. The number and the types of the treated teeth in the groups are as shown in Table 3.

No statistically significant difference was found between group T and group P in terms of demographic data, American Society of Anesthesiologists scores, duration of intraoperative anesthesia, and the number of teeth treated during RCT (p>0.05) (Table 2).

There was no difference between the averages of Beck Anxiety scores in the preoperative period in both groups, and both groups were found to have mildmoderate preoperative anxiety scores (Table 4).

In terms of postoperative pain values at 5th minute (VAS 1), statistically significant lower VAS scores were observed in group T compared to group P (p=0.010) (Table 4). Similarly, in the postoperative pain values at the 2nd hour (VAS 2), statistically significantly lower VAS score averages were observed in group T compared to group P (p=0.019) (Table 4). Considering the differences in change over time, the effect of drugs on the mean of VAS score over time in both group P and group T was not statistically significant (p=0.452). Both drugs decreased the VAS score to the same extent over time (Figure 2). However, there was no significant difference between group T and group P in terms of rescue analgesia need (p=0.571) (Table 4).

Postoperative side effects were observed in 2 patients in group T (nausea-vomiting), in 1 patient in group P (mild epistaxis due to nasotracheal

| Table 2. Demographic data and intraoperative characteristics | | | | |
|--|----------------------------------|--------------|-------|--|
| | Tenoxicam | Paracetamol | р | |
| Age | 31.10±10.87 | 30.17±11.91 | 0.665 | |
| Gender (f/m) (n) | 21/18 | 14/15 | 0.808 | |
| Weight (kg) | 72.07±10.25 | 73.00±10.40 | 0.691 | |
| Anesthesia duration | 234.74±51.70 | 238.10±52.54 | 0.960 | |
| Number of tretaed teeth | 1.79±0.97 | 1.75±0.83 | 0.925 | |
| ASA I/II (n) | 32/7 | 24/5 | 0.940 | |
| *Mean ± standard deviation. F: Female, m: Male, ASA | : American Society of Anesthesio | ologists | | |

intubation), and in 2 patients in group P (headache). No side effects were observed in other patients.

Discussion

According to the findings of the present study, it was observed that significantly lower postoperative pain values were observed in both early period measurements (5 minutes and 2 hours after) in patients who received tenoxicam in endodontic treatments performed under general anesthesia compared to those who received paracetamol. Therefore, the first null hypothesis was rejected. Since, there was no statistically significant difference between the two groups in terms of the need for rescue analgesia, the second null hypothesis should be accepted.



Figure 2. The distribution of mean VAS scores between groups for checked time periods

| VAS: | Visual | ana | log | score |
|------|--------|-----|-----|-------|
|------|--------|-----|-----|-------|

Pain is a condition that is oftentimes more important than the disease itself and often needs to be treated guickly (23). Since the most common clinical complication after RCT is pain (14), there are many studies in the literature on the management of pain after RCT (24,25); however, there is no study in the literature regarding the management of early pain after RCT under general anesthesia. Therefore, the results of the present study may highlight major issues in the literature. While intra-operative pain is prevented in endodontic treatments with effective local anesthesia methods and operative techniques, paracetamol, non-narcotic analgesics containing NSAIDs and narcotic analgesics are being used in postoperative pain management (16,24,25). An IV analgesic may be the preferred choice for patients who are unable to take drugs administered orally in the early postoperative period after general anesthesia and need rapid onset of analgesia (26). Tenoxicam is a NSAID with high potential in terms of its analgesic and anti-inflammatory effects, and due to its possible use in IV form, it is frequently preferred after surgical procedures under general anesthesia where oral administeration is not possible. Due to its long halflife and the sufficiency of a single dose tenoxicam has moved to the forefront in postoperative pain control for outpatient surgeries compared to other NSAI groups (27). Regarding these reasons, tenoxicam was chosen as an NSAID in the present study. However,

| Table 3. The number and types of the treated teeth in the groups | | | | | |
|--|-------------|--------------|-------------|--------------|--|
| | Paracetamol | | Tenox | icam | |
| | Maxilla (n) | Mandible (n) | Maxilla (n) | Mandible (n) | |
| Incisors | 9 | 5 | 11 | 8 | |
| Canine | 8 | 3 | 9 | 9 | |
| Premolars | 7 | 6 | 10 | 7 | |
| Molars | 6 | 8 | 9 | 10 | |
| Sum | 52 | | 73 | | |

| Table 4. Visual analog scores and anxiety levels | | | | | |
|---|-----------------------------------|---------------------------------------|--------|--|--|
| | Tenoxicam | Paracetamol | p | | |
| VAS 1 (5 th minute) | 2.94±0.21 | 3.82±0.25 | 0.010* | | |
| VAS 2 (2 nd hour) | 1.20±0.75 | 1.86±0.20 | 0.019* | | |
| Rescue analgesia need | 1 | 2 | 0.571 | | |
| Anxiety level ⁸ 14.69 ± 0.17 16.24 ± 6.60 0.452 | | | | | |
| Mean ± standard deviation. *p≤0.05, ^B Total anxiet | ty score according to the Beck An | xiety scale. VAS: Visual analog score | | | |

NSAIDs have some undesirable side effects on many body systems, especially the gastrointestinal system, as well as their proven analgesic effects, reducing platelet aggregation and prolonging the bleeding time (28).

Paracetomol is also an another agent which can be administered intravenously, has a proven analgesic efficacy and less side effects compared to NSAIDs (26,29), hence it is an another agent of choice in pain control after endodontic treatment. Cheung and Rodrigo (30) used a single oral dose of 40 mg tenoxicam and 1,000 mg paracetamol in 30 dental surgery cases and reported that both drugs provided similar postoperative analgesia. Similar to our results, it has been reported that when administered as IV, tenoxicam provides an effective analgesia at doses of 20 mg and 40 mg especially after oral surgeries (29). Likewise, Gunusen et al. (31) reported that IV tenoxicam reduced both postoperative pain and additional need of morphine compared to paracetamol in abdominal hysteroctomy cases. However, unlike these studies, there are also studies that have found a superior postoperative efficiency with paracetamol (32). Hyllested et al. (32) argued that paracetamol is an appropriate alternative to NSAIDs, especially due to its low incidence of side effects, and that it should be a preferred option in high-risk patients. Khalili et al. (33) reported that there was no difference between paracetamol use alone and combined use of paracetamol with oxicam group NSAIDs especially in orthopedic operations. We are of the opinion that these different findings in analgesic efficacy comparison studies may be due to different surgery types.

In the present study, no significant side effects were observed due to the use of either paracetamol or tenoxicam. In the literature, there are different interpretations about side effects as well as increased analgesia efficacy regarding the use of both groups of drugs separately and in combination. Hyllested et al. (32) stated that combining paracetamol with NSAIDs may be appropriate due to the increased analgesic efficacy, but attention should be paid to the potential increase in side effects resulting from their combined use. The risk increases especially in longterm use without lowering the dose. Ong et al. (34) reported that the combination of long-acting NSAIDs such as paracetamol and tenoxicam theoretically has the disadvantage of pharmacokinetic incompatibility because tenoxicam has a much longer elimination half-life than paracetamol. On the other hand, Merry et al. (35) stated that the combination of NSAID and paracetamol minimizes the need for rescue analgesia and the side effects caused by opioid use. It is known that there is a relationship between plasma paracetamol concentrations and analgesic efficacy. Attempting to continually maintain paracetamol plasma concentrations may cause the dose to be increased above the required threshold during postoperative follow-up, increasing the risk of hepatotoxicity.

The most important limitation of this study is the small sample size. Surgical, prosthetic and periodontological procedures, which may effect postoperative pain, were also performed in patients who underwent dental procedures under general anesthesia, often with endodontic treatments. As a result, the population of the study was limited due to the exclusion of these processes.

The incidence of post operative pain after RCT has been associated with various factors in the literature such as age, gender, pulpal and periradicular status, tooth type, preoperative pain, sinus tracts, and operational factors (36,37). For his reasons, many factors such as tooth type, pulp and periradicular status of the patient have been tried to be standardized in studies related to postoperative pain after canal treatment in the literature (13,14,36,37). However, as stated above, the most important limitation of this study is its small sample size. Therefore, due to the limited number of patients evaluated in this study, standardization of other factors had to be ignored. Therefore, this issue is another limitation of this study. Consequently, we think that the results of this study should be reconfirmed in larger patient populations with new studies.

Conclusion

As a result, IV tenoxicam provides more effective postoperative analgesia than IV paracetomol in the management of postoperative pain after RCTs performed in single visit under general anesthesia. In addition, since there is no difference between the two drugs in terms of rescue analgesia frequency and paracetomol has less side effects than NSAIDs, it makes IV paracetomal administration preferable in RCT treatments under general anesthesia.

Ethics

Ethics Committee Approval: This study was conducted with an approval from the Non-Invasive Clinical Research Ethics Committee (protocol no: 2020/75, date: 02.07.2020) of the Faculty of Medicine Aydın Adnan Menderes University.

Informed Consent: Retrospective study. Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.D.Ö., Ö.K., S.Y.Ö., P.A.O., Design: Ö.K., H.D.Ö., Supervision: Ö.K., H.D.Ö., Fundings: H.D.Ö., Ö.K., S.Y.Ö., P.A.O., Materials: H.D.Ö., P.A.O., Ö.K., Data Collection or Processing: Ö.K., Analysis or Interpretation: Ö.K., Literature Search: Ö.K., H.D.Ö., Writing: Ö.K., H.D.Ö., Critical Review: S.Y.Ö., P.A.O.

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Influence of Different Plaque Control Methods and Hydrothermal Aging on Structural Properties of Monolithic Zirconia

Farklı Plak Kontrol Yöntemleri ve Hidrotermal Yaşlanmanın Monolitik Zirkonyanın Yapısal Özelliklerine Etkisi

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Keywords

Monolithic zirconia, hydrothermal aging, scaling instruments, air-abrasive powder

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Monolitik zirkonya, hidrotermal yaşlanma, kazıma aletleri, aşındırıcı toz

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Abstract

Objective: This study aimed to investigate the effect of hydrothermal aging and various plaque removal methods, which are a part of professional dental cleaning, on zirconia's structural properties.

Materials and Methods: Seventy-two disk-shaped monolithic zirconia specimens (diameter 12 mm and thickness 1 mm) divided into six groups were subjected to no surface treatment, instrumentation with steel curette and ultrasonic steel scaler, and air abrasion with sodium bicarbonate, erythritol, and glycine before being aged in an autoclave at 0.2 MPa and 134 °C for 2 h. Specimens were analyzed using X-ray diffraction, scanning electron microscopy with energy dispersive X-ray spectrometry, and atomic force microscopy to evaluate crystal structure, microstructure, and surface roughness. Further, the contact angle and Vickers hardness measurements were performed for wettability and hardness evaluations. A biaxial bending test was applied to measure the durability of the material.

Results: According to the results, no significant change was found in the crystal structure, surface roughness, and bending strength of zirconia (p>0.05). In contrast, a substantial decrease in surface hardness values and a significant increase in wettability values were observed in the steel curette and ultrasonic steel scaler groups compared with other groups (p<0.05).

Conclusion: The use of abrasive powders in dental plaque control after prosthetic treatment can help maintain periodontal health and long-term use of prosthesis after restoration of monolithic zirconia.

Öz

Amaç: Bu çalışma, profesyonel diş temizliğinin bir parçası olan plak uzaklaştırma yöntemleri ile hidrotermal yaşlanmanın zirkonyanın yapısal özelliklerine etkisini araştırmayı amaçlamıştır.

Gereç ve Yöntemler: Altı gruba bölünmüş 72 adet disk şeklinde monolitik zirkonya örnek (çap 12 mm ve kalınlık 1 mm) otoklavda 0,2 MPa ve 134 °C'de 2 saat hidrotermal yaşlandırma öncesi çelik küret, ultrasonik çelik kazıyıcı, sodyum bikarbonat, eritritol ve glisin abraziv toz ile yüzey işlemine tabi tutuldu. Örnekler, kristal yapıyı değerlendirmek için X-ışını kırınımı yöntemi, mikro yapı için taramalı

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elektron mikroskobu ve yüzey pürüzlülüğü için atomik kuvvet mikroskobu kullanılarak analiz edildi. Ayrıca ıslanabilirlik ve sertlik değerlendirmeleri için temas açısı ve Vickers sertlik ölçümleri yapıldı. Malzemenin dayanıklılığını ölçmek için ise çift eksenli bükme testi uygulandı.

Bulgular: Sonuçlara göre zirkonyumun kristal yapısında, yüzey pürüzlülüğünde ve eğilme dayanımında önemli bir değişiklik olmadığı görüldü (p>0,05). Çelik küret ve ultrasonik çelik kazıyıcı gruplarında diğer gruplara göre yüzey sertlik değerlerinde önemli düşüş ve ıslanabilirlik değerlerinde anlamlı artış gözlendi (p<0,05).

Sonuç: Monolitik zirkonya restorasyon uygulamasından sonra periodontal sağlığın sürdürülmesi ve protezin uzun süreli kullanımı için protetik tedavi sonrası dental plak kontrolünde aşındırıcı tozlardan faydalanmak uygun bir seçenek olabilir.

Introduction

The term "monolithic restoration" isn't new for prosthodontic dentistry; namely, they are applied for several years as full ceramic crowns and bridges. Monolithic zirconia systems have increasing demands by both patients and clinicians because of their high esthetic features and durability. Monolithic restorations have been produced from a single piece of highly translucent zirconia through computeraid design/computer-aid manufacturing (CAD/ CAM). While assessing monolithic zirconia's clinical performance, it can be seen that the survival rates are reported between 82.7% and 100% for single crown and fixed prosthesis (1).

Zirconia is a polymorphic material, whose structural situation is defined by its mechanical and optical properties. There are three crystalline phases of zirconia in nature at different temperatures: monoclinic (m) form (room temperature-1,170 °C), tetragonal (t) form (1,170-2,370 °C), and cubic (c) form (2,370 °C-melting point) (2). Crystalline configuration transforms between these phases when the crystalline structure's atomic bonds break apart under different stimuli such as mechanical, thermal, and combined stresses. During the cooling of zirconia from sintering temperature to room temperature, the transformation of t→m occurs at ~950 °C spontaneously, known as phase transformation toughening (PTT) (3,4). Throughout transformation, volumetric expansion eventuates within the grains at the monoclinic phase. It contributes to the mechanical strength of the material to some extent, but it should be under control because excessive expansion can give rise to catastrophic failures itself. Some metal oxides such as CaO, MgO, Y₂O₃ or CeO₂ are added to stabilize the t phase of zirconia at room temperature to benefit from PTT clinically (5).

The most commonly used form of zirconia in prosthetic dentistry is the yttria-stabilized t phase

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(Y-TZP) zirconia. It is partially stabilized at room temperature, referred to as metastable state, which means that particular conditions such as humidity, mechanical stress, temperature, surface roughness, can provoke the spontaneous and proceeding transformation of t \rightarrow m (5). Y-TZP is susceptible to a humid environment, even there is no mechanical stress (6). This transformation differs from PTT in terms of the process known as a low-temperature degradation (LTD) phenomenon. So, the LTD process begins with water sorption, then t phase transforms into *m* phase on the surface and deep into the bulk of Y-TZP as the volume of altered grains increases. This volumetric expansion induces surface uplifts, removing the grains and microcracks, which originate material degradation without mechanical stress (7). As long as this process goes on, microcracks became bigger (8) and finally, fracture strength of Y-TZP decreases due to the transformation of %50 of the surface crystals (9). When we think about the LTD phenomenon's clinical effects, it comes to mind that it can be crucial for monolithic zirconia restorations to have no porcelain layer so that they immediately interact with saliva which will expedite LTD. Monolithic zirconia has high flexural strength, needs more conservative tooth preparation, gives minimal antagonist wear, displays more satisfying esthetic, saves time both in laboratory and dental procedures (10). More importantly the reason for its popularity is the absence of chipping complications that have been shown to be a high rate of failure concerning the cohesive fracture of veneering ceramic in clinical studies (11).

