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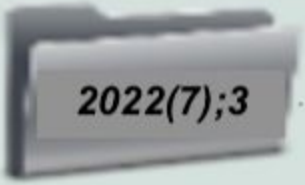

Articles

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Comparison of the short-term effects of intragastric balloon and botulinum toxin injection on weight loss

İntragastrik balon ve botulinum toksin enjeksiyonunun kilo kaybı üzerine kısa dönem etkilerinin karşılaştırılması

Muzaffer Al [1]

Abstract

Aim: To compare the effects of endoscopic intragastric balloon (IGB) placement and intragastric botulinum toxin-A (BTX-A) injection in terms of weight loss among patients with non-morbid obesity.

Methods: This retrospective cohort study was conducted between 01.08.2020 and 01.01.2022. A total of 39 patients with a body mass index (BMI) of <40 without comorbidities were included in the study. Nineteen underwent intragastric BTX-A injection and 20 underwent IGB placement. Patients were evaluated 1 month and 6 months after the procedures.

Results: Mean age was 39.4 ± 8.6 in the BTX-A group and 37.3 ± 10.4 in the IGB group (p = 0.496). 78.9% of the BTX-A group and 75.0% of the IGB group were female (p = 1.000). In both groups, the median weight 1 month after the procedure was significantly lower than before the procedure, and the median weight 6 months after the procedure was significantly lower than 1 month after the procedure (p<0.001 for both groups). The median weight loss in the IGB group at both the 1st and 6th months was significantly greater than the corresponding values of the BTX-A group (p < 0.001 for both).

Conclusion: IGB insertion appears to be a more successful endoscopic bariatric procedure than intragastric BTX-A injection, as measured by weight loss at post-intervention 1 month and 6 months. IGB may be preferred in patients with a BMI below 40 without obesity-related comorbidity.

Keywords: Obesity, endoscopic bariatric procedures, intragastric balloon placement, intragastric botulinum toxin-A injection, weight loss.

Öz

Amaç: Morbid obez olmayan hastalarda endoskopik intragastrik balon (IGB) yerleştirme ve intragastrik botulinum toksin-A (BTX-A) enjeksiyonunun kilo kaybı açısından etkilerini karşılaştırmak.

Yöntemler: Bu retrospektif kohort çalışması 01.08.2020 ile 01.01.2022 tarihleri arasında gerçekleştirildi. Beden kitle indeksi (BKİ) <40 olan ve komorbiditesi olmayan toplam 39 hasta çalışmaya dahil edildi. Olguların 19'una intragastrik BTX-A enjeksiyonu ve 20'sine IGB yerleştirmesi yapıldı. Hastalar işlemlerden 1 ay ve 6 ay sonra değerlendirildi.

Bulgular: Ortalama yaş BTX-A grubunda 39,4 ± 8,6 ve IGB grubunda 37,3 ± 10,4 idi (p = 0,496). BTX-A grubunun %78,9'u ve IGB grubunun %75,0'ı kadındı (p=1.000). Her iki grupta da işlem öncesi ile karşılaştırıldığında işlemden 1 ay sonra ve işlemden 1 ay sonrası ile karşılaştırıldığında işlemden 6 ay sonra ortanca ağırlık anlamlı düzeyde azaldı (her iki grup için p<0,001). BTX-A grubu ile karşılaştırıldığında hem 1. hem de 6. ayda medyan kilo kaybı IGB grubunda anlamlı düzeyde daha fazlaydı (her ikisi için p < 0,001).

Sonuç: Çalışmamızda müdahale sonrası 1. ve 6. ayda kilo kaybı ile ölçüldüğü üzere, IGB yerleştirilmesi intragastrik BTX-A enjeksiyonundan daha başarılı bir endoskopik bariatrik prosedür gibi görünmektedir. Obezite ile ilişkili komorbiditesi olmayan BKİ 40'ın altında olan hastalarda IGB tercih edilebilir.

Anahtar Kelimeler: Obezite, endoskopik bariatrik prosedürler, intragastrik balon yerleştirme, intragastrik botulinum toksin-A enjeksiyonu, kilo kaybı.

[1] **Near East University, Faculty of Medicine, Department of Surgery, Nicosia, Cyprus.**

MA: 0000-0002-0187-3247

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Sorumlu yazar / Corresponding author:
Muzaffer Al

Adres/Address: Department of Surgery, Near East University, Faculty of Medicine, Nicosia, Cyprus.

e-mail: drmuzaffer61@hotmail.com
Tel/Phone: +90542 262 7500

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Introduction

Obesity is a significant threat to human health owing to the high prevalence of morbidity and mortality caused by the cdition itself and associated comorbidities [1]. Current guidelines suggest bariatric surgery as the most potent treatment tool for patients with class-3 obesity or those with class-2 obesity compounded by an obesity-related comorbidity [2-4]. However, although treating obesity in early stages is advised before the development of comorbidities, bariatric surgery is not a first-line option [2, 4-6]. Endoscopic bariatric procedures (EBPs) are more effective than pharmacotherapy and lifestyle changes and offer a lower rate of side effects compared to bariatric surgery [7, 8]. Therefore, EBPs have evolved tremendously in last decade and can be applied to patients in all the stages of obesity [6, 9].

EBPs can be categorized as follows: space-occupying devices, gastric restrictive methods, malabsorptive procedures, regulating gastric emptying, and others [6]. Intragastric balloon (IGB) placement, defined as the insertion of a space-occupying device into the stomach with the aid of endoscopy, is a reversible nonsurgical bariatric procedure available since the 1980s [6, 10, 11]. It was designed to reduce food intake by inducing early satiety [10, 11]. Its safety and efficacy has been reported in various publications [12, 13]. IGB can be applied both as a bridge procedure before surgery in severely obese patients and as a primary procedure for less-severe patients [4, 14, 15]. Close follow-up with a dedicated dietitian and surgeon increases the likelihood of success, yielding comparable outcomes to surgery [4, 9]. However, with this procedure, it has been reported that maintaining weight loss is difficult in the long-term [16].

Endoscopic intragastric botulinum toxin-A (BTX-A) injection is a procedure which primarily regulates gastric emptying by causing gastroparesis [6]. BTX-A injection allows early satiety, extends the duration of satiety, inhibits the release of acetylcholine (delaying gastric emptying), and inhibits ghrelin release (a potent hunger-stimulating hormone) [1, 6, 17]. Although its application as an EBP is known to be safe, results concerning weight loss are inconsistent, particularly in the long-term [2, 7, 18, 19].

