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Contents

We completed the 1st International Congress on Multidisciplinary Studies in Health Sciences, in which a considerable number of academicians from various countries took part on the Scientific and Arbitration Board, with the participation of more than a hundred scientists, in collaboration with Altınbaş University and IKSAD, on 3-5 June 2020. Today, online seminars and conferences are gaining more importance after the health alert of the Covid-19 pandemic worldwide. In accordance with this awareness, we are proud to be a leading university that holds an online congress by international standards.

The congress was successfully carried out thanks to the coordinated work and frequent meetings that we had initiated long before the due date. Facilitating question and answer sessions in 2 separate halls where panels and scientific presentations were held for 3 days, our congress was accredited with 23 credits by the Turkish Medical Association Continuing Medical Education (TMA-CME) and Accreditation Council for Continuing Professional Development. Accommodation and transportation expenses, which play an effective role in organizing congresses, were eliminated through online arrangements. Therefore, the scientists were provided with easier, more effective and wider participation opportunities by allocating less time and financial resources.

Health sciences in our country, as in the world, have a close relationship with all disciplines, especially the fundamental life sciences. Thus, eminent academicians and scientists who pursue their studies in the fields of Medical Sciences (Internal, Basic, Surgery), Dentistry, Pharmacy, Veterinary Medicine, Nursing, Physiotherapy and Rehabilitation, Nutrition and Dietetics, Midwifery, Child Development, Emergency and Disaster Management, Gerontology, Life Sciences (Biology, Chemistry, Physics etc.), Healthcare Management, Social Services, Public Health and Epidemiology, Health Information Systems, Bioengineering and other Multidisciplinary Health and Life Sciences, have contributed to the world of science with panels and oral presentations.

In this respect, we believe that our congress will shed light on the future in the name of health and life sciences. We would like to thank the scientists, who work in the fields of health sciences and vocations, as well as all our devoted contributors of the academy.

We wish to meet in the next scientific meetings.

Prof. Dr. Turgut İpek

Chairman of the Congress

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Research Article

Investigation of Knowledge and Behaviour of Adult Individuals in Terms of Sustainable Nutrition

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Abstract: The objective of this study was to evaluate the knowledge and behaviour of individuals aged 18 years or above on the subject of sustainable nutrition. The study was conducted between April and May 2019 and involved a total of 202 adult individuals (85 female, 117 male), all of whom are resident in Istanbul and over 18 years of age. The socio-demographic characteristics of the participants, their knowledge on sustainable nutrition, nutritional behaviours and food preferences were determined using a questionnaire. 64,40% of the participants with an average age of 32,60 ± 13,20 had not heard of the concept of sustainable nutrition concept before. While there was no statistically significant difference between gender and being aware of the concept of sustainable nutrition, it was found that women exhibited more sustainable nutrition behaviours compared to men ($p < 0.05$). It was observed that the participants learned the concept of sustainable nutrition mostly from health professionals (31.9%) and social media (26.3%). 39.1% of the participants responded that they agreed with the statement "I consume vegetables and fruits grown during the season" and 36,60% of them agreed with the statement "I consume fish caught during the season with appropriate methods". Most of the respondents (44.50% and 34.60% respectively) agree with the statements "I'm careful about not wasting the food" and "I use economic foods". 44.50% of the respondents agreed with the statement "I have less food waste". In conclusion, studies on public awareness campaigns can be beneficial.

Keywords: *Sustainability; sustainable nutrition; food; environment*

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1. Introduction

The concept of "Sustainable Nutrition" has evolved over the last two decades. Although there is no universally accepted definition, the United Nations Food and Agriculture Organization (FAO) defined the definition of sustainable nutrition as 'diets with low environmental impacts that contribute to food and nutritional security for a healthy life in present and future generations' in 2010 (Miller and Auestad, 2013). Sustainable diets are protective and respectful to biodiversity and ecosystem, culturally acceptable, accessible, economically affordable and acquirable, nutritionally adequate, safe and healthy, and use natural and human resources in the best way. This definition reveals that human health and ecosystems are not independent of each other (Alsaffar, 2016; Miller and Auestad, 2013). Global changes such as climate change, loss of biodiversity are pose a major threat to healthy and reliable nutrition. For a healthier planet and healthy people, a healthy and reliable diet as well as sustainable production and consumption are required (World Health Organization, 2018). According to the 'Global Food Losses and Food Waste' study by the United Nations Food and Agriculture Organization, four billion tons of food is produced per annum for global consumption and approximately one-third of this food is lost and wasted (FAO, 2011). Developed countries account for 56% of food loss and waste, while developing countries account for the remaining 44% (Demirbaş, 2018).

The food we consume and the diets we choose are the main social indicators of health and well-being. Based on the experiences over the last half-century and current trends, drastic change in our current food strategy is required along with the promotion of fair, culturally appropriate, biodiversity-based, sustainable diets. Therefore, food companies, trade bodies, nutritionists and other health personnel, government and individuals have important duties (Burlingame and Dernini, 2012).

It is emphasized that sustainability has increased in recent years. Awareness studies on this issue are increasing worldwide. However, the number of studies on this subject is quite low in Turkey. The objective of this study was to investigate 'Sustainable Nutrition' behaviours and knowledge in adult individuals.

2. Materials and Methods

This study was conducted with 202 adult individuals (85 male, 117 female) over the age of 18 and resident in Istanbul. The study was conducted between April 2019-May 2019. Individuals were included by random sampling. Voluntary individuals were included in the study. The study was approved by Bahçeşehir University Scientific Research and Publication Ethics Committee on 10/04/2019. A questionnaire consisting of 17 questions was prepared by literature review and applied by a face to face interview method in order to determine the demographic characteristics of the participants, their knowledge and behaviours on sustainable nutrition.

SPSS 15.0 program was used to evaluate the analyses. Statistical significance was accepted as $p < 0.005$.

3. Results

A total of 202 adults, 117 (57.9%) female and 85 (42.1%) male, aged between 18 and 67 years participated in the study. 35.6% of the participants have previously heard of the sustainable nutrition concept and 64.4% of them have never heard of the sustainable nutrition concept. No statistically significant difference was found between gender and knowledge of the concept of sustainable nutrition (p>0,05). When the profession and working status of those who are aware of the concept of sustainable nutrition are examined, the participants who are students (37.6%) are in the majority and this difference is statistically significant (p = 0.032).

31.9% of the participants who know the concept of sustainable nutrition heard the concept from healthcare professionals (doctors/dietitians), 26.3% from social media, 15.2% from conferences/scientific meetings, 5.5% from newspapers/magazines and 5.5% from television programs such as advertorials/news.

The participants reported that the concept of sustainable nutrition is most related to "environmentally friendly food" (55.4%) and least related to "equal and fair trade" (12.9%). 36.6% of participants indicated that the concept of sustainable nutrition is related to 'biodiversity, environment, climate'; 54.5% of participants indicated it is related to 'food safety'; 43.1% of participants indicated it is related to 'food availability'; 45% of participants indicated it is related to 'nutrient/nutrient needs'; 36.1% of participants indicated it is related to 'local food'; 49% of participants think it is related to 'seasonal food'; 13.4% of participants think it is related to cultural heritage and 40.60% think it is related to 'public health and welfare'. 39.1% of the participants responded that they agreed with the statement "I consume vegetables and fruits grown during the season" and 36.6% of them agreed with the statement "I consume fish caught during the season with appropriate methods". 44.5% of the respondents agreed with the statement "I have less food waste" and "I am careful about not wasting food". Substantial proportion of the respondents (36.6%) responded that 'I neither agree nor disagree' to the statement 'I separate my food packaging wastes for recycling'. Only 27.7% of the participants disagreed with the statement "I use my own water container instead of using a pet bottle'.

Considering the relationship between gender of those who answered 'I agree' to the following statements: 'I consume high amounts of fruits and vegetables', 'I consume vegetables and fruits grown during the season', 'I consume fish caught during the season and with appropriate methods', 'I consume traditional/regional foods', 'I consume organic foods', 'I have an adequate and balanced diet' and 'I don't eat one type of food only, I eat a diversity of foods', an increase was observed in favour of women and this difference was statistically significant (p< 0,05).

Conclusion

A limited number of studies have been conducted in Turkey with respect to sustainability and sustainable nutrition. The studies on these subjects in the international scientific literature focus on nutrition models and greenhouse gas emissions. The objective of this study was to find out the knowledge and behaviours of the participants about sustainable nutrition. Our study indicated that the concept of sustainable nutrition was mostly communicated by health professionals and social media. While physicians and dieticians play

an important role in raising public awareness, the effective use of social media is of utmost importance in terms of raising awareness. There is no valid scale that measures knowledge and behaviours about the concept of sustainable nutrition. Further studies are needed to increase public awareness on the subject and to create a valid scale that measures awareness.

Conflict of Interest

Authors declare no conflict of interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Bahçeşehir University Scientific Research and Publication Ethics Committee, 30/04/2019-E.1232).

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Research Article

Application of Tramadol Hydrogel as a Transdermal Drug Delivery with Sonophoresis Device to Rats

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Abstract: Transdermal drug delivery offers an appealing alternative to injections and oral medications. However, applications of transdermal drug delivery are constrained to only a few drugs due to low skin permeability. Application of low-frequency ultrasound enhances skin permeability, a phenomenon called as low-frequency sonophoresis. The skin consists of two important layers called epidermis and dermis, which are on the fatty layer called hypodermis (subcutaneous tissue). The epidermis is the outermost layer of the skin. It consists mainly of cells called "keratinocytes". This is caused by the evolution of cells formed in the lower layer and their accumulation on top of each other. At the top is the stratum corneum epidermidis layer from almost completely dead cells. Stratum corneum acts as a primary barrier to drug delivery, transdermal drug delivery technique precedes to conventional drug delivery process. In this study, tramadol hydrogel is an opioid-like analgesic with much less adverse impact was carried out to rat skin. The tramadol hydrogel was applied on rat skin by using a novel developed sonophoretic device. There were 4 groups of Sprague Dawley male rats that were examined to evaluate analgesia. The first group was control group, the second was intraperitoneal (i.p.) application group, the third was tramadol hydrogel without sonophoresis application and the last group was tramadol hydrogel with sonophoresis application. It was shown that tramadol used with sonophoresis increased analgesic effect three-fold than tramadol hydrogel group 30 minutes later. Hot-plate analgesia meter was used and the efficacy was measured on 16 rats. Tramadol dosage was 28 mg per kilogram for each rat. Low frequency sonophoresis device transducer was adjusted to 40 kilohertz (kHz) frequency for up to 60 minutes. Measurements were carried out at 0, 10, 20, 30, 40 and 60 minutes. There was a statistically significant difference between tramadol hydrogel and tramadol hydrogel with sonophoresis groups ($p<0.05$, by Kruskal Wallis test). Moreover, the developed sonophoretic device application was successful and application low frequency 40 kHz was safe. Neither burn nor erythematous streaks were observed on rat skin by using low frequency sonophoresis. The administration of tramadol hydrogel and tramadol hydrogel with sonophoresis groups were examined, the absorption of tramadol increased by 2-3 times transdermally.

Keywords: *Tramadol hydrogel; hot plate analgesia test; sonophoresis device; transdermal drug delivery; Spraque Dawley rats; low frequency*

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1. Introduction

The skin is one of the most critical organs inside the frame and takes a huge role for penetration of drug delivery structures (Trommer and Neubert, 2006). Transdermal drug delivery systems have essential advantages. Transdermal drug release has many advantages. These advantages are as following: drug release is provided non-invasively, the degradation of gastrointestinal (GI) enzymes is avoided, the transdermal drug release system does not produce "first-pass effect" in the liver, systemic toxicity decreases, drug absorption is provided by manipulation, drug bioavailability increases, plasma drug level is maintained as constant, it is given as an analgesic to patients who have moderate or strong pain. The transdermal drug delivery system adjusts the frequency and amount of drug dosing, damages tissues less and is cost-effective (Paudel et al., 2010). The skin talents as a barrier to inhibit drug delivery, stratum corneum layer is that the outermost layer of the skin, has a structure in which corneocytes are densely packed in a lipid matrix, forming the 'bricks and mortar' and that is the first crucial barrier (Lampe et al., 1983). The stratum corneum of base layer is known as granular layer is the formation of mobile cell junction which block the drug from penetrating via the structure. The drug penetrates the stratum corneum initially, secondly passes were through the deeper epidermis. Thanks to this penetration, in the dermal layer there is no drug accumulation (Guy and Hudgraft, 2003). Elimination half-life of tramadol is about 6 hours (Lehmann et al.,1997). Tramadol has a high solubility in the oral cavity. It is also known as tramadol hydrochloride prepared with Pluronics 127, it has both opioid and non-opioid properties (Mitragotri et al., 2010). It is primary effective at the central nervous system (CNS). According to the structure tramadol is similar to codeine and morphine. It has 6000-times less side effect than morphine and is 10-times less powerful than codeine (Thang et al., 2001). It provides serotonin (5-HT) reuptake due to inhibition of ache distribution inside the spinal cord (Bamigbade and Langford, 1998). Sonophoresis facilitates to penetrate from stratum corneum absorption (Schoellhammer et al., 2014). Felllinger and Schmidt published an article on sonophoresis in early 1950s for the treatment of polyarthritis. It was applied hydrocortisone on the hand's digital joints (Smith et al., 2007). This technique provided us better results considered to hydrocortisone injections for bursitis treatment (Liu et al., 2006). Sonophoresis can also be applied on a variety of drugs which have capability to assist the penetration as well. One of the most important applications of this method is for local anesthetics transdermal application (Mitragotri et al., 2014). Transdermal drug release has been examined in 2 subgroups as active and passive methods (Kurz et al., 1989). Passive methods are that the optimization of the drug method or delivery to enhance skin permeability (Smith et al., 1995). However, these techniques have limits for the development of the skin permeability of bio-macromolecules (Bartek et al., 1987). On the contrary, the active strategies which comprise of physical or mechanical techniques even for bio-macromolecules (Fernyhough et al., 1992). These techniques

are micro-needles, iontophoresis, chemical penetration enhancers and sonophoresis. There are four main ultrasound parameters which are frequency, intensity, duty cycle, and application of time. Low-frequency sonophoresis has an important breakthrough on the formation and collapse of gaseous cavities (acoustic). Moreover, with the usage of acoustic spectroscopy, quantifying inertial cavitation has become more handy (Tezel et al., 2002). It can produce intense micro streams, that is going up the bioavailability of the drugs (Terahara et al., 2002). Cavitation takes place due to the nucleation of small gaseous cavities all through the negative stress cycles of ultrasound. As a result, cavitation provides the ordering of the lipid bilayers and formation of aqueous channels ensures to penetrate easily in the skin (Mitragotri et al., 1995). Levy et al. demonstrated that when convection and cavitation had been mixed with mannitol, inulin, they enhanced transport to skin (Levy et al., 1989). Mitragotri et al. carried out a work of the synergistic effect of low-frequency ultrasound that is using 20 kHz with sodium lauryl sulfate (SLS) (Levy et al., 1989). The addition of 1% SLS to the solution reduced the threshold to about 18 joules/cm^2 (Mitragotri, 2000).

1.1. *Low-Frequency Sonophoresis*

Biotechnology has its milestone on low-frequency sonophoresis which has studied by scientist for the last 10 years. Sonophoresis provides electrical energy to turn into mechanical energy or vice versa. Low-frequency sonophoresis helps to increase diffusion and ultrasound waves causes convection. The most powerful feature of low-frequency sonophoresis is measuring frequency and drug delivery ratio which can be controlled by an ultrasonic transducer. Low-frequency sonophoresis helps to delivery of low and high molecular (macromolecule like heparin and glucose) of drugs which includes hydrophilic drugs. Hence, it has an important technique for drug delivery systems.

Low-frequency sonophoresis presents advantages over other transdermal delivery methods. It can be tested by application time and ultrasound parameters (Mitragorti, 2000). So it provides local delivery. The other advantage is that it can be controlled by varying frequency and intensity of ultrasound. The other advantage is that it can also be used with drug-containing patch. It is the effective release of prescribed medications cannot be easily achieved by conventional patches, since the dose may be discharged or released. For the solution of this problem, controlled therapeutic systems are preferred by physical means. It can monitor blood analyses as well as blood glucose for diabetes (Kost et al., 2000).

Low frequency sonophoresis was used for therapeutic purposes with the help of piezoelectric disc, it is formed by the addition of mechanism. When rapid change in voltage with transducer motion, it provides therapeutic penetration of drug. It consists of high frequency pressure wave (ultrasound). The active substance is provided from the ultrasound device. It is provided by a contacting agent which transmits energy to the skin. Mechanical changes in the skin affect the stratum corneum layer of the skin. This mechanical change takes place in keranitocyte cells thanks to cavitation (cavity formation), allowing permeation and cell destruction increases rapidly in a reversible way.

1.2. *Dependence of Transport on Ultrasound Parameters*

Ultrasound links to skin barriers. These barriers are stratum corneum thickness, high skin impedance, low skin hydration, low useable area for solid transportation, age, blood flow, follicles such as sweat and hair, trauma on skin, humidity and temperature, presence of chemicals and chronical usages of drugs.

There are four main ultrasound parameters which are frequency, intensity, duty cycle, and application of time. Low-frequency sonophoresis has an extensive study on the dependence of permeability enhancement on frequency and intensity in the low-frequency which has been shown by Tezel et al. (Tezel et al., 2001).

1.2.1. *The Frequency*

Emitted wave frequency is related to the size of the crystal. Attenuation of an acoustic wave is inversely proportional to its frequency. If the frequency increases, ultrasound penetrates into less deeply under the skin. High frequencies range from 1-3 Mhz while low frequency ranges from 20 to 100 kHz. High frequencies were first surveyed as physical enhancers for transdermal delivery of drugs (Neeter et al., 2003).

1.2.2. *Mechanisms of Low-Frequency Sonophoresis*

Many of variables affect low-frequency sonophoresis. These are cavitation (pore induction), frequency, amplitude, intensity and application of time.

1.2.3. *Cavitation*

Low-frequency sonophoresis has an important breakthrough on the formation and collapse of gaseous cavities (acoustic). Cavitation means the collapse and formation of gas bubbles in a liquid environment and the resulting collapse when exposed to a sound wave in such an environment. Cavitation happens with the coupling medium (coupling medium means liquid is that found between the ultrasound transducer and the skin). The frequency and acoustic pressure amplitude are related to the maximum radius of the cavitation bubbles. During low-frequency sonophoresis, cavitation occurs within 15 micrometers of stratum corneum and in order to overcome this, inert cavitation is created in the skin layers. Moreover, with the usage of acoustic spectroscopy, quantifying inertial cavitation has become more manageable (Husseini et al., 2005). It can produce violent micro streams, which goes up the bioavailability of the drugs. As a result, cavitation provides the ordering of the lipid bilayers and formation of aqueous channels provides to penetrate easily in the skin.