Preventing inflammatory periodontal disease and/ or dental caries by controlling plaque accumulation as well as prosthodontic treatment quality is vital for a dental prosthesis's long-term survival (12). Plaque control by patients should be carried out regularly to maintain a healthy oral condition and by dentists when the patients cannot remove dental plaque in hard-to-reach parts and when there is mineralized dental plaque (calculus) present. It is known that using hand instruments (periodontal curettes) and power-driven instruments (sonic/ultrasonic scaler) for plague removal is very efficient through intraoral scaling (13). Also, air-powder jet devices enable the removal of dental plaque (14). The scaler tip of the ultrasonic scaler oscillates at about 30 kHz for generating micro-vibrations to elevate dental plaque and calculus under water cooling. Using an ultrasonic scaler provides an advantage of the clinicians in terms of working time and physical effort (15). Therefore, many clinicians widely prefer spending more time on ultrasonic scaling than hand instrumentation for tooth cleaning in dental offices. But instrumentations with Gracey curette and ultrasonic scaler causes unwanted effects like disturbance, pain and defects on dental material (16). In such a case, air-powder polishing systems utilizing pressurized air, water and an abrasive powder can be a less unpleasant, easy and quick option (14). The first air powder application was sodium bicarbonate, a very abrasive material (17). Less abrasive powders such as glycine and erythritol have been developed to eliminate the detrimental effect of sodium bicarbonate over soft and hard tissues and restorative material's surfaces (18).

Once after the prosthetic treatment, especially for a fixed prosthesis, plaque accumulation should be monitored carefully at regular intervals. So, plaque formation can begin for the first year of a prosthesis and affect the abutment teeth (19). Thus, prosthodontic restorations may be exposed to different mechanical plaque control methods and their effects repeatedly. As a result, mechanical surface treatment and LTD may induce the sensitivity to degradation of monolithic zirconia's structural features and clinical fractures (20). The tested hypothesis in this study was that surface treatments stem from different plaque control methods and LTD does not generate any differences in the structural properties of monolithic Crystalline structure, micro-hardness, zirconia. surface roughness, wettability, fracture strength and microstructure of monolithic zirconia were analyzed through the present study to investigate whether or not periodontal surface treatment methods affect the material.

Materials and Methods

Preparation of Specimens and Surface Treatments

Seventy-two disc-shaped specimens (12 mm in diameter, 1 mm thick) of monolithic zirconia were milled out from pre-sintered 3Y-TZP blanks (Nacera Pearl 1, Doceram, Dortmund, Germany) by a CAD/ CAM system according to DIN EN ISO 6872:2019 (21). The specimens sintered at 1,450 °C for 2 h, according to the manufacturer's instructions were divided into six groups (n=12) related to specified treatment after sintering; group 1: untreated control (C), group 2: scaling by a steel curette (H6/H7 DE Scaler, Hu-Friedy, Chicago, USA) (Sc), group 3: scaling by ultrasonic scaler with a steel tip (Cavitron, Dentsply Sirona, Charlotte, USA) (USc), group 4: air-polishing with sodium bicarbonate powder (Na), group 5: air-polishing with erythritol powder (Er), group 6: air-polishing with glycine powder (Gl). All specimens except the untreated control group were autoclaved to perform the LTD phenomenon. The conditions of accelerating the aging test in an autoclave (Andromeda Vacuum XP, Tecno-Gaz S.p.A., Parma, Italy) were determined according to the previous study (22). The specimens were exposed to autoclaving for 2 h at 134 °C and 0.2 MPa.

Surface treatment procedures were performed by a particular operator with at least 10 years of clinical experience as a periodontal specialist to standardize the instrumentations. Scaling with a steel curette was made by five strokes and 10 times in the same direction and location. Blades were contacted to the zirconia surface at an angulation of 70 degrees (23,24). The ultrasonic scaler with a steel tip was utilized for 1 min and repeated 10 times under water cooling. The ultrasonic scaler tip was placed on the zirconia surface to contact its lateral surface with an inclination of almost 0 degrees. Scaling motions were executed all over the surface of the specimens briefly, continuously, and equally in the same direction (25). Powders were applied using the standard unit (Air-Flow Master, EMS SA, Switzerland) by the same periodontal specialist. For air-polishing treatment, a nozzle of the air-polishing device was located 5 mm away at a 90° angle to the surface of the zirconia specimen (26). In clinical situations, the nozzle is moved usually during spraying and powder doesn't affect a particular area for the presumed treatment time. Therefore, it was decided that air-polishing procedures were performed for 10 seconds at a pressure of 1.8 bar. Before autoclaving, the specimens with different surface treatments were ultrasonically cleaned in pure water for 5 min.

Assessment of Structural Properties

Crystalline Structure Analysis-X-ray Diffractometer

X-ray diffractometer (XRD) analysis was carried out to detect the amount of tetragonal and monoclinic phases on the surface of a specimen for each group zirconia. Monolithic zirconia specimens were selected randomly from each group. We used a diffractometer (Empyrean, Malvern Panalytical Ltd, United Kingdom) using CuK α radiation recorded within the range of 20°-80°, a step size of 0.04° and a scanning time per step of 10 sec at 40 kV and 40 mA to analyze the specimens. According to this, Im (-111) monoclinic peak intensity is around 28.2° 20, Im (111) monoclinic peak intensity is around 31.5°, 20, and the It (101) tetragonal peak intensity is around 30.2°, 20. The ratio of the monoclinic phase (Xm) at the surfaces of zirconia was calculated using the formula below (32):

Xm = [Im (-111) + Im (111)] / [Im (-111) + Im (111) + It (101)]

The volume ratio of the monoclinic and tetragonal phase was calculated according to Toraya et al. (27) by using the following formula.

Vm = 1.311 Xm / (1+0.311 Xm)

Xm: Complete intensity of monoclinic phase, Vm: Monoclinic phase volume ratio.

Surface Roughness

The surface roughness of zirconia specimens was evaluated using an atomic force microscope (AFM) (Alpha 3100R, WITec, Ulm, Germany). During the surface analysis, three specimens were randomly selected from each group to determine surface roughness profile values (Ra), and a 5x5 mm area on the specimen was scanned at 0.1 Hz and observed for cracks, etc. This procedure was repeated 3 times on each specimen and a mean Ra was specified for the specimen to identify the roughness of the zirconia surface.

Biaxial Bending Test

To the biaxial flexural strength test, we used piston on three-ball method through a universal test machine (Mts Ceriterion model 42, MTS Systems Corporation, USA) with an apparatus that was specially produced for this test according to ISO 6872 and mounted on the upper and lower supportive arms of the test machine at head-speed of 1 mm/min. There were three steel balls with a diameter of 2.5 mm in the lower part of the apparatus, and they were positioned 120° with each other. A flat punch of 1.4 mm diameter in the upper part of this apparatus applied pressure to the center of the zirconia specimen with a cross speed of 1 mm/min to the point of fracture.

A computer connected to the testing machine recorded the force when fracturing eleven specimens for each zirconia group. It converted the test results from N to MPa according to the international standards (ISO 6872) using the following formula;

 $S = -0,2387P(X-Y)/d^2$

S: Maximum center tensile stress (MPa), P: Total load causing fracture (N)

X= $(1+^{\vee})$ In $(r2/r3)^2$ + $[(1-^{\vee})/2](r2/r3)^2$, Y= $(1+^{\vee})[1+$ In $(r1/r3)^2]$ + $(1-^{\vee})(r1/r3)^2$

($^{\vee}$): Poisson ratio (We took ' $^{\vee}$ ' as 0.25 which should be used if the value is unknown in this study.) r1: Radius of the support circle (mm), r2: Radius of the loaded area (mm), r3: Radius of the specimen (mm), d: Thickness of the specimen at fracture origin (mm).

Microstructure Analysis

After the biaxial bending test, a specimen for each group was observed by field emission scanning electron microscope (FE-SEM) (Jeol SEM-7100-EDX, The Netherlands). For the FE-SEM characterization, the images were taken at a magnification of x500. The chemical composition of monolithic zirconia and amount of stabilizer Y_2O_3 , HfO₂ and ZrO₂ on the surface were analyzed using energy-dispersive X-ray spectrometry (EDX) to evaluate whether there is a quantitative change due to the surface treatments.

Wettability

Pure water was dripped via a micro syringe on the surface of a specimen for each group zirconia to evaluate the contact between liquid and surface of the specimen. When a droplet touched the surface, a contact angle meter (CA-X; Kyowa Interface Science, Saitama, Japan) measured the contact angle of the droplet within 5 sec.

Measurement of Vickers Micro-hardness Value

A micro-hardness device (Shimadzu HMV-G, Japan) was used to measure the hardness of the specimens. After the biaxial bending test, all zirconia specimens were fixed to the testing device and 1 kg (9.8N) force with a speed of 0.015-0.07 mm/sec. A diagonal notch was created on the surface of the zirconia, then the notch was measured employing a microscope attached to the device. Micro-hardness values (HV) were calculated via the device's software using the following formula:

HV= 1.8544 (P/d²)

P: Load (kgf), d: The average length of the two diagonal lines of the notch (mm).

Statistical Analysis

Data were analyzed with SPSS V23 (IBM, New York, USA). Shapiro-Wilk examined compliance with a normal distribution. One-Way ANOVA was used for comparisons according to groups. Multiple comparisons were analyzed using the Tukey HSD test. Data are presented as mean ± standard deviation. The level of significance was taken as p<0.05.

Results

Crystalline Structure Analysis-XRD

X-ray diffractograms of all groups are shown in Figure 1. XRD patterns of monolithic zirconia are similar in all groups. A quantitative comparison showed that surface treatments did not affect the



Figure 1. Representative X-ray diffractometer spectrum of monolithic zirconia specimens with different surface treatment. a. Control group. b. Scaler group. c. Ultrasonic scaler group. d. Sodium bicarbonate powder group. e. Erythritol powder group. f. Glycine powder group

peak intensities of Im (-111) and Im (111) after calculating the monoclinic fraction (Table 1).

Surface Roughness

Although there was no significant difference between the Ra values of the surface-treated samples (p>0.05), it was seen that the specimens in the USc group had rougher surfaces according to the threedimensional AFM images obtained. The C group samples show that the roughness is less than the treated surfaces (Figure 2).

Biaxial Bending Test

Biaxial bending strength ranged from 366.6 MPa (Sc) to 301.7 MPa (Na). Surface treatments applied had no significant effect on zirconia specimens' bending strength (p>0.05). The biaxial bending strength values of monolithic zirconia samples are shown in Table 2.

FE-SEM and EDX Evaluation

Microscopic observation showed that the surface of the monolithic zirconia disc was not much affected by different surface treatments in Figure 3. It is seen that there is no quantitative change of Y, Hf and Zr percentages by weight on the surface after different surface treatments. EDX findings are shown in Table 3.



Figure 2. Representative three-dimensional atomic force microscope topographic images of all groups. a. Control group. b. Scaler group. c. Ultrasonic scaler group. d. Sodium bicarbonate powder group. e. Erythritol powder group. f. Glycine powder group

| Table 1. Quantitative data related to monoclinic phase volumes of the groups measured by XRD (Vm, %) | | | | | | | |
|---|--------|---------|---------|---------|---------|---------|--|
| C Sc USc Na Er Gl | | | | | | | |
| Xm | 0.6029 | 0.60873 | 0.6146 | 0.60232 | 0.59295 | 0.6256 | |
| Vm | 0.6656 | 0.67101 | 0.67645 | 0.66506 | 0.65633 | 0.68658 | |
| Xm: Complete intensity rate of monoclinic phase, Vm: Monoclinic phase volume ratio, XRD: X-ray diffractometer | | | | | | | |

Wettability

The contact angle value varies according to the groups (p<0.05). Accordingly, the contact angle in the USc (26.3°) was obtained the lowest, while the C group was the highest (80.5°). Group C is different according to all groups statistically. There was no difference between the Na, Er and Gl groups; 46°,62° and 58° (p>0.05). The results of contact angle measurements are summarized in Figure 4.

Vickers Micro-hardness Values

Vickers micro-HVs of monolithic zirconia specimens are shown in Table 2. Vickers values analyzed by One-



Figure 3. Representative images of scanning electron microscope analysis at 500x of monolithic zirconia disc **a.** Control group. **b.** Scaler group. **c.** Ultrasonic scaler group. **d.** Sodium bicarbonate powder group. **e.** Erythritol powder group. **f.** Glycine powder group

Way ANOVA showed significant differences among groups (p<0.05). Sc and USc groups were significantly lower than the other groups, 1232.6±86.2 and 1109.7±45.5 MPa.

Discussion

The present study was designed to examine the effect of repeatedly using different plaque removal methods and hydrothermal aging on monolithic zirconia's structural properties. According to the study's findings, we accepted the hypothesis that plaque removal methods and thermal aging would



Figure 4. Contact angle of a pure water droplet on the monolithic zirconia subjected to different surface treatments. a. Control group. b. Scaler group. c. Ultrasonic scaler group. d. Sodium bicarbonate powder group. e. Erythritol powder group. f. Glycine powder group

SD: Standard deviation

Table 2. Mean and standard deviation of micro-hardness, roughness and biaxial flexural strength values of the zirconia with different surface treatment

| Group | Vickers mean ± SD (MPa) | Ra mean ± SD (nm) | Biaxial mean ± SD (MPa) | | |
|------------------------------|--|-------------------|-------------------------|--|--|
| С | 1473.8±44.2° | 136.1±29.9 | 329.2±125.7 | | |
| Sc | 1232.6±86.2 ^b | 175.3±15.2 | 366.6±133.7 | | |
| USc | 1109.7±45.5 ^c | 182.12±40.2 | 336.2±135.1 | | |
| Na | 1311.5±20.5ª | 166.2±70.6 | 301.7±94.4 | | |
| Er | 1387.5±31 ^a | 142.9±29.2 | 303.4±93.8 | | |
| Gl | 1291.9±127.4ª | 142.9±29.2 | 316.5±100.7 | | |
| The different lower case let | The different lower case letters a, b, c indicate significant statistical differences ($p < 0.05$). SD: Standard deviation | | | | |

| Table 3. The weight percent of Y, Hf, Zr analyzed by EDX in different groups (weight %) | | | | | | | |
|---|---|------|------|------|------|------|--|
| C Sc USc Na Er Gl | | | | | | | |
| Υ | 2.73 | 2.37 | 2.78 | 2.42 | 2.50 | 2.49 | |
| Hf | 1.45 | 1.31 | 1.24 | 1.18 | 1.19 | 1.18 | |
| Zr 79.63 70.88 71.11 71.1 73.34 72.04 | | | | | | | |
| EDX: Energy-dispers | EDX: Energy-dispersive X-ray spectrometry | | | | | | |

not cause any changes in the determinants examined to predict the behavior of zirconia.

Dental plaque is accepted as the main etiological factor in the pathogenesis of periodontal diseases (28). Rough surfaces in the mouth have an essential effect on plaque formation. Because microorganisms primarily adhere to areas with surface irregularities (29). Dental plaque can accumulate on the surface of the restorative material as well as on the tooth surface. Some surface properties of the restorative material, such as the material's chemical structure, surface roughness, surface topography, and ion release can strongly affect plague formation and bacterial adhesion (30). Dental plaque control emerges as an essential factor in preventing periodontal diseases (31). In this study, we simulated plaque control procedures performed by the dentist at least every six months after prosthetic treatment (32).