The number of studies in the literature comparing the success of these two EBPs, whose indications are similar to each other, is quite limited. Overall, the literature suggests greater bariatric success and fewer procedural complaints from IGB placement [20-22]; however, as mentioned, there are various inconsistencies. Thus, we aimed to compare the success in weight loss of both modalities with a follow-up of 6 months, and additionally, to assess short-term bariatric effects.

Material and methods

Study design and ethical issues

This retrospective cohort study was initiated after the local ethical committee approval (Ethical Committee of Buyuk Anadolu Hospital, 21.05.2020/05-218614) and conducted according to the principles of the Declaration of Helsinki and its later amendments at our bariatric surgery Center of Excellence (COE), Department of General Surgery, Büyük Anadolu Hospital, Samsun, Turkey between 01.08.2020 and 01.01.2022.

Participants and data collection

A total of 39 patients who were overweight or had class 1 or class 2 obesity without comorbidity underwent EBPs during the study period. Nineteen underwent endoscopic intragastric BTX-A injection, and 20 underwent endoscopic IGB placement. Patients younger than 18 years, patients with obesity related comorbidities, individuals whose treatment was terminated and/or switched to another treatment protocol as a result of intolerance or complications, those who had undergone EBP for other purposes (before other operations, such as orthopedic surgery or bariatric surgery), patients with any psychiatric disorder, and subjects in whom follow-up data were unavailable or missing were excluded from the study.

Retrospective data including sociodemographic, anthropometric, surgical and weight loss at follow-up were obtained from a prospectively-maintained database.

Endoscopic procedures

The indication for EBP was defined in overweight or obese patients who did not respond positively to diet, exercise, and lifestyle modification for at least 6 months and met the following criteria: (i) having a body mass index (BMI) of <40 and (ii) not being diagnosed with any obesity-related comorbidity [6, 15]. The advantages and disadvantages and possible complications of the procedures were explained to the patients and the procedure to be applied was determined according to the patient's preference. Written informed consent forms were obtained from each patient before the procedure.

Endoscopic intragastric botulinum toxin-A injection: The procedure was applied in an outpatient endoscopy care unit under sedation anesthesia (midazolam 0.05 mg/kg, propofol 1 mg/kg). First, the patients underwent routine gastroscopy procedure. The patients were checked for any gastric or duodenal pathology. A total of 500 IU [7] Clostridium botulinum type-A toxin hemagglutinin complex (Dysport™; Ipsen Biopharm Ltd., UK) diluted with 20 ml of saline solution [21] was injected into the muscular layer of the stomach. Injections were made as follows: 10 spots (250 IU) at the antrum relatively close to the incusura angularis and 5 spots (125 IU) each to the corpus and fundus through a sclerotheray needle (Interject™ 23G; Boston Scientific, USA). Each spot received 1 ml of injection volume. In the fundus, meticulous care was taken to not penetrate the diaphragm or myocardium. After checking for bleeding, patients were monitored for 1 hour after the procedure for any possible complication. A low-calorie liquid diet (1200 calories) was administered during the first week, a soft-solids diet in the second week, and a low-carbohydrate diet in the third week was provided for the patients under the follow-up of a dedicated dietician. Feeling of satiety and weight loss were monitored in follow-up visits. Moderate physical activity was recommended for the patients.

Endoscopic intragastric balloon placement and removal: The procedure was applied in an ambulatory endoscopic care unit under sedation anesthesia (midazolam 0.05 mg/kg, propofol 1 mg/kg), in the left lateral decubitus position, and the removal procedure was done in the same way. Firstly, a routine gastroscopy procedure was performed to exclude any pathologies. Then, an intragastric fluid-filled balloon (Bariglobe™; Russia) was applied through the oropharyngeal route with the help of endoscopy according to the manufacturer's instructions. Under direct gastroscopic view, the balloons were filled with 500 ml of saline mixed with 10 ml of methylene blue. Tubing of the balloon was removed and the patient was monitored for 1 hour after the operation. A proton pump inhibitor (PPI) (pantoprazole 20 mg oral, once daily) and an antiemetic agent (ondansetron 8 mg oral, twice daily) were prescribed after the procedure. Patients were advised to continue PPI medication for the entire 6 months of follow-up. All patients were advised to adhere to a low-calorie liquid diet (1200 calories) in the first week, a soft-solid diet in the second week, and a normal diet in the third week after the

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procedure. All subjects were continuously monitored by a dedicated dietician until the IGB was removed. Moderate physical activity was recommended for the patients. At 6–12 months after placement, IGB was removed through upper gastrointestinal endoscopy under sedation anesthesia.

Follow-up

As a routine practice, patients are called for follow-up evaluations after surgery in the 1st week, 1st month, 3rd month and 6th month when these procedures are applied in our department. The 1st month and 6th month information recorded in these follow-up evaluations were obtained from the hospital records and were included in the analyses of this study.

Outcomes

The primary outcome was to compare weight loss success of two procedures and the secondary outcome was to compare the two approaches with regard to their efficacy in treating non-morbid obesity.

Statistical analysis

Data collected quantitatively were evaluated with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Continuous data of groups were analyzed using the Mann-Whitney U test for non-parametric data, while the independent samples t-test was used for parametric data. The Chi-square test was used for categorical comparisons. Quantitative values were summarized with mean ± SD values and median (minimum-maximum) values, depending on normality of distribution. Categorical values were reported with frequency and percentage. A p value less than 0.05 was regarded to show statistical significance.

Results

The overall mean age of patients was 38.3 ± 9.5 years. In the BTX-A group, mean age was 39.4 ± 8.6 years, while this value was 37.3 ± 10.4 years in the IGB group (p = 0.496). 78.9% of the BTX-A group and 75.0% of the IGB group were female (p = 1.000). The baseline median BMI of the IGB group [31.2 (29.2 - 33.3)] was significantly higher than that of the BTX-A group [32.5 (30.1 - 38.9)] (p = 0.016) (Table 1).

Table 1. Distribution of demographic, height and BMI characteristics by groups

	Total	IGB group	BTX-A group	p
Gender				
Male	9 (23.1%)	5 (25.0%)	4 (21.1%)	1.000
Female	30 (76.9%)	15 (75.0%)	15 (78.9%)	
Age (year)	38.3 ± 9.5	37.3 ± 10.4	39.4 ± 8.6	0.496
Height (m)	1.6 (1.5 - 1.9)	1.6 (1.5 - 1.8)	1.6 (1.5 - 1.9)	0.687
BMI (kg/m^2)	31.6 (29.2 - 38.9)	32.5 (30.1 - 38.9)	31.2 (29.2 - 33.3)	0.016

Normally distributed numerical data are presented as mean ± standard deviation, non-normally distributed numerical data are presented with median (minimum - maximum) values, categorical data are presented as number (percentage) values.
Abbreviations; BMI: Body-mass index, BTX-A: Botulinum toxin-A, IGB: Intragastric balloon.