1.2.4. *Convection*

Convection is a significant factor for low-frequency sonophoresis. Acoustic streaming (convective process) can be increased by lidocaine. Levy et al., 2014, demonstrated that when convection and cavitation were mixed with mannitol, inulin, they enhanced delivery to skin.

1.2.5. *Thermal Effects*

Attenuation of ultrasound wave leads to thermal increasement for low-frequency sonophoresis. Ultrasound waves cause heating of the medium. Thermal effects cause to increase skin permeability. It provides to increase kinetic energy and diffusion of drugs, dilates points of entry of the skin, promotes drug absorption and enhances circulation of blood for *in vivo* experiments. Duty cycle and ultrasound intensity are parameters that are directly related to thermal effects. Therefore, these parameters must be arranged for low-frequency sonophoresis application.

1.2.6. *Synergistic Effect with Other Enhancers*

Ultrasound application is not effective compared to usage of low-frequency ultrasound combinations with other enhancers which has been shown to be more efficient. Moreover, increasing transdermal transport, especially with the combination of ultrasound with other enhancers causes to decrease the enhancers needed to help the drug flux. Therefore, combination of ultrasound with other enhancers will definitely increase the reliability with decreasing the strength of selected enhancers.

1.2.7. *Ultrasound and Chemicals*

Mitragotri et al. carried out a work of the synergistic effect of low-frequency ultrasound that is using 20 kilohertz with SLS (Hama and Sagen, 2007). It has been shown that the administration of SLS causes an approximately 3-fold increase in mannitol permeability and is only about 8-times greater than that of ultrasound for 90 minutes. It was also observed that the induced sulphate solution increased approximately 200-fold in the skin permeability of mannitol.

In particular, with insufficient surfactant penetration effect, the threshold ultrasound energy was about 141 joules/cm^2 to produce a detectable change in skin impedance. Mitragotri et al. has showed the addition of 1% SLS to the solution reduced the threshold to about 18 joules/cm^2. The various results of this synergistic effect indicated that low frequency ultrasound indicated better spread and diffusion of the surfactant in the skin.

1.2.8. *Ultrasound and Iontophoresis*

The synergy between low frequency ultrasound and iontophoresis are of great importance as it increases transdermal transport. In fact, this combination is particularly useful in the treatment of transdermal transport by Park et al., 2019, By using heparin as a model drug, it has been shown to have a better and easier way to investigate the synergistic effect of ultrasound and iontophoresis on transdermal transport by Long et al., 2000. Approximately 10 minutes prior to the administration of iontophoresis, the skin was once treated with 1% dodecyl pyridinium chloride solution. As a result, the increase in heparin flux of ultrasound and iontophoresis applications was recorded approximately 56-fold increased with these applications.

1.3. *Equipment and Devices*

1.3.1. *Tramadol Pharmacology*

Tramadol is a centrally acting analgesic agent with μ-opioid agonist properties, blocks NE uptake. Tramadol hydrogel is a similar molecule with 4-phenyl-piperidine analogue of codeine, which is acting as analgesic. It can be used by patients in the orthopedics spine clinic and may even be beneficial in patients with poor cardiopulmonary function, including older patients, obese and smokers, patients with liver or renal dysfunction and patients using non-steroidal anti-inflammatory disorders. It can be also used in post-operative pain relief. Its elimination half-life is about 6 hours.

Tramadol has a high solubility in the oral cavity. It is also known as tramadol hydrochloride (Tr HC) and has opioid and non-opioid properties. It is primary effective on the central nervous system (CNS). This drug is similar to codeine and morphine as considered to structurally. However, it is 6000-times less active than morphine and is 10-times less effective than codeine. However, in 1995, it was rated as a treatment of acute pain with Food and Drug Administration. Tramadol hydrochloride effects are on low-affinity m-opioid and k-opioid receptors, and NE, blocking monoamine receptor systems. It provides 5-HT reuptake due to inhibition of pain distribution in the spinal cord. It has also a lower incidence of adverse effects.

1.3.2. *Hot Plate Analgesia Test*

The hot plate is one of the most widely preferred test for analgesia. Because it is helpful to determine the analgesic efficacy of experimental drugs in rodents. In this experiment it was used the guidelines developed by Ankier S.I. (1974). A hot plate, May AHP 0603 is brand name, has been adjusted to 54°C and the latency of the first reaction (licking of the paws or jumping response- a jump has been identified by all 4 paws leaving the heated surface) has been recorded. A cut-off period of 60 seconds has been considered to avoid any damage to the paws. Rats were placed on the hot plate one by one and response latency was measured with a stopwatch (rats were used from YÜDETAM, Yeditepe University). Observations showed that the majority of animals reacted to the heat by licking their paws.

2. Materials and Methods

2.1. *Development of Transdermal Sonophoresis Device*

Transdermal sonophoresis device was developed at Yeditepe University Biomedical Engineering Laboratories. Lm555 oscillator, Texas Instrument, has been used for this experiment. On this experiment, the aim is to produce square wave pulses provided continuously by the 555 timer IC. On the other hand, the 555 timer IC has connected either in its monostable mode therefore it generates a back and front type switching action. Connection of the 555 timer IC in an unstable mode is a tricky part. When it was approved highly precise free roaming waveform, very stable 555 oscillator has to used. Also, RC circuit has to be connected to oscillator which contains 2 resistors and capacitors. The 555 timer IC can be used which generates stabilized square wave output waveforms. Its duty cycle is between 50-100%.

The device has stopped working until for the next trigger pulse. It initiates to act as an unstable multi vibrator. It has a great importance to continuously re-trigger effect of circuit. Pin 2 which provides triggering process connecting to 555 timer and threshold input to pin 6 acts as an unstable oscillator with together. Single timing resistor has a key act on this device because it has been split into two different resistors which are R1 and R2. Pin 7 which is discharge input has been linked to their junctions (Figure 3).

2.2. *Tramadol Hydrogel Formulation*

In this study, firstly 20 grams of Pluronic F 127 was weighed and dispersed into the 40 mL purified water. The dispersed polymer was put into the refrigerator overnight and was dissolved homogenously as a hydrogel. Then hydrogel was incubated 2 days at 37°C. The dispersed polymer was sterilized at room temperature. The solution was placed to eppendorf tube and then tramadol solution was incorporated into hydrogel. Finally, solution was sterilized at cabinet with ultraviolet for 30 minutes.

2.3. *Drug Loading*

The reason for mixing tramadol hydrogel with Pluronic F 127, Sigma Aldrich Chemical Co., it is more or less permeable to body fluids and also it does not avoid from transition to body fluids as useful substances such as food and oxygen. It has little friction to the surrounding tissues. It has also shown low adhesion to the mucous membrane and tissues. Epithelial cells in the stomach are protected from the acidic stomach acid thanks to the gel. Taking advantage of Blankenship's studies, it was concluded that 28 mg/kg of tramadol hydrogel was the effective dose in rats, and since each of the rats had a weight of 250 grams, 7 mg/kg was administered to each *in vivo* study.

2.4. *Hot Plate Analgesia Test*

Four groups were determined for measuring the analgesia effect on rats (Figure 2). The first was determined as a control group. 3 rats were placed with sonication at 40 kHz at 0, 10, 20, 30, 40 and 60 minutes. The second was tramadol hydrogel group (GT), Contramal®, Abdi İbrahim Company. In this group, only tramadol hydrogel was put on rats directly on their backs that were shaved. The third was intraperitoneal group. Each rat has administered 7 mg tramadol (28 mg/kg, each rat is 250 gram). The last was sonication application group with tramadol hydrogel was applied on rats with sonophoresis device. Tramadol hydrogel was supplied with 40 kHz ultrasonic transducer; provided with a 15 volt via power supply. In conclusion, on each time jumping or paw licking response has been noted to understand analgesic effect (Jóhannesson and Woods, 1964).

3. Result

Using low frequency sonophoresis, acoustic cavitation is created on the skin, increasing the pore and permeability on the skin. As a result of the cavitation, acoustic microjets on the skin cause inhomogeneous pore formation (Bird et al., 1960). *In vivo* experiments consisted of tramadol hydrogel and tramadol hydrogel with low frequency sonophoresis application group. Tramadol hydrogel improved drug penetration as

it provides the destruction of the organic barrier (Chaturvedi et al., 2011). A hydrogel which could stick finely to the epithelium can increase the time retention of the system at (Hussain et al., 2011). Therefore, it has provided sufficient drug dose for the desired therapeutic healing effect. (Peppas and Sahlin, 1996). Extensive efforts were made to expand bio-adhesive hydrogels to enable advanced drug delivery (Reece et al., 2001). Ultrasound-brought about disruption of ionic cross-links to set off bursts of drug launch became observed (Bouhadir et al., 2001). Low frequency sonophoresis can instant disrupt the hydrogel structure (Bommannan et al., 1992). It is very advantageous due to its deep penetration inside tissues (Mitragotri et al., 2005). No effect was observed on latency in response to acute thermal pain in any of the rats that were given transdermal tramadol as hydrogel with sonication application at initial, 10, 20 and 30 minutes later. It was calculated that the transdermal as hydrogel with sonication application is not effective until 40 minutes. Spraque Dawley rats that obtained 28 mg tramadol per kilogram body weight i.p. and transdermal packages with sonication had behavioral responses to tramadol that included minimized responsiveness to tactile stimuli and decreased cage interest no impact was discovered on latency. Acute thermal pain in any of the rats that have been given transdermal tramadol as hydrogel with sonication application at 10, 20 and 30 minutes (Taber et al., 1969).

In this study, it was found that administering 40-60 minutes sonication was found effective. The maximum latency in response to acute thermal pain that was observed after 60 minutes. The bioavailability of the transdermal hydrogel with sonication was increased almost two and three times (respectively after 40 and 60 minutes) more than transdermal hydrogel application. Hot plate latency test was used to compare latency in response to acute thermal pain after transdermal tramadol application with sonication (40 kHz) (Tilson et al., 1973). This device investigated the possibility of developing transdermal tramadol with sonication application allowing fast analgesic effect of tramadol in a 40-60 minutes (Figure1). Finally, it was observed 40 kHz was useful for this study, when the comparison with the high frequency sonophoresis, low frequency provided larger bubbles (Polat et al., 2011).

4. Discussion and Conclusion

The utility of sonophoresis to the pores and skin will increase its permeability and provides penetrating of drug substances (Tezel et al., 2003). Transdermal delivery of hydrophilic substance like tramadol causes problems due to their lack of ability of integrating with cellular membrane and penetrating through stratum corneum (Mitragotri and Kost, 2000). In this study, it was observed that the efficacy of tramadol hydrogel was increased with sonophoresis as a trigger effect after 40 minutes. Tramadol drug penetration was tested with hot plate analgesia test. Results were tested Kruskal Wallis test for statistical analysis. At the end of the study, any skin irritation was not observed with low frequency sonophoresis technique. It was safe at 1.5 W/cm^2 energy density and 40 kHz frequency. In this way, low-frequency sonophoresis sooner or later causes greater modifications to the skin, particularly for high-molecular weight drugs (Yu and Ding, 2008). In the simultaneous treatment, the drug and ultrasound had been performed at the same time and for this reason pores and skin transmitting changed into better diffusion as a result of structural modifications inside the skin and also because of convection ultrasound (Guvendiren et al., 2012).

Figure 1. Tramadol hydrogel (28 mg/kg) latency times in rats versus time (min) n=6. Between 3 groups tramadol hydrogel (GT), tramadol hydrogel with sonophoresis (GTS) and control group

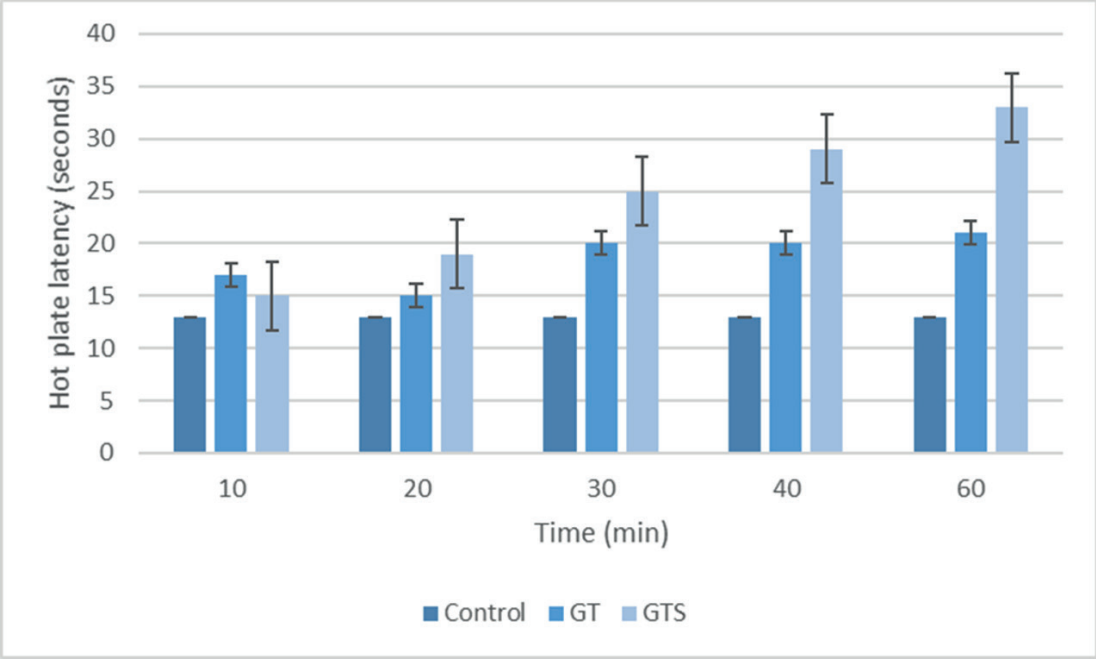


Figure 2. Sonophoresis device application to rats

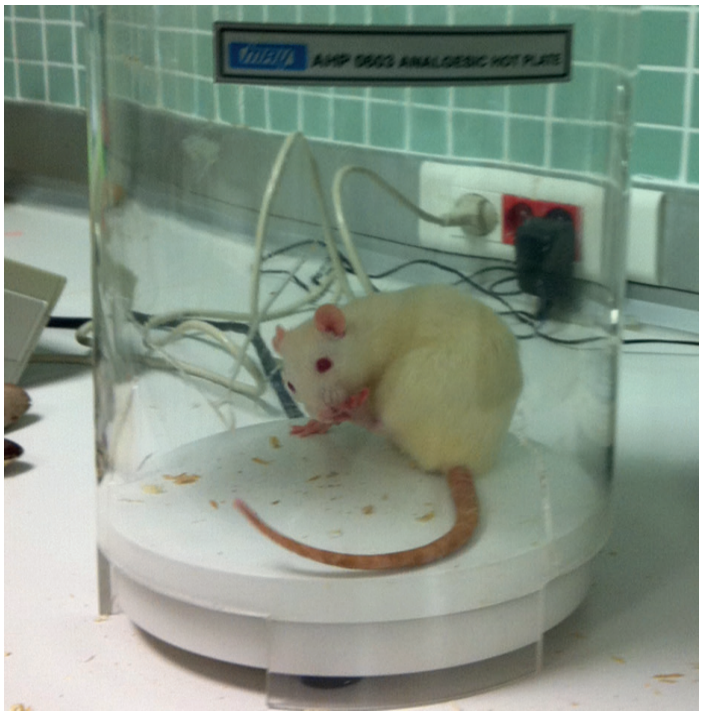
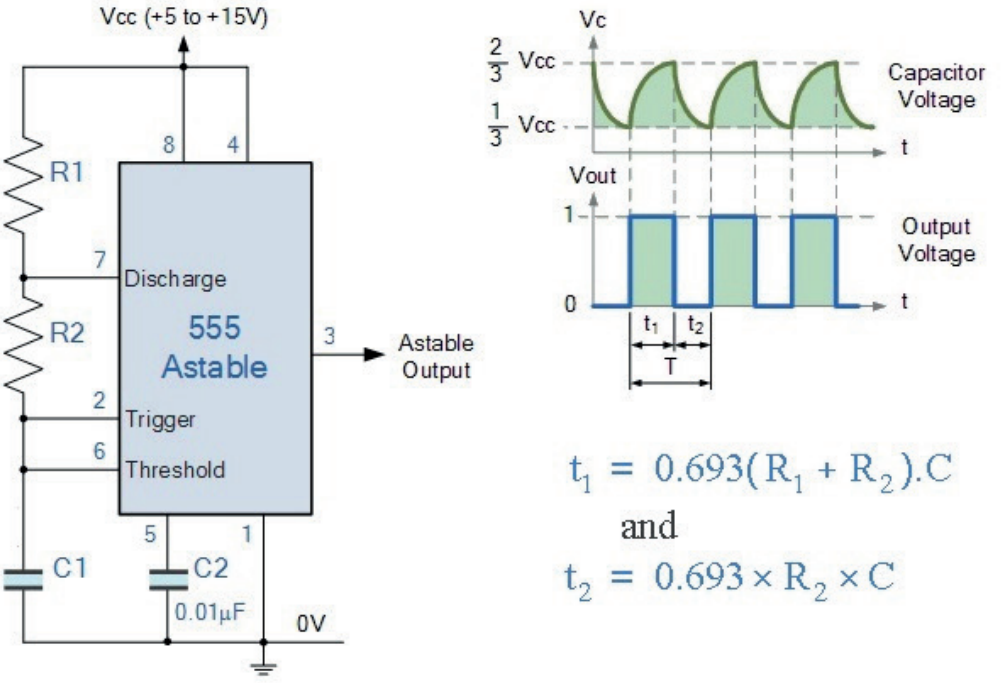


Figure 3. Sonophoresis device circuit



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Conflict of Interest

Authors declare no conflict of interest.

Ethical Approval

All procedures performed in studies involving experimental animals were in accordance with the ethical standards of the institutional and/or national research committee (Yeditepe University Experimental Animal Ethics Commitee 01.06.2018/674).