In our study, AFM analysis shows no significant difference between the different surface treatments applied for plague control and aging in terms of surface roughness values (Ra). Our findings regarding the effect of Sc and USc on roughness (175.3±15.2 nm and 182.12±40.2 nm) are consistent with other studies. The previous research observed by Lee et al. (33) to investigate the optical properties and surface roughness of different restorative materials has shown that ultrasonic scaling with steel tip does not cause any changes on the surface roughness of zirconia. Another study examining bacterial adhesion on varied restorative materials after plaque removal via scaling both steel curette and ultrasonic scaler points to scalers did not affect zirconia surface roughness (34). In contrast to the present study, Nakazawa et al. (25) reported that ultrasonic scaling increases the surface roughness with or without aging. They observed that small pits were formed on the zirconia surface instead of scratches, and they concluded that this occurred due to particle break off from the surface due to LTD. Vigolo, too, examined the effect of steel and titanium curettes on zirconia and lithium disilicate surfaces and concluded that the steel curette increased the zirconia surface roughness (35). Methodological differences like instrumentation time, pressure and operator's skill in the surface treatment may explain the variability of results among so-called studies. Previous studies investigating the effect of air-abrasive powders on teeth and dental materials

showed that sodium bicarbonate powder increases the roughness of tooth and composite surfaces. Glycine and erythritol also have surface changing effects, but they are less abrasive (26,36,37). Glycine powder causes the least surface damage during the removal of plaque on different restorative materials (38). Although the Ra values are higher in the Na, Er and Gl groups (166.2±70.6 nm, 142.9±29.2 nm and 142.9±29.2 nm, respectively) than the C group (136.1±29.9 nm) in our study, air-abrasive powders do not affect the roughness of the material owing to zirconia's surface hardness that is higher than the abrasive particles used.

In this study, a piston-on-three-ball test applied for biaxial bending strength to simulate pure bending and prevent edge loss. It is less sensitive than uniaxial tests such as 3-point or 4-point bending tests to the undetectable defect of the material at a loaded position. In addition, its easy use resulted in fewer errors than other tests and provided clinically adaptable results (39). The results show that biaxial bending strength of zirconia is not affected by the surface treatments and aging effects (p>0.05). Although different aging and different abrasive powders are used, there are studies in the literature that are compatible with our study results (40,41). Mogbel et al. (42) detected an increase in biaxial flexural strength of zirconia after aging and surface treatment with alumina particle and polishing. They explained the different results by hardening strength caused by compressive stresses during monoclinic phase transformation increased the amount of force required to break the samples. In this study, no significant difference was observed between the flexural strength results due to $t \rightarrow m$ phase transformation on the zirconia surface was lower and the diameter, hardness, and application pressures of the abrasive powders used were different from previous research.

Zirconia is composed of different crystal phases. The t phase determines the mechanical properties of the material at room temperature (43). t \rightarrow m phase transformation caused by dental stresses such as etching, sandblasting, and hydrothermal aging (LTD) causes deterioration of zirconia's superior mechanical properties (42). LTD is time-dependent phenomenon and aging time is affecting t \rightarrow m phase transformation. The current aging process of the zirconia specimens to simulate the LTD effect in this in-vitro study depends on a previous study by Chevalier et al. (22). Chevalier stated that one hour of autoclave treatment at 134 °C and 2 bar (0.2 MPa) pressure had theoretically corresponded to a similar effect as 3-4 years aging at 37 °C in the oral environment.

During the m phase transformation due to mechanical stress, the compression pressure created by the volumetric expansion of the particles increases the durability of the material by preventing the cracks' progress on the surface (44). Without mechanical stress, the m phase transformation based on humidity and temperature occurs slowly in the particles contact with water. Meantime, a progressive process occurs that causes the mechanical properties of the material to deteriorate with a rise in the surface, followed by microfracture and pull-out of the particle on the surface (6,45). Studies have not fully understood the effect of LTD on the mechanical properties of zirconia. So much so that studies are showing that it affects mechanical properties positively and studies showing that it does not affect $t \rightarrow m$ phase transformation (42,46,47). Our phase transformation results analyzed utilizing an XRD show that aging and different surface treatments do not significantly impact t \rightarrow m phase transformation since the two-hour aging period in our study may not have increased the activation energy for the tetragonal to monoclinic transformation on the zirconia surface. A previous study investigating the effect of ultrasonic scaling and LTD on phase transformation stated that ultrasonic scalers did not affect the phase transformation on the zirconia surface. But independent of the ultrasonic scaling processes, LTD increased the t \rightarrow m phase transformation and decreased the material's surface hardness (25). Although our findings are partially compatible with the study mentioned above, the phase transformation percentages differed from ours due to the extended aging time for LTD. Sc and USc groups indicated lower surface hardness results, but there were no important changes in the other groups. Micro-fractures occurring on the surface during scaling may have caused transformation hardening on the surface. This discrepancy might be an artifact of measurement that linked to the manufacturing process causing micro-notches. It might be thought that these notches make it challenging to evaluate hardness test results.

While investigating the phase transformation on the surface of monolithic zirconia, evaluating the

changes in the amount of stabilizers $(Y_2O_3, HfO_2, and ZrO_2)$ can provide useful information. Some studies have reported an increase in the Y_2O_3 ratio on the surface decreases t \rightarrow m phase transformation arise as an effect of aging (48). Research on LTD effects said that Y concentration on zirconia surface decreased and Y-TZP structure weakened when they are kept in a humid environment (49). Y and Hf ratios by virtue of EDX analysis in surface treatment groups kept up with the C group in this study. The findings show no stabilizer loss, so there is no phase transformation on the material surface as presented by XRD analysis.

Biofilm formation over dental materials in the mouth is related to the surface roughness, wettability, and the interaction of bacteria with the surface (50). John et al. (51) reported that hydrophilicity is a more significant factor than surface roughness for dental plaque accumulation. Regarding the effects of different surface treatments, we detected substantial change in the wettability of monolithic zirconia. The most hydrophobic group was the non-treated C group, with a contact angle of 80.5°. The hydrophilic properties of zirconia specimens in Sc and USc groups (contact angle 26.3° and 32°) increased after different surface treatments. The air-abrasive powders caused decrease in the contact angle compatible with previous research studied by Sturz et al. (52). A previous study informed that hydrophilicity could increase only with LTD. Besides, they said that LTD and surface treatment with ultrasonic scaling using a steel tip caused hydrophobic surface. Because of the aging time in that study, LTD may stimulate to release of hydroxyl groups due to the degradation of Zr-O-Zr bonds that specify the hydrophilicity may have been removed from the surface during ultrasonic scaling (25).

The limitation of this in-vitro study is that only the thermal conditions were applied similar to the oral environment were evaluated. Still, mechanical loading is a factor that did not assess in the present study. Although the current study showed promising results about the usage of air-abrasive powders to professional plaque control after prosthetic treatment for monolithic zirconia restoration, the structural behavior of this zirconia needs to be investigated under thermal and mechanical loading in the aqueous environment. Therefore, further studies should be considered to address these issues before definitive conclusions can be drawn.

Conclusion

Considering the results of our study, using airabrasive powders for professional plaque control in the supportive treatment maintaining post-prosthetic periodontal health may be an appropriate treatment for monolithic zirconia restorations.

Ethics

Ethics Committee Approval: This study does not require ethics committee approval.

Informed Consent: This study does not require informed consent.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: H.Ö.U., Design: H.Ö.U., Ç.A., Supervision: H.Ö.U., Ç.A., Fundings: H.Ö.U., Materials: H.Ö.U., Data Collection or Processing: H.Ö.U., Ç.A., Analysis or Interpretation: H.Ö.U., Literature Search: H.Ö.U., Writing: H.Ö.U., Ç.A., Critical Review: H.Ö.U., Ç.A.

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Oral Pathological Lesions in the Aegean Region: A 30-Year Retrospective Study

Ege Bölgesinde Oral Patolojik Lezyonlar: 30 Yıllık Retrospektif Bir Çalışma

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Keywords

Oral

Abstract

Öz

amaclamaktadır.

Objective: Oral pathological lesions in the mouth vary greatly. However, few studies have evaluated these lesions with long-term data. This study aimed to analyze the demographic parameters (i.e., age, gender, anatomical location, and incidence) of oral pathologies in the Aegean Region.

Materials and Methods: In this retrospective study, histopathological reports of 30 years in the Department of Oral Pathology, Faculty of Dentistry, Ege University, were analyzed. Data on sex, age, lesion location, and histopathologic diagnosis were analyzed.

Results: The histopathological data of 6,330 patients were evaluated. Most of the pathological oral lesions were osseous lesions (n=3,858), and 2,472 soft tissue pathologies were identified. The posterior mandible was the most common location of these lesions (n=2,011).

Conclusion: Determining the variety and frequency of oral pathological lesions at a societal level is important for the management of these lesions.

Amaç: Ağız içinde görülen oral patolojik lezyonlar geniş bir yelpazeye sahiptir. Bununla birlikte, birkaç çalışma tüm bu lezyonları uzun sürede çok sayıda verilerle

değerlendirmiştir. Bu çalışma Ege Bölgesi'ndeki oral patolojilerin demografik

parametrelerini (yaş, cinsiyet, anatomik yerleşim ve insidans) incelemeyi

Gereç ve Yöntemler: Bu retrospektif çalışmada Ege Üniversitesi Diş Hekimliği Fakültesi Ağız Patoloji Anabilim Dalı'nda toplanan 30 yıllık histopatolojik raporlar

Anahtar Kelimeler

lesions,

retrospective study, histology

Oral lezyonlar, patoloji, prevalans, retrospektif çalışma, histoloji

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prevalence,

sunulmuştur. Cinsiyet, yaş, lezyonun yeri ve histopatolojik tanı ile ilgili bilgiler analiz edilmiştir. **Bulgular:** Toplam 6.330 histopatolojik veri değerlendirildi. Ağızdaki patolojik lezyonların çoğu yumuşak doku lezyonlarıydı (n=2.472). Alt çene arka bölge, bu

lezyonların en sık yerleşim yeriydi (n=2.011). Sonuç: Bir toplumdaki oral patolojik lezyonların çeşitliliğinin ve sıklığının belirlenmesi bu lezyonların yönetimi açısından önemlidir.

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Introduction

A thorough understanding of the frequency and anatomical distribution of oral pathological lesions is imperative to guide the clinicians through the process of identification and clinical diagnosis of oral lesions.

Evaluation of the demographic distribution of oral lesions and their prevalence in the community is necessary for determination of risk groups and provision of health care services (1).

Histopathological examination is the gold standard to confirm-clinical diagnosis of oral pathology. Early diagnosis and treatment is essential to limit morbidity and improve quality of life. Additionally the accuracy of the preliminary diagnosis is prerequisite for timely and successful management of these cases (2).

Oral pathological lesions constitute a broadspectrum of lesions presenting with miscellaneous symptoms, findings and prognosis. Various classifications are made by many authors depending on tissue origin, radiographic features or clinical behavior of the lesion (3). Racial, hereditary and geographical factors influence the incidence of oral lesions; further studies are important to evaluate demographic, clinical and epidemiologic characteristics in different populations (4).

The aim of this study is to provide clinical guidance in the diagnosis of oral pathologies thorough evaluation of the data acquired from the management oral pathologies over a period of 30-years. This study aims to analysis, the demographic parameters (age, sex, anatomic location and incidence) of oral pathologies presenting in Aegean Region of Turkey.

Materials and Methods

In this retrospective study all of the histopathological analysis reported in the Department of Oral Pathology of Ege University, Faculty of Dentistry, thorough 1984 to 2014 were evaluated. Demographic data and tissue diagnosis of 6,330 patients' histopathological reports were analyzed. This retrospective study was approved by the Ethics Committee of Ege University Faculty of Medicine (decision no: 19-10.1T/46, date: 16.10.2019). Data including age, gender, anatomic location of the lesion, clinical and histopathologic diagnosis were recorded. Notes of patients lacking the above information were excluded from the study.

Classification of Oral Pathological Lesions

Oral pathological lesions in our study were divided into 7 main groups (Table 1). These; inflammatory lesions, benign bone pathology, malignant tumors, odontogenic tumors, lesions of odontogenic and non-odontogenic origin and soft tissue lesions. The first 6 groups of these were intra osseous lesions. Intra osseous oral pathological lesions were classified according to Neville's Text Book of Oral and Maxillofacial Pathology (5).

Statistical Analysis

Data was analyzed using Microsoft Excel Software to reveal statistical prevalence values, frequency distribution tables and graphs.

Results

A total of 6,330 histopathological diagnosis reported over a period of 30-years were analyzed in

| Table 1. Age distribution of oral pathological lesions | | | | | |
|--|-----------------|----------|-------|-------------------|--|
| Oral pathological lesions | Number of cases | Mean age | SD | Age range (years) | |
| Inflammatory lesions | 182 | 51.97 | 16.59 | 2-85 | |
| Benign bone pathology | 1,144 | 37.54 | 18.39 | 0-93 | |
| Malignant tumors | 103 | 57.78 | 16.16 | 13-86 | |
| Odontogenic lesions | 2,175 | 37.11 | 16.61 | 0-84 | |
| Non-odontogenic lesions | 94 | 44.72 | 16.49 | 10-81 | |
| Odontogenic tumors | 160 | 29.44 | 17.29 | 1-76 | |
| Soft tissue lesions | 2,472 | 40.68 | 17.87 | 0-89 | |
| Total | 6,330 | 39.26 | 17.89 | 0-93 | |
| SD: Standard deviation | ^ | ^ | | | |

this retrospective study. There were 3,223 (50.9%) female and 3,107 (49.1%) male patients. There was no significant difference between the sexes (p=0.005). The mean age of the patients was 39.26 (standard deviation: 17.89 years). The age range varied from newborn to 93 years old (Table 2).

Locations of oral pathological lesions were grouped as posterior mandible (n=2,011; 31.8%), anterior maxilla (n=1,492; 23.6%), anterior mandible (841; 13.3%), posterior maxilla (811; 12.8%), miscellaneous region (not recorded or, unknown) (n=287; 4.5%), cheek mucosa (n=244; 3.9%), maxilla (n=184; 2.9%), palatal mucosa (n=132; 2.1%), mandible (n=131; 2.1%) lip mucosa (n=116; 1.8%), and tongue (n=74; 1.2%) (Table 3). Intraoral pathologies were most commonly seen in male patients and posterior mandible (male: 1,062/female: 949). Tongue pathologies were the rarest and were more common among male patients (male: 40/female: 34). The distribution of these lesions according to age and location is shown in Figure 1.

Out of the 6,330 oral pathologies, 2,472 (39%) were classified as soft tissue pathologies and 3,858 (60.9%) were osseous pathologies. The most common intraosseous pathologies were odontogenic pathologies (n=2,175; 34.4%), followed by benign bone tumors



Figure 1. Intraoral region and sex distribution

(n=1,144; 18.1%), inflammatory lesions (n=182; 2.9%), odontogenic tumors (n=160; 2.5%), malignant tumors (n=103; 1.6%) and non-odontogenic pathologies (n=94; 1.5%) (Figure 2).

Distribution of pathological lesions according to age is shown in Table 3. Soft tissue pathologies were more common among female patients (n=1,436). Non-odontogenic lesions were the rarest pathologies that were seen in female patients (n=37) (Figure 3).

Most of the "soft tissue lesions" (n=2,472) were grouped under "others" (n=996). Others were soft tissue lesions which diagnosis could not be fully determined.