The median weight of the EBP groups at baseline and comparisons of weight loss (within-group and intergroup) during the post-procedure follow-up studies are summarized in Table 2 and Figure 1. In both groups, the median weight 1 month after the procedure was significantly lower than before the procedure, and the median weight 6 months after the procedure was significantly lower than both before the procedure and 1 month after the procedure (p < 0.001 for both groups). The median weight loss of the IGB group at both the 1st and 6th months was significantly higher than the BTX-A group (p < 0.001 for both times). No severe complications were observed during the administration of either of the EBPs. Of note, although various mild, self-limiting side effects including nausea, vomiting, abdominal pain and abdominal discomfort were reported by some of the patients, none of these side effects required therapeutic intervention.

Table 2. Comparison of pre- and post-intervention weight values between the groups.

	Total	IGB group	BTX-A group	p*
Pre-procedural weight (kg)	84.0 (72.0 - 111.0)^a	84.0 (74.0 - 106.0)^a	80.0 (72.0 - 111.0)^a	0.283
Post-procedural 1st month weight (kg)	78.0 (63.0 - 103.0)^b	77.0 (63.0 - 97.0)^b	78.0 (64.0 - 103.0)^b	0.876
Post-procedural 6th month weight (kg)	69.5 (51.0 - 93.0)^c	66.0 (51.0 - 83.0)^c	72.0 (55.0 - 93.0)^c	0.330
p**	<0.001	<0.001	<0.001	
Weight loss at 1st month (kg)	7.0 (2.0 – 12.0)	9.0 (5.0 – 12.0)	6.0 (2.0 – 8.0)	<0.001
Weight loss at 6th month (total weight loss) (kg)	16.0 (1.0 – 30.0)	19.0 (13.0 – 30.0)	13.0 (1.0 – 19.0)	<0.001

Data are presented with median (minimum - maximum) values.
a,b,c: There is a statistically significant difference between consecutive measurements shown with different letters.
* Inter-group comparison, ** Intra-group comparison.
Abbreviations; BTX-A: Botulinum toxin-A, IGB: Intragastric balloon.

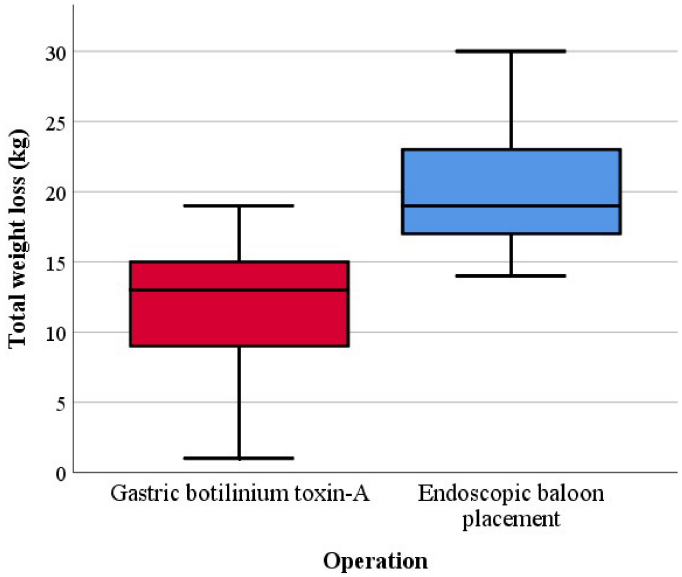

Figure 1. Comparison of weight loss at 6 months (total weight loss) between the two procedures.

Discussion

We found that the median weight loss values of IGB recipients at both 1 month and 6 months were significantly greater compared to BTX-A recipients. Although IGB appears to be superior in terms of short-term weight loss among patients with non-morbid obesity, it should also be noted that both interventions yielded significant weight loss from baseline to 1 month and from 1 month to 6 months.

Lifestyle changes and bariatric surgeries are both effective in the treatment of obesity; however, the former approach is often difficult for patients and the expensive bariatric surgeries may result in complications. These possible problems demonstrate the importance of EBP procedures and highlight the underlying reasons of their rising popularity [6, 10, 11, 14, 23, 24].

ACEM

IGB placement and intragastric BTX-A injection have the advantages of being reversible in the great majority of subjects, lower risks, and being feasible in patients who are not suitable for laparoscopic or open bariatric surgery or are at high surgical risk [6, 11, 14]. In this study, the bariatric success of these commonly used EBPs were compared. It was observed that the weight loss values in the 1st and 6th months of the patients who underwent IGB placement were significantly greater. There are very few results that have compared endoscopic IGB placement with endoscopic intragastric BTX-A injection in terms of weight loss success. In one of them, it was reported that IGB insertion was more successful than intragastric BTX-A injection (100 IU) in weight change (compared to baseline) at 1 week, 1 month, and 3 months [20]. In another study from Turkey, the success of BMI reduction after 6 months was compared in patients who received only IGB (group 1), only intragastric BTX-A injection (group 2), and the combination of the two procedures (group 3). While the decrease in BMI was significant in all three groups, it was reported that the amount of improvement was highest in group 3 and lowest in group 1 (group 3 > group 2 > group 1), and the same ranking was also valid for treatment tolerance [21]. In a systematic review and meta-analysis, the effects of some bariatric procedures (including both of these procedures) on gastric emptying and weight loss were investigated. As a result, IGB placement was found to be more effective than intragastric BTX-A injection in gastric emptying and gastric emptying-related weight loss. In addition, an interesting result of this study was that fluid-filled balloons delayed gastric emptying to a greater degree comparted to air-filled balloons, and injections of >300 IU BTX-A also delayed gastric emptying more than lower doses [22].

The two methods have similarities such as being endoscopically applicable, being less invasive than bariatric surgery, having similar indications, and inferior long-term weight loss success [2, 7, 16]. Although both methods are safe and effective, BTX-A injection is reportedly more reliable which is an important advantage despite the fact that IGB placement has better short-term bariatric success, regardless of BTX-A dosage. IGB insertion may cause self-limiting side effects such as nausea, vomiting, generalized abdominal pain and/or discomfort, back pain, and acid reflux, and more severe side effects such as partial or complete gastrointestinal obstruction, injury to the lining of the digestive tract, stomach or esophagus; and gastric perforation [10, 16, 25, 26]. One review reported the adverse event rate of IGB as 28.5% [27]. In another study, it was reported that at least 1 device-related adverse event was seen in 98% of the patients undergoing IGB placement [28]. Otherwise, no significant side effects or neurophysiologic changes were reported after BTX-A injection [18, 29]. On the other hand, the efficacy of BTX-A is suggested to demonstrate a gradual decrease after surgery, especially towards the 6th month [2, 30]. Although the same BTX-A injection procedure was applied for each patient in the study, procedure standardization may not have been achieved, as BTX-A injection is a relatively more complex and operator-dependent procedure than IGB placement, and this may have affected the results.