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Research Article

Evaluation of Preoperative Tests in Elective Surgeries of Asymptomatic Patients During Covid-19 Pandemic

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Abstract: With the Covid-19 pandemic, some changes have been made in health practices. In this study, the action plan applied in the preoperative evaluation of patients with no symptoms and contact history planned during the pandemic was presented in light of the Ministry of Health communique and the literature. Preoperative Evaluation Action Plans were determined in each hospital. The first aim is to distinguish patients who are asymptomatic and have no contact history. Then, these patients are evaluated before the operation with the tests and physical examination. Various changes were made in the tests used in preoperative evaluation during the pandemic process. Initially, the first preferred test was thorax computed tomography, while the polymerase chain reaction test is now recommended. Accurate information and compliance with determined action plans are of great importance in the planning of elective surgeries. It is evident that preoperative evaluation criteria may change according to the characteristics of the pandemic process.

Keywords: *Consent forms; Covid-19, elective surgical procedures, pandemic; PCR; thorax computed tomography*

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1. Introduction

After the new coronavirus was accepted as a pandemic, the Ministry of Health had suggested postponing elective surgery and endoscopic procedures with its notification. With the resumption of elective surgeries, the application of surgery to asymptomatic patients poses the risk of both the spread of the disease and healthcare professionals. It is reported that Covid-19 may cause hospital infections that seriously threaten

surgical staff and hospitalized patients (Liang, 2020). In this study, the action plan applied in the pre-operative evaluation of asymptomatic and non-contact patients is presented in light of the Ministry of Health communique and literature.

2. Materials and Methods

In order to identify symptomatic patients and people with contact/suspect contact, all patients are triaged in the emergency room upon arrival at the hospital. The presence of contact history, fever, cough, and respiratory distress are questioned with someone diagnosed with Covid-19 in the past 14 days. Routine examinations are requested during anesthesia pre-operative examinations. Then the second triage is done by the anesthesia team. The anesthesiologist evaluates the tests through the automation system. Patients with the presence of signs are referred to the infectious diseases outpatient clinic as possible cases and their operations are delayed. With the previously determined road plan of these patients, they are allowed to go to the infection outpatient clinic without approaching other patients. Those who do not find a feature in their examination (no suspect contact-no complaint) are evaluated face to face in the anesthesia outpatient clinic. In this evaluation, Anesthesia Policlinic Isolation Rules (anesthesiologist must wear surgical mask-visor-gloves) are followed. "Written consent" is obtained from the patients that they have answered the questions correctly. A detailed physical examination is done. After the approval of anesthesia, from the patient, carrying, peri-operative or post-operative symptomatic, hospital-related transmission risks are stated and "Covid-19 Special Informed Consent Form" is signed, which states that "surgery is not urgent and can be delayed".

3. Results

In this study, the changes made in parallel with the explanations of the Ministry of Health and the practical applications in our institution before any algorithms have been published are examined. Diagnostic tests are very important especially in asymptomatic people during the pandemic. Molecular tests with genetic material and serological tests with antigens or antibodies against the virus are used in laboratories (Gürbüz, 2020).

Current molecular tests are techniques that detect the genetic material of the virus using a method based on real-time reverse transcription polymerase chain reaction (RT-RT-PCR) (Li et al., 2020). RT-PCR tests in Turkey Ministry of Health Directorate General of Public Health Microbiology Reference Laboratory is done at authorized centers by.

4. Discussion

Due to technical reasons, such as virus mutation or RT-PCR inhibition, or due to insufficient viral material in the sample, the negativity of the RT-PCR test is not sufficient to rule out the disease (Gürbüz, 2020). The total positive rate of RT-PCR in the diagnosis of Covid-19 was reported to be approximately 30% to 60% in the first presentation (Yang et al., 2020). Development of antibody tests to ensure rapid screening of symptomatic or asymptomatic carriers in laboratories should be targeted (Calucho, 2020).

At the beginning of May, when elective surgeries started, there was no opportunity for RT-PCR tests for people without symptoms at the centers authorized by the Ministry of Health. When this is the case, the respiratory system that the virus most affected affects lung imaging methods. In a study, the sensitivity of RT-PCR test in the early period of the disease was reported as 71%, and thorax computed tomography (CT) as 98% (Xie et al., 2020). The sensitivity of chest x-ray is reported between 30-60% in showing disease involvement (Kong and Agarwal, 2020).

The most common findings are the radiographic view of ground glass on chest x-ray in the diagnosis of Covid-19 or bilateral frosted glass in CT and accompanying consolidation (Özdemir et al., 2020). Though RT-PCR test is the gold standard in the diagnosis of Covid-19, it has been reported that thorax CT is becoming more and more important in the diagnosis because it can give false-negative results (Ai et al., 2020; Xie et al., 2020). According to the data of this literature, we determined the Preoperative Evaluation Action Plan in elective cases, and performed thoracic CT imaging in asymptomatic individuals. In some of the papers, it was stated that because CT contains ionizing radiation, it should be used as a problem-solving method in patients who have negative RT-PCR but are clinically interrupted rather than a scanning method (Erturk, 2020). Turkish Anesthesiology and Reanimation Association (TARD) published a guideline titled "Recommendations to Start Elective Surgeries" on May 21, 2020 (Ergil et al., 2020). Stating that social awareness and individual patient education are important, TARD recommended that the RT-PCR test be extended (Ergil et al., 2020). Then, on June 1, 2020, the Ministry of Health stated in her communique that she published the method proposals to be followed regarding elective surgeries (Ministry of Health, 2020). In this guide, it was suggested that thorax CT should not be requested for screening patients. It was stated that RT-PCR test was recommended in asymptomatic and hospitalized patients who are not in contact with the known or suspected Covid-19 patient and in regions of prevalence and/or test positivity rates (≥2%). In the same study, "surgeries should be done within the first 7 days after the negative test result." the statement said. After the 1st of June, 2020, people without symptoms were given the opportunity to apply RT-PCR test via HSYS. After this date, as an institution, we started to use RT-PCR test in asymptomatic patients who will have surgery instead of thorax CT.

Conclusion

In the planning of elective surgeries in the Covid-19 pandemic, harmony, cooperation, and accurate information is of great importance among patients, patient relatives, anesthesiologists and surgical team. It is obvious that pre-operative evaluation criteria may change according to the characteristics of the pandemic process. Consistent policies are needed to protect both patients and health professionals as long as the pandemic continues. Besides the legislative will, professional organizations, civil society organizations should also take an active role in determining these policies.

Conflict of Interest

Author declares no conflict of interest.

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Review

Importance of Medical Imaging Methods in Medicine

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Abstract: Medicine, it is a multidisciplinary science. It is based on the principle of obtaining clearer information about diseases through the cooperation of many branches. In the medical field, radiology science has an important place especially in diagnosis and treatment of diseases. With the development of radiology science, in other words, medical imaging methods, the diagnosis of diseases has become easier. Imaging techniques are mainly based on the process of making the invisible parts of the human body visible by various methods. Radiology; It can basically be classified under two titles: diagnostic radiology and interventional radiology. For diagnosis, there are seven basic methods in radiology and nuclear medicine clinics: x-ray, mammography, computed tomography (CT), magnetic resonance (MR), ultrasonography (US), single photon emission computed tomography (SPECT) and positron emission tomography (PET). While ionizing radiation sources such as X-ray and gamma-ray are used in some of these methods, radiation is not used in some, instead there are methods that use radio waves and supersonic waves. In terms of interventional radiology, biopsies, and ablation treatments samples can be shown. Apart from these methods, there are various devices for special use with the developing technology. In this study, basic imaging methods will be mentioned. It is very important for both patients and healthcare professionals to know the devices containing radiation and to have information.

Keywords: *Radiology; medical imaging methods; diagnostic radiology; interventional radiology; radiation*

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1. Introduction

In order to get clearer results in the medical field, various branches of science have to work in partnership with this field. One of these fields of science is radiology. The word radiology consists of the combination of the words radius (ray) and logos (word) in ancient Greek and it is described as ray science (Kaya et al., 1997). The radiology science was born on December 22, 1895, after Wilhelm Conrad Rontgen discovered his X-rays and the projection on photography, on December 22, 1895, at the Wurzburg physics institute, on December 22, 1895 (Riesz, 1995). In the first quarter of the twentieth century, the science of radiology entered the clinic as a branch of medicine. Thanks to radiology methods, it is quite easy to diagnose the diseases.

2. Materials and Methods

Radiology is used in the field of science, which uses radiation for the purpose of imaging and diagnosing diseases, or for guiding the way to enter the body through interventional methods. Radiology, it can be classified under two headings as diagnostic radiology (diagnostic-radiodiagnostic) and interventional radiology. Diagnostic radiology has five basic methods: x-ray, computed tomography (CT), magnetic resonance (MR), ultrasonography (US) and nuclear medicine (NM). Some of these methods like X ray, CT and NM use ionizing radiation sources like X ray and gamma ray while MR, US don't use radiation sources. In addition, mammography (Egan, 1966), angiography (Ovit et al., 1980), bone mineral densitometry (Stain et al., 1987), and dental imaging methods (Olaf et al., 2002) can be added to X-ray imaging methods. In terms of interventional radiology, angiography and ablation treatments are examples. Apart from these methods, there are various devices special for use with the developing technology (Bushong, 1997).

2.1 *Diagnostic Radiology*

2.1.1 *X-ray (Roentgen)*

X-ray is an imaging method that involves conventional operations and uses the X-ray source for imaging the relevant region (Tunacı ve Tiryaki, 2007). The planar, 2-dimensional image of the patient is taken. It is basically divided into two as radiography and radioscopy. In both methods, images are created by lowering the energies of X-rays from the patient onto image-receiving systems. While films are used as the image acquisition system in radiography, fluorescent screens are used in radioscopy and live images are obtained

Various cross-sectional imaging methods have come to the fore in order to obtain more detailed and clear images with the developing technology. However, the prevalence of X-ray shots in diagnosis continues (Kocaer et al., 2018).For example, the method that provides data in a forearm fracture or a chest radiography in such a cheap and simple way is again X-ray.

2.1.2 *Computed Tomography*

Computed tomography also uses X-ray sources, as in X-rays. Unlike X-ray, image acquisition systems are detectors (Bushong, 1997). The signals coming through the detectors are converted into numerical data in computer environment and images are created. Computed tomography is a cross-sectional imaging method. By rotating the X-ray tube and detectors around the patient together, 3D cross-sectional images are obtained and detailed view of the relevant region is provided. Computed tomography is mostly used in intracranial traumas, thorax and abdomen imaging (Kocaer et al., 2018).

2.1.3 *Mammography*

With the mammography device used in the diagnosis of lesions in the breast, the image of the region related to X-rays applied at low doses is obtained. With these devices, which have a very important place for the diagnosis of breast cancer, the breast of the patient is compressed thanks to the device units, so that the overlapping breast tissues are opened and thinned, and in this way, the patient is given a low dose of radiation (Kaya et al., 1997). These are devices that have evolved and diversified over time.

2.1.4 *Magnetic Resonance Imaging*

Magnetic resonance imaging method is a cross-sectional imaging method used mostly in imaging soft tissues. Radio waves are used as an energy source in the MR system. Proton atoms in the body are used as data source (Tekin et al., 2018). Thanks to radiofrequency energy, these protons are stimulated, causing a change in their current directions. Then, when this arousal is interrupted, protons leave a signal to the environment as they return to their former positions. These digitalized signals are converted into images in computer environment. An important advantage of the MR method is that the patient can take images in any plane without changing their position. It is used mostly in the central nervous system, musculoskeletal system, sometimes in the lungs, mediastinum imaging, separation of the uterus layers, etc.(Tekin et al., 2018).

2.1.5 *Ultrasonography*

On ultrasonography, unlike other radiology methods, supersonic waves are used. Sound energy, which is a type of mechanical energy, consists of the propagation of molecular vibration in the medium in a wave. Thanks to the probe heads used in the device, these sound waves are sent to the relevant area of the patient and the image is instantly displayed on the screen with the echoes made by these sound waves in the body (Rumack, 1991).

2.1.6 *Nuclear Medicine*

Nuclear medicine is a branch of medicine that provides diagnosis by monitoring the image obtained as a result of the detection and processing of gamma rays emitted using radioactive materials by the scanners using planar or tomographic methods. Generally, with this method, organs such as the brain, bones, heart, kidneys, digestive tube, liver and spleen can be examined in detail (Demir, 2000).

2.1.6.1 *PET (Positron Emission Tomography)*

In this technique, photons occurring at the same place and spreading in opposite directions are detected at the same time. The patient is injected with radioisotopes emitting positron. Positrons are positively charged electrons, and when they collide with (-) charged electrons on their path, the event of mass conversion into energy occurs. As the colliding masses disappear, the 511 KeV-powered anilation photon is released in opposite directions at an angle of 180° to each other. These anilation photons turn into scintillation by hitting the detectors. Scintilations turn into electrical signals in photo-multiplier tubes. Electric signals are processed in other electronic circuits and converted into images (Ayaz, 2017).

2.1.6.2 *SPECT (Single Photon Emission Computed Tomography)*

SPECT is the only computerized photon tomography system. The gamma photons emitted in one direction from the radiopharmaceuticals delivered to the body in the SPECT technique are based on the principle of creating a cross-sectional image by detecting them by the SPECT detectors and processing them in the computer unit. Power to separate images in SPECT, it is of poor quality than planar system, but the fact that organ depths are displayed at a higher contrast in SPECT compared to the planar system, and the fact that the numerical measurement of volume, size and activity is realized with high accuracy has made use of SPECT devices (Ayaz, 2017).

2.2 *Interventional Radiology*

Interventional radiological procedures are based on the process of imaging the relevant region under the guidance of other imaging methods by entering the body in various ways and it can be classified under various headings like biopsies, fluid drainages, percutaneous nephrostomies, biliary drainage, ablation procedures (Şirikçi, 2015).

3. Results

Medical imaging methods, in other words, the use of radiological methods in medicine, is quite common. With the use of these methods, diagnosis and treatment of diseases has become easier. The sensitivity of imaging methods is different for each tissue and organ. Therfore, these methods are developing day by day. In this study, all these methods are mentioned in detail.

4. Discussion

All medical imaging methods used for diagnosis have advantages and disadvantages. While CT, X-ray methods are preferred for anatomical anomaly due to hard tissues such as bones and joints; MR, nuclear medicine scintigraphy methods are preferred for physiological anomaly due to soft tissues such as brain and liver. In addition, among all these methods involving radiation, reducing the doses that patients and healthcare personnel will be exposed and should be a priority. For this reason, alternative methods such as ultrasound should be preferred in imaging of tissues and organs, especially near the surface, such as thyroid gland, kidney.

The device technologies used in cancer diagnosis and staging, which are very popular in radiology, are also in continuous development. While PET devices used in clinical routine have been used in combination with PET-CT until recently, today it is planned to be reduced in patient dose and produced as PET-MR combination. In addition, tomography techniques played a very important role in the diagnosis and follow-up of the treatment in the Covid-19 pandemic, which started in late 2019 in China's Wuhan region and spread all over the world. Republic of Turkey Ministry of Health, in conjunction with other health authorities, but negative PCR test to diagnose the disease in people with symptoms and clinical follow-up treatment has the effect of emphasizing the importance of shooting and suggested tomography (URL-1). We think that tomography shots will play an important role in the subsequent processes of the pandemic and in determining the damage to the tissues and organs of people who overcome the disease.

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Conflict of Interest

The authors declare no conflict of interest.

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Review

Gender Mainstreaming in Health

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Abstract: The study aims to evaluate gender inequality faced by women working at healthcare services sector and to create awareness. The term "gender" expresses the socially determined roles and responsibilities of women and men and it may vary among populations and over time. Gender equality can be ensured not only through access to healthcare services, professional equality, justice and equity, but also by equal distribution of responsibilities and income between men and women. The study reviewed the literature particularly by screening the recently printed papers on gender mainstreaming, especially in association with the health sector. According to World Economic Forum Global Gender Gap 2020, Turkey is ranked 130 among 153 countries in terms of gender equality. This fact may be secondary to low engagement of women in the labor force. Although working hours of men and women are equal in Turkish health sector, the monthly wage equals to 201.9 hours for men and 200.5 hours for women. Another indicator of gender gap is the gender-based violence against women. According to a study conducted by Ministry of Health in 2018, women are mostly exposed to violence in health sector by 62.5%; 48.1% of healthcare professionals are exposed to verbal violence and 64.9% of crimes of violence are committed by men. Women account for majority of professionals employed in health sector. Considering their health professions, approximately 70% of nurses are women, while the figure is 100% for midwives and approximately 50% for medical doctors.

In conclusion, gender-based discrimination may occur in terms of taking advantage of the opportunities, allocation and use of resources and access to services. Women are far worse affected by aforementioned discrimination, as they are more disadvantageous and have lower social status than men. This study advises a perspective that focuses on "gender parity" better regarding policies, strategies and processes in the delivery of healthcare services.

Keywords: *Gender; health; gender gap; gender mainstreaming*

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1. Introduction

On the contrary to the biological sex, gender gap emerges in the socialization process; therefore, it may or may vary among populations and cultures. Gender configures life of both men and women and ultimately, the diversity conveys a meaning that determines the gender gap in terms of access to resources beyond just "being different". This gap is prominently represented in the distribution of income. Today, women account for 70% of poor people worldwide. The situation, also called "feminization of poverty", applies to both rich and poor countries and it is an indicator that reflects the unequal status of women in work life and low status at home.

Although many women have no employment opportunity, female employees are paid an amount that is, averagely, three-fourths of the income gained by men (SBU, 2017). Globally, women account for half of the world population but they represent 1/10 of global income, 2/3 of working hours and 1/100 of properties (Akın, 2010). Their social status is low, while the life expectancy is longer but quality of life is poorer.

2. Gender Mainstreaming in Health

Healthcare sector is among professions that are obliged for uninterrupted services both in our country and at global scale. Operations modes are irregular and professionals face busy schedules due to the quality of the service. Healthcare professionals, while rendering healthcare services for patients, are at greater risk of occupational accident and disease along with professional deformation than other professions. One of the factors that lead to common existence of such problems in the sector is the insufficient increase of qualified personnel despite the recent climb in the demand to the healthcare.

Although number of medical doctors and nurses per patient is very high in our country, these two professions are so wearing and deterrent, as they need to undertake the roles that are beyond their professions. When Turkish data is compared to the health data of OECD, number of persons per medical doctor is 498.2 and mean 341.3 for Turkey and OECD, respectively. Moreover, number of persons per nurse is 431.2 in Turkey, while the figure is mean 102 in OECD countries (OECD, 2018).