Figure 2. The distribution of oral pathological lesions



Figure 3. Sex distribution among oral pathological lesions

| Table 2. Demographic data | | | | | | |
|---------------------------|--------|---------|---------|-------|-------|--|
| Variables | Number | Minimum | Maximum | Mean | SD | |
| Age | 6,330 | 0 | 93 | 39.26 | 17.89 | |
| | | Count | | % | | |
| | Total | 6,330 | | 100 | | |
| Cau | Male | 3,107 | | 49.1 | | |
| Sex | Female | 3,223 | | 50.9 | | |
| SD: Standard deviation | | | | | | |

Radicular cyst (n=853) was the most common odontogenic lesion (n=1,755). Peripheral giant cell granuloma (PGCG) (n=448) was the most common benign bone pathology (n=1,144). Ameloblastoma (n=89) was the most common odontogenic tumor (n=160). Squamous cell carcinoma (SCC) (n=74) was the most common malignant tumor (n=103). Incisive canal cyst was the most common (n=85) non-odontogenic lesion (n=94) (Table 4).

| Table 3. Distribution of age according to locations of oral lesions | | | | | | |
|---|-----------------|----------|-------|-------------------|--|--|
| Region | Number of cases | Mean age | SD | Age range (years) | | |
| Miscellaneous region | 287 | 38.52 | 17.81 | 1-79 | | |
| Anterior mandible | 841 | 40.74 | 18.69 | 0-85 | | |
| Posterior mandible | 2,011 | 38.73 | 17.84 | 2-86 | | |
| Anterior maxilla | 1,492 | 37.11 | 17.51 | 0-93 | | |
| Posterior maxilla | 818 | 39.53 | 17.69 | 0-84 | | |
| Lip mucosa | 116 | 39.72 | 18.27 | 1-76 | | |
| Buccal mucosa | 244 | 46.08 | 15.26 | 8-89 | | |
| Palatal mucosa | 132 | 47.31 | 17.45 | 7-80 | | |
| Mandible | 131 | 41.24 | 17.01 | 7-70 | | |
| Maxilla | 184 | 37.24 | 17.53 | 1-79 | | |
| Tongue | 74 | 44.26 | 19.50 | 9-83 | | |
| Total | 6,330 | 39.26 | 17.89 | 0-93 | | |
| SD: Standard deviation | | | | | | |

| Table 4. Histopathologic diagnoses in each category | | | | | | |
|---|--------|------|--------|-----------|------------------|-------|
| Diagnosis | Number | Male | Female | M:F ratio | Mean age (years) | SD |
| Soft tissue lesions | 2,472 | | | | | |
| Adenocarcinoma | 16 | 10 | 6 | 1.67 | 51.59 | 18.42 |
| Actinomycoses | 19 | 9 | 10 | 0.9 | 35.86 | 16.34 |
| Fibrolipoma | 25 | 10 | 15 | 0.67 | 33.28 | 15.53 |
| Fibroma | 208 | 83 | 125 | 0.66 | 12 | 7.07 |
| Hemangioma | 37 | 15 | 22 | 0.68 | 43.56 | 19.7 |
| Hyperparakeratosis | 37 | 21 | 16 | 1.31 | 25.07 | 15.6 |
| Intradermal nevus | 7 | 1 | 6 | 0.17 | 41.86 | 18.35 |
| Irritation hyperplasia | 552 | 211 | 341 | 0.62 | 53.63 | 14.78 |
| Leukoedema | 2 | 1 | 1 | 1 | 44.58 | 22.05 |
| Mucosel | 78 | 45 | 33 | 1.36 | 55.24 | 16.61 |
| Papilloma | 113 | 52 | 61 | 0.85 | 37.47 | 16.86 |
| Pleomorphic adenoma | 38 | 14 | 24 | 0.58 | 40.97 | 17.57 |
| Pyogenic granuloma | 303 | 103 | 200 | 0.52 | 45.19 | 14.18 |
| Nicotinic stomatitis | 5 | 3 | 2 | 1.5 | 33 | 5.66 |
| Verruca vulgaris | 36 | 16 | 20 | 0.8 | 38.37 | 20.48 |
| Others | 996 | 442 | 554 | 0.79 | 43.11 | 19.17 |
| Odontogenic lesions | 2,175 | | | | | |
| Apical periodontal cyst | 203 | 127 | 76 | 1.67 | 35.51 | 14.53 |
| Dentigerous (follicular) cyst | 497 | 334 | 163 | 2.05 | 31.85 | 17.53 |
| Keratocysts | 442 | 295 | 147 | 2.01 | 41.41 | 16.87 |

Table 4. continued

| Odontogenic cyst | 108 | 69 | 39 | 1.77 | 37.92 | 18.22 |
|--|-------|-----|-----|------|-------|-------|
| Radicular cyst | 853 | 513 | 340 | 1.51 | 37.54 | 15.37 |
| Residual cyst | 72 | 39 | 33 | 1.18 | 45.24 | 14.42 |
| Benign bone pathologies | 1,144 | | | | | |
| Aneurysmal bone cyst | 9 | 0 | 9 | 0 | 24.22 | 10.28 |
| Exostoses | 8 | 2 | 6 | 0.33 | 42.38 | 13.18 |
| Fibrous dysplasia | 34 | 9 | 25 | 0.36 | 36.35 | 18.09 |
| Ossifying fibroma | 278 | 85 | 193 | 0.44 | 35.36 | 16.35 |
| Osteoma | 84 | 30 | 54 | 0.56 | 38.37 | 15.59 |
| Peripheral giant cell granuloma | 448 | 191 | 257 | 0.74 | 41.19 | 18.85 |
| Central giant cell granuloma | 251 | 98 | 153 | 0.64 | 34.03 | 20.15 |
| Cemento ossifying fibroma | 32 | 6 | 26 | 0.23 | 34.38 | 14.62 |
| Inflammatory lesions | 182 | | | | | |
| Osteomyelitis | 182 | 83 | 99 | 0.84 | 51.97 | 16.59 |
| Odontogenic tumors | 160 | | | | | |
| Ameloblastoma | 89 | 48 | 41 | 1.17 | 36.02 | 15.97 |
| Compound odontoma | 24 | 13 | 11 | 1.18 | 26.58 | 18.58 |
| Complex odontoma | 47 | 17 | 30 | 0.57 | 18.45 | 12.69 |
| Malignant tumors | 103 | | | | | |
| Differentiated spinocellular carcinoma | 9 | 5 | 4 | 1.25 | 57.11 | 6.25 |
| Spinocellular carcinoma | 3 | 2 | 1 | 2 | 44.24 | 15.25 |
| Mucoepidermoid carcinoma | 17 | 8 | 9 | 0.89 | 60.78 | 16.11 |
| Squamous cell carcinoma | 74 | 40 | 34 | 1.15 | 61.66 | 5.51 |
| Non-odontogenic lesions | 94 | | | | | |
| Epidermoid cyst | 5 | 3 | 2 | 1.5 | 36.2 | 18.44 |
| Globulomaxillary cyst | 4 | 2 | 2 | 1 | 33 | 30.29 |
| Incisive canal cyst | 85 | 52 | 33 | 1.58 | 45.78 | 15.49 |
| SD: Standard deviation | | | | | * | |

Discussion

In the 30-year retrospective evaluation, 6,330 oral pathologies were evaluated. Of these evaluations, 996 soft tissue lesions could not be determined precisely due to missing data entry. While 3,107 oral pathological lesions were seen in men, 3,223 of them were seen in women. This shows that there is no difference in terms of gender. In accordance with other studies (1-4,6-18) male-female ratio was almost equal in our study. The age range is 0-93 years old as 6,330 oral pathologies constitute a diverse and massive cohort,

the average age is 39.26. This situation is compatible with other studies (1-3,11,12,15-18).

Most of the oral pathological lesions were seen in the posterior mandible, in coordination with other studies (2-4,6-9,12,13,16,19-23). This finding could possibly be associated with the presence of adjacent anatomical structures such as tongue, cheek mucosa and salivary glands in the lower jaw (2). Contrary to our findings, Selvamani et al. (24) emphasized that some intraoral lesions were mostly seen in the maxilla. While other studies state that some pathological lesions in the mouth are seen equally in both jaws (15,25). There is no definitive explanation regarding the site predilection of oral pathologies in the literature.

In many retrospective studies of oral pathological lesions (1,4,6-9,11,14,16,18), the presence of excess amount of soft tissue lesions was noticeable as in our study (Table 3). Among these soft tissue lesions, irritation hyperplasia was the second commonest after "others" group (Table 4). Oral mucosa is prone to developmental disorders, irritation, inflammation and neoplastic conditions as it's constantly under the effect of different internal and external stimuli. Reactive lesions are tumor-like hyperplasia that develop in response to a low-grade irritation or injury, such as chewing, food impaction, calculus, iatrogenic injuries such as mechanical irritation caused by ill-fitting dentures, fillings and crowns. Irritation hyperplasia, pyogenic granuloma, PGCG, and cemento-ossifying fibroma are common reactive lesions seen in the oral cavity. Reactive lesions are commonly seen in the gingiva followed by in no particular order tongue, palate, cheek and floor of the mouth. Clinical characteristics of these lesions consist of sessile or pedunculated masses with smooth or irregular surfaces, and present with different colors, from bright pink to red (26). Irritation hyperplasia is the most common tumor like and submucosal reactive lesion in the oral cavity that is composed of fibrous or connective tissue caused by mechanical trauma of irritants such as calculi, foreign bodies, chronic biting, overhanging restoration margins, sharp spicules of bones and over extended borders of appliances (27). The findings of our study confirm that in our society, particularly in the elderly edentulous group, poor oral hygiene and less than ideal management of restorative treatment needs remain as an issue to be solved by the health authorities.

Odontogenic lesions originate from odontogenic epithelium of tooth germ, and these lesions occur frequently during the development of teeth in the first two decades of life (4). Radicular cyst is an inflammatory cyst that is associated with odontogenic infections. It is also associated with increased maxillofacial trauma (13,17,21,24,28). In accordance with other studies (1,3,7,10,11,13,15,17-19,21,24) radicular cysts were found to be the commonest odontogenic pathology. The incidence of radicular cysts were found to be higher in men (Table 4). However a couple of retrospective studies by Silva et al. (6) and Prosdócimo et al. (14) found that dentigerous cysts were the commonest odontogenic lesion.

In our study, the commonest benign bone tumor was found to be the PGCG. It has a predilection for gingiva and poor oral hygiene plays a role in the etiology (4). A PGCG is a reactive, exophytic lesion that occurs primarily in gingiva and alveolar ridge. It originates from the periosteum or periodontal membrane in both dentate and edentulous areas (16,29). Radiographic findings are widening of the adjacent periodontal space and the adjacent interdental septum is more radiolucent than the normal surrounding bone that shows a normal trabecular structure (29). In accordance with the current study, it was previously shown that PGCG has a slight predilection for female gender (16,18).

Osteomyelitis is an intraosseous inflammatory process encompassing cortical bone and periosteum that is characterized by progressive inflammatory osteoclasia with ossification. Osteomyelitis can be seen in any bone including the femur, humerus, or jaws. The most typical pathogenesis is an infection with bacteria such as *Staphylococcus aureus* or *Mycobacteria*, but it may also be induced by trauma, radiation, or specific drugs (30). Osteomyelitis is rarely seen in the jaws and in our study it was classified as an inflammatory lesion. In the current study male to female ratio is found to be 0.84 and the average age is 51.97. These values are very close to the values shown by Andre et al. (31). Osteomyelitis was extremely rare in our study.

Odontogenic tumors constitute a heterogeneous group of pathological lesions, arising from dental mesenchymal cells or its remnants. Biologically, some of these lesions present as hamartomas with varying degrees of differentiation, while the rest are benign or malignant neoplasms with variable aggressiveness and potential to develop metastasis (12,16,18,20,23). Since the odontogenic tumors are generally asymptomatic, patients do not notice until it reaches large sizes. Odontogenic tumors are more commonly seen in the 4th decade of life (12,16,18,20,23). However, our findings show that odontogenic tumors are more common in the third decade of life. In accordance with the literature, ameloblastoma is the commonest odontogenic tumor in the current study (1,3,4,11,12,16,18,20,23). Although there is no significant gender predilection in other and the current study, Jaafari Ashkavandi et al. (4) state a slight male predilection.

SCC constitutes 90% of malignant tumors in the mouth. It has a male predilection and commoner in the 6th decade of life (32-35). In accordance with these studies SCC is the commonest maxillofacial malignant tumor. The male to female ratio was 1.15 and the average age was 61.66.

Non-odontogenic cysts are developmental or reactive lesions. These lesions develop from non-odontogenic epithelium and are more common in men (2,13,15,17,18). The commonest non-odontogenic lesion is incisive canal cyst (1,3,11,14). Our findings are consistent with these literatures.

Conclusion

In this study, the 30-year demographic distribution of oral pathologies in the Aegean region is documented. Soft tissue pathologies were the commonest oral pathologies and posterior mandible was the most frequently affected anatomical site. A slight female predilection that was not significant was noted. Findings of the current study can contribute to formulating a clinical working diagnosis hence management issues surrounding oral pathologies.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Ethics Committee of Ege University Faculty of Medicine (decision no: 19-10.1T/46, date: 16.10.2019).

Informed Consent: All participants provided written consent to the approved protocol as they were free to decline their participation. The personal data of the participants were kept confidential.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.Ç., C.E., H.K., Design: A.Ç., C.E., H.K., Supervision: A.Ç., C.E., H.K., Fundings: A.Ç., C.E., H.K., A.M., Materials: A.Ç., C.E., Data Collection or Processing: A.Ç., C.E., H.K., A.M., Analysis or Interpretation: A.Ç., A.M., Literature Search: A.Ç., C.E., H.K., Writing: A.Ç., Critical Review: A.Ç., C.E.

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Characteristics of Term Neonates Admitted to the Neonatal Intensive Care Unit: A Single-center Experience

Yenidoğan Yoğun Bakım Ünitesine Yatırılan Term Yenidoğan Bebeklerin Özellikleri: Tek Merkez Deneyimi

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Keywords

Term, newborn, intensive care unit, admission, indication

Anahtar Kelimeler

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Abstract

Objective: Considerable research has been reported about the problems of preterm neonates admitted to the neonatal intensive care unit (NICU); however, the number of studies examining the problems of term neonates is limited. Thus, this study examined the problems of term neonates admitted to the NICU.

Materials and Methods: The demographic and clinical characteristics of mothers and term neonates admitted to the NICU between January 1, 2015, and December 31, 2020, were retrospectively examined from the medical records. Neonates with major congenital anomalies, diagnosed with genetic syndromes, or referred to another hospital for any reason were excluded from the study. Categorical variables are expressed as n and percentage (%) and numerical variables as median (25th-75th percentile) values.

Results: In total, 1,221 term neonates were enrolled, of which 349 (28.6%) were referred from other centers. The mean gestational age of the infant was 38 weeks (37-39) and the median birth weight was 3.560 g (3,210-3,672). The most common reason for admission to hospital was respiratory distress (n=399, 32.7%), followed by neonatal jaundice (n=370, 30.3%), infections (n=181, 14.8%), hypoxic-ischemic encephalopathy (HIE) (n=98, 8%), hypoglycemia (n=40, 3.3%), small for gestational age (n=25, 2%), poor feeding (n=16, 1.3%), and others (n=92, 7.6%). The median length of hospital stay was 5 (3-8) days. The mortality rate was calculated as 1.1%. Mortality occurred in seven neonates due to infection during the study and in seven due to HIE.

Conclusion: Term neonates represent a significant proportion of patients admitted to the NICU. In light of admission causes, various antenatal practices may help reduce the admission frequency of these neonates.