In this study, the median weight loss at 1 month and 6 months after IGB placement was 9 and 19 kg, respectively. In two randomized clinical trials, some of the patients with a BMI between 30 and 40 underwent 12-month lifestyle modification only (control group), while other patients received an IGB for the first 6-month period in addition to this 12-month lifestyle modification. In both studies, it was reported that significantly more weight loss was achieved in the IGB group in the second 6-month period [28, 31]. In another RCT comparing air-filled IGB to a non-balloon sham capsule (placebo), patients undergoing IGB placement had twice as much weight loss as the control group and sustained high weight loss at 48 weeks [32]. In some studies, IGB placement is applied before bariatric surgery as a pre-surgical bridging procedure [4, 6, 14, 15]. In this regard, Ashrafian et al. [14] presented their 16-year experience. They reported that short-term effective weight loss success of IGB placement alone was temporary, while long-term effects were much more pronounced when combined with bariatric surgery. Ball et al. [4] also showed that the use of IGB as the first step before definitive bariatric surgery significantly contributed to weight loss. Studies also show that the IGB should be removed 6-12 months after insertion [33]. A recently published meta-analysis of 20 RCTs reported significant results on short-term weight loss with the IGB procedure, but the sustainability of this weight loss could not be demonstrated [16]. Although we did not encounter any serious intraoperative or postoperative complications, more studies are needed to clarify potential complications.

Injection of BTX is widely used in patients with gastrointestinal smooth muscle disorders such as achalasia, diffuse esophageal spasms, gastroparesis, and Oddi sphincter dysfunction. In recent years, intragastric BTX-A injection has gained considerable popularity [34]. In the present study, after intragastric BTX-A injection, the median weight loss was 6 kg in the 1st month and 13 kg in the 6th month. However, available literature is exceedingly inconsistent [2, 7, 18, 19]. In a double-blind RCT, patients who underwent intraparietal endoscopic gastric BTX-A injection had significantly greater weight loss (11 vs 5.7 kg) and BMI reduction (4 vs 2 kg/m2) compared to placebo at 8 weeks [18]. Bang et al.'s meta-analysis also showed that intragastric BTX-A injection was effective for the treatment of obesity [7]. However, in another meta-analysis comparing the results of BTX-A versus saline injection, it was concluded that intragastric BTX-A injection was ineffective [2]. Also, other studies reported that BTX-A had no significant effect on weight loss [19, 30]. Methodological differences such as total toxin dose, the number of injections, the injection site, the distance between injections, injection needle gauge, auxiliary method (endoscopy only or combined endoscopy and ultrasound) may play a role in these conflicting findings [7, 22, 30, 34, 35]. The presence of other factors that may affect gastric emptying, such as pyloric tonus [36], and the high probability that the success of this procedure may be affected by the operator seem to be other such factors [36]. Another important issue is that intragastric BTX-A injection is a self-reversing procedure since effects disappear around 3 to 6 months after injection [2, 30]. Although this is an advantage with respect to the ease of terminating / changing intervention, it is also a considerable disadvantage since patients often expect such procedures to have long-lasting effects.

Some limitations of the study should be considered when evaluating the results. Since this was a single-center study and the number of participants was small, the generalizability of the results is limited. Another limitation regarding generalizability is the fact that the results are procured from a set of patients with non-morbid obesity who did not have comorbidities. Although data was collected from a prospectively-maintained database, the effects of additional possible factors such as adherence to diet, exercise or drug use, which may affect weight loss, could not be investigated. The absence of a control group can also be considered as a limitation. It has not been investigated whether weight loss is sustained after 6 months following either procedure (after balloon removal in the IGB group).

In conclusion, IGB insertion was found to be more successful than intragastric BTX-A injection in terms of weight loss both 1 month and 6 months after the procedures. It was

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observed that both IGB placement and intragastric BTX-A injection continued to yield weight loss until the 6th month. Since only a specific subset of obese patients were included in this study, there is an apparent need for comprehensive studies involving obese patients with different characteristics in order to be able to draw definitive conclusions regarding the efficacy of these two bariatric procedures as primary treatment tools in obesity.

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Ferric carboxymaltose versus ferrous glycine sulfate for treatment of iron deficiency anemia and their effect on vitamin B12 and folic acid: A retrospective study

Demir eksikliği anemisinin tedavisinde ferrik karboksimaltoz ile demir glisin sülfatın karşılaştırılması ve bu iki ajanın B12 vitamini ve folik asit üzerine etkisi: Retrospektif bir çalışma

Mustafa Genco Erdem[1]

Abstract

Aim Anemia is a major public health problem, affecting about one-third of the world's population, and is most commonly caused by iron deficiency. Iron deficiency anemia requires oral or intravenous iron replacement therapy. The purpose of this study was to assess the change in several hematological parameters, vitamin B12, and folic acid from baseline to the first month of follow-up following therapy with oral ferrous glycine sulfate or intravenous ferric carboxymaltose.

Methods: All patients who received oral ferrous glycine sulfate or intravenous ferric carboxymaltose for the treatment of iron deficiency anemia between January 1, 2016, and December 31, 2018, were included in the trial. Along with age and gender information, values of hemoglobin, ferritin, transferrin saturation, mean corpuscular volume, vitamin B12, and folic acid were derived from patients' records at the beginning of treatment and first month follow-up.

Results: Laboratory values obtained after treatment showed statistically significant improvement in both groups (intra group, $p<0.001$). When the percentage of change between groups was compared: Percentage-based increases in hemoglobin, mean corpuscular volume, transferrin saturation and ferritin values were significantly higher in the ferric carboxymaltose group ($p<0.001$). The percentage decrease in vitamin B12 and folic acid values was higher in the ferric carboxymaltose group ($p=0.005$ and $p=0.01$, respectively) when compared with oral ferrous glycine sulfate group.

Conclusions: According to the findings of our study, iron deficiency anemia can be treated very successfully using ferric carboxymaltose; however, it should be remembered that concurrent supplementation of elements such vitamin B12 and folic acid is necessary for the appropriate progression of erythropoiesis.

Keywords: Ferric carboxymaltose, ferritin, folic acid, iron, iron deficiency anemia, vitamin B12.