3. Role of Woman in Healthcare Sector Regarding Professional "Feminization"

Woman is responsible for "care" of households according to the gender roles that have differentiated over historical process. Households include children, husband, elders and sick family members. Therefore, "care service" has been existing worldwide since very ancient times. Today, nursing care is the profession that clarifies this situation best (Eser, 2017). Gender roles differentiate in medicine. Men prefer surgical departments more, while women take part rather in medical departments. Here, the exception proves the rule. For example, there are more women in gynecology and obstetrics and pediatric surgery comparing to other surgical departments. Female medical doctors prefer departments that are characterized by less burden of night shift, less invasive procedures and less wearing (Urhan and Etiler, 2011). Female medical doctors also prefer pediatrics, family medicine, gynecology and obstetrics, dermatology and otolaryngology that are more compatible with female role and are not dominated by men (Ünver et al., 2010). A journal

published in British Medical Journal (Wallis et al., 2017) compared male and female surgeons regarding patients undergoing elective surgeries, post-operative morbidity, post-discharge re-hospitalization and one-month mortality. Although there was no difference between male and female surgeons in terms of post-operative morbidity and re-hospitalization, post-operative month 1 mortality was significantly lower for patients operated on by female surgeons than the patients operated on by male surgeons (TTB, 2019).

Number of female medical doctors with managerial positions, such as head of institute, dean, head of department, chief doctor and deputy chief doctor in universities, medical faculties and teaching and research hospitals, is disproportionally lower than number of female medical doctors working in the field of medicine. For example, only 3 of 10 deputy chief doctors are female in a teaching and research hospital, where the chief doctor is man; moreover, there is no female manager in many organizations (TTB, 2019). Considering participation of women to decision-making processes, there are 38 senior managers in Central Organization of Ministry Health; excluding the staff with no clear detail or empty positions, it is determined that only one of 24 senior managers is a woman (Danayiyen and Kıyak, 2017).

According to 2018 statistics of Ministry of Health, number of medical doctors, nurses, midwives and other healthcare professionals working at all sectors (public, university, private) are 91,559, 126,891, 52,495 and 121,206, respectively (Health Statistics, 2018). Women account for majority of professionals employed in health sector. According to OECD data, women represent 40% of all medical doctors in Turkey (Orhan and Yücel, 2017). Considering their health professions, approximately 70% of nurses are women, while the figure is 100% for midwives and approximately 50% for medical doctors (İlkkaracan, 2010). When the profession of health is compared with other fields, it is characterized by highest working hours, mean 42.5 hours per week. As already known, upper limit of the legally allowed working hours per week is 45 hours. Turkey is also characterized by highest working hours in healthcare sector among European countries (Etiler, 2012). Although working hours of men and women are equal in Turkish health sector, the monthly wage equals to 201.9 hours for men and 200.5 hours for women (Etiler, 2015). Another indicator of gender gap is the gender-based violence against women. According to a study conducted by Ministry of Health in 2018, women are mostly exposed to violence in health sector by 62.5%; 48.1% of healthcare professionals are exposed to verbal violence and 64.9% of crimes of violence are committed by men (TTB, 2019).

Conclusion

Gender-based discrimination deprives women of the right to life and education as well as professional life, equal wage and participation to decision-making processes, briefly of "benefiting from human rights". Gender of a person may be the underlying cause of discrimination regarding use of opportunities, allocation of resources and access to services in the field of health. Women are worse affected by aforementioned discrimination, as they are more disadvantageous and have lower social status than men. Considering the health sector, women should be allowed to take managerial roles along with being a labor force and their way should be smoothened in educational and scientific fields. The fact that female labor is both quantitatively and qualitatively intense in health sector clearly reveals out the importance of gender mainstreaming problem. The most effective way to ensure gender parity is to develop policies

that take the gender mainstreaming into account and to integrate a perspective that focuses on gender mainstreaming into laws and programs of the country.

Conflict of interest

Authors declare no conflict of interest

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Review

The Use of Therapeutic Ultrason in Control of Biofilm Infections

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Abstract: The purpose of this study is to evaluate the effectiveness of the antibiofilm feature of ultrasound by compiling researches on the use of therapeutic ultrasound in biofilm removal. The literature was scanned with the keywords "biofilm removal", "therapeutic ultrasound". Therapeutic ultrasound application can generate two possible bacterial responses, in the form of inducing bactericidal and bacterial growth. The bactericidal effect has been reported in different studies where high intensity occurs at low frequency, induction of bacterial growth occurs at low intensity and low frequency. For bactericidal effect with antibiofilm properties, ultrasound should be applied at high intensity and low frequency. The combined use of ultrasound with other methods, especially antimicrobials, ensures effective destruction of biofilms and prevents the development of antibiotic resistance.

Keywords: *Therapeutic ultrasound; biofilm removal; antibiotic resistance; antibiofilm; microbubble; cavitation effect*

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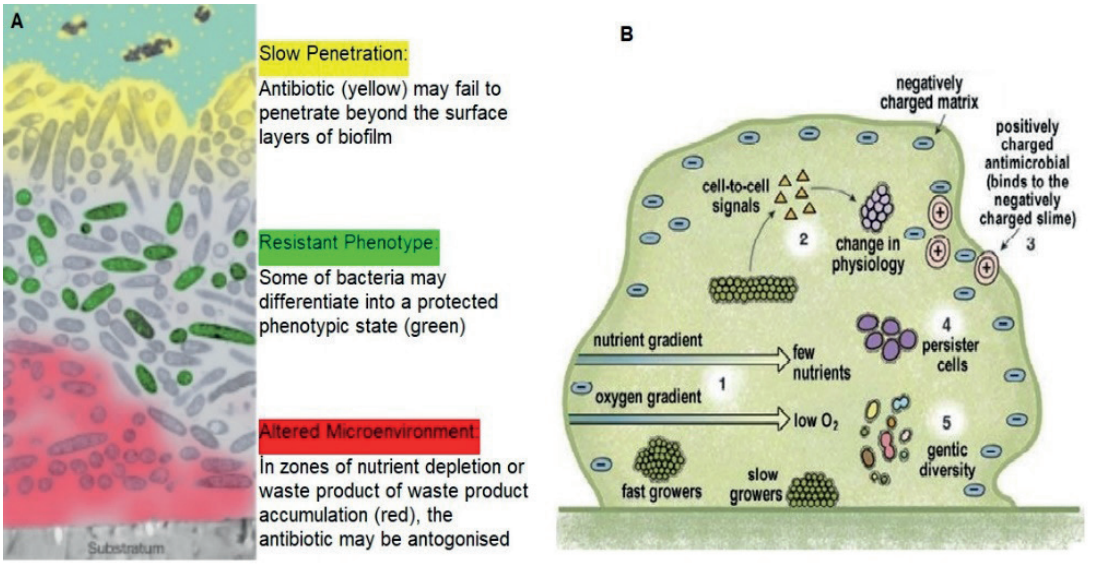
1. Introduction

Biofilm is a form of living together by attaching to a surface or each other with exopolysaccharide (EPS) created by microorganisms themselves. The concept of biofilm was first expressed in Costerton's studies (Costerton et al., 1987). Biofilm structure can be found on various surfaces such as water systems, living tissues, medical devices (Bayrakal and Baskın, 2018). Biofilms, it can show high tolerance against external threats such as mechanical stress, heat, UV radiation, disinfectants, antimicrobials and host immune system. Due to this tolerance, bacteria in a biofilm are a thousand-times more resistant to antibiotics (Mah, 2012). The National Institutes of Health (NIH) has suggested that 80 percent of human infections are related to biofilms. İn addition to this the Centers for Disease Control and Prevention (CDC) has announced that more than 65 percent of infections, transmitted from the emergency clinic, are inferable from biofilms (Percival, 2017). Various hypotheses describing antimicrobial resistance mechanisms in biofilm are presented in Figure 1A and 1B (Harrison et al., 2005; Stewart, 2001). Negatively charged EPS

ties to positively charged antimicrobials. EPS blocks phagocytosis and complement activation (Percival, 2004). Antimicrobials are significantly more effective against fast growing cells. Microorganisms in the depth of the biofilm grows slowly because they are exposed to low oxygen and supplements. So, they can escape antimicrobial effects. Intercellular signals change the physiology of the biofilm, allowing bacteria to produce molecular pumps that pump out antibiotics. Persister cells do not grow in the presence of antibiotics, however, the drug is removed, causing a normal bacterial colony. Genetical and physiological variety allow a few cells to endure.

Figure 1. Antimicrobial resistance mechanisms in biofilm (Harrison et al., 2015; Stewart, 2001)



Biofilm removal can be provided by physical, chemical and biological methods. Treatments such as heat shock therapy and ultrasound are physical methods. Enzyme treatment such as proteases and nuclease to EPS are examples of the chemical method. In the biological method, bacteriophages are used. Bacteriophages by multiplying inside biofilm bacteria disrupt the biofilm. Combined use of biofilm removal methods with antibiotic treatment is recommended by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), as an approach that increases the treatment success (Hoiby et al., 2015). Therapeutic ultrasound is used in physical therapy, rheumatic diseases, oncology brain tumors, control of biofilm infections, acceleration of wound healing, modulation of drug release in pharmacy and canal-root disinfection in dentistry. The biological effects of therapeutic ultrasound occur in a thermal and non-thermal way. The effects associated with heat during the application of ultrasound are thermal effects and the effects caused by cavitation and acoustic flow are non-thermal effects. The biofilm removal bactericidal characteristic of ultrasound is associated with the transient cavitation effect occurring at high intensity and low frequency (Erriu et al., 2014).

2. Materials and Methods

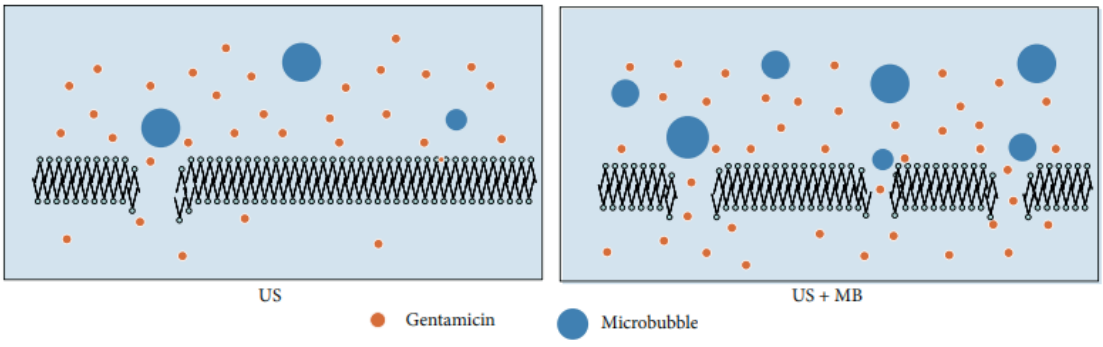
PubMed database was searched with the keywords "biofilm removal" and "therapeutic ultrasound". Among the searched articles, those related to food and environmental biofilm removal were eliminated. 48 articles published between 1980-2020, containing therapeutic ultrasound and antibiotic combined application for clinical use only, were evaluated. Articles considered as important in Table 2 have been summarized.

Table 2. Researches on biofilm removal of low frequency ultrasound (LFU)

Authors (Years)	Results
Pitt and Ross (2003)	Applying US at low frequency and intensity stimulates the growth of cells.
Al Bsoul et al. (2010)	LFU (93%) removed biofilm better than HFU (43%).
Seth et al. (2013)	LFU has a significant impact on biofilm-infected wounds.
Karosi et al. (2013)	LFU is a reliable method for biofilm removal.
Crone et al. (2015)	Biofilms were disrupted by the application of low frequency UAW.
Li et al. (2015)	Ultrasound, combined use of microbubble and HBD-3 provided good biofilm removal.

Low frequency ultrasound creates mechanical damage to membranes with cavitation effect. The combined use of microbubble agents that trigger bubble formation with LFU increases the therapeutic efficacy (Zhu et al., 2014). Increased therapeutic efficacy in microbubble use is presented in Figure 2.

Figure 2. Increasing the treatment efficacy by adding micro bubble (Zhu, 2014).



3. Results and Suggestions

Therapeutic ultrasound can generate two possible bacterial responses: inducing either bactericidal characteristic or bacterial growth. It has been reported in different studies that the bactericidal effect occurs at low frequency high intensity, induction of bacterial growth occurs at low intensity and low frequency. Therefore, it is recommended to apply ultrasound at high intensity and low frequency to provide bactericidal effect with antibiofilm properties. It is stated that the combined use of ultrasound with antimicrobial agent and/or the addition of agents such as microbubbles that increase the cavitation efficiency to the application environment may increase the treatment effectiveness. Applying combined treatments offers a great advantage in preventing the increase in antibiotic resistance rates as a result of unnecessary and wrong use of antibiotics. Since wrong applications can create unstable cavitations in the tissue and cause hemolysis, necrosis and bleeding, the way and duration of the application of ultrasound is very important in treatment.

Conflict of Interest

Author declares no conflict of interest.

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Review

The Role of Cardiopulmonary Rehabilitation in Patients with Infected COVID-19

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Abstract: The 2019 new type of coronavirus, or 2019-nCoV (with new name is SARS-CoV-2), is closely related to the coronavirus (batSL-CoVZC45 and bat-SL-CoVZXC21), which have similar characteristics like as severe acute respiratory syndromes. Spread of the virus happens from person to person with droplets or direct contact. The average incubation period of the infection is 5-6 days (2-14 days). In patients recovered from Covid-19 pneumonia and acute respiratuar disstress sendrome (ARDS). However, post-acute physiotherapy and rehabilitation needs for the patients are not completely known. According to the informations from other viral infections such as H1N1 and SARS, respiratory and physical function losses (muscle mass and muscle function loss, myopathy, contractures, neuropathy and/or weakness acquired in intensive care) are observed after acute illness, ARDS and intensive care processes. Furthermore cognitive and emotional dysfunctions (anxiety, depression, post traumatic stress syndrome) may affect participation and quality of life. Rehabilitation interventions should be started as early as possible in mild and moderate cases. The short-term goal of cardiopulmonary rehabiliation is to alleviate dyspnea, anxiety and depression, the long-term goal is to maximize the funcutionality of the patient, improve the quality of life and facilitate her return to society. Cardiopulmonary rehabilitation programme should be done mainly via videos, brochures, remote consultations or online to prevent cross infection for the patients with Covid-19. Guidelines for Covid-19 show that physiotherapy and rehabilitation practices should practised an individual basis, based on the results of multidisciplinary evaluation, when clinically necessary. Current guidelines and protocols state that applications using airway cleaning techniques, breathing exercises and assistive devices, exercise training and respiratory muscle training should not be applied in the acute period.

Keywords: *Coronavirus; Covid-19; cardiac rehabilitation; pulmonary rehabilitation*

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1. Introduction

1.1. *Cardiac Rehabilitatıon*

It includes a multidisciplinary approach carried out under the coordination of many disciplines such as physicians, physiotherapists, nurses, dieticians, psychologists, social workers to improve the physical, psychological and social functions of patients with cardiac disease to stabilize the progression of the disease and reduce mortality, allowing a more active life (Kim et al., 2019).

Cardiac rehabilitation is strongly recommended by the American Cardiology Association (ACC) and the American Heart Association (AHA) for the treatment of patients with coronary artery disease and chronic heart failure, as it has strong evidence levels (Scherrenberg, 2020). Core components of cardiac rehabilitation: healthy behaviour changes and education, lifestyle risk factor manegement, physical activity and exercise, diet, smoking cessation, psychosocial health, medical risk factor management, cardioprotective therapies, long-term management, audit and evaluation (Kim et al,. 2019).

1.2. *Pulmonary Rehabilitation*

In the declaration published by the American Thoracic Society and the European Respiratory Society in 2006, pulmonary rehabilitation is recommended to all chronic respiratory patients with symptomatic, have limited activities and/or whose disease cannot be controlled despite optimal medical treatment. Pulmonary rehabilitation is an interdisciplinary approach. It consists of a pulmonologist, a physiotherapist, a nurse, a dietician, a psychologist, a social worker, and a healthcare professional suited to the patient's needs (Nici et al., 2006). Core components of pulmonary rehabilitation: exercise training, supplemental oxygen during exercise, breathing low density gas mixtures, mechanically assisted ventilation, nutritional supplementation and advice, anabolic steroids, education, breathing retraining techniques, respiratory muscle training, neuromuscular electrical stimulation (Nici et al., 2006).

2. Covid-19 Infection Origined New Type Coronavirus (SARS-CoV-2)

The 2019 new type of coronavirus, or 2019-nCoV (with new name is SARS-CoV-2), is closely related to the coronavirus (batSL-CoVZC45 and bat-SL-CoVZXC21), which has similar characteristics of severe acute respiratory syndromes. The virus spreads from person to person through droplets or direct contact. The average incubation period of the infection is 5-6 days (2-14 days) (Vanessa, 2020). Based on the increasing evidence of increasing infection incidence we can say that due to the possibility of transmission by asymptomatic carriers, the SARS-CoV-2 shows a high pandemic. The most common symptoms of Covid-19 infection are dyspnea, tachypnea, oxygenation disorder SpO2<93%, PaO2/Fio2 ratio<300 infiltration of the lung area in 24-48 hours (Vanessa, 2020).

Patients with moderate or severe Covid-19 cannot seperated from medical managements. Decubitus, peripheral muscle weakness, muscular retractions, articular limitations, balance/postural disorders, and physical deconditioning are caused by prolonged bed rest. This complications could dramatically reduce

the chances of returning to pre-infection functional status (Brugliera, 2020). According to the severity of the disease, patients with uncomplicated (mild) Covid-19 infection**,** patients with moderate Covid-19 infection (viral pneumonia), patients who developed ARDS due to severe Covid-19 infection (Brugliera, 2020).

2.1 *Cardiopulmonary Rehabilitation in Patients with Infected Covid-19*

Physiotherapists are likely to have a role in the management of patients admitted to hospital with confirmed Covid-19. Globally, physiotherapists often work in acute hospital wards and intensive care units (ICU). In particular, cardiorespiratory physiotherapy focuses on the management of acute and chronic respiratory conditions and aims to improve physical recovery following an acute illness (Thomas, 2020).