Öz

Amaç: Yenidoğan yoğun bakım ünitesine (YYBÜ) yatırılan preterm bebeklerin sorunları ile ilgili çok sayıda araştırma bulunmakta iken, literatürde term bebeklerin sorunlarını inceleyen kısıtlı sayıda çalışma bulunmaktadır. Bu çalışmada hastanemizin YYBÜ'de yatan term bebeklerin sorunları incelenmiştir.

Gereç ve Yöntemler: 1 Ocak 2015 ile 31 Aralık 2020 tarihleri arasında YYBÜ'de yatan term bebeklerin ve annelerinin demografik ve klinik özellikleri tıbbi kayıtlardan geriye dönük olarak incelendi. Majör konjenital anomalisi olan, genetik sendrom

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tanısı alan ve herhangi bir nedenle başka bir hastaneye sevk edilen bebekler çalışma dışı bırakıldı. Kategorik değişkenler frekans (n) ve yüzde (%) olarak, nümerik değişkenler ise ortanca (25 persantil-75 persantil) olarak verildi.

Bulgular: Çalışmaya 1,221 term bebek dahil edildi. Bu bebeklerin 349'u (%28,6) diğer bir sağlık merkezinden sevk ile yatırılmıştı. Çalışmaya alınan bebeklerin ortanca gebelik haftası 38 hafta (37-39), bebeklerin ortanca doğum ağırlığı 3,560 g (3.210-3.672) idi. Hastaneye yatış nedenleri değerlendirildiğinde, en sık nedenin solunum sıkıntısı (n=399, %32,7) olduğu görüldü. Bunu sırası ile yenidoğan sarılığı (n=370, %30,3), enfeksiyonlar (n=181, %14,8), hipoksik-iskemik ensefalopati (HİE) (n=98, %8), hipoglisemi (n=40, %3,3), düşük doğum ağırlığı (n=25, %2), beslenme sorunları (n=16, %1,3) ve diğer nedenler (n=92, %7,5) takip ediyordu. Ortanca hastanede yatış günü 5 (3-8) idi. Çalışma süresince yedi bebeğin yenidoğan enfeksiyonu olduğu, yedi bebeğin de HİE nedeni ile eksitus olduğu görüldü ve mortalite oranı %1,1 olarak belirlendi.

Sonuç: Günümüzde YYBÜ'de yatan hastaların önemli bir kısmını term bebekler oluşturmaktadır. Yatış nedenleri göz önüne alındığında bazı antenatal uygulamaların ve ebeveyn eğitiminin bu bebeklerin yatış sıklığını azaltmada yardımcı olabileceği düşünülmüştür.

Introduction

The neonatal period is one when the baby endeavors to adapt to extrauterine life, and when marked physiological changes occur. A significant proportion of deaths in the first year of life are observed during this time when the baby is most defenseless (1). The fact that three out of four deaths in the neonatal period occur in the first week of life heightens the importance of the care provided for the baby (2). Infant death rates are one of the criteria used to determine countries' level of development and also reflect the accessibility and effectiveness of health services.

Prematurity and low birth weight are the most important risk factors for neonatal morbidity and mortality. Numerous studies have therefore examined the problems of preterm babies. However, analysis of all neonatal intensive care unit (NICU) admissions shows that term babies constitute more than 50% of such infants (3). A study from Ireland reported that 54% of babies admitted to the NICU had birth weights of 2,500 g or more (4). Similarly, term babies were reported to constitute 60% of admissions to the NICU in the UK in 2012-2013 (3). In addition to the potential complications and high treatment costs associated with admission to the NICU, the separation of the mother and neonate after birth damages motherinfant bonding, reduces the physiological benefits of bonding, and disrupts the feeding of the infant (5).

The purpose of this study was to evaluate the clinical and demographic characteristics and the reasons for admission of term neonates in our hospital, which has one of the largest tertiary NICUs in its region.

Materials and Methods

Term neonates (\geq 37 birth weeks) admitted to the NICU of the university hospital between 1 January 2015, and 31 December 2020, were included in this retrospective, cross-sectional study. Medical records of mothers during pregnancy and babies' detailed NICU admission records were examined in detail. When identifying the reasons for babies' admission, a single basic cause of admission to the hospital was recorded. Babies with major congenital anomalies, diagnosed with genetic syndromes, or referred to another hospital for any reason were excluded from the study. Ethical committee approval was received before the study commenced from Aydın Adnan Menderes University (decision no: 11, date: 22.04.2021).

Definitions

Gestational age was calculated based on the date of the last menstrual cycle and/or fetal ultrasound measurements performed in the first trimester. Babies with birth weights below the 10th percentile for the birth week were defined as small for gestational age (SGA) (6). Respiratory distress was defined as tachypnea commencing immediately after birth, contraction in the respiratory muscles and use of auxiliary respiratory muscles, grunting, cyanosis, apnea, or oxygen requirement. Respiratory distress syndrome (RDS) was diagnosed based on cyanosis, tachypnea (respiratory rate >60 breaths/ min), intercostal retractions, grunting, a diffuse reticulogranular appearance, and air bronchograms on chest X-rays, starting in the first hours after birth and exceeding 24 h in duration. Transient tachypnea of the newborn (TTN) was diagnosed with grunting and tachypnea commencing in the first 6 h after birth

and lasting at least 12 h, together with a pronounced pulmonary vascular bed on lung X-rays, increased aeration, perihilar fullness, and fluid in fissures (7). Pneumonia was diagnosed in the presence of typical lung X-ray findings in respiratory difficulty accompanied by acute phase reactant elevation (7). Meconium aspiration syndrome (MAS) was diagnosed based on amniotic fluid being stained with meconium and an increased oxygen requirement, together with the absence of any pathology capable of causing respiratory difficulty and/or observation of typical radiological changes on chest X-rays (8). Hypoglycemia was defined as venous blood glucose lower than 47 mg/dL (9). Hypoxic-ischemia encephalopathy (HIE) was diagnosed based on Apgar scores of less than 5 at 5 minutes and 10 minutes, presence of marked metabolic acidosis (pH <7.0 or base deficit <12 mmol/L, or both together) in blood gas taken from umbilical cord blood or in the first hour after birth, the observation of neurological findings such as seizure, and multiple organ failure (10). Chorioamnionitis was diagnosed based on maternal body temperature elevation plus at least two or more of the following: maternal leukocytosis (>15,000 cells/mm³), maternal tachycardia (>100 beats/min), fetal tachycardia (>160 beats/min), uterine tenderness or purulent amniotic fluid (11). Infection was diagnosed as a pathological process caused by the invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic organisms. Neonatal sepsis diagnosed as, presence of clinical signs and symptoms of infection (hypotension, seizure, increase oxygen requirement, apnea, intercostal retraction, tachypnea, weak pulse, delayed capillary refill, bradycardia or tachycardia, irritability, hypotonia, lethargy, feed intolerance) and abnormal laboratory results (increased C-reactive protein, leukocytosis or leukopenia, thrombocytopenia, elevated immature: total neutrophil ratio) with or without the presence of positive blood culture (12). Neonatal jaundice was evaluated in line with Turkish Neonatal Society protocols (13).

Statistical Analysis

Statistical analyses were performed using SPSS version 19 software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). Descriptive statistics (kurtosis and skewness), visual methods (histograms), and

analytical tests (Shapiro-Wilk test) were employed to determine the normal distribution of numerical variables. Categorical data were presented as n and %, and numerical data were mean ± standard deviation if normally distributed, and as median values (25-75%) if non-normally distributed. Spearman's correlation test was used for non-normally distributed data. A p-value less than 0.05 was considered statistically significant.

Results

A total of 3,439 neonates were admitted to the NICU during the study period, of which 1,855 (54%) were term. Six hundred thirty-four infants were excluded from the study, and 1,221 term infants were enrolled (Figure 1). The demographic and clinical characteristics of the neonates and mothers included in the study are presented in Tables 1 and 2. The median age of the mothers was 29 (25-33) years, and 91.8% had received regular prenatal follow-up. In addition, 70.2% of births were by cesarean delivery, and 98% of babies were singletons. The babies' median birth weight was 3,560 g (3,210-3,672) and median gestational age was 38 weeks (37-39). Six hundred eighty-three babies (55.9%) were boys (male: female ratio 1.2). Three hundred forty-nine (28.6%) babies were referred from another hospital.

Forty-nine percent of babies were admitted within the first 24 h after birth. Respiratory distress was the most frequent reason for admission (32.7%). TTN was the most common respiratory morbidity (55.6%). The other causes of the admission in respiratory distress group were pneumonia (27.6%), RDS (7%), pneumothorax (6.8%), and MAS (3%). The median admission time among neonates with respiratory morbidity was postnatal 1 (1-3) day. Mechanical ventilation requirement of these neonates was 85%, and 15.1% received surfactant therapy. The median length of stay of the hospital was 5 (3-8) days in respiratory distress group.

The second most common cause of admission to the NICU was neonatal jaundice (30.3%). The median time of admission of babies with jaundice was postnatal 3 (1-5) days. ABO incompatibility was present in 32.4% of these infants, Rh incompatibility in 12.1%, ABO and Rh incompatibility in 2.4%, subgroup incompatibility in 1.9%, glucose 6-phosphate dehydrogenase deficiency in 1.9%, and other causes in 49.3%. The median length of stay in NICU was 3 (2-5) days in



Figure 1. Diagram of inclusion and exclusion

| Table 1. The demographic and clinical characteristics of mothers | | | | |
|--|-------|------|--|--|
| Variable | n | % | | |
| Maternal age (years) | _ | | | |
| <18 | 40 | 3.4 | | |
| 18-34 | 935 | 76.6 | | |
| ≥35 | 245 | 20 | | |
| Parity | | | | |
| Primipara | 455 | 37.2 | | |
| Multipara | 766 | 62.8 | | |
| Assisted reproductive technology | 10 | 0.8 | | |
| Regular prenatal care | 1,121 | 91.8 | | |
| Twin status | 25 | 2 | | |
| Diabetes | 171 | 14 | | |
| With insulin | 39 | 3.2 | | |
| Preeclampsia | 60 | 4.9 | | |
| Hyperthyroidism | 3 | 0.2 | | |
| Hypothyroidism | 86 | 7 | | |
| Placenta previa | 22 | 1.8 | | |
| Placental abruption | 5 | 0.4 | | |
| Premature rupture of membrane | 44 | 3.6 | | |
| Chorioamnionitis | 13 | 1 | | |
| Cardiac disease | 11 | 0.9 | | |
| Autoimmune disease | 11 | 0.9 | | |

neonates with jaundice. Seven neonates (1.9%) with jaundice were treated with exchange transfusion. Kernicterus developed in one baby who was treated with exchange transfusion with a diagnosis of glucose 6-phosphate dehydrogenase deficiency.

One hundred eighty-one (14.8%) neonates were followed up due to neonatal infection. Blood culture positivity was observed in 51 (28.1%) of these infants. The most commonly isolated microorganisms were *Staphylococcus aureus* (21.5%), coagulase-negative *staphylococci* (21.5%), *Escherichia coli* (19.6%) and *Klebsiella pneumoniae* (16.6%).

Ninety-eight (8.1%) of term neonates were admitted with diagnoses of HIE. Sixty-one (62.2%) of these neonates were started on hypothermia therapy. Eighty-seven (88.8%) of the babies with HIE were referred from another hospital, and 62 (63.2%) were born by vaginal delivery. The mean length of hospitalization among these patients was 7 (5-11) days.

Forty patients (3.3%) were admitted due to hypoglycemia, 25 (2.0%) due to SGA, 16 (1.3%) due to feeding problems, and 92 (7.6%) for other reasons (neonatal abstinence syndrome, social indication, admission for some diagnostic tests, cardiac arrhythmia, etc.).

Seven neonates with HIE and seven neonates with sepsis died during the study period and the mortality rate was 1.1%.

Table 2. The demographic and clinical characteristics of term neonates

| Variable | n | % | | | |
|--|-------|------|--|--|--|
| Sex | | | | | |
| Male | 683 | 55.9 | | | |
| Gestational age at birth (weeks) | | | | | |
| 37-38 | 319 | 26.1 | | | |
| 38-39 | 535 | 43.8 | | | |
| 39-40 | 215 | 17.7 | | | |
| 40-41 | 114 | 9.3 | | | |
| 41-42 | 25 | 2 | | | |
| ≥42 | 13 | 1.1 | | | |
| Birth weight (g) | | | | | |
| <2,500 | 92 | 7.5 | | | |
| 2,500-3,990 | 1,050 | 86 | | | |
| ≥4,000 | 79 | 6.5 | | | |
| Mode of delivery | | | | | |
| Cesarean delivery | 858s | 70 | | | |
| Postnatal age at admission (days) | | | | | |
| <24 h | 599 | 49 | | | |
| 24 h-1 week | 366 | 30 | | | |
| 1 week-2 weeks | 103 | 8.5 | | | |
| ≥2 weeks | 153 | 12.5 | | | |
| Reason for admission | | | | | |
| Respiratory distress | 399 | 32.7 | | | |
| Jaundice | 370 | 30.3 | | | |
| Infection | 181 | 14.8 | | | |
| HIE | 98 | 8 | | | |
| Hypoglycaemia | 40 | 3.3 | | | |
| SGA | 25 | 2 | | | |
| Poor feeding | 16 | 1.3 | | | |
| Others | 92 | 7.6 | | | |
| HIE: Hypoxic ischemic encephalopathy, SGA: Small for gestational age | | | | | |

The length of stay in NICU was longer among babies with neonatal infection, HIE, and hypoglycemia than in babies admitted for other reasons (p<0.001) (Table 3). Besides, there was no correlation between the gestational age and length of stay in NICU (r=0.041, p=0.154).

Discussion

Although term babies are regarded as being at low risk of admission to the NICU, 5-18% of these babies

| Table 3. Length of stay in a neonatal intensive care unit | | | | |
|---|----------|----------|--|--|
| Reason for admission Length of stay (days) | | p* | | |
| Respiratory distress | 5 (3-8) | | | |
| Jaundice | 3 (2-5) | | | |
| Infection | 7 (4-9) | <0.001** | | |
| HIE | 7 (5-11) | | | |
| Hypoglycaemia | 7 (4-9) | | | |
| SGA | 4 (3-8) | | | |
| Poor feeding | 3 (2-4) | | | |
| Others | 4 (2-7) | | | |
| HIE: Hypoxic ischemic encephalopathy, SGA: Small for gestational age Data were given as median (25-75 percentile) *Kruskal-Wallis test, **Infection, HIE, and hypoglycemia vs. the other diagnoses | | | | |

are admitted to intensive care (14). Consistent with previous studies, the present study showed that term neonates constituted more than half of NICU admissions (3). An epidemiological study from the USA performed in 2007-2012 reported that babies with a birth weight exceeding 2,500 g constituted more than half of NICU admissions (15). Overall, 1,221 term neonates had been included in the study period. Among them, male neonates were a little more than female neonates, which is consistent with the previous studies (16,17). It was reported that male neonates born at all birth weights had higher mortality rates up to 18 years of age than female neonates (18). The study by Ito et al. (19) reported that the mortality rates of male neonates are higher than the mortality rates of female neonates because of the higher incidence of respiratory and gastrointestinal diseases in male neonates. Moreover, cultural factors could lead to males receiving more consideration from parents than females.