Öz

Amaç: Dünya nüfusunun yaklaşık üçte birini etkilemesiyle önemli bir halk sağlığı sorunu olan anemi, en sık demir eksikliğinden kaynaklanır. Demir eksikliği anemisi, oral veya intravenöz demir replasman tedavisi gerektirir. Bu çalışmanın amacı, oral demir glisin sülfat veya intravenöz ferrik karboksimaltoz tedavileri altında başlangıçtan birinci ay takibine kadar çeşitli hematolojik parametrelerin, vitamin B12 ve folik asidin değişimini incelemektir.

Yöntemler: Çalışma, 1 Ocak 2016 ve 31 Aralık 2018 tarihleri arasında oral ferröz glisin sülfat veya iv ferrik karboksimaltoz ile demir eksikliği anemisi nedeniyle tedavi edilen tüm hastaları içermiştir. Hastaların dosyalarından elde edilen yaş ve cinsiyet verilerinin yanısıra, tedavi başlangıcında ve tedaviden sonraki birinci ay kontrollerinde alınan hemoglobin, transferrin satürasyonu, ferritin, ortalama korpüsküler hacim, vitamin B12 ve folik asit değerleri kayıt edildi.

Bulgular: Tedavi sonrasında elde edilen laboratuvar değerleri her iki grupta da istatistiksel olarak anlamlı iyileşme göstermiştir (grup içi, $p<0,001$). Gruplar arasındaki değişim yüzdesi karşılaştırıldığında: Hemoglobin, ortalama korpusküler hacim, transferrin satürasyonu ve ferritin değerlerindeki yüzde bazlı artışlar ferrik karboksimaltoz grubunda anlamlı olarak daha yüksekti ($p<0,001$). B12 vitamini ve folik asit değerlerindeki yüzde düşüş, oral demir glisin sülfat grubuyla karşılaştırıldığında ferrik karboksimaltoz grubunda daha yüksekti (sırasıyla $p=0,005$ ve $p=0,001$).

Sonuç: Çalışmamızın bulgularına göre, demir eksikliği anemisi, ferrik karboksimaltoz kullanılarak başarılı bir şekilde tedavi edilebilir; ancak, eritropoezin uygun gelişimi için B12 vitamini ve folik asit gibi faktörlerin eş zamanlı takviyesinin gerekli olduğu unutulmamalıdır.

Anahtar Kelimeler: Ferrik karboksimaltoz, ferritin, folik asit, demir, demir eksikliği anemisi, vitamin B12.

[1] **Beykent University, Faculty of Medicine, Dept of Internal Medicine, Istanbul, Turkey.**

MGE: 0000-0002-7783-8130

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Sorumlu yazar / Corresponding author:

Mustafa Genco Erdem

Beykent Üniversitesi, Avalon Kampüsü, Beylikdüzü, İstanbul, Türkiye.

e-mail: m.gencoerdem@gmail.com

Tel/Phone: 0 555 634 10 37

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Introduction

Iron deficiency anemia (IDA) is a common condition that affects people of all ages. The World Health Organization (WHO) defined anemia as a hemoglobin (Hb) concentration of less than 13 g/dL for men and less than 12 g/dL for non-pregnant women [1].

The global prevalence of anemia was found to be 32.9% in 2010 [1]. Iron deficiency is the leading cause of anemia [2]. The treatment of IDA can be divided into two groups: oral and intravenous iron replacement therapies. Oral iron replacement therapy is cost-effective, but it requires daily usage for up to 6 months and has side effects including constipation and abdominal pain. In contrast, intravenous (iv) iron preparations, particularly ferric carboxymaltose, are expensive but restore iron stores after one or two infusions (lasting around 20 minutes) [3-5]. The low side-effect profile of ferric carboxymaltose treatment and its rapid results have made it the first choice, especially in countries with high incomes. Yet, there is no definitive guideline about which agent should be the first choice in treatment.

In erythropoiesis, erythroblasts need folic acid and vitamin B12 (Vit B12) during differentiation [6,7]; in the absence of these two factors, megaloblastic anemia is known to occur due to ineffective erythropoiesis [8,9]. Although many studies have compared the efficacy of oral versus intravenous iron replacement in patients with iron deficiency anemia [10-12], very few have examined the changes in additional factors such as Vit B12 and folic acid concurrently with intravenous ferric carboxymaltose.

The purpose of this study was to compare several hematological parameters at baseline and one month after therapy with oral ferrous glycine sulfate (Ferro Sanol Duodenal®, Turkey) and intravenous ferric carboxymaltose (Ferinject®, Germany). In addition, we designed this study to assess the effects of intravenous ferric carboxymaltose on other erythropoiesis-related factors like Vit B12 and folic acid.

Material and methods

Study

In this single-center retrospective study, from January 1, 2016, to December 31, 2018, all adult patients treated for IDA at the internal medicine outpatient clinic were consecutively included. The patients' medical records were reviewed for one month since the time of inclusion. Demographic and clinical data were collected by hospitals information system. The study protocol was approved by Medicalpark Fatih Hospital's institutional review board (approval number: 2021 – 1 – 10). All of the procedures were in accordance with the World Medical Association Helsinki Declaration of 1964 and later versions. The written consent could not be taken due to the retrospective design of the study.

Patients

WHO defines anemia as Hb 13 g/dL in men and 12 g/dL in women; IDA is defined as transferrin saturation <20% and ferritin <25 ng/mL in anemic patients [1,13]. Inclusion criteria were as follows: age >18 years, having been treated for IDA, having first month follow-up one. Exclusion criteria included pregnancy, having active inflammatory bowel diseae, macrocytic anemias (folic acid or Vit B12 deficiency) or any other chronic disease (an infection, a rheumatic or malignant disease), incomplete medical records or incomplete follow-up.

Patients' demographics (age, gender), type of medication, and the results of the hematological parameters [Hb (g/dl), mean corpuscular volume (MCV) (fL), transferrin saturation (TS) (%), ferritin (ng/mL), Vit B12 (pg/mL), and folic acid (ng/mL)] were recorded.

Eligible patients were divided into two groups depending on the iron therapy at the time of enrollment. Subjects on ferrous glycine sulfate received a daily dose of 567.7 mg given orally for one month. Subjects on ferric carboxymaltose therapy received a single dose of a single dose of 1000 mg, in a slow intravenous infusion over 20 min. Following the first infusion of ferric carboxymaltose or ferrous glycine sulfate prescription, none of the patients in ferric carboxymaltose group received oral iron therapy and none in ferrous glycine sulfate group received intravenous iron treatments during the follow-up.

The data was compared between oral ferrous glycine sulfate group and intravenous ferric carboxymaltose group. The primary endpoint of the study was the change in Hb, MCV, TS, and ferritin from the beginning of the study to the first month of intragroup follow-up; and the secondary outcome was the change of Vit B12 and folic acid among the groups.