Patients with uncomplicated (mild) Covid-19 infection

Almost all of these cases are recovering. It does not contain viral pneumonia. In an average of 80% of cases, there are symptoms fever, muscle/joint pain, cough, sore throat and nasal congestion. Airway secretion burden is extremely low. Respiratory physiotherapy and rehabilitation practices are not effective on the course of the disease. In cases with mild Covid-19 infection, it is recommended to be physically active at home, although it is stated that there is no indication for respiratory physiotherapy. In addition, the patients who are in quarantine at home can reduce their anxiety with relaxation exercises, pursed lip breathing, thoracic expansion exercises, respiratory control in prone lying down (İnce et al., 2020).

Patients with moderate Covid-19 infection (viral pneumonia)

In patients are observed ARDS in 67% acute kidney damage in 29%**,** acute cardiac damage in 23%**,** liver dysfunction in 29%**,** multiple organ failure after intensive care. It was reported that ARDS and/or multiple organ failure developed in 6% of the cases requiring intensive care hospitalization. Affected systems in the acute period are respiratory system, the cardiovascular system, the circulatory system, blood parameters, muscular system, neurological system (Vanessa, 2020).

Physiotherapy and rehabilitation in the acute period of Covid-19 infection

Guidelines for Covid-19 show that physiotherapy and rehabilitation practices should practised an individual basis, based on the results of multidisciplinary evaluation, when clinically necessary (İnce et al., 2020; Thomas, 2020). Current guidelines and protocols state that applications using airway cleaning techniques, breathing exercises and assistive devices, exercise training and respiratory muscle training should not be applied in the acute period. In the acute period of patients infected with Covid-19, airway secretion burden is extremely low. Therefore, Covid-19 infection does not require the use of airway cleaning techniques (Lazzaeri, 2020).

There is no indication for use of respiratory physiotherapy methods for the patients with moderate Covid-19 infection (viral pneumonia). Oxygen therapy may be required in half of the hospitalized patients due to Covid-19 pneumonia (İnce, 2020; Polastri, 2020). However, patients with moderate severity of Covid-19

infection (viral pneumonia) exercises in the bed, getting out of bed, sitting balance, standing, walking and upper/lower extremity exercises can be applied. Mobilization and exercises can be done with brochures and tele-rehabilitation applications (training videos, video calls, phone calls) for the effective and safe operation of physiotherapists (İnce et al., 2020; Vanessa, 2020).

Patients who developed ARDS due to severe Covid-19 infection (severe viral pneumonia)

It is especially severe in the patients with advanced cardiovascular and metabolic comorbidities. Negative hematological changes are seen more often in patients with severe disease: lymphocytopenia in 83.2%, thrombocytopenia in 36.2%, leukopenia in 33.7%. the high level of C-reactive protein reduce frequently, but alanine aminotransferase, aspartate aminotransferase, creatine kinase and D –dimer levels increase (Litao, 2020). Some of these cases show ARDS, sepsis, septic shock, and multiple organ failure, which are characterized by acute hypoxemic respiratory failure. Intubation and invasive mechanical ventilation are required in these patients who are followed up in the ICU. There is no indication for respiratory physiotherapy including airway cleaning techniques in viral pneumonia and ARDS (İnce et al., 2020). Physiotherapists who practise in the ICU can assist in positioning patients with severe respiratory failure associated with Covid-19, including the use of prone position to optimise oxygenation (Avard et.al., 2020).

Applications are beneficial such as 30-45 degree high lying. Passive/active joint opening exercises and mobilization can be done. Passive and active mobilization techniques should not be applied or cut off in the below cases; high fever, worsened dyspnea, breathing frequency>30 breaths/min, SpO2 <93% during the oxygen therapy FiO2> 50% during NIMV implementation, PEEP or CPAP>10cmH2O, presence of respiratory distress, the presence of arterial hypertension, bradycardia or tachycardia, arrhythmias, shock, deep sedation (İnce et al., 2020).

Physiotherapy and rehabilitation after Covid-19 acute period (post-acute)

In patients recovered from Covid-19 pneumonia and ARDS, the post-acute physiotherapy and rehabilitation needs are not completely known. Physiotherapy may play a vital role in the respiratory management and rehabilitation of patients with SARS-CoV-2/Covid-19. A cardiorespiratory therapist contributes a significant role in the management of patients with confirmed/suspected SARS-CoV-2/Covid-19 (Avard et al., 2020).

Information obtained from viral infections such as H1N1 and SARS, after acute illness, ARDS and intensive care processes; respiratory and physical function losses (muscle mass and muscle function loss, myopathy, contractures, neuropathy and/or weakness acquired in intensive care) indicate that cognitive and emotional dysfunctions (anxiety, depression, post-traumatic stress syndrome) may affect participation and quality of life (Beeching, 2020).

Patients who have successfully recovered from the acute Covid-19 enfection will require health support to define and quantify the consequences of the disease. Indeed, it is not clear if Covid-19 will leave permanent lung and/or physical damage. Alterations of lung tissue such as ground-glass opacities, consolidation,

vascular thickening, bronchiectasis, pleural effusion, crazy paving pattern and irregular solid nodules, may progress in over 80% of patients (Polastri et al., 2020).

In cases recovering from Covid-19 infection, physiotherapy and rehabilitation applications may be needed due to respiratory and physical function losses, cognitive disorders and emotional problems during the rehabilitation phase (Beeching, 2020). Prone positioning in intensive care can cause pressure sores, brachial plexus injury and plantar flexion contractures (İnce et al., 2020). Continued infection risk period (first 6-8 weeks); physiotherapy and rehabilitation can also contribute to reduce anxiety and depression in patients who experience delirium, anger, fear, dysthymia, insomnia, panic attacks or isolation due to isolation and intensive care during treatment or who show risk of non-compliance (İnce et al., 2020). In hospitalized patients with Covid-19; kidney dysfunction, hypertension, diabetes mellitus, comorbidities such as chronic heart disease and obesity cancer are observed (Scherrenberg et al., 2020). It is important for possible complications to be followed by telerehabilitation after discharge. Planning of blood pressure pulse and oxygen saturation controlled physical activities in kidney patients infected with Covid-19 (Scherrenberg et al., 2020).

Avoiding exercise and activities related to upper extremities that increase peripheral resistance. Exercise and activity should cut off if the pulse increases more than 20 beats and the blood pressure increases above 20 mmHg after the activity and post-exercise compared to rest. Planning of exercise and physical activity by individual follow-up. It should be kept in mind when when exercise describe. Because, Covid-19 can cause arrhythmia and/or myocarditis with cardiac involvement. Furthermore the drugs used in the treatment of Covid-19 can cause arrhythmia. Physiotherapists contribute to the functional levels of patients after discharge. While being included in the treatment program in this patient group, they should be monitored strictly and their clinical status should be monitored. Possible cardiac problems (e.g. arrhythmia, myocarditis) that may occur in the hospital period before starting rehabilitation should be controlled and stabilized (Sheehy, 2020). During the discharge from the hospital, it should be recorded the patient's emergency needs in terms of rehabilitation (e.g. safe mobility, symptom control (dyspnea, fatigue, pain), supplemental oxygen demand, adequate nutrition, adequate psychological/social support) and an individual assessment, including short/medium term needs (Gómez, 2020).

During the first 6-8 weeks of the patient's homelife, if no exercise capacity assessment has been made, infected patients are recommended to perform low-intensity physical activity/exercises on probability (including functional strengthening; the value of dyspnea and/or fatigue in the modified Borg Scale (0-10) points). Safe and effective communication solutions should be considered between patient and physiotherapist using video calling, digital resources (Sheehy, 2020). Do not use non-invasive ventilator support during exercise training in Covid-19 patients in infectious period, or use with patient-specific equipment supply (Gómez, 2020).

Covid-19: Time to reach the center stage of alternative models in cardiac rehabilitation

In the current pandemic, all options are to continue the delivery of cardiac rehabilitation. Using technology-based cardiac rehabilitation (TDCR) can increase accessibility to CR in areas where healthcare is difficult to

deliver. The short-term goal of pulmonary rehabilitation is to alleviate dyspnea and anxiety and depression, while the long-term goal is to maximize the patient's functionality, improve the quality of life and facilitate return to society (Sheehy, 2020).

Rehabilitation interventions should be started as early as possible in mild and moderate cases. Operations that can increase the risk of infection should be minimized. To avoid from the infection, a closed plastic bag should be used to close the mouth during expectoration. In addition, pulmonary rehabilitation of patients with Covid-19 should be done mainly through training videos, brochures, remote consultations or online instruction to prevent cross-infection. In acute care it may be necessary to take patients earlier than usual (İnce et al., 2020).

Patients should stay in their rooms. Group therapy and therapy should be prohibited in rehabilitation gyms; therapy should be provided in the patient rooms. Shared equipment should be decontaminated among patients; where possible, use disposable equipment (e.g. TheraBands instead of hand weights). Electrode sponges, hydrocollator heat packs, gels, topical lotions, dexterity training items, etc. special attention should be paid. When possible, plan therapeutic activities to minimize the number of staff involved. The number of staff should be reduced minimize when entering a patient's room (Gómez, 2020).

International Physical Activity Survey, Physical Activity Scale for the Elderly and The Barthel Index can be used to measure activities of daily living (ADL). Physiotherapy should begin at the inpatient treatment center and continue after inpatient rehabilitation. Early mobilization should include frequent changes of position, in-bed mobility, sitting position, simple bed exercises, and ADLs. Active limb exercises should be accompanied by progressive muscle strengthening (recommended program: 8-12 reps, 1 to 3 sets with 2 minutes of rest between sets, 3 sessions per week for 6 weeks).Neuromuscular electrical stimulation can be used to help strengthen. Walking, cycling or arm ergometry can apply (İnce et al., 2020).

Initially, aerobic activity should be kept below 3 MET. Then, progressive aerobic exercise should be increased to 20-30 minutes 3-5 times a week. Balance work should be included. Occupational therapy should focus on targeted interventions to facilitate functional independence and prepare patients for discharge as well as ADL guidance. Speech-language pathologists should evaluate and treat dysphagia and voice disorders caused by prolonged intubation (Sheehy, 2020).

Increasing aerobic capacity can provide short-term safe improvements in the function of the immune and respiratory systems in coronovırus patients. This can be produced mainly by three mechanisms: first, it can improve immunity by increasing the level and function of immune cells and immunoglobulins, regulating CRP levels, and reducing anxiety and depression. Second, it can improve respiratory system functions by acting as antibiotics, antioxidants and antimycotic by restoring normal lung tissue elasticity and strength. Finally, Covid-19 can act as a protective barrier to reduce risk factors, helping to reduce the incidence and progression of Covid-19 (Gómez, 2020).

Conflict of Interest

We declare that we have no conflict of interest.

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Review

The Relationship Mechanism Between Covid-19 and Renin-Angiotensin System

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Abstract: Coronaviruses (CoVs) are a group of ribonucleic acid (RNA) viruses that can cause respiratory, intestinal and central nervous system infections in humans and animals. Especially two strains caused severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). In addition to these strains, SARS-coronavirus 2 (SARS-CoV-2), appeared in Wuhan, China in December 2019. It soon affected the whole world and was declared a pandemic by the World Health Organization. The disease caused by the SARS-CoV-2 virus is called coronavirus disease (Covid-19). There are studies in the literature, infection mechanism of Covid-19, is binding of the virus to the receptor of angiotensin converting enzyme-2 (ACE2) and subsequently internalization of the complex by the host cell. The recognition of ACE2 as a co-receptor for SARS-CoV-2 suggest that there is cellular entry in ACE2 expressing tissues, including lung, heart, kidney, brain and intestine. The studies, have extensively studied the RBD-ACE2 complex, spike protein, and free RBD systems of SARS-CoV-2 and SARS-CoV using protein-protein docking and molecular dynamics simulations. The free binding energy of SARS-CoV-2 to RBD-ACE2 has been shown to be lower than the free binding energies of other coronavirus types. It was emphasized that this situation could be related to the more contagious SARS-CoV-2. While it seems such as clear that SARS-CoV-2 infects with binding mechanism the human ACE2 receptor of the RBD domain, the molecular mechanisms still remain mysterious. The present findings are expected to be useful for the disease prevention and control as well as drug and vaccine development of Covid-19.

Keywords: *Covid -19; ACE1; ACE2; renin; angiotensin*

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1.Introduction

Coronaviruses (CoVs) are a group of RNA viruses. Coronaviruses can cause respiratory, intestinal, liver, and central nervous system infections in humans and animals (Chen & Guo, 2016; Fang, 2020). Six coronavirus strains have been identified that can infect humans. Especially two strains caused severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), two large-scale pandemics (He, 2020). In addition to these strains, a new SARS-CoV-2 appeared in Wuhan, China in December 2019. It soon affected the whole world and was declared a pandemic by the World Health Organization (WHO). The disease caused by the SARS-CoV-2 virus is called coronavirus disease (Covid-19). The epidemic has become a global public health crisis with its continuous development and rapid spread (He, 2020; Sun et al., 2020). Covid-19, is also called SARS-CoV-2 due to its close relationship to SARS-CoV (Sun et al., 2020). The most common clinical manifestations of the patients are fever, cough, shortness of breath and fatigue, and some patients have radiographic ground-glass lung changes and finally died from acute respiratory distress syndrome (ARDS) (Sun et al., 2020; Zhou et al., 2020). Covid-19 was found to be caused by SARS-CoV-2 virus-induced pneumonia by clinicians based on clinical symptoms and other criteria, including a rise in body temperature, decreased lymphocyte count, and decreased white blood cells (Zhou et al., 2020). SARS-CoV-2 cell penetration occurs through the receptors. This receptor binding sites (RBD) of SARS-CoV-2 on the protein coat are functional for infection and virus viability in the host cell. Although the binding mechanism of SARS-CoV-2 human cell infection by RBD and angiotensin converting enzyme 2 (ACE2) receptor seems clear, its molecular mechanisms are still unknown. According to some studies showing that the mechanism of infection of Covid-19 is binding of the virus to the receptor of ACE2 and infects by the host cell (He, 2020). This review will examine physiological aspects of the Covid-19 and renin-angiotensin system (RAS) in different organs/systems. It is shown in the literature that the studies on this subject are contradictory.

2. Covid-19 in ACE2 and Renin Angiotensin System

When the molecular structure of SARS-CoV-2 is investigated it consists of spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins (Du L., 2009; Sun et al., 2020). The S protein has two regions. The role of the S1 protein is to bind to the receptor on the host cell membrane. The S1 protein also has an N-terminal domain (NTD) and three C-terminal domains (CTD1, CTD2, CTD3). S2 protein is responsible for fusion to the host membrane (Gui et al., 2017; Li, 2016; Wu et al., 2020). SARS-CoV the RBD is located in the CTD1 of the S1 region. SARS-CoV attaches to RBD protein by binding of human host cells to ACE2. Therefore, the prerequisite for the infection of SARS-CoV to human is the interaction between RBD and ACE2. Due to the high similarity between SARS-CoV and Covid-19, Covid-19 was expected to use the ACE2 molecule as a receptor to infect humans (Song, Gui, Wang, & Xiang, 2018; Xu et al., 2020). Studies show that Covid-19 has a higher affinity for binding ACE2 than SARS-CoV (Wrapp et al., 2020). The total free energy of S protein of SARS-CoV-2 appears to be low compared to that of SARS-CoV. This may also provide insight into the evolution of SARS-CoV-2 because SARS-like CoVs are thought to be caused by bats known to have a higher body temperature than humans (Cui, Li, & Shi, 2019; He, 2020). SARS-CoV-2's RBD has better solubility than SARS-CoV may explain that Covid-19 has higher infectivity than SARS-CoV (He, 2020). ACE2 is the aminopeptidase responsible for the separation of angiotensin-I (AngI) and angiotensin-II

(AngII) into angiotensin-(1-9) and angiotensin-(1-7) peptides (Mali et al., 2020). It is expressed in a variety of tissues in the human body, including the lung, heart, kidney, small intestine, vascular endothelium, renal proximal tubular epithelium, intestinal epithelium, macrophages and the brain. Testis ACE, which has a smaller ACE isoform, is expressed only in the adult testicle (Masuyer et al., 2014). ACE2 expression in the lungs is concentrated in type II alveolar cells, macrophages and moderate bronchial and tracheal epithelial cells (Hamming et al., 2004; Kai, 2020).

3. Treatments Targeting ACE2 and AngII

Covid 19 disease has been observed to be higher in individuals with chronic disease. There are concerns about whether to increase the severity of Covid-19 in hypertension and cardiovascular disease (CVD) patients who take their angiotensin receptor blocker (ARB) and ACE inhibitor (ACEI) (Kang et al., 2020). In contrast, it has attracted attention in publications that argue that ARBs are useful in the prevention and treatment of lung damage caused by Covid-19 (Vaduganathan M, 2020). There are no data on the effects of ARBs and ACEIs on lung ACE2 expression in animal models or humans (Kai, 2020). A small case study reported that plasma AngII levels were markedly elevated and linearly associated with viral load and lung injury severity in Covid-19 pneumonia patients. (Liu et al., 2020). The beneficial net effects of ARB have been proposed in acute lung damaged rodents infected with SARS-CoV (Kai, 2020; Kuba K, 2005). Another treatment is transmembrane protease serine 2 (TMPRSS2), a membrane protease for ACE2 preparation, a very important step for Covid-19 and fusion of target cell membranes and consequently entry into viral cells (Hoffmann M, 2020). Clinical studies on TMPRSS2 inhibitors for the treatment of Covid-19 are ongoing (Kai, 2020).

Conclusion

This review is written considering the data from the most recent studies on Covid-19 and the renin-angiotensin system mechanism. The contradictions in the literature clearly attract attention. We think that the ongoing clinical studies on RAS will eliminate the existing uncertainty.

Conflict of Interest

Authors declare no conflict of interest.

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Review

Evaluation of the Content of National News Reflected on the Internet about Covid-19 Pandemic

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Abstract: The coronavirus, which started in China and spreads almost all over the world, and whose source is not known exactly, but is regarded as illegally sold, can have a fatal effect on humans. Today, the number of people caught with coronavirus (Covid-19) is rapidly increasing. In order to eliminate this disease caused by the coronavirus, quarantine applications are carried out in many countries, curfews, curfews out of the country or out of the city, wear a mask, etc. Health professionals work day and night. However, the vaccine of the coronavirus has still not been found. In response to this situation, the World Health Organization has declared the Covid-19 epidemic as a pandemic. This study was carried out with the aim of evaluating the national news published in digital media regarding the coronavirus, which is declared as a pandemic worldwide. For this purpose, the keywords "Coronavirus, Koronavirüs, Covid-19, Pandemi, Covid 19, Kovid-19" were entered into the Google search engine. January 1, 2020-May 1, 2020 during the ten newspaper archives can be accessed on the number of the highest circulation national news website in Turkey, 150 news content was evaluated. In the study, content analysis, one of the qualitative research techniques, was used to analyze the data. As a result of the research, it has been determined that the most handled issues regarding Covid-19 in the news sites of the related newspapers are general information about Covid-19, about the current situation in Turkey coronavirus, the effects of coronavirus and that the coronavirus in the world, respectively. It has been determined that the least discussed issues in the news sites of the related newspapers are: the statements of the World Health Organization (WHO) regarding the coronavirus, the criticisms about the corona virus, post-pandemic life and coronavirus data presented in famous individuals.