In the present study, the most common cause of admission to NICU was respiratory distress consistent with literature data (16). A cohort study investigating risk factors in NICU admissions in babies with gestational ages exceeding 36 weeks reported that respiratory morbidity represented 49.3% of reasons for admission (20). In the present study, 74% of babies admitted due to respiratory morbidity were born before 39 weeks, 76% were born by cesarean delivery. This may be attributable to antenatal risk factors such as diabetes, preeclampsia, and infection being more frequent among mothers of babies
born before the 39th week of pregnancy and the greater prevalence of cesarean deliveries in births occurring before that week. Horowitz et al. (21) reported an increased incidence of admission due to respiratory distress in births before 39 weeks, and a greater incidence of cesarean delivery among these neonates. The risk of respiratory distress in neonates born by elective cesarean delivery, cesarean delivery performed after the onset of labor, and neonates born by the vaginal delivery equalized in the 39th week (22). Elective cesarean delivery is therefore recommended in the 39th week (23). We think it is important for such information to be provided to parents scheduled for cesarean delivery. In addition, there are many advances to reduce the incidence and severity of respiratory distress including ensuring lung maturation with prenatal steroids, follow-up of highrisk pregnancies in tertiary perinatal centers, and noninvasive mechanical ventilation techniques. In the present study, non-invasive mechanical ventilation support was given to 30% of the neonates' admissions due to respiratory distress which is consistent with previous studies (24).

Neonatal jaundice was the second most frequent reason for admission to NICU, at a rate of 30.3% in this study. The rate of admission to the NICU due to indirect hyperbilirubinemia has increased following the shortening of postpartum hospital stay (25). Indirect hyperbilirubinemia is one of the most common neonatal problem and can give rise to severe conditions such as kernicterus (26). Exchange transfusion was performed in one patient diagnosed with glucose 6-phosphate dehydrogenase deficiency in the present study, but due to late presentation, kernicterus development could not be prevented. A retrospective cohort study from the UK reported that birth after the 37th gestational week increased the incidence of admission to intensive care due to jaundice (3). Before discharge, it is important for parents to be informed about neonatal feeding and jaundice, particularly in the presence of risk factors, and concerning when the baby should be brought for control examination (13).

In the present study, 14.8% of neonates were admitted due to neonatal infections. Neonatal infections are still an important cause of morbidity and mortality in the neonatal period in both developed and developing countries (27). Yang and

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Meng (16) reported a rate of 6.5% for admission to the NICU among term babies because of neonatal infections. Despite all the many advances in the field of neonatology, neonatal infections retain their clinical importance because there is no finding entirely showing infection, and due to the lack of a specific marker showing neonatal infection. Rapid initiation of empiric antibiotic therapy in case of suspected infection can be life-saving. Antenatal prophylaxis, hand washing, using an aseptic technique during invasive procedures, infection control education of all staff, and the determination of hospital infectious agents and sensitivity rates play a leading role in infection control policies. In the present study, seven babies died due to neonatal sepsis. Eighty-five percent of these babies had been referred to our NICU from another hospital. Therefore, we think that this situation may have caused a delay in the initiation of empirical antibiotic therapy and appropriate treatment.

The incidence of HIE is 1.5 per 1,000 live births in developed countries (28). According to Turkish Neonatal Society HIE Working Group data, the incidence of HIE in babies with gestational ages >37 weeks is 2.6 per 1,000 live births (29). In the present study, 8.1% of babies were admitted due to HIE. It was noteworthy that 90% of the babies in this patient group had been referred from other hospitals, and that while the rate of vaginal delivery among all babies was 29.8%, the rate was 63% in these infants. Martinez-Biarge et al. (30) reported a higher risk of HIE in vaginal births compared to elective cesarean births. A similar risk of HIE has been reported in operative vaginal deliveries and emergency cesarean section with full cervical dilation (31). In the present study, none of the neonates treated with hypothermia were born by elective cesarean section. The study investigating the intrapartum risk factors for HIE reported that operative vaginal delivery (2.34) and emergency cesarean section (2.17) were both associated with an increased risk of encephalopathy compared to spontaneous vaginal delivery (32). In addition, considering the heterogeneity of the etiological causes and possible relations with the antepartum period, elective cesarean delivery is not recommended to reduce the risk of asphyxia (33). Due to the lack of data on an operative vaginal delivery, no comment could be made on this subject in the present study. Seven babies died from HIE in this study. Identifying at-risk pregnant, intrauterine transport of infants, appropriate antenatal care of the mother, and the provision of periodic neonatal resuscitation program training sessions for health personnel can all be effective in reducing perinatal asphyxia-related mortality (34,35).

The fact that one-third of the term neonates admitted to the NICU were followed up less than three days suggests that the admission criteria for term babies need to be reviewed in this study. In a cohort study in which 19 NICUs were examined retrospectively, babies born at gestational weeks between 35-42 and admitted to the NICU were investigated, and no identifiable cause was found in 10.8% of patients (36). In addition, intensive care admission can be prevented by various antenatal procedures in some term babies. Considering that admitting babies to the NICU represents a significant source of anxiety for families, babies being followed up in the same room with their mothers, if babies expected to be admitted for short periods, will contribute to bonding between mother and the baby and maintenance of feeding of infant (37).

The present study had a few limitations. The study involves results from a single-center it reflects data from the local region, and the results may not, therefore, be capable of being generalized to the entire population. Moreover, kernicterus developed in one baby in this study. Since kernicterus can also be diagnosed at post-discharge follow-up, our findings may not reflect the true results. In addition, this study was unable of measuring results beyond the NICU admissions.

Conclusion

Term neonates represent a significant proportion of admissions to the NICU. This study reported the clinical characteristics and reasons for admission of term babies. In light of the reasons for admission of term neonates, we think that various antenatal measures and parental education may help reduce the incidence of admission among these babies. We think that evaluation of the reasons for term neonate admissions and the measures to be taken to reduce the rate of admission of these babies in our country, in which the number of NICU beds is critical, is a matter of considerable importance. Reducing the incidence of hospitalization of term neonates will reduce morbidity and complications during admission and lower costs, as well as preventing the adverse consequences of separating mother and baby.

Ethics

Ethics Committee Approval: Ethical committee approval was received before the study commenced from Aydın Adnan Menderes University (decision no: 11, date: 22.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.A., D.İ.G., A.B.A., G.E., Design: A.A., D.İ.G., A.B.A., G.E., Supervision: A.A., D.İ.G., G.E., Data Collection or Processing: A.A., D.İ.G., G.E., M.K.T., Analysis or Interpretation: A.A., D.İ.G., G.E., M.K.T., Literature Search: A.A., D.İ.G., G.E., M.K.T., Writing: A.A., D.İ.G., G.E., M.K.T., Critical Review: A.A., D.İ.G., G.E., M.K.T.

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Validity of Metric Assessment of Mastoid Triangle in Sex Determination: An Anatomical Study

Cinsiyet Belirlemede Mastoid Üçgenin Metrik Değerlendirmesinin Geçerliliği: Anatomik Bir Çalışma

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Keywords

Mastoid triangle, sexual dimorphism, skull, temporal bone

Anahtar Kelimeler

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Abstract

Objective: This study aimed to evaluate the validity of the mastoid triangle anthropometric measurements and area between the three craniometric points, namely porion (po), asterion (ast), and mastoidale (ms) as a sex determinant.

Materials and Methods: A total of 60 dry skulls (30 males and 30 females) were assessed for 10 morphometric measurements with a compass, and a total of 120 mastoid triangles were evaluated.

Results: Statistically significant differences were found in all the mastoid triangle measurements between males and females ($p \le 0.01$). Discriminant function analyses revealed that the left po-ms length and the total area of the mastoid triangle were two variables with the highest sensitivity at an accuracy rate of 90%. The models with three mastoid triangle variables including the total po-ms, total ms-ast, and total po-ast measurements, in combination, provided high discriminant potentials of 96.7% and 93.3% in females and males, respectively. When the total po-ms, total ms-ast, and total po-ast were used together, a greater sexual dimorphism was observed, correctly classifying the sex with a 95% accuracy rate. The mean value of the total area which is preferred due to the asymmetry between the sides of the skull was 1455.2 mm² in males and 1341.2 mm² in females.

Conclusion: In the light of the obtained results, the discriminant function analyses of the mastoid triangle measurements are concluded to be reliable in sex determination and preferable in forensic medicine and anthropology.

Öz

Amaç: Bu çalışmanın amacı, porion (po), asterion (ast) ve mastoidale (ms) olmak üzere üç kraniyometrik nokta arasındaki mastoid üçgen antropometrik ölçümlerinin ve alanının cinsiyet belirleyicisi olarak geçerliliğini değerlendirmektir.

Gereç ve Yöntemler: Toplam 60 kuru kafatası (30 erkek ve 30 kadın) kullanılarak kaliper ile on adet ölçüm gerçekleştirildi, 120 mastoid üçgen değerlendirildi.

Bulgular: Erkekler ve kadınlar arasında tüm mastoid üçgen ölçümlerinde istatistiksel olarak anlamlı farklılık bulundu (p≤0,01). Diskriminant fonksiyon analizinde sol poms uzunluğu ve mastoid üçgenin toplam alanının %90 doğruluk oranıyla en yüksek duyarlılığa sahip iki değişken olduğu bulundu. Toplam po-ms, toplam ms-ast ve toplam po-ast ölçümlerini bir arada içeren üç mastoid üçgen değişkenli modeller,

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kadınlarda ve erkeklerde sırasıyla %96,7 ve %93,3'lük yüksek diskriminant potansiyeli sağladı. Total po-ms, total ms-ast ve total po-ast birlikte kullanıldığında, cinsiyeti %95 oranında doğru sınıflandıran daha fazla cinsel dimorfizme sahiptiler. Kafatası kenarları arasındaki asimetri nedeniyle tercih edilen toplam alanın ortalama değeri erkeklerde 1455,2 mm², kadınlarda 1341,2 mm² olarak bulundu.

Sonuç: Elde edilen sonuçlar ışığında mastoid üçgen ölçümlerinin diskriminant fonksiyon analizlerinin cinsiyet belirlemede güvenilir, adli tıp ve antropolojide tercih edilebilir olabileceği sonucuna varılabilir.

Introduction

Clinically, knowledge of the morphometric assessment of the cranium may be important for neurosurgeons so that they may avoid inadvertent procedures during various surgical approaches (1,2). More importantly, skeletal features of the cranium are considered important in terms of sex determination in legal medicine and forensic anthropology. Thus, it is of great importance for paleoanthropologists to identify sex confidentially by using skeletons, which constitutes the basis for later evaluations. In particular, discriminant function analysis of the human skull has become important in legal medicine and forensic anthropology (3-5). Classically, two methods have been used for sex determination based on bone characteristics, that is, morphological (non-metrical) and metrical (5,6).

The results of morphometric measurements on the bones in sex determination are of great importance at all times. Therefore, we aimed to perform a morphometric method easily applicable with high accuracy and very little observer error in this study. Processus mastoideus and the surrounding space can be used for sex determination. Since recent studies focused on whether the landmark of asterion (ast) was reliable, we investigated its role in sex determination (3,7,8). Many authors have drawn attention to preservation of the petrous portion of the temporal bone and its use in identity and sex determination. Compact structure and protected position of the petrous bone at the base of the skull have made it preferable in sex determination (1,3,9). As a result of these craniometric features, the mastoid triangle is an important anatomic area in terms of sex determination.

In this study, the method was based on measurements of the distances between three craniometric points, easily identified as porion (po), ast and mastoidale (ms). The measurements of the triangle drawn between these three points and the measurement of the triangular area were used to identify sex (3,7,8).

Materials and Methods

We performed morphometric measurements of 60 adult craniums which belonged to 30 females and 30 males in the Laboratory of the Department of Anatomy, Aydın Adnan Menderes University Faculty of Medicine, Aydın, Turkey. The skulls with intact craniometric points and with no evidence of trauma or deformations in the mastoid space were selected for this study.

Metric Assessment of Mastoid Triangle

In this study, a total of 10 randomly selected craniums were assessed independently by two examiners with regard to parameters. A week later, the same measurements were repeated and interand intraobserver reliability were assessed. Thus, a total of 120 mastoid triangles were assessed by a single observer to minimize observer error on the right and left side. The mastoid triangle was defined by between three points; po the superior surface of the meatus acusticus externus, as the craniometric point at the junction of the sutura lambdoidea, sutura occipitomastoidea, sutura parietomastoidea, and ms the lowest craniometric point at the mastoid process (Figure 1). The po, ast and ms both on the right and left sides were identified in each skull and the mastoid triangle was obtained when three lines were drawn between these three points. Dimensions of the triangle were measured with a compass sensitive at 0.01 mm, similar to those of (8,10). Measurement results were expressed in mm and mm².

Linear measurements of the triangle were as follows: Po-ms, distance between po and ast; msast, distance between ms and ast; po-ast, distance between po and ast. Firstly, the circumferences (C) of the triangles both on the right and the left were measured and each triangular area was estimated based on the Heron's formula, as described below (8). Heron's formula: A = V [s(s-a) (s-b) (s-c)]

A= triangular area, a: po-ms distance, b: ms-ast distance, c: po-ast distance, s; semi-circumference of the triangle calculated with s=(a+b+c)/2

Then, similar measurements obtained from the right and left sides of the same cranium were summed and total po-ms distance, ms-asc distance, po-ast distance, mastoid triangle circumference and area were calculated according to the method described by de Paiva and Segre (11). The calculated measurements were as follows: total po-ms, sum of right and left po-ms distances; total ms-ast, sum of right and left ms-ast distances; total po-ast, sum of right and left po-ast distances; mastoid triangle circumference, three dimensions of the triangle on one side (po-ms + ms-ast + po-ast); total circumference, the sum of the C of the



Figure 1. Mastoid triangle drawn between three points; asterion, porion and mastoidale, lateral view of the skull

right and left mastoid triangles; mastoid triangle area based on Heron's formula using semi-circumference; and total area, sum of right and left mastoid triangles area on the same cranium.

Statistical Analysis

Statistical Package for Social Sciences (Version 18.0, SPSS Inc., Chicago, IL, USA) software was used for analysis of the data obtained in this study. The normality of the data was evaluated with the Shapiro-Wilk test and expressed as the mean ± standard deviation (SD) since all of them showed normal distribution. Statistical difference was evaluated with Student's t-test between genders and paired t-test between right and left sides. Discriminant function analysis was performed to determine the effectiveness of parametric variables in separating genders from each other.