Statistical Analysis

Statistical analysis was performed using the MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013). The normality of continuous variables was investigated by Shapiro-Wilk's test. Descriptive statistics were presented using mean and standard deviation for normally distributed variables and median (and minimum-maximum) for the non-normally distributed variables. Non-parametric statistical methods were used for values with skewed distribution. For the comparison of two non-normally distributed independent groups, Mann Whitney U test was used. For the comparison of two non-normally distributed dependent groups, Wilcoxon Signed Rank test was used. The comparison of categorical variables was performed by using the Chi-Square test. Statistical significance was accepted when the two-sided p value was lower than 0.05.

Results

A total of 333 patients were included in the study. The ferrous glycine sulfate group included 186 patients and the ferric carboxymaltose group included 147 patients. The flow chart of the study is shown in Figure 1.

Table 1 shows the demographics of 333 patients included in the study. There were no statistical differences between groups according to age and gender distribution values (p=0.072, p=0.947, respectively).

Table 1. Demographic characteristics of the study groups.

	Ferrous glycine sulfate Group	Ferric carboxymaltose Group	p
Gender †			0.072[1]
Female	93 (50)	88 (59.9)	
Male	93 (50)	59 (40.1)	
Age (years) ‡	43 (18-70)	40 (18-78)	0.947[2]

†: n (%), ‡: median (min-max), [1]: Chi-Square test, [2]: Mann Whitney U test.

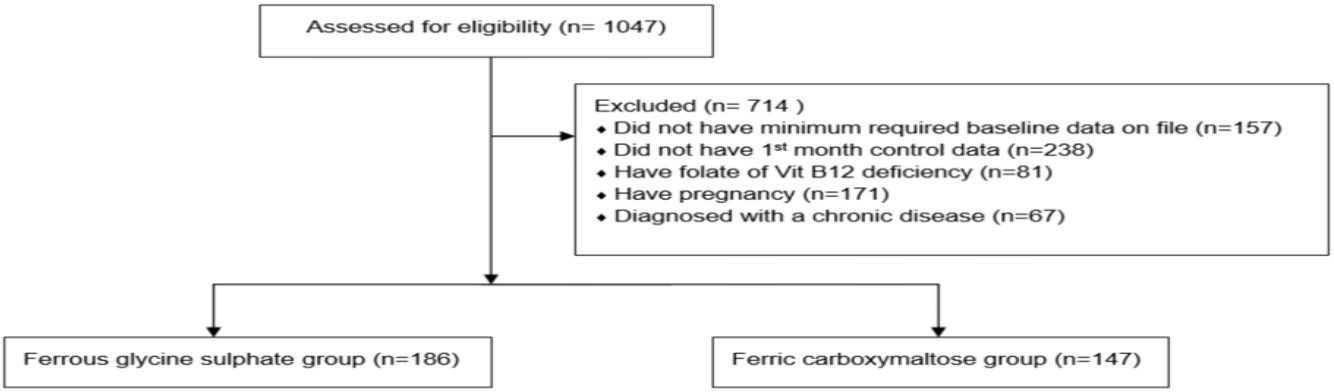

Figure 1. Flowchart of the study.

There was no significant difference between the groups regarding baseline Hb and TS values (p=0.100, p=0.850, respectively) (Table 2).

Table 2.

	Ferrous glycine sulfate group	Ferric carboxymaltose group	$p^{1/3}$
Hemoglobin-baseline (g/dL)	8.9 (8-11)	8.9 (8-10)	0.100[1]
Hemoglobin-first month (g/dL)	10.1 (9-12.7)	11.4 (9.7-13.5)	<0.001[1]
Difference	1.2 (0.4-1.8)	2.5 (1.3-3.5)	<0.001[3]
Δ % change	13.8 (4.6-22.2)	27.9 (14.4-42.7)	<0.001[3]
p^2	<0.001	<0.001	
MCV-baseline (fL)	74 (65-79)	72 (65-79)	0.002[1]
MCV-first month (fL)	79 (69-89)	83 (73-93)	<0.001[1]
Difference	5.5 (-2-15)	11(8-14)	<0.001[3]
Δ % change	7.6 ((-2.6)-23.1)	15.8 (10.3-21.5)	<0.001[3]
p^2	<0.001	<0.001	
TS-baseline (%)	0.1 (0.01-0.2)	0.1 (0.01-0.2)	0.850[1]
TS-first month (%)	0.2 (0.06-0.3)	0.3 (0.2-0.5)	<0.001[1]
Difference	0.1 (0.1-0.2)	0.2 (0.2-0.4)	<0.001[3]
Δ % change	100 (29.4-1400)	250 (79-2800)	<0.001[3]
p^2	<0.001	<0.001	
Ferritin-baseline (ng/mL)	9 (1-15)	7 (1-15)	<0.001[1]
Ferritin-first month (ng/mL)	36 (7-60)	209(155-261)	<0.001[1]
Difference	28 (5-48)	201 (148-260)	<0.001[3]
Δ % change	323.6 (64.3-4200)	2950 (1233.3-26000)	<0.001[3]
p^2	<0.001	<0.001	
Vit B12-baseline (pg/mL)	290 (199-324)	267 (210-320)	<0.001[1]
Vit B12-first month (pg/mL)	267 (181-306)	231 (198-288)	<0.001[1]
Difference	-22 (-30-(-10)	-29 (-111-75)	0.018[3]
Δ % change	-7.47 ((-11.4)-(-3.2))	-11 ((-35.7)-35.2)	0.005[3]
p^2	<0.001	<0.001	
Folic acid-baseline (ng/mL)	7 (5-10)	7.7 (4.5-11)	0.006[1]
Folic acid-first month (ng/mL)	5.8 (4.3-7.8)	5.7 (3.2-10)	0.947[1]
Difference	-1.3 (-5.6-2.8)	-1.7 (-3.2-1.1)	0.009[3]
Δ % change	-18.2 ((-56)-56)	-23.1 ((-47.6)-23.4)	0.010[3]
p^2	<0.001	<0.001	

All values were represented by median (min-max).
p^1 :Intergroup comparison, Mann Whitney U test, p^2: intragroup comparison, Wilcoxon Signed Rank Test, p^3: other comparions, Mann Whitney U test.
MCV: mean corpuscular colume, TS: transferrin saturation, Vit B12: vitamin B12.

Significant differences were detected in terms of baseline MCV, ferritin, Vit B12, and folic acid. Median MCV, ferritin, and Vit B12 baseline values were significantly higher in ferrous glycine sulfate group than in ferric carboxymaltose group (p=0.002, p<0.001, p<0.001, respectively). The median folic acid baseline value was significantly lower in ferrous glycine sulfate group compared to ferric carboxymaltose group (p=0.006).