Keywords: *Covid-19; pandemic; epidemic; coronavirus; news; content analysis*

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1. Introduction

Humanity had to fight various diseases for centuries. When it comes to the 21st century, it has seen that countries have to struggle with many diseases despite the developments in medicine and the advancement of technology. The Covid-19 outbreak (coronavirus) is one of these diseases. According to the Ministry of Health General Directorate of Public Health (2020), the coronavirus is a disease that started in China (December 31, 2019) and whose source is not fully known but is still sold as illegal.

As the beginning of March 2020 slowed down the pandemic in China, Covid-19 incidents and related deaths started to increase rapidly in Iran, South Korea and Italy. As of March 2020, cases have been reported in over 100 countries worldwide. Covid-19 first cases were detected in Turkey on March 11, 2020 (Ministry of Health General Directorate of Public Health, 2020). Table 1 represents information about the Covid-19 pandemic in some countries.

Table 1. The number of Covid-19 cases by countries (21.05.2020)

	Countries	Total Cases	Total Deaths	The Mortality rates by Case Numbers (%)	Total Recovered
1	USA	1.588.383	95.066	6	369.625
2	Russia	317.554	3.099	1	92.681
3	Brazil	310.921	20.082	6,5	125.960
4	Spain	280.117	27.940	10	196.958
5	UK	253.032	36.151	14,3	10.517
6	Italy	228.006	32.486	14,2	134.560
7	France	181.951	28.242	15,5	63.976
8	Germenay	179.021	8.309	4,6	158.087
9	Turkey	153.548	4.249	2,8	114.990
10	Iran	129.341	7.249	5,6	100.564

As cited in: Eriş, H. and Ayhan, Z. (2020). Covid-19 perceptions and attitudes of health workers in Turkey. Journal of Critical Reviews, 7 (12), 1142-1150.

Countries have begun to take various precautions due to the rapid increase in the number of individuals caught with coronavirus, the virus has a lethal effect on individuals, and the vaccine is still not available today. In addition, the coronavirus has been declared a pandemic by WHO. The word "pandemic" usually refers to a common epidemic of infectious diseases across an entire country or simultaneously across one or more continents (Honigsbaum, 2009; Qiu et al., 2016, 2017). Today, the phenomenon of pandemic has not become just a personal, biological problem but also political, economic, social and technological problem (Eriş and Ayhan, 2020). Many scientists working in various fields state that different approaches from the past will emerge and be adopted in many fields with the effect of the Covid-19 pandemic (Yılmaz, 2020).

This study was carried out with the aim of evaluating national news on digital media related to Covid-19 pandemics. In this direction, firstly, the summary and introduction sections are included in the study, and then the research section is included in the material and method section. By analyzing the content in the material method section of the study, the distribution of the news in the digital media regarding the Covid-19 pandemic according to the topics and sources, etc. are included. Then, findings, discussion and conclusion are included.

2. Materials and Methods

Research January 01 in Turkey 2020-01 May 2020 was carried out on the date of circulation of newspaper archives can be achieved the highest number of national news websites. Thus, 150 news have been evaluated considering the headlines of the news. In the study, content analysis, one of the qualitative research techniques, was used to analyze the data. In Table 2, the websites and keywords where the news on coronavirus are examined are given:

Table 2. National websites and keywords reviewed in the research

Websites	**Sabah, Hürriyet, Sözcü, Milliyet, Türkiye, Posta, Akşam, Yeni Şafak, Takvim ve Korkusuz**
Keywords	"Koronavirüsü", "Koronavirüs","Covid-19","Pandemi", "Covid-19", "Kovid 19"

Table 2 shows the keywords searched in the Google search engine and the limitations of the research in the study. In addition, the websites included in the research were preferred because they are the top ten newspapers with the highest triage in gazetetirajlari.com.

3. Results

The news obtained from the websites of the related newspapers has been examined in terms of the publication date of the news, the source of the news, the title of the news, etc. The news examined were handled by the researchers according to their subject matter in Table 3.

Table 3. Distribution of all news reviewed in the research by topic

Subject of the News	**Number of News**	**Percentage of News (%)**
General information	25	17
Current status of the coronavirus in Turkey	22	15
Effects of coronavirus	18	12
Coronavirus in the world	18	12
Symptoms of the coronavirus	10	7
Measures taken	9	6
Vaccine studies	7	5
Information about pandemic	8	5
Success of health workers	6	4
Treatment processes of coronavirus	5	3
Pandemic hospital	5	3
The sacrifices made by healthcare professionals	3	2
Social assistance fees	3	2
Other (Treatment costs related to coronavirus, second wave, social isolation)	3	2
Life after a pandemic	2	1
Statements of the WHO for corona	2	1
Coronavirus in famous individuals	2	1
Reviews of the data presented	2	1
Total	150	100

In Table 3, the news on newspaper websites examined in the research are mostly published the subjects of general information about the coronavirus, the current state of the coronavirus in Turkey, the effects of coronavirus and coronavirus in the world.

If the distribution of all the news examined in the research according to their sources is examined, it was determined the news was published mostly in Sözcü (40%), Milliyet (23%) and Sabah (17%) newspapers, respectively.

In the literature, it was found that the national news examined were published in digital media mostly in March 20 (68 news, 45% of all news) and April (82 news, 55% of all news). The reason of this is considered as the first case of Covid-19 in Turkey has been emergenced on March 11, 2020. It is determined that the news about the Covid-19 pandemic in the world on March 2020 has been published mostly about the subjects of coronavirus (19%), general information of Covid-19 (19%), the effects of the coronavirus (15%) and coronavirus current situation in Turkey (12%) respectively. The order of the most published news in April is seen about the subjects of: coronavirus current situation in Turkey (17%), general information of Covid-19 (15%), coronavirus effects (10%) and coronavirus symptoms (10%). It was determined that the news about the Covid-19 pandemic, published in March, were mostly received from Sözcü (45%), Milliyet (25%) and Sabah (17%) websites and the news published in April were mostly received from the websites of Sözcü (36%), Milliyet (21%) and Sabah (18%).

In this research, the most published news related to coronavirus has been examined in all three newspapers with Covid-19 pandemics. According to this in the newspaper website of Sözcü, the most published news regarding to subject respectively is coronavirus effects (15%), general information about coronavirus (13%), the world coronavirus (12%) and the current status of coronavirus in Turkey (12%). In the Milliyet newspaper website it is general information about coronavirus (24%), the current status of coronavirus in Turkey (21%), the world coronavirus (18%) and the effect coronavirus (9%). And the Sabah newspaper website is respectively coronavirus effects (19%), the world coronavirus (15%), coronavirus symptoms (12%) and current status of coronavirus in Turkey (8%).

4. Discussion

In the literature, it has been determined that there are studies related to Covid-19 pandemics since 2020 (Bostan et al., 2020; Çetintepe, 2020). However, no study analyzing the news on the websites of the related newspapers for Covid-19 pandemics has been found. Therefore, this research is thought to be the first in terms of revealing the analysis of national news in digital media regarding the Covid-19 pandemic.

Conclusion

The following results were reached in this study: In digital media, it was determined that the most addressed issues relating to Covid-19 is: general information, the current status of the coronavirus in Turkey, the coronavirus in the world and the effects of the coronavirus. It was determined that the news related to the subject were published mostly on the websites of Sözcü, Milliyet, Sabah newspapers and

published most in April. It has been determined that the most discussed issues related to the Covid-19 pandemic in March and April of 2020 were similar. It can be said that the news distributions according to the newspapers were also similar. This study is thought to be beneficial in terms of guiding future studies. For the content analysis studies on Covid-19 pandemics in the future, researchers may be advised to examine a longer period of time or turn to the effects of the coronavirus.

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Conflict of Interest

The authors declare no conflict of interest.

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Review

Precautions Taken in Radiotherapy Clinics in Covid-19 Pandemic

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Abstract: It has been shown that cancer patients may have a higher risk of Covid-19 than non-cancers, and cancer patients are affected more rapidly than Covid-19. Covidien Turkey as well as in all the world-pandemic period 19 measures taken urgently in the radiotherapy clinic and has been implemented. The scope of measures and applications taken in this study was evaluated. One-to-one interviews with radiotherapy clinics have determined the precautions taken in the clinics. The measures proposed by the Ministry of Health and the Turkish Radiation Oncology Association and the measures applied by the American Radiation Oncology Association were compared. Hygiene, which is the first precaution for Covid-19, has been emphasized in all clinics and measures have been taken regarding the use of necessary protective equipment. By making arrangements in the patient hours, the confrontation of patients in the waiting rooms is minimized. Before each treatment, the risk of transmission in the clinics was reduced by asking for additional tests from those with suspected Covid-19 by measuring the fever of the patients and monitoring the patient. Patients who were diagnosed with Covid-19 were discontinued from their general condition by stopping their treatment until they recovered. The measures taken are similar to those taken worldwide. It is pleasing that the number of patients decreases day by day and the number of cases seen in clinics is low. It should be taken into consideration that additional measures will be needed in case of new attack periods.

Keywords: *Covid-19; radiotherapy; protection methods; treatment change; hygiene measures; overtime planning*

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1. Introduction

The coronavirus, first seen in China about 17 years ago, caused the death of millions with the SARS outbreak (Liang et al., 2020). Later, it was determined that the virus, which evolved with the transition between species, could be transmitted to human and striking facts were shown by experiments. The virus has been reported to affect the respiratory tract and has to cease close contact. It was a concern that the vaccines obtained did not provide complete protection. In late 2019, there was fear, and the virus was

transmitted to humans and spread rapidly to the world. Due to its spreading rate and an increasingly bad situation, a pandemic occurred in a short time, and countries faced rapidly increasing deaths against taking urgent measures in order (Combs et al., 2020).

Symptoms seen by transmission of the virus to humans have been reported as high fever, cough and shortness of breath. The first case was reported on March 10, 2020 in Turkey. With the announcement of the pandemic, the Ministry of Health sent instructions to hospitals to take necessary measures (Wang et al., 2020).

Radiotherapy is a radiation therapy used in the treatment of cancer patients. Most of the treatments of cancer patients are covered by radiotherapy. Radiotherapy can sometimes be accompanied by surgery and chemotherapy. Radiotherapy is a long-term treatment given to the patient in fractions. Treatments can last for about 5-6 weeks. This increases the risk of close contact and transmission in radiotherapy clinics ("Radiotherapy-Ministry of Health," 2017).

Wang et al.(Wang et al., 2020) and Liang et al. (Liang et al., 2020) showed that cancer patients may have a higher risk of Covid-19 and cancer patients are affected faster than Covid-19 compared to non-cancerous individuals. Radiotherapy clinics are going through a new and difficult period with Covid-19.

Keeping oncology clinics in operation during this period has brought some special precautions. The Ministry of Health has reported the measures to be taken in radiotherapy clinics in a letter. Similarly, the Turkish Radiation Oncology Association (TROD) has sent a recommendation letter containing measures to be followed by the clinics ("Ministry of Health Precautions," 2020; TROD, 2020). The American Clinical Oncology Association (ASCO) has provided recommendations to colleagues and precautions to be taken based on the conditions they face across the World ("ASCO," 2020).

Employees, patients and patient relatives should be informed about the symptoms of Covid-19 and ways of prevention. Face to face interviews with patients should be kept as short as possible. Informations should be made by phone. Patient appointments should be well organized and the necessary free time period should be provided between each patient. Attention should be paid to hygiene rules first, and situations that would threaten both the patients and their relatives should be avoided with the new emergency plans created ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020).

As the primary way of protecting against Covid-19 is hygiene and close contact, necessary measures should be taken in general radiotherapy units and patient waiting rooms in control and treatment rooms ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020). Adequate disinfectant should be provided and patients and staff should be trained on the effective use of disinfectants. For surface disinfectants, it is important to use fast active solutions ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020). Relatives of the patients should be prevented to accompany the treatment as much as possible. Thus, the number of people contacted in the clinic should be tried to be reduced. A critical issue in this particular pandemic is the availability of protective clothing. Treatments will not be disrupted as long as there are sufficient protective equipment ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020).

It should be noted that masking to personnel and patients protects both sides. Care must be taken in this regard and unmasked patients should not be taken. As a more advanced personal protection equipment, disposable coveralls, disposable gowns and face shields should be used. Considering the difficulty of working with the mask for a long time, the working times applied to the staff should be arranged according to the patient appointments. The personnel's right to leave should be observed and should not be overworked. Treatment planning should be made at a certain time of the day for patients known or suspected of Covid-19. For patients at high risk of Covid-19 (such as patients with lung cancer), treatment planning should be done at a different time than Covid-19 patients. Separate access and equipment should be used for patients without Covid-19 and for patients with known or suspected Covid-19. In order to detect the early onset of typical Covid-19 symptoms (fever, cough, sore throat, shortness of breath, fatigue) in patients treated in the department of radiation oncology, it is recommended that both employees and patients who come to the treatment be checked daily and subjected to a short questionnaire including symptoms. Treatment of patients should be revised and hypofractionated treatments should be initiated when necessary ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020).

The time period between the treatment periods of patients should be extended and all equipment used after each patient should be disinfected. In patients undergoing radiotherapy and suspected of having typical symptoms of Covid-19, treatment should be discontinued immediately and the test results should be followed by sending the patient to a pandemic clinic. Radiotherapy and Covid-19 patients are at risk for serious complications such as pneumonia and hospitalization. According to the Zhang et al. article (Zhang & Zhang, 2020), there is a strong relationship between radiotherapy and the serious effects of Covid-19 infection (HR=4.079, 95% CI 1.086-15.322, P=0.037). Although these data are limited, interruption of radiotherapy should be considered in patients with active Covid-19, since continued treatment can lead to more serious complications. There are no clear indications of how long a patient should overcome the symptoms of Covid-19 before starting radiotherapy. However, treatment should not be continued until to be sure that the virus is no longer available. In Covid-19 positive patients who do not start treatment, it should be recommended to start treatment after recovery. It is recommended to postpone cancer screening procedures such as mammograms and colonoscopy. It is recommended that cancer screening procedures continue with benefit/loss analyzes. It is deemed appropriate to suspend the follow-up of the follow-up patients except for emergencies and re-plan according to the current risk ("ASCO," 2020; "Covid-19/Ministry of Health," 2020; TROD, 2020; Wang et al., 2020).

As a result, the measures taken are similar to those taken worldwide. It is pleasing that the number of patients decreases day by day and the number of cases seen in clinics is low. It should be taken into consideration that additional measures will be needed in case of new attack periods. The important thing is to understand how much these measures are applied in clinics. Our work on flour continues.

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Conflict of Interest

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Review

The Importance of Antimicrobials in the Public Health

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Abstract: As in the past, today, antimicrobial products remain important in public health. Antimicrobial products used to protect against epidemic during the pandemic attracted the attention of the public. Antimicrobial agents stops or decelerates the spread of microorganisms. Microorganisms include bacteria, viruses, protozoans, and fungi. Increasing the effectiveness of antimicrobial products against microorganisms is very important today. Antimicrobial products we can see in every area of our daily life in house, workplace, or at school. In this review, we aimed to give brief information under the headings impact mechanisms of antimicrobials, production sources of antimicrobials new generation antimicrobials; what is safe antimicrobial in public health?

Keywords: *Antimicrobials; antifungal; antibacterial; antiviral*

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1. Introduction

Antimicrobials are defined as substances that have the power to reduce the presence of microorganisms or kill them completely. Antimicrobials can be classified according to their functions and the organism it acts on. Antibiotics that prevent the reproduction of bacteria are one of our most particularly weapon in fighting bacterial infections (Törün et al., 2017). Coronavirus-19 (Covid-19) appeared in Wuhan, China in December 2019 and with the announcement of this pandemic, the importance of antimicrobials became even more understandable. The use of antimicrobial effective disinfectants and antiseptics has increased rapidly today.

Antimicrobial drugs can be grouped based on the microorganisms to which they are effective. For example, antibiotics against bacteria and antifungals against fungi are used. They can also be classified

according to their functions. Agents that kill microorganisms are called microbicide, and only agents that inhibit their growth are called biostatic (Antimicrobial; https://en.wikipedia.org/wiki/Antimicrobial accessed; 30.06.2020). Microbicides are used for the purpose of microorganisms such as viruses or bacteria. Biocide is define intended to destroy, deter, render harmless, or exert a controlling effect on any harmful organism. Any biocidal compound that is to reduce its infectivity or substance. We can give wood tar as an example. The use of antimicrobial drugs to treat infection is called Antimicrobial Chemotherapy. Antimicrobial Chemotherapy can be classified as Antibacterial Chemotherapy Antifungal Chemotherapy Antihelminthic Chemotherapy Antiprotozoal Chemotherapy Antiviral Chemotherapy. Also, the use of antimicrobial drugs to prevent infection is called Antimicrobial Prophylaxis. (Antimicrobial; https://en.wikipedia.org/wiki/Antimicrobial accessed; 30.06.2020).

1.2. *Antibacterials*

Bacterial infections are among the important infectious diseases. Hence, over 60 years of extensive researches have been launched for achieving new antimicrobial medicines isolated from different sources. Despite progress in development of antibacterial agents, there are still special needs to find new antibacterial agents due to development of multidrug resistant bacteria (Moghadamtousi et al., 2014)

1.3. *Antivirals*

Lack of effective therapeutics for the most of viral diseases, emergence of antiviral drug resistance, and high cost of some antiviral therapies necessitate finding new effective antiviral compounds (Lemoine et al., 2013; Moghadamtousi et al., 2014; Tomei et al., 2005) Antiviral drugs are a class of medication used specifically for treating viral infections. Like antibiotics, specific antivirals are used for specific viruses.