Results

In this study, all measured and calculated parameters of which are mean, SD, minimum and maximum values are given in Table 1, were found to be statistically significant higher in males than females with a 95% confidence interval ($p \le 0.01$). In Table 2, gender specific Student's t-test values of the measurements are shown. The results of paired t-test used to detect differences according to right and left sides are presented in Table 3. As shown in the Table 3, there was not a significant difference between any of the individual mastoid triangle measurements in both males and females (p > 0.05). Regardless of gender

| Table 1. Summary statistics of parametric measurements by gender, right and left sides | | | | | | |
|---|------------------------------------|---------------|-----------------|--------------------------------------|-----------------|-----------------|
| Measurements | Male (n=30) Mean ± SD (min-max) | | | Female (n=30) Mean ± SD (min-max) | | |
| | Right | Left | Total | Right | Left | Total |
| Po-ms | 32.2±3.2 (26.6- | 32.2±3 | 64.7±6.0 | 26.1±3 | 26.8±2.1 (20.8- | 52.9±4.7 (40.8- |
| | 40.7) | (28.9-41) | (55.6-81.7) | (20.0-30.6) | 29.8) | 59.8) |
| Ms-ast | 49.8±5.7 | 48.7±4.8 | 98.5±10.1 | 46.3±4.5 | 45.4±4.5 | 91.7±8.5 (70.5- |
| | (36-61) | (41-62.7) | (79.5-123.7) | (35-56.8) | (35.5-55.8) | 112.6) |
| Po-ast | 46.6±3.2 | 47.3±2.6 | 93.9±5.0 | 42.9±2.7 | 42.8±3.3 | 85.7±5.2 |
| | (41-55) | (42-53.6) | (85-105.5) | (36.0-48.5) | (35.4-48) | (71.4-94.3) |
| с | 128.6±10.2 | 128.6±9.1 | 257.2±18.2 | 115.3±8.1 | 115±8.6 | 230.3±15.5 |
| | (107.8-151.7) | (112-150.2) | (224.6-294.8) | (92.4-131) | (93.7-128.4) | (186.1-259.4) |
| A | 723.9±111.5 | 731.3±103.4 | 1455.2±201.2 | 545.6±77.9 | 556.8±73.5 | 1102.3±137.4 |
| | (516.4-1050.4) | (563.5-963.7) | (1107.3-1990.9) | (361.8-678.9) | (382.7-662.3) | (744.4-1341.2) |
| SD: Standard deviation, min: Minimum, max: Maximum, po-ms: Porion, ms-ast: Mastoidale asterion, po-ast: Porion, C: Mastoid triangle circumference, A: Mastoid triangle area | | | | | | |

| Table 2. The distribution of gender specific differences by measurements | | | | |
|--|-------|-------|----|---------------------|
| Measurements | Side | t | df | p (sig. two tailed) |
| Do mo | Left | 8.514 | 58 | p<0.01 |
| Po-ms | Right | 7.719 | 58 | p<0.01 |
| Die och | Left | 2.723 | 58 | p<0.01 |
| IVIS-ASL | Right | 2.627 | 58 | p<0.01 |
| | Left | 5.957 | 58 | p<0.01 |
| PO-ast | Right | 4.769 | 58 | p<0.01 |
| Cincumference | Left | 5.951 | 58 | p<0.01 |
| Circumference | Right | 5.612 | 58 | p<0.01 |
| A | Left | 7.537 | 58 | p<0.01 |
| Area | Right | 7.181 | 58 | p<0.01 |
| Total po-ms | | 8.524 | 58 | p<0.01 |
| Total ms-ast | Both | 2.804 | 58 | p<0.01 |
| Total po-ast | both | 6.226 | 58 | p<0.01 |
| Total circumference | | 6.152 | 58 | p<0.01 |
| Total area | | 7.934 | 58 | p<0.01 |
| | | | | |

Po: Porion, ms: Mastoidale, ast: Asterion, t: The test statistics, df: The degrees of freedom for the test, Sig.: Significance. The p-value corresponding to the given test statistic t with degrees of freedom df

| Table 3. Distribution of the side differences by gender | | | | | |
|--|---------|-------|----|---------------------|--|
| Measurements | Gender | t | df | p (Sig. two tailed) | |
| | Males | 0.923 | 29 | 0.364 | |
| po-ms | Females | 1.978 | 29 | 0.058 | |
| Ma ast | Males | 1.877 | 29 | 0.071 | |
| IVIS-dSL | Females | 1.619 | 29 | 0.116 | |
| | Males | 1.347 | 29 | 0.188 | |
| po-ast | Females | 0.321 | 29 | 0.751 | |
| Circumforonco | Males | 0.032 | 29 | 0.975 | |
| Circumierence | Females | 0.277 | 29 | 0.784 | |
| A + 00 | Males | 0.536 | 29 | 0.596 | |
| Area | Females | 0.961 | 29 | 0.344 | |
| Po: Porion, ms: Mastoidale, ast: Asterion, t: The test statistics, df: The degrees of freedom for the test, Sig.: Significance. The p-value corresponding to | | | | | |

Po: Porion, ms: Mastoidale, ast: Asterion, t: The test statistics, df: The degrees of freedom for the test, Sig.: Significance. The p-value corresponding to the given test statistic t with degrees of freedom df

(n=60), there were no significant side differences except for two lengths of the triangles. As seen in Table 4, only po-ms and ms-ast were statistically different between the left and right sides.

The results of the discriminant function analysis performed to determine the importance of the measurements in terms of sex determination are given in Table 5. Discriminat analysis showed that left po-ms and total area values were the most reliable variables at an accuracy rate of 90%. The second and third most reliable variables were total po-ms at an accuracy rate of 88.3% and right and left triangular area at an accuracy rate of 83.3% respectively. Besides, the least reliable measurement in sex determination was found to be right ms-asth distance at an accuracy rate of 63.3%. The second and the third least reliable measurements were left ms-ast at an accuracy rate of 66.7% and total ms-ast at an accuracy rate of 68.3% respectively. Overall, the discriminant function of the individual measures from the female skulls yielded a

| Table 4. The distribution of side differences regardless of gender | | | | |
|--|-------|----|---------------------------|--|
| Measurements | t | df | p value (Sig. two tailed) | |
| Po-ms | 2.105 | 59 | 0.040 | |
| Ms-ast | 2.497 | 59 | 0.015 | |
| Po-ast | 0.725 | 59 | 0.472 | |
| Circumference | 1.039 | 59 | 0.828 | |
| Area | 0.219 | 59 | 0.303 | |

Po: Porion, ms: Mastoidale, ast: Asterion, t: The test statistics, df: The degrees of freedom for the test, Sig.: Significance. The p-value corresponding to the given test statistic t with degrees of freedom df

| Accuracy rates of discriminate function (%) | | | |
|---|--------|------|-------|
| Measurements | Female | Male | Total |
| Left po-ms | 96.7 | 83.3 | 90.0 |
| Left ms-ast | 70.0 | 63.3 | 66.7 |
| Left po-ast | 70.0 | 80.0 | 75.0 |
| Left circumference | 73.3 | 73.3 | 73.3 |
| Left area | 86.7 | 80.0 | 83.3 |
| Right po-ms | 83.3 | 80.0 | 81.7 |
| Right ms-ast | 66.7 | 60.0 | 63.3 |
| Right po-ast | 73.3 | 73.3 | 73.3 |
| Right circumference | 76.7 | 76.7 | 76.7 |
| Right area | 83.3 | 83.3 | 83.3 |
| Total po-ms | 90.0 | 86.7 | 88.3 |
| Total ms-ast | 73.3 | 63.3 | 68.3 |
| Total po-ast | 80.0 | 70.0 | 75.0 |
| Total circumference | 80.0 | 83.3 | 81.7 |
| Total area | 96.7 | 83.3 | 90.0 |
| Total po-ms, ms-ast, po-ast | 96.7 | 93.3 | 95.0 |
| Left and right po-ms | 96.7 | 83.3 | 90.0 |

higher accuracy rate of sex determination and so did the discriminant function of multiple variables.

Accuracy rates increased when more than one measure of the mastoid triangle especially total values of all three dimensions of both the left and the right triangles, i.e. total po-ms, ms-ast and po-ast was used. It was striking that the measure of the right and left po-ms had a high accuracy rate without ast. The discriminant function of total po-ms, total ms-ast and total po-ast provided accuracy rates of 96.7% and 93.3% for sex determination in females and males respectively. An overall assessment showed that the individual measurements had a higher discriminant function in the females and the multiple variables yielded similarly higher rates of accuracy in the females.

Discussion

When one has to determine sex of a skeleton dating back to old times and broken into pieces, both morphological and metric features of the skeleton can be utilized (5,6). In this study, measurements of the mastoid triangle in skulls were evaluated for sex determination.

Many authors have proposed that an analysis of characteristics of the mastoid process is an indicator

of sexual dimorphism (9). There have been studies on the presence of sexual dimorphism in the mastoid triangle with conflicting results (8,10). Some authors described morphologic indicators from South African indigenous skulls different from the classic indicators described by Krogman (12). Kemkes and Gobel (8) did not obtain accuracy rates sufficient to discriminate sex from the mastoid triangle; they reported a better sensitivity of the method in females. On the other hand, Suazo et al. (10) drew the conclusion that the mastoid triangle was underestimated in sex determination inwomen, hence being of less utility in practice, which is not compatible with the results of the present study. Our results differ from them but similar to de Paiva and Segre (11). Consistent with the results of a study by de Pavia and Segre (11), we found that mastoid triangle dimensions had a high rate of discriminant function for sex determination. In fact, we found significant differences not only in the total triangle area but also all dimensions and the circumference of the triangle between male and female skulls (p<0.01). We think that the real indicator should have an application in sex determination and a good sensitivity in both sexes.

In the current study, we used the same compass as the one described by Kemkes and Göbel (8) and Suazo at al. (10). However, de Paiva and Segre (11) used a xerographic copy of a structure of certain convexity and all of them are lineal dimensions. de Paiva and Segre (11) reported that the mean total area, which is the preferred measurement because of the asymmetry between the sides of the skull, was 1505.32 mm² for male skulls, which was greater than the maximum value obtained in the female skulls. In this study the mean total area for female skulls was 1221.24 mm², which was lower than the minimum total area for the male skulls, which is consistent with the results of the study of de Paiva and Segre (11). In fact, we found that the mean total cranial area was 1455.2±201.2 mm² in the males, which was larger than the maximum total cranial area in the females and that the mean total cranial area was 1102.3±137.4 mm² in the females, which was smaller than the minimum total cranial area in the males (1107.3 mm²). de Pavia and Segre (11) noted that values of \geq 1447.40 mm² for the total triangle are typical of male crania, while values of ≤1260.36 mm² are indicative of female skulls at a confidence interval of 95%.

Discriminant analysis, made to determine which parameter better differentiates gender, showed that using more than one measure of the mastoid triangle, i.e., summation of three dimensions of the triangles on the left and the right yielded an accuracy rate of 95% for sex determination. Toneva et al. (13) measured mastoid triangle edge and area values in 148 computed tomography scans in Bulgarians, and performed discriminant function analysis to investigate the usability of these measurements in sex determination. They found that the po-mastoidal distance was statistically higher on the right side in males unlike our study. Besides, they found that mastoid triangle edge and area measurements were significantly different in both genders, similar to our study. The mastoid triangle dimensions showed sufficient discriminating power for sex estimation among Bulgarians (up to 89%), and the total mastoid triangle area is found to be the best single-sex discriminating trait (13). Another study (14) using a total of 102 lateral cephalograms in Nigerians, reported that the only mean values of the ast-ms distance and mastoid triangle area were found to be higher in males than females. Sinhorini et al. (2) reported that the use of mastoid triangle parameters had an accuracy of 80.8% for sex estimation in a hundred Brazilian skulls.

In our study, the mean total cranial area in both females and males overlapped and therefore, it is not a cranial feature than can be used for sex determination. To the best of our knowledge, however, this is the first study reporting the metric assessment of the mastoid trianglein Turkish population for sex determination in forensic medicine and anthropology.

The ast has got various positions. Its reliability has been put into question due to its population-specific variability in position (15). Kemkes and Gobel (8) emphasized that variability of the location of the ast lessened the value of the mastoid triangle as a marker of sex determination. Therefore, we performed a discriminant analysis of po-ms only without the ast and found that it had a high discriminant capability at a rate of 90%. Discriminant function of the measures including the ast was the least reliable for sex determination. In fact, the least reliable mastoid triangle dimension was the right ms-ast at a rate of 63.3%, followed by left ms-ast at a rate of 66.7% and total ms-ast at a rate of 68.3%.

Conclusion

The results of the present study underline the role of the mastoid triangle in sex determination. It can be concluded that several metric values of the cranium can be reliable and yield a high rate of accuracy in paleoanthropological studies when morphological features of the bones such as the cranium cannot be used or when these bones have suspicious features.

Ethics

Ethics Committee Approval: Ethics committee approval is not required to carry out this study.

Informed Consent: Informed consent approval is not required to carry out this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.K.B., N.G.Ç., M.T., Design: H.K.B., N.G.Ç., M.T., Supervision: H.K.B., N.G.Ç., M.T., E.D.İ., Fundings: H.K.B., N.G.Ç., M.T., Materials: H.K.B., N.G.Ç., M.T., E.D.İ., Data Collection or Processing: E.D.İ., G.S., Analysis or Interpretation: H.K.B., N.G.Ç., M.T., E.D.İ., G.S., Literature Search: H.K.B., N.G.Ç., M.T., E.D.İ., G.S., Writing: H.K.B., N.G.Ç., M.T., E.D.İ., G.S., Critical Review: H.K.B., N.G.Ç., M.T., E.D.İ., G.S.

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The Relationship Between the Activity Level, Internet Addiction, and Depressive Symptoms of University Students During the Coronavirus Disease-2019 Outbreak Cross-Sectional Study

Koronavirüs Hastalığı–2019 Salgınında Üniversite Öğrencilerinin Aktivite Düzeyi, İnternet Bağımlılığı ve Depresif Belirtiler ile İlişkisi: Kesitsel Çalışma

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Keywords

Physical activity, internet addiction, depressive symptoms, COVID-19 outbreak, university student

Anahtar Kelimeler

Fiziksel aktivite, internet bağımlılığı, depresif belirtiler, COVID-19 salgını, üniversite öğrencisi

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Abstract

Objective: The coronavirus disease-2019 (COVID-19) pandemic significantly disrupted normal activities globally. Social restriction measures were encountered during the pandemic process, which resulted in students staying at home for a long time. This study aimed to investigate the relationship between physical activity, internet addiction, and depressive symptoms of university students during the COVID-19 pandemic.

Materials and Methods: This cross-sectional study was conducted with 160 students studying at Aydın Adnan Menderes University Söke Health Services Vocational School between July and August 2020. A Personal Identification Form, Short Form of Young's Internet Addiction Test, Beck Depression Scale, and International Physical Activity Questionnaire (IPAQ) were used to collect the research data. Spearman correlation test and Student's t-test were used for data analysis.

Results: The IPAO revealed that 28.2% of the students were active. The students' mean depression scores were 8.8 ± 6.6 (0-37) and the internet addiction mean score was 25.1 ± 7.2 (12-47). A moderately significant positive correlation was found between the mean scores of internet addiction and depressive symptoms (r=0.303; p<0.01). No difference was found between the mean scores of depressive symptoms and internet addiction in active and inactive students (p>0.05). Contrarily, a relationship was determined between internet addiction and depressive symptoms. **Conclusion:** Improving the physical and psychological health of university students during the pandemic process is important for public health. Therefore, various multi-sectoral approach developments, such as online physical activity programs, are recommended. Additionally, students should be made aware of how to balance the time spent in front of the computer or the internet.

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) pandemisi, küresel olarak normal aktiviteleri önemli ölçüde bozmuştur. Pandemi sürecinde karşımıza çıkan sosyal kısıtlama önlemleri öğrencilerin uzun süre evde kalmasını gerekli kılmıştır. Çalışmanın amacı, COVID-19 pandemisinde üniversite öğrencilerinde fiziksel aktivite düzeyi, internet bağımlılığı ve depresif belirtiler arasındaki ilişkiyi incelemektir.

Gereç ve Yöntemler: Bu kesitsel çalışma, Temmuz ve Ağustos 2020 tarihleri arasında Aydın Adnan Menderes Üniversitesi Söke Sağlık Hizmetleri Meslek Yüksekokulu'nda okuyan 160 öğrenci ile yapıldı. Araştırma verileri Birey Tanıtım Formu, Young İnternet Bağımlılığı Testi Kısa Formu, Beck Depresyon Ölçeği ve Uluslararası Fiziksel Aktivite Anketi (IPAQ) kullanılarak toplandı. Veri analizi için Spearman korelasyon testi ve Student's t-testi kullanıldı.