Significant improvements were detected in both groups (intra-group) in terms of laboratory values obtained after treatment (p<0.001). There were significant differences between the groups (inter-group numerical) except for folic acid in median laboratory values at the end of the first month. For subjects receiving oral ferrous glycine sulfate, Hb increased from baseline of 8.9 (8-11) to 10.1 (9-12.7) g/dL at first month follow-up (p<0.001). For subjects receiving ferric carboxymaltose, Hb increased from baseline of 8.9 (8-10) to 11.4 (9.7-13.5) g/dL at at first month follow-up; (p<0.001). MCV, TS, and ferritin values were significantly higher in ferric carboxymaltose compared to ferrous glycine sulfate group (p<0.001).

At baseline Vit B12 value in ferric carboxymaltose group was significantly lower than ferrous glycine sulfate group (p<0.001); conversely the baseline folic acid value was significantly lower in ferrous glycine sulfate group (p=0.006). When we compare the first month follow-up values: There was no significant difference in folic acid value between groups (p=0.947); but Vit B12 value was significanty lower in ferric carboxymaltose group (p<0.001).

When the delta percentage change between groups (inter-group %) is compared: The delta percentage change increase in Hb, MCV, TS, and ferritin values were significantly higher in ferric carboxymaltose group than in ferrous glycine sulfate group (p<0.001). The delta percentage change decrease in Vit B12 and folic acid values were higher in ferric carboxymaltose group than in ferrous glycine sulfate group (p=0.005, p=0.010, respectively).

Discussion

In our study, Hb increase was more significant in ferric carboxymaltose patients than in ferrous glycine sulfate patients. Furthermore, as can be seen by ferritin and TS value increases, replenishment of iron stores was significantly greater in the iv ferric carboxymaltose group than in the oral ferrous glycine sulfate group. These numeric and percentage based increases in the first month, consistent with previous studies, are promising for patients who need rapid correction of anemia and have difficulty using oral iron preparations due to gastrointestinal disturbances.

Treatment of IDA can be challenging due to side effects of chosen drug or compliance of patient to the length of the treatment. Oral iron has a history of non-compliance and is linked

to more frequent adverse events; in contrast, older IV iron treatments carried their own risks and were not consistently demonstrated to be superior to oral iron in randomized controlled trials. Fortunately, this perception started to shift as ferric carboxymaltose became more widely used [10-13]. The low compliance with oral iron treatments due to the gastrointestinal discomfort they cause may be one of the obvious factors influencing our study's primary outcome. Due to the retrospective nature of our study, we were unable to investigate the patients' adherence to oral medicine and anticipate how low treatment compliance would affect the results.

When oral iron therapy is given, the patient is usually reassessed two to four weeks after initiation; the hemoglobin level is checked, the tolerability of oral iron is reviewed. With intravenous iron, we usually see patients four to eight weeks after the iron is given. Four weeks should be the minimum interval because after iv iron is given, there is a significant fluctuation in blood iron parameters such as iron, TS and ferritin [14-16]. We did our follow-up at the end of first month because 4 weeks is the intersection cluster for monitoring both oral and iv iron treatment efficacy.

In one of the few studies in which iv ferric carboxymaltose did not produce a more significant Hb increase than oral iron therapy, Bager et al. [17] conducted a study in 64 upper gastrointestinal bleeding patients, which showed no significant difference in Hb increase between oral ferrous glycine sulfate and iv ferric carboxymaltose. This may be because the participants in Bager's study had baseline hemoglobin levels that were higher than those in the current investigation (mean Hb at baseline was, respectively, 10.1 and 9.7 g/dL in the oral and iv iron groups). Still, the restoration of iron depots was faster by iv ferric carboxymaltose than oral ferrous glycine sulfate. In many other studies, ferric carboxymaltose treatment outperformed oral iron treatment in terms of Hb level increase and correction time. In REPAIR-IDA study performed by Onken JE et al. [18], patients with chronic kidney disease and IDA were randomly assigned to receive a total dose of 1500 mg ferric carboxymaltose in 1 week or 200mg iron sucrose in up to five infusions in 2 weeks. Increases in Hb, ferritin, and TS values were superior for patients receiving ferric carboxymaltose compared with patients receiving iron sucrose. In another study, Lichtensten et al. [19] conducted a study that they pooled data from four other studies; they took 191 patients treated for IDA with ferric carboxymaltose; in this study improvements in Hb, TS, and ferritin values were significantly greater ($p=0.001$) than patients receiving oral iron therapies. Ferrer-Barceló et al. [20] performed a prospective study of 61 patients with acute gastrointestinal bleeding who were treated with iv ferric carboxymaltose or oral ferrous glycine sulfate; ferric carboxymaltose provided a significant Hb, TS, and ferritin increase and was better tolerated than oral ferrous glycine sulfate. Finally, in 2021, Cirillo et al. [21] conducted a retrospective, monocentric, observational study reviewing 349 non-dialysis-dependent chronic kidney disease patients. 239 patients were treated with a single dose of iv ferric carboxymaltose and 110 with one or two daily dose of 325 mg oral ferrous glycine sulfate. They reported that iv ferric carboxymaltose treatment in non-dialysis-dependent chronic kidney disease patients results in better replenishment of iron stores when compared to oral ferrous glycine sulfate.

In the light of all these and new studies, iv iron carboxymaltose therapy has begin become the first choice of treatment in more and more patients since it fills iron stores faster, has a low side effect profile and high treatment compliance compared to oral iron replacement therapy [22-24].

We also evaluated baseline and first month follow-up Vit B12 and folic acid blood levels in this study. After one month from the first day of therapy, both factors have been decreased. When we compare groups, there was no significant difference in folic acid values but Vit B12 value in iv ferric carboxymaltose group was significantly decreased compared to oral ferrous glycine sulfate group. Additionally, when we examined the percentages between the two groups at the first month follow-up, we found that the levels of folic acid and vitamin B12 in the IV ferric carboxymaltose group were significantly lower than those in the oral ferrous glycine sulfate group.

This result occurred because erythroblasts require Vit B12 and folic acid to proliferate during their differentiation [6]. Vit B12 is used as a cofactor during the synthesis of tetrahydrofolic acid. Tetrahydrofolic acid is used during the synthesis of deoxythymidine monophosphate; in the end, deoxythymidine monophosphate is required for DNA synthesis in erythropoiesis [25]. Therefore, after we restored the iron depots, erythropoiesis began to work. Consequently, Vit B12 and folic acid were utilized at a rate proportional to erythropoiesis. This process explained the decline in folic acid and vitamin B12.