1.4. *Antifungal*

Antifungals are used to kill or prevent growth of fungi. Fungal and human cells are similar at the molecular level, making it more difficult to find a target for an antifungal drug to attack that does not also exist in the host organism. In addition to their use in medicine, antifungals are often preferred to control fungal growth in humid or wet places, especially indoors. Sodium bicarbonate (baking soda) blasted on to surfaces acts as an antifungal.

2. Non-Pharmaceutical Antimicrobials

A wide variety of chemical and natural compounds are used as antimicrobials, organic acids and salts; lactic acid, citric acid, acetic acid are used in food either as food additives or as disinfectants. For example, acids are usually sprayed on the beef carcasses, and then washed or steamed to reduce the amonunt of *Escherichia coli*. Copper alloy surfaces have antimicrobial properties due to their natural structure and can kill microorganisms such as *E. coli* and *Staphylococcus*. In addition to regular cleaning, antimicrobial copper alloys are installed in some health facilities and metro transit systems. Other heavy metal cations such as Hg^{2+} and Pb^{2+} (cive and lead ions) have antimicrobial activities, but they may be toxic. Also it is known

that laurel, ceramic, carnation and thyme oils are most effective against food-borne bacterial pathogens. Its active ingredients are generally terpenoids and secondary metabolites. Many of these agents appear to have different structures and modes of action than antibiotics in use, that detection the concern that cross-resistance may be minimum with the agents currently in use. The resistance of a bacterium that has lost its sensitivity to an antibiotic against other antibiotics with similar chemical structure or similar mechanism of action is called cross-resistance.

3. Classification of Antimicrobial Agents

The efficiency of an antiseptic must be measured in relation to three main factors: concentration, time, and temperature. It is desirable to know the minimum concentration at which an antiseptic will be effective. Some antiseptics such as phenol lose their antiseptic activity after a certain dilution, whereas mercurial preparations still inhibit bacterial growth at very high dilutions. Most antiseptics act faster under increased temperatures; the activity of coal-tar derivatives, for instance, is doubled by a rise in temperature from that of a cool room to body heat. Many antiseptics destroy certain types of microorganisms and not others. Many others will kill bacteria but not their spores, which are walled, usually dormant, reproductive bodies. Alcohols are among the most widely used antiseptics, especially ethyl and isopropyl alcohol, which are commonly used in a 70% concentration in water. They are also widely used in combination with other antiseptic agents. The phenols contain a large number of common antiseptics and disinfectants, among them phenol (carbolic acid) and creosote, while such bisphenols as hexyl resorcinol and hexachlorophene are widely used as antiseptic agents in soaps. Chlorine and iodine are both extremely effective agents and can be used in high dilution. The quaternary ammonium compounds are more widely used as disinfectants than as antiseptics. Certain acridine dyes are used as antiseptics, as are some aromatic, or essential, oils (Antimicrobial Agent, https://www.britannica.com/science/antimicrobial-agent Accessed; 30.06.2020)

4. New Generation Antimicrobials

It includes the development of small molecule libraries customized for bacterial targets, as well as by applying metagenomics to increase the number of isolations from various media or to identify bioactive compounds produced by microorganisms that are currently unknown and not cultured. Recently, many bacterial species, fungi, algae and plants are employed to produce clean, nontoxic, biocompatible and environmentally friendly silver nanoparticles (SNPs). The advantage of biogenic SNPs are that the molecule can be coated with proteins (secreted by microorganisms such as fungi) allowing them more stable in the aqueous solutions (Korani et al., 2015). Nanomaterials today are a promising platform for alternative measures to control bacterial infections as they offer prolonged antimicrobial activity with negligible toxicity, compared with small molecular antimicrobial agents that display short-term activity and environmental toxicity. The antimicrobial nanoparticle physically destroys cell membranes of the organism which prevent development of drug-resistance microbes (Farouk at al., 2018). Usually, after a unique pioneering natural product is discovered, modifications are made on the molecule to increase the existing activity or to obtain new activities. By using chemical synthesis reactions, biotransformation, combinatorial biosynthesis or a combination of these techniques, high quality molecule libraries can be created for drug discovery studies (Güner et al., 2019).

5. Aydin Adnan Menderes University Department of Biology and Antimicrobials

Aydın Adnan Menderes University, Biology Department, Microbiology Science has been working on classical and new generation antimicrobial activities for the last fifteen years. (Biyik et al., 2018; Çoban et al., 2017; Çoban et al., 2018; Torun et al., 2018). We investigate the effects of chemically synthesized (BOR) "Vic-dioxime derivatives and metal complexes, heteroaromatic hydrozone groups and metal complexes, methylbenzohydrazide and metal complexes, thiosemicarbazone glyoxime and metal complexes, hydrazone-oxime ligands and metal complexes, imidazole salts and derivatives, gipsimogenin derivatives complexes, 1,2 Diboran compounds and derivatives on clinically important bacteria, yeast and microfungi (ADÜ-BAP-2020).

Conflict of Interest

No conflict of interest is declared by the authors.

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Review

Using Theory to Nursing Research

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Abstract: In recent years, the interest in the use of models in nursing research is gradually increasing. Nursing theories are important in the synthesis of the relationship between research process and nursing knowledge. In addition, improving and testing nursing knowledge and initiatives make it possible to present study results within a scientific framework. In this review, there are some doctoral theses made using theory.

Keywords: *Nursing; theory; research; thesis*

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1. Introduction

The use of models and theory in research directs practices, provides systematic thinking, guides the researcher in the selection of research design, identification of appropriate measurement tools, analysis and interpretation of data. It also determines the factors that will be used to reach the goal by providing the factors that affect the behavior as a whole. All these save nursing from being a work-oriented profession and make it possible to focus on nursing role and practice, rather than medical applications. Today, there is an increase in the studies conducted using the model in nursing research in Turkey frequently used theories/models; Health Promotion Model, Health Belief Model, Roy Adaptation Model, Social Cognitive Theory, Diffusion of Innovation Theory, Neuman Systems Model, Piaget's Theory of Cognitive Development, Watson' Theory of Human Caring and Self-Care Deficit Nursing Theory.

If the study examples using the theory/model are examined, the most commonly used one is Health Promotion Model and Health Belief Model. When we consider the Health Promotion Model in general, variables represented as "Individual Characteristics and Experiences" are 'prior related behavior' and 'personal factors'. "Behavior-specific cognitive factors" in the model are 'perceived benefit and barriers', 'perceived self-efficacy', 'activity-related effect', 'interpersonal influences', and 'situational influences', which are major motivational mechanisms of gaining and maintaining health promotion behavior. There are also concepts

of 'commitment to a plan of action' and 'meeting immediate demands and preferences'. Also The Health Belief Model consists of three components: individual characteristics, perceptions and cues to action. In this model, individual variables show socio-demographic and psychological characteristics, whereas the perception component consists of susceptibility, severity, barriers, self-efficacy, and health motivation.

In the study titled "The Impact of Nursing Interventions with Health Promotion Models on Early Diagnosis Behaviors of Poor Women for Breast and Cervical Cancer" (Aydoğdu, 2012), in which Health Promotion Model and Health Belief Model are used together; with the nursing interventions planned using the model, it was aimed to improve the early diagnosis behaviors of breast and cervical cancer of poor women. It is stated that the use of model concepts together in the study will be effective in planning initiatives for behavioral change in poor women.

Roy Adaptation Model is one of the most frequently used theories in studies. When we look at the model briefly, four adaptive modes have been identified within the model. Each adaptive mode interacts with others. Any stimulus that affects one of the adaptive modes, affects other three modes as well. This complex relationship between adaptive modes demonstrates the holistic nature of human. For this reason, nurses must assess how each of these modes affects others. Roy Adaptation Model was used in the study titled "An Investigation of the Effect of Support Group Intervention After Liver Transplant on Patients' Knowledge, Symptoms and Life Quality Level" (Ordin, 2013). This study consists of 3 stages. The purpose of the first stage is to explain patients' experience and adaptation period after liver transplantation, second stage is to adapt "the 59-Item Transplant Symptom Occurrence and Symptom Distress Scale" into Turkish for patients who underwent liver and kidney transplantation and test its validity and reliability and aim of last stage is to examine the effect of "support group" intervention based on Roy Adaptation Model on physical, psychological and social adaptation level of patients who underwent liver transplantation. In the first phase of the study, the data were collected according to adaptive modes of Roy Adaptation Model. In this research, focal stimulus is having undergone liver transplantation. The contextual stimuli are patient's socio-demographical characteristics (age, gender, marital status, education, employment status) and liver disease status (etiology, date of LT, donor type, immunosupressive drugs used). The aim of the support group intervention applied in the 3rd phase of the study was to influence physiological, self concept and interdependence adaptive modes of patients who underwent liver transplantation.

Another dissertation conducted with infertile women based on Watson's Theory of Human Caring is titled "The Effects of Nursing Care Based on Watson's Theory of Human Caring on Anxiety, Coping and Distress of Women Who Receive Infertility Treatment" (Ozan, 2013). The purpose of the study is to investigate the effects of nursing care based on Watson's theory of human caring on anxiety, coping and distress of women whose infertility treatment failed. In this dissertation, the theory was used in order to understand infertile women, create a framework for their nursing care and form appropriate nursing interventions.

Another doctoral dissertation based on the Social Cognitive Theory is titled "Investigation of the Effectiveness of the Program Developed for Bullying in Primary Schools" (Karataş, 2011). Bullying, accepted to be an aggressive behavior, is tried to explain with different theories and models in the literature. The Social Cognitive Theory is one of the most commonly used among these theories. The aims of the study are testing validity and reliability of the Parent Monitoring Scale in a Turkish sample, identifying the relationship

between bullying and parent monitoring status and identifying the relationship between bullying and health issues and evaluating the effectiveness of the program developed for bullying in primary schools. Model's concepts of interdependence, self-efficacy, self-regulation, and vicarious learning capacity were decisive in planning of interventions to be used in the study. In addition, individuals to be included in the training program, topics to be addressed in the training program, and methods and techniques to be used to explain these topics throughout the program were determined in accordance with the principles of the theory.

The Self-Care Deficit Nursing Theory was used in a dissertation study titled "Effects of Web-Based Diabetes Training on Care Outcomes: A Randomized Controlled Study" (Avdal 2010). The Self-Care Deficit Nursing Theory consists of six core concepts and one peripheral concept. The six core concepts are self-care, therapeutic self-care demand, self-care agency, self-care deficit, nursing agency, and nursing system. The seventh concept is basic situational factors that affect individual's self-care agency. The purpose of the dissertation is to investigate the effects of web-based diabetes training given to individuals with Type 2 diabetes on their A1c levels and check-up attendance behavior. The researcher states that the use of Self-Care Deficit Nursing Theory in this dissertation allows for a systematical study, a diabetes patient-centered thinking and makes it possible for diabetes patients to set their own goals.

Betty Neuman's System Model is one of the most commonly used theories in studies. According to the model, a person is a dynamic combination of relationships between physiological, psychological, sociocultural, developmental and spiritual variables. A system approach is adopted in the model in order to explain how the system remains its balance against stressors. Neuman's System Model was used in the dissertation titled "Effects of Coping Group and Social Support Group on Nurses' Level of Burnout" (Günüşen, 2009). The purpose of the thesis is to investigation of effects of increasing the coping skills and social support levels of nurses with medium or high burnout scores through coping and social support groups on their level of burnout; and determination of opinions of nurses who fully attended, fully skipped and partly attended the interventions regarding the program. Individuals included in the study were given coping training and a social support group was held in order to strengthen their lines of resistance. This is called secondary prevention in the Neuman Systems Model. The characteristic of secondary prevention is that it is applied after the occurrence of reaction against stress. The intervention is considered to be secondary prevention in Neuman Systems Model, since nurses with high levels of burnout were included in this study. The aim is to strengthen lines of resistance and reduce the reaction level. In this study, an attempt was made to strengthen psychological and sociocultural variables in nurses' lines of resistance through coping and social support groups and reduce their levels of burnout.

Working examples using the model have recently gained momentum. The use of theory is important in creating a universal language as well as providing generalizability of study results. The use of theory also provides an insight to the researcher, helps to see the whole, provides systematic thinking in a wide range from defining the problem to research design and interpretation of the findings. In this context, the use of models in nursing researches, as well as theses, will contribute to the development of the nursing profession.

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Case Report

Selective Retreatment of a Three-Canalled Mandibular Premolar using Cone Beam Computed Tomography: 5-Year Follow-up

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Abstract: Root canal retreatment is traditionally considered an "all or none" treatment approach. However, the use of three-dimensional imaging such as cone-beam computed tomographic imaging allows for a more accurate evaluation of the periapical status of individual roots associated with multi-rooted teeth. This information has introduced a novel and conservative treatment alternative for previously endodontically treated teeth with multiple roots presenting with post-treatment disease. This new approach is termed *selective root retreatment*. This case report presents the selective retreatment by using CBCT and 5-year follow-up of the lower second premolar tooth, which has been previously treated with canal treatment but has recurrent infection symptoms. The patient was followed up for 6 months, 1 year and 5 years. At control appointments, the patient was asymptomatic and radiographic evaluation showed that periapical infection had healed. This case report shows that the selective retreatment method can be successfully applied to multi-rooted teeth with symptoms of recurrent infection after root canal treatment.

Keywords: *Cone beam computed tomography; multi-rooted tooth; reinfection; selective retreatment*

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1. Introduction

The fundamental aims of root canal therapy are properly preparing and disinfectioning of all pulp spaces and its wholly filling it in three-dimensions with an biocompatible obturation material to avoid reinfection of the tooth (Schilder, 1967; Schilder, 1974). Initial root canal treatment has been stated to result in a desirable consequence between 86% and 98% of the time (Friedman et al., 2003, Friedman and Mor, 2004). This shows that the endodontically treated teeth that developed post-treatment pathosis or presenting persistence of disease were dramatically rate. Previous studies informed failure percentages of 14%–16% for initial root canal treatment (Torabinejad et al., 2007). Causes of failure are based on persistent intraradicular infection residing in initially untreated canals, dentinal tubules, or the complicated root canal

system (Nair, 2006; Peters et al., 2004). The extraradicular reasons of endodontic lack of success attribute periapical actinomycosis (Tronstad et al., 1990), a foreign body reaction induced by extruded endodontic materials (Nair et al., 1990), an accumulation of endogenous cholesterol crystals in the apical tissues (Nair, 1999) and an unresolved cystic lesion (Ramachandran Nair et al., 1996). Treatment alternatives for the endodontically treated teeth with post-treatment disease are restricted. They comprise non-surgical retreatment, surgical treatment (including intentional replantation), or a combination of both procedures.

Root canal retreatment is a non-surgical process that includes removal of root canal filling materials from the root canal, and after that cleaning, shaping and filling of the canals. Root canal retreatment is conventionally considered an "all or none" treatment modality (Roda, 2006). However, the use of three-dimensional imaging such as cone-beam computed tomographic visualization permits for a more correct assessment of the periapical condition of individual roots interrelated with multi-rooted teeth. This data has asserted a modernistic and conservative treatment option for initially endodontically treated teeth with multiple roots exhibiting with post-treatment disease. This new procedure is entitled *selective root retreatment*. New generation imaging permits the clinician to manage presumable treatment determination in terms of the presence or absence of periapical disease of individual roots as opposed to guessing about the tooth completely (Nudera, 2015). In that way, retreatment could be restricted to a single root or roots evidently indicating periapical pathosis while leaving the root(s) with no apparent or noticed pathosis untouched. The aim of this case report is to present the selective retreatment by using CBCT and 5-year follow-up of the lower second premolar tooth, which has been previously treated with canal treatment but has recurrent infection symptoms.

2. Description of the Case

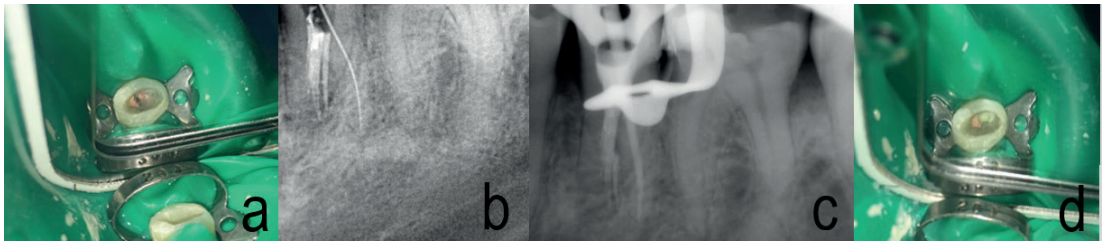
A 38-year-old male patient with a non-contributory medical history was referred to our clinic with the complaint of swelling and pain the previous two weeks in the lower left mandibular region. Extraoral examination demonstrated swelling in the left mental area. Clinical and radiographical examination presented that there was a root canal treatment in the second mandibular premolar tooth, but there was a lesion in the periapical area. It is thought that there might have been a missing extra canal. In the intraoral examination, the tooth was tender to percussion and palpation tests and exhibited no mobility. Probing depths were within normal limits for the tooth. Also, cone-beam computed tomography sections were taken to determine the exact diagnosis and lesion borders. As a result of the examined sections, it was determined that the second mandibular premolar tooth, which is generally single-rooted and single canals, had three canals. Two root canals were treated and a root canal was missed out. The periapical lesion originated from the missing root canal (Figure 1).

Figure 1. CBCT sections that taken from the tooth.

The treatment of the tooth was completed in two appointments. At the first visit, under local anesthesia, an access cavity was opened by applying rubber-dam to the tooth (Figure 2a). The root canal, which was missed out previously, was localized by endodontic sond without any intervention to other root canal fillings. Working length was determined using a radiograph with stainless steel hand #10 K file and electronic apex locator (Root ZX mini; J Morita Co, Kyoto, Japan) (Figure 2b). Cleaning and shaping of the canal was performed with rotary nickel-titanium system (ProTaper Next, Dentsply Maillefer, Ballaigues, Switzerland) up to X2. During the instrumentation, the canal was irrigated with copious amounts of 2.5% sodium hypochlorite. After the final irrigation (5.25% sodium hypochlorite, 17% ethylene diamine tetra acetic acid and 2% chlorhexidine) the canal was dried with paper cons, and dressed with a calcium hydroxide paste (Calasept, Nordiska Dental, Angelholm, Sweden), and the access was sealed with temporary filling material (Cavit W, 3M Espe, Seefeld, Germany).

When the patient came for control two weeks later, the patient did not have any symptoms (pain, swelling). The medication paste was removed with irrigation solutions. Final preparation was made with the X2 file. After the final irrigation, the root canal was dries with paper cons and was filled with gutta-percha and AH Plus sealer (AH Plus, Dentsply, De Trey, UK) with cold lateral compaction method. Then the tooth was restored with flowable and bulk-composite filling material. (Figure 2c and 2d).