Bulgular: Öğrencilerin %28,2'sinin IPAQ'a göre aktif olduğu belirlendi. Öğrencilerin depresyon puan ortalamaları 8,8±6,6 (0-37), internet bağımlılığı puan ortalamaları 25,1±7,2 (12-47) olarak saptandı. İnternet bağımlılığı puan ortalamaları ile depresyon puan ortalamaları arasında pozitif yönde orta derecede anlamlı bir ilişki tespit edildi (r=0,303; p<0,01). Aktif olan öğrenciler ile inaktif olanlar karşılaştırıldığında depresyon ve internet bağımlılığı puan ortalamaları arasında fark bulunmadı (p>0,05). Buna karşın internet bağımlılığı ile depresif belirtiler arasında ilişki olduğu belirlendi.

Sonuç: Pandemi sürecinde üniversite öğrencilerinin fiziksel ve psikolojik sağlık durumlarını geliştirmek halk sağlığı açısından önemlidir. Bunun için online fiziksel aktivite programları gibi çeşitli çok sektörlü yaklaşımların geliştirilmesi önerilmektedir. Ayrıca bilgisayar ya da internet başında geçirilen sürenin dengeli olması konusunda öğrenciler bilinçlendirilmelidir.

Introduction

Coronavirus disease-2019 (COVID-19) emerged in Wuhan, China in December 2019 and started to spread rapidly in many countries (1). COVID-19 is not only a health problem, but it also brings about serious economic, educational, and social consequences. Understanding the behavioral and mental health consequences of this crisis is critical in order to be ready for future pandemics. There have been changes in the mental health levels around the world during the COVID-19 pandemic (2,3).

University students are a particular social group that is under pressure from all aspects in their daily life, educational life, and emotions. Because of the immaturity of their psychological development and variability in their emotions, psychological conflicts often arise when they are faced with a problem of physiological, psychological, and social adaptation (1). Fear, anxiety, and other negative emotions are more likely to occur in a sudden, life-threatening, and uncertain situation. Young people subjected to social isolation measures during the COVID-19 pandemic period were forced to leave their friends and school environments (2). In China in January 2020, and then in the United States, Italy, Spain, England, and Turkey, among many others, distance education has replaced in-class education in many universities. Young people, who usually have an active lifestyle, have suddenly started to spend most of the day on computers and

smartphones. Young people, who already spend most of their time on digital platforms, have increased their screen time with distance education. It is stated that this situation will create a basis for further increase in internet addiction in youngsters (4). The impact of the COVID-19 epidemic on university students in China, an increase in anxiety and depression levels has been reported in university students due to social isolation (5). In additionaly studies have shown that depressed people are more likely to suffer from social media addiction. For example, depression has been shown to be positively associated with Facebook addiction (6) and mobile phone addiction (7). Despite the positive effects of social isolation on the spread of the disease, the potential increase in sedentary behavior due to isolation can be harmful to health (8). Especially increased sitting time decreases regular physical activity, which, in addition to the development of chronic health problems (9), can lead to an increase in anxiety, stress, and depression, and a decrease in mental health and psychological vitality (10).

There exist few studies on the mental health conditions and internet addiction of university students who are subjected to the pandemic. Although there are studies examining the physical activity levels of university students during the pandemic period (11), there exists no study regarding the relationship between depression, internet addiction, and physical activity levels during social isolation periods due to the pandemic. In this study, it was aimed to examine the relationship between physical activity levels, internet addiction, and depressive symptoms in university students exposed to social isolation during the COVID-19 pandemic.

Materials and Methods

Study Design and Setting

This cross-sectional study was conducted in students at Aydin Adnan Menderes University Söke Health Services Vocational School between July and August 2020. The participants eligible for inclusion were students who agreed to participate in the research by giving verbal consent and filled the forms completely. We excluded individuals who had disabilities, language problems and not internet access.

Sampling Description

The total number of students registered at the school was 640. A minimum sample size of 138 students was calculated using the G*Power v.3.1 software based on previous research (12) and assuming a 95% statistical power, α =0.05 with type 1 error frequency, and 0.3 effect size. Due to the possibility of 15% loss, 160 students were planned to include in the study. Students were randomly selected from their attendance lists.

Data Collection and Processing

A semi-structured questionnaire form was used to collect data from students by sending questionnaires to their e-mail addresses. Each student was given a due date to return the questionnaire. If the questionnaire was not returned by the deadline, or an incomplete questionnaire was returned, the questionnaire was sent again. After this reminder, all of the students returned the questionnaire.

The questionnaire form consisted of four major sections: 1) Personal Identification Form, 2) Short Form of Young's Internet Addiction Test (YIAT-SF), 3) Beck Depression Scale (BDS), 4) The International Physical Activity Questionnaire (IPAQ).

Personal Identification Form

This form included questions about students' age, sex, education, height, weight, place of residence, presence of a diagnosed disease, medication use, presence of any disability, time spent sitting during the day and night, day sleep times, time spent in front of TV, time spent on social media, time spent at home, presence of changes in weight during COVID-19, and regular exercise status before the pandemic.

Short Form of Young's Internet Addiction Test

YIAT-SF consists of 12 items on a 5-point Likert scale ranging from 1 (rarely) to 5 (always). The total score of the test ranges from 12 to 60 and represents an individual's tendency to internet addiction. In this study, we used a Turkish adaptation of the test (13).

Beck Depression Scale

The severity of depressive feelings was evaluated by the BDS. The Turkish adaptation of the scale was performed by Aydemir and Köroğlu (14). This scale consists of 21 questions, each with four possible answers (score: 0-3). Higher total scores indicate increased depressive symptoms [minimum (min): 0, maximum (max): 63]. Cut of point was determined as 17.

The International Physical Activity Questionnaire

The Turkish adaptation of the scale was performed by Karaca and Turnagöl (15). Following standard IPAQ procedures, the number of days was multiplied by the number of hours reported for each component in order to calculate metabolic equivalent (MET) scores. Activity categories (inactive, active, and very active) were determined based on the total MET scores. Those who were not designated as active and very active were considered to be inactive.

Statistical Analysis

The SPSS software version 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA) was used for statistical analysis. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. After examining the normality of distributions of the responses, descriptive statistics are presented as means ± standard deviation (min-max) and median values for continuous variables and as percentages for the categorical variables. Correlation between depression and internet addiction scores were analyzed by Spearman correlation statistics. The relationship between depression and internet addiction scores between inactive and active students was evaluated with the Student's t-test. A 5% type 1 error level was used to infer statistical significance.

Ethical Issues

This research was conducted in adherence to the Declaration of Helsinki. Prior to the research, the students provided their informed consent and participated in the study on a voluntary basis. The study was approved by Faculty of Medicine Non-Invasive Clinical Research Ethics Committee of a Aydın Adnan Menderes University in Turkey (protocol no: 2020/95, date: 04.06.2020). The participants were informed about the objectives of the study and that their confidentiality would be respected and their responses would not be judged.

Results

It was found that 63.8% of the participants were women, 97.5% were living with their families, 98.8% were associate degree graduates, and 96.3% did not have a physician-diagnosed disease and did not use any drug regularly.

As seen in Table 1, the mean body mass index was within normal limits. When the BDS and YIAT-SF lower and upper limit values were considered, it was seen that the mean BDS was quite low and the mean YIAT-SF was moderate.

As shown in Table 2, the students stated that they were at home for an average of 87.3±35.0 days from the beginning of the pandemic until the date of the

study; 5.6% were obese and 15.6% were overweight according to their declared weight and height measurements. It was found that 38.1% (n=61) of the university students sleep during the day and the average sleeping time during the day was 3.8 ± 2.4 (1-12) hours; the average sleeping time at night was 7.0 ± 2.2 (0-10) hours; the time spent sitting during the day was 7.3 ± 3.0 (1-16) hours; the time spent in front of the television was 1.5 ± 1.6 (0-10) hours; and, the time spent on the computer/phone was 4.7 ± 2.6 (0-15) hours.

According to the IPAQ, 71.8% of the students were inactive, and only 28.2% of them were active or highly active during the restriction period. Depressive symptoms were present in 12.5% of the students. A moderately significant positive correlation was found between the students' mean scores for internet addiction and depression scores (r=0.303; p<0.01). The mean internet addiction score of the students showing depression symptoms was 28.7±10.0, and this value was 24.6±6.5 for students showing no symptoms of depression (t=2.445; p=0.016). The addiction score was higher in students with depression.

When the students who were active and those who were inactive were compared according to the IPAQ, no difference was found between the mean scores of depression and internet addiction (p>0.05).

| Table 1. The age and BMI characteristics of the participants and results of outcome measures (n=160) | | | |
|---|------------------------------------|--|--|
| Variables | Mean ± SD (min-max)/median | | |
| Age (years) | 20.1±1.3 (17-27)/20 | | |
| BMI (kg/m2) | 22.5±5.2/21.5 | | |
| IPAQ (min/week) | 2448.2±3868.7 (130.5-31279.5)/1272 | | |
| BDS | 8.8±6.6 (0-37)/8 | | |
| YIAT-SF | 25.1±7.2 (12-47)/24 | | |
| SD: Standard deviation, BMI: Body mass index, min: Minimum, max: Maximum, BDS: Beck Depression Scale, YIAT-SF: Short Form of Young's Internet Addiction Test | | | |

| Table 2. Changes in the daily activities of students during the social isolation period of | compared to pre-pa | ndemic values |
|--|--------------------|---------------|
| | | |

| Changes in daily activities | n | % |
|--|-----|------|
| Increase in mobile phone usage time | 125 | 78.1 |
| Increase in time spent on computer games | 49 | 30.6 |
| Increase in TV watching time | 61 | 38.1 |
| Increase in internet usage time | 139 | 86.9 |
| Changes in sleep habits | 104 | 65.0 |
| Weight change (increase in 76 students, decrease in 28 students) | 106 | 66.3 |

According to our research findings, the BDS mean score of the inactive students was 8.5 ± 6.4 , while that of active students was 8.8 ± 6.3 (t=-0.218, p=0.828) (Figure 1); and inactive students' mean YIAT-SF score was 24.9 ± 7.1 , while active students' mean YIAT-SF score was 26.1 ± 7.9 (t=-0.925, p=0.357) (Figure 2).

Discussion

Findings of this study showed that, 71.8% of the students were inactive in the early pandemic period and no difference between physically active and inactive students in terms of depression and internet addiction scores. There exists no research in the literature directly related to our research findings. It



Figure 1. Distribution of depression scores according to students' activity status

BDS: Beck Depression Scale, IPAQ: International Physical Activity Questionnaire



Figure 2. Distribution of internet addiction scores according to students' activity status

YIAT-SF: Short Form of Young's Internet Addiction Test

was reported that the use of computers and electronic devices has increased due to the sedentary life style that comes with the pandemic (16). Sedentary life style is associated with depression (17). Since the beginning of the pandemic, researchers have noted a strong relationship between being physically active at home and being healthy and having a stronger immune system (9). Due to social isolation, working from home, attending distance education at home, and talking with friends or family members via the Internet, as opposed to face-to-face gatherings, have increased internet usage (18,19). In studies examining the relationship between physical activity and internet addiction, it has been found that internet use is more common in people who do not perform regular physical activity (11). Due to the COVID-19 pandemic and related social isolation, physical activity in gyms or outdoor was restricted. While some perform webbased physical activities, physical activity levels have decreased in some segments with low social support and high anxiety about getting infected. Studies have reported that as physical activity increases, psychological distress decreases (20-22). Similarly, it has been reported that depressive symptoms decreased in those who performed moderate-tosevere physical activity during the pandemic (23). Xiang et al. (1) conducted a study in 1,396 university students, and reported that 52.3% of the students had low physical activity level and the depression rate was 41.8%. Depressive symptoms were identified in 12.5% of the students in this study. Since the present study was conducted in the initial period of the pandemic, the short-term effects of restriction period were evaluated in this study. The higher rate in Chinese study, may be that the disease was first described in China and at the beginning of the pandemic, there were many unknowns about the disease that effected psychological well-being.

Another finding obtained in this study was that a moderately significant positive correlation was found between internet addiction scores and depressive symptom scores. Internet addiction scores were found to be higher in students with depressive symptoms. There are studies reporting similar results in parallel with our findings. In a study conducted with Chinese college students, it was determined that anxiety and depression were correlates for internet addiction (24). In a study conducted by Alaca (25), it was found that the students in the group with internet addiction had higher daily internet usage duration and depression scores compared to the group without internet addiction. In another study, dental students who were depressed were nearly six times more likely to be internet addicted than not-depressed students (26). In a study conducted by Fazeli et al. (27) in 1,512 students, internet addiction was found to cause disconnection from real life and increased insomnia. and as a result, it was reported that quality of life was affected, and internet addiction was found to be associated with depression and anxiety. Another study in Italy showed significant relationship between internet usage and depression in 809 university students (28). In this study, there was an increase in the internet usage of university students during the hours before bedtime. Due to the fact that education continues remotely with social isolation, university students who spend a significant part of the day on the computer or smartphone continue to use them after online course sessions. This situation causes irregularities in sleeping habits such as going to bed later and thus getting up later. Decrease in sleep quality has been associated with severe depression. Although sleep quality was not evaluated in our study, the change in sleep habits was declared by the students.

In this study, it was found that only 28.2% of the university students were active according to the IPAQ, and their mean depression score was 8.8±6.6 (0-37) and mean internet addiction score was 25.1±7.2. In addition, it was concluded that there was an increase in durations of TV watching, mobile phone usage, computer game playing, and internet usage. Romero-Blanco et al. (29) sitting time during the day among university students increased during the COVID-19 period. As physical activity plays an important role in reducing the pressure not only on the body but also on the mind, its importance has elevated especially during the pandemic (30).

In studies conducted before COVID-19, the rate of internet addiction among university students was determined to be 3.2-6% (31,32). However, it was found between 7.7% and 24.4% in studies conducted during the COVID-19 outbreak (8,24). Since the YIAT-SF was used in our study and there was no cut-off point, the frequency of internet addiction in students was not obtained. In the COVID-19 process, it is reported that internet usage rates have increased all over the world, and internet addiction rates have also increased. Also, it was determined that anxiety and depression were correlated with internet addiction (24). Compared to the pre-pandemic period, 86.9% of the students stated that there was an increase in their internet usage, 78.1% had an increase in mobile phone usage, and 65% had a change in their sleep habits. Being aware of the screen time, and regulating it (balanced use) is required. World Health Organization has established general health guidelines for the staying home period that includes useful tips for physical activity, mental health, internet addiction (33). There is a need for such guidelines for young people as well.

Since this study was planned and carried out with after onset of the COVID-19 pandemic, the fact that the participants' pre-pandemic physical activity status, depressive symptoms, and internet addiction rates were not known was a limitation of the study. After the pandemic, the change in the students' daily living activities could only be recorded according to their self-reports. In addition, it should not be noted that the findings obtained are short-term results since the study was conducted right after the first trimester of the pandemic.

Conclusion

This study showed that there was no difference between physically active and inactive students in terms of depression and internet addiction scores. However, in our study conducted at the beginning of the COVID-19 process, the average score of students with depression symptoms was found to be higher than those without depression symptoms. This finding provides further evidence of the association between depression symptoms and internet addiction in adolescents, and emphasizes the need to provide supportive online training (digital training videos, etc.) with a multidisciplinary approach to improve the mental and physical health of these young people.

Ethics

Ethics Committee Approval: The study was approved by Faculty of Medicine Non-Invasive Clinical Research Ethics Committee of a Aydın Adnan Menderes University in Turkey (protocol no: 2020/95, date: 04.06.2020).

Informed Consent: The participants were informed about the objectives of the study and that their confidentiality would be respected and their responses would not be judged.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.Ö., Design: E.G.Ö., N.Ö., Supervision: E.G.Ö., Data Collection or Processing: N.Ö., Analysis or Interpretation: F.A., Literature Search: N.Ö., Writing: F.A., N.Ö., Critical Review: E.G.Ö., F.A.

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