Figure 2. a) Clinical view of the tooth after access cavity b) Radiographical view of localized missing canal c) Radiographical view of master con d) Clinical view of the tooth after filling the canal and placing flowable composite



The patient was followed up for 6 months, 1 year and 5 years. At control appointments, the patient was asymptomatic and radiographic evaluation showed that periapical infection had healed (Figure 3 and 4).

Figure 3. After 1-year follow-up radiograps

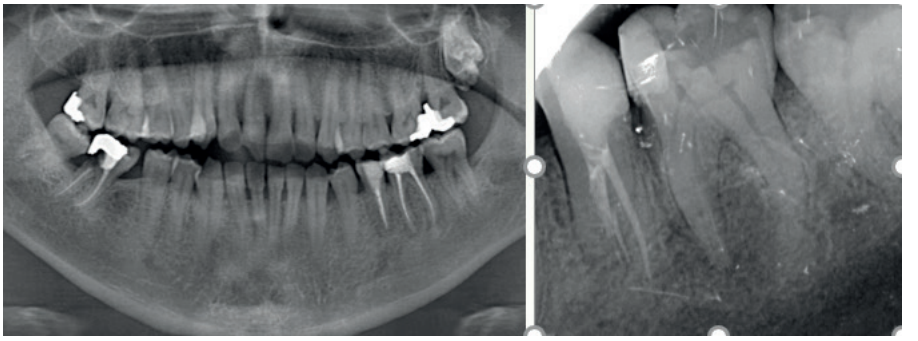
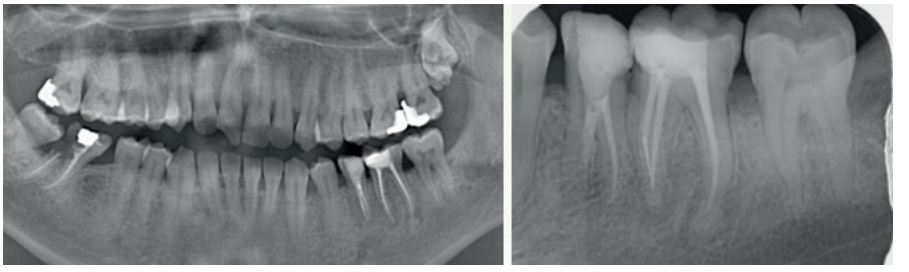


Figure 4. After 5-year follow-up radiographs



3. Discussion

The presence of untreated root canals may be a reason for failure of endodontic therapy. Because of this, to achieve a satisfactory root canal therapy, the clinician should be aware of the multiple and complex variations that can occur during root formation and identify the different canal configurations (Parekh et al., 2011). The importance to have the knowledge of extra root canals and their locations with respect to the main respective canal depicts the success rate of their endodontic therapy (Maggiore et al., 2002; Vertucci and Haddix, 2011). Although mandibular 1st and 2nd premolar teeth are usually single-rooted and single-canalled, they can show variations in terms of the number of roots and canals. In the study of Prakash et al. two-rooted mandibular second premolars were found (Prakash et al., 2008). Vertucci and Francois 1986 reported that the mandibular first premolar had single canal at the apex in 74.0% of the teeth researched, two canals at the apex in 25.5%, and three canals at the apex in the rest 0.5% of the teeth. Only 12% of mandibular second premolars studied had a second or third canal. They also stated that the second premolar had one canal at the apex in 97.5% and two canals at the apex in only 2.5% of the teeth researched (Vertucci and Francois, 1986).

In 1991, Bram and Fleisher revealed a mandibular second premolar with four canals (Bram and Fleisher, 1991). Lotfi et al. mandibular second premolars with three canals and atypical orifices were studied. They found one distolingual and one distobuccal at the same level and one mesiolingual on the wall of the second premolar (Lotfi et al., 2008). Mandibular premolars with three canals were stated in other previous studies (Aguiar et al., 2010; Chan et al., 1992; Cleghorn et al., 2008; Poorni et al., 2010). As seen in

mentioned above studies, the incidence of second premolar teeth with atypical morphology with more than one root and canal is considerably higher. As a result of that, these extra canals can be overlooked when performing canal treatment and this situation may cause post-treatment lesions.

Conservative treatment options are limited for teeth with recurrent or persistent infectional disease. These alternative approaches are the non-surgical retreatment (by removal of all root canal filling and restorations), surgical root treatment, or extraction. Although favourable results can be achieved with all these options, present technology may allow a more conservative and equally successful approach. It is generally recommended that all restorative and obturation materials be removed from all roots irrespective of the presence or absence of periapical pathosis in traditional root canal retreatment. However this treatment approach had some disadvantages. Weakening of the tooth structure through unnecessary removal of dentin and possible iatrogenic mistakes can generate difficulties for re-building after nonsurgical retreatment. Additionally, undesired heat generation can occur during post-removal and it may harm the tooth and its connecting periodontium (Davis et al., 2010). These risks could cause tooth loss. Besides these, removal of whole restorations is never practical and in the interest of patient. Patients usually refer to root canal retreatment with restorations considered to be short while ago builded. Patients are generally reluctant to undertake the financial and/or psychological pressure of a full restoration removal and reconstruction. Also, removal completely the existing restoration can cause loss of time for patients.

Previously, treatment planning and finding permorfing has been confined by two-dimensional radiographic imaging. Cone-beam computed tomographic (CBCT) imaging has become a worthy device for the objective of endodontics (Patel, 2009). This improved imaging dramatically enhances the clinician's facility to forseeable estimate root morphology, internal anatomy, and periapical pathosis before treatment (Barnett Abbott et al., 2011). This provides us to perform a differential diagnosis of which root arises the periapical pathosis, and selective retreatment could be managed more accurately.

As a conclusion, clinicians should be aware of root canal configuration malformations and be able to apply this knowledge in radiographic and clinical interpretation. It is the rationalist method to apply the selective retreatment method, which is the most conservative treatment approach, in teeth that developed post-treatment lesions due to the lack of internal anatomy knowledge. Meanwhile, CBCT can be used for precise diagnosis of the individual roots and canals. In this way, no attempts can be performed on root canal obturations that do not have pathosis and appear healthy. Also access cavity reformings may be required for unrestricted entry to complex anatomy and missing canals.

The main aim of this case study is to report a successful selective retreatment of a mandibular second premolar with three canals. In our case report, CBCT imaging confirmed the presence of an untreated root canal in the lower second premolar tooth. Owing to the fact that, there was no deficiency in filling and no periapical pathosis of other roots, no intervention was done to them. Thus, weakening of the roots and whole tooth is prevented without the unnecessary additional interventions.

Conflict of Interest

Author declares no conflict of interest.

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Case Report

Digital Planning and Mucosa-supported Guided Implant Surgery: A Case Report

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Abstract: Guided implant surgery simplifies the execution of implant placement procedures and provides optimal clinical outcomes. The aim of this report was to demonstrate digital implant surgery process and to evaluate implant deviations at apex and platform. Case: A 55-year-old man with no relevant medical history and having an edentulous maxilla referred to the department of oral and maxillofacial surgery. Mucosa-supported guide and implant locations based on the desired prosthetic design was planned via Codiagnostix® software. Six implants were inserted and immediate provisional prosthesis was adapted to the maxilla. To analyze implant deviations, pre-planned image and post-operative cone beam computed tomography were superimposed. Digitally guided implant surgery is a beneficial and minimal invasive method for providing pre-treatment prosthetic evaluation and reducing intraoperative human error and surgery time. Although implant deviations were diagnosed in all implants with different degrees, final prosthetic rehabilitation was successfully achieved.

Keywords: *Digital planning; guided implant surgery; hybrid prosthesis; deviations; mucosa-supported guide; cone beam computed tomography*

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1. Introduction

Implant therapy has become a routine procedure to rehabilitate the edentulous patient. As the demand for the implant therapy has increased, several treatment modalities have been recommended to manage the complex cases. Guided implant surgery has been used for many years in practice to place implants in a correct position and reduce intraoperative human factor (Rosenfeld et al., 2006). The most important factors which affect the implant success are stable and healthy tissues surrounding the implant, precise placement of an implant based on the prosthetic and esthetic needs to prevent bone loss and compromised esthetics (Tardieu et al., 2007).

The most important advantage of guided implant surgery is the ability to anticipate the needs for the prosthetic and esthetics prior to the surgery and incorporate them into the surgical planning (Ganz, 2008; Jacobs, 2003; Parashis and Diamantopoulos, 2008; Schnitman et al., 2014). This method allows the surgeon to insert the implants into the sufficient hard and soft tissue at the pre-determined locations. The objective of this case report was to show the steps of guided implant surgery and to compare the digitally pre-planned and post-operative implant locations via CBCTs.

2. Case

A 55-year-old man with no relevant medical history presented for the replacement of his missing maxillary teeth, which had been removed three months ago (Figure 1). Mucosa supported guided implant surgery including an immediate provisional prosthesis was planned. A teeth set up was prepared to ensure accurate esthetics and function prior to the surgery. As a scanning appliance, an acrylic material and teeth with radiopacity were used to make it distinguishable in the radiographs. Pre-operative tomography scan was obtained with the scanning prosthesis mounted to the maxilla. All pre-operative and post-operative computed tomography scans were taken with a 1 mm slice thickness and 0.5 mm voxel size.

To obtain digital intraoral impressions of the maxillary edentulous jaw, provisional scanning prosthesis and stone cast of the upper jaw were scanned via laboratory digital scanner (Strauman 7series, Dental Wings, Canada). The prosthetic plan and CBCT data of the subject were imported into the digital planning software (CoDiagnostiX®). Before superimposition, three different points on the teeth and bone were used for image fusion of the intraoral scan data and CBCT data.

Figure 1. Frontal and intraoral views of the patient

2.1. *3D Implant Planning*

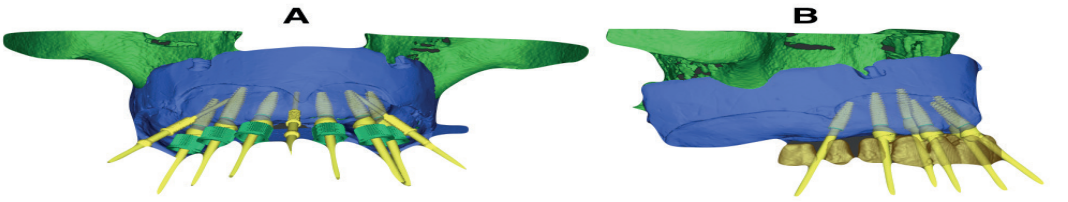
By considering the desired prosthetic plan, locations for six implants in variable lengths and diameters were determined (Figure 2). Implant positions, diameter and lengths of all implants were given in Table 1.

Table 1. Implant Properties

Position	**Model**	**Length**	**Diameter** (Ø)
15	Bone Level Tapered Roxolid® SLA® (NC)	10.00 mm	3.30 mm
14	Template Fixation Pin, Ø 1.3mm	28.00 mm	1.30 mm
13	Bone Level Tapered Roxolid® SLA® (NC)	12.00 mm	3.30 mm
12	Template Fixation Pin, Ø 1.3mm	28.00 mm	1.30 mm
11	Bone Level Tapered Roxolid® SLA® (NC)	10.00 mm	3.30 mm
21	Bone Level Tapered Roxolid® SLA® (NC)	10.00 mm	3.30 mm
23	Bone Level Tapered Roxolid® SLA® (NC)	10.00 mm	3.30 mm
24	Template Fixation Pin, Ø 1.3mm	28.00 mm	1.30 mm
25	Bone Level Tapered Roxolid® SLA® (NC)	10.00 mm	3.30 mm

Once virtual implant planning was finished, the DICOM files were transferred to the Rapid Shape P30 printer (Rapid Shape GmbH, Heimsheim, Germany). A single guide was manufactured to manage the whole steps of the surgery (from mucosal excision to the implant insertion). The guide, then was visually checked for fit. Pre-determined sleeves were adapted to this surgery guide.

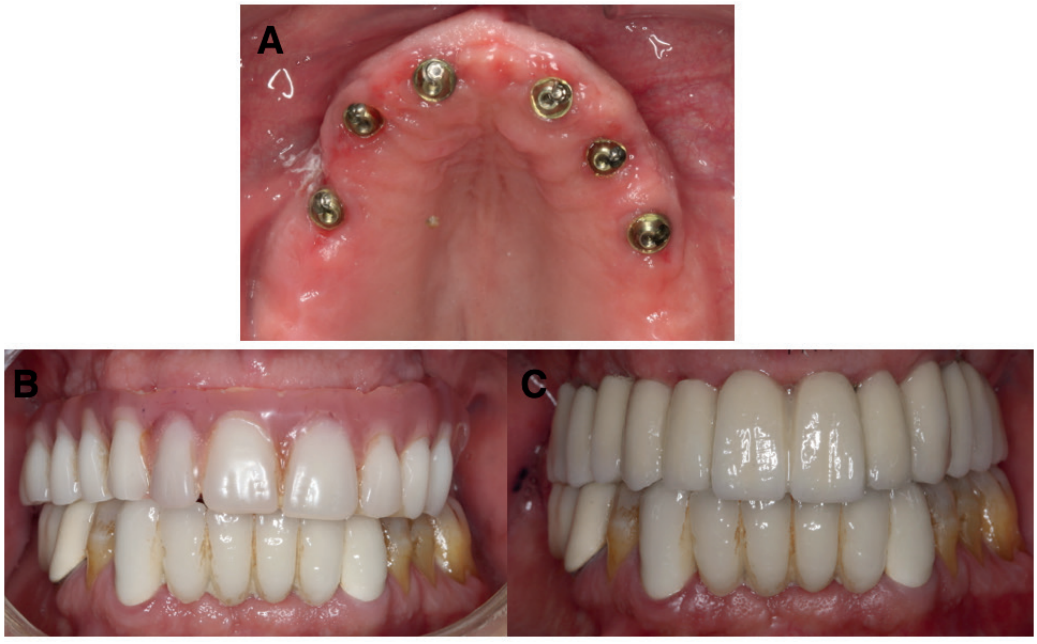
Figure 2. Representation of six designated implant locations based on the desired prosthetic plan. A) Frontal view, B) Sagittal view



2.2. *Surgical Protocol*

Putty (polyvinyl siloxane impression material) was used to ensure the accuracy of the position of the guide. The putty material was seated and adapted intraorally to avoid the deviation between the guide and the maxillary basis at every steps. The patient received local articaine anesthesia at the beginning of the intervention. Full seating of the surgical guides was verified by touch sensivity and direct visualization. Digital pressure around the premolar-molar region was bilaterally applied to immobilize the guide before inserting three template fixation pins buccally to further secure the guide. Sequential guided surgery protocol was performed according to the manufacturer (Straumann®). 3.3×10mm and 3.3×12 mm bone level tapered implants (Roxolid®, SLA®, Straumann Ag, Basel, Switzerland) were inserted. Key height handpieces were used inside the metal sleeves to match every drill. Guide position and immobilization were checked during every drilling and implant insertion step. Immediate provisional prosthesis was adapted to the implants via abutments and final hybrid prosthesis was adapted two months later (Figure 3).

Figure 3. A) Locations of six implants, B) Immediate provisional prosthesis, C) Final hybrid prosthesis



2.3. *Radiologic Diagnosis and Deviations*

Virtually planned image and post-surgical CBCT scan were superimposed in STL files to compare the differences between the pre- and post-operative implant locations using the same surfaces of teeth and bone. Apex or platform measurements were taken from the apical/platform center of the virtual implant to the apical/platform center of the placed implant. 3D deviation at implant crest and implant apex (Figure 4) were measured and all values were shown in Table 2.

Figure 4. A) Sagittal view of the implant, B) Coronal view of the implant, C) Comparision of pre- (blue) and post-operative (red) implant positions and representation of implant deviations at apex and platform regions

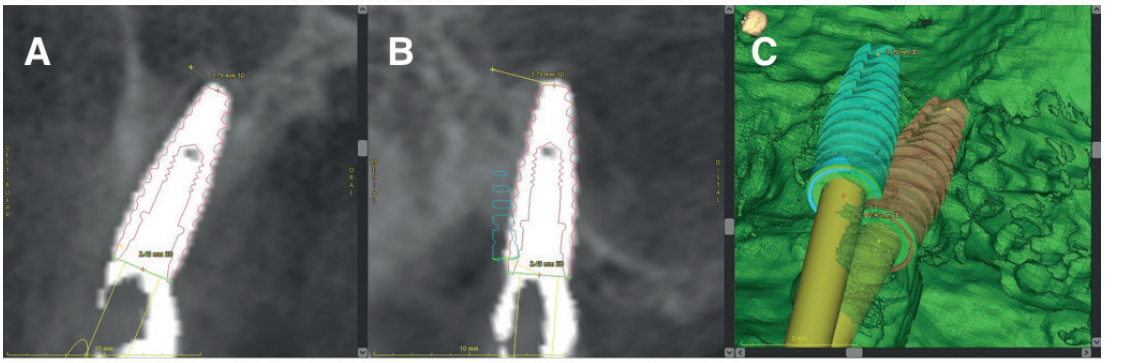


Table 2. Evaluation of treatment outcomes (IP: Implant position, ID: Implant diameter (mm), IL: Implant length (mm), DP: Deviation at platform (mm), DA: Deviation at apex (mm))

IP	ID(mm)	IL (mm)	DP (mm)	DA (mm)
11	3.3	10	0.95	1.61
21	3.3	10	0.80	0.99
13	3.3	12	0.98	1.21
23	3.3	10	1.60	2.57
15	3.3	10	0.86	1.77
25	3.3	10	2.45	3.79

The highest 3D deviation value around the implant (25#) was recorded in millimeters. Left side values for 3D deviation were found to be higher than right side values. Improper alignment and registration between the digital scanned model and the cone beam computed tomography model, manufacturing process used for fabrication of surgical guide, positioning error of the template, opposite side to the senior surgeon and posterior location of the implant may affect the accuracy of the pre-operative planning (Tatakis et al., 2019; Widmann and Bale, 2006).

Conclusion

Guided implant surgery can be an accurate and clinically advantageous procedure when implant therapy is indicated. However, pre-operative and intraoperative factors impact the final accuracy of the process. It is possible to reduce the possible risks with complete understanding of the guided implant surgery process and adequate case preparation.

Conflict of Interest

Authors declare no conflict of interest.

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