Only two studies in the literature examined these two factors' baseline values during iv ferric carboxymaltose treatment, and just one of them included first month follow-up values. Venturini et al. [26] analyzed 106 patients with IDA on admission to a cardiac rehabilitation unit after cardiac surgery. They treated patients with iv ferric carboxymaltose or oral sucrosomial iron. Unfortunately, they could only reach the baseline Vit B12 and folic acid levels before the treatment; obtained data show that folic acid deficiency is quite frequent after cardiac surgery, detected in 60.4% of patients; meanwhile, only 6.6% of this group had Vit B12 deficiency. In the other study, contrary to our findings, Huguet et al. [27] found no significant change in Vit B12 and folic acid values compared to the baseline value after one month of a single 500mg ferric carboxymaltose dose in iron deficiency patients without anemia. The main reason for reaching this result can be that patients in the study did not have anemia; also the relatively low amount of iv ferric carboxymaltose used can be considered as another reason.

As a result, if Vit B12 and folic acid levels are not controlled before therapy, this decline may result in a deficit of these two vitamins and diminish the efficiency of the treatment. Furthermore, low levels of Vit B12 and folic acid can even lead to severe neurological deficits in the long run. Therefore, supplementing Vit B12 and folic acid at the beginning of ferric carboxymaltose treatment may be a simple, effective, inexpensive solution to prevent adverse events.

Being a single-center and a retrospective study can be cited as the limitations of this study. We think that prospective studies with more patients will make new contributions to the literature.

In conclusion, our study's results indicate that ferric carboxymaltose treatment is very effective for restoring iron depots in IDA, it should be kept in mind that concomitant, adequate supplementation of factors such as Vit B12 and folic acid is essential for the proper progression of erythropoiesis.

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Effects of exercise on coronary flow reserve and biochemical parameters in patients with type 2 diabetes mellitus

Aerobic egzersizin tip 2 diyabet hastalarında koroner akım rezervi ve biyokimyasal parametrelere etkisi

Göksel Güz [1], Hüseyin Oflaz [2]

Abstract

Aim: Coronary, peripheral and cerebral vascular diseases are the most important causes of mortality and morbidity in diabetic patients. The aim of our study was to determine the dysfunction in the epicardial coronary arteries and microvascular circulation noninvasively by measuring the coronary flow reserve (CFR) by transthoracic echocardiography, and to examine the effect of regular aerobic exercise on CFR in diabetic patients.

Methods: Forty patients with diabetes mellitus and 20 healthy volunteers were included in the study. These patients were those who had been using oral antidiabetic drugs for at least 3 years, had no ischemia symptoms and did not exercise regularly. At the beginning of the study, the CFR obtained from the distal left anterior decendant artery (LAD) flow in the transthoracic echocardiography of diabetic patients was compared with the health control group. Diabetic patients were divided into two groups as those who were included in a regular exercise program and those who were not. The exercise group was given regular aerobic exercise for 8 weeks in the department of sports medicine. Post-exercise CFR values of diabetic patients included in aerobic exercise program were compared with pre-exercise values.

Results: Basal CFR values of diabetic patients were statistically significantly lower than healthy volunteers ($p<0.001$). A significant improvement was found in the post-exercise CFR values of the diabetic patients who were included in the exercise program compared to the pre-exercise levels ($p<0.001$).

Conclusion: Regular aerobic exercise can reduce the risk of cardiovascular complications by improving coronary flow reserve in diabetic patients.

Keywords: Exercise, coronary flow reserve, type 2 diabetes mellitus.

Öz

Amaç: Diyabetik hastalarda en önemli mortalite ve morbidite nedenleri koroner, periferik ve serebral hastalıklardır. Çalışmamızın amacı, epikardiyal koroner arterler ve mikrovasküler dolaşımdaki disfonksiyonu transtorasik ekokardiyografi ile koroner akım rezervinin (CFR) ölçülerek noninvaziv olarak belirlemek, düzenli aerobic egzersizin diabetik hastalarda CFR üzerindeki etkisini incelemekti.

Yöntemler: Çalışmaya 40 diabetus mellitus hastası ve 20 sağlıklı gönüllü dahil edildi. Bu hastalar en az 3 yıldır oral antidiyabetik ilaç kullanan, iskemi semptomu olmayan ve düzenli egzersiz yapmayan hastalardı. Çalışmanın başlangıcında diyabetik hastaların transtorasik ekokardiyografisinde distal LAD (left anterior decendan artery) akımından elde edilen CFR, sağlık kontrol grubu ile karşılaştırıldı. Diyabetik hastalar düzenli egzersiz programına alınanlar ve egzersiz konusunda yönlendirilmeyenler olarak iki gruba ayrıldı Egzersiz grubuna spor hekimliği anabilim dalında 8 hafta süreyle düzenli aerobik egzersiz verildi. Aerobik egzersiz programına alınan diyabetik hastaların egzersiz sonrası CFR değerleri egzersiz öncesi değerleri ile karşılaştırıldı.

Bulgular: Diyabetik grupların bazal CFR değerleri sağlıklı gönüllülere göre istatistiksel olarak anlamlı derecede düşüktü ($p<0.001$). Egzersiz programına alınan diyabetik hastaların egzersiz sonrası CFR değerlerinde egzersiz öncesi düzeylere göre anlamlı iyileşme tespit edildi ($p<0.001$).

Sonuç: Düzenli aerobic egzersiz, diyabetik hastalarda koroner akım rezervini düzelterek kardiyovasküler komplikasyon riskini azaltabilir.

Anahtar Kelimeler: Egzersiz, koroner akım rezervi, tip 2 diabetus mellitus.

[1] Medicana International Hospital, Department of Cardiology, Beylikduzu, Istanbul, Turkey.

[2] Istanbul University, Istanbul Faculty of Medicine, Department of Cardiology, Istanbul, Turkey.

GG: 0000-0002-8386-9160

HO: 0000-0003-1937-7038

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Sorumlu yazar / Corresponding author:

Göksel Güz

Adres/Address: Beylikdüzü cad. No: 3, Beylikdüzü Medicana İnternational Hastanesi. Beylikdüzü, İstanbul, Türkiye

E-mail: gokselguz@yahoo.com

Tel/Phone: +90 05057748831

Introduction

Diabetes mellitus is one of the most important threats to human health in modern society. The most prominent mortality and morbidity causes in diabetic patients are coronary, peripheral and cerebral diseases [1]. Cardiovascular mortality is increased by 3 to 4 folds in diabetic patients compared to patients without diabetes [2]. Endothelial dysfunction, proinflammatory state, tendency to thrombosis, autonomic dysfunction and disruptions in lipoproteins are the mechanisms responsible for cardiovascular incidents [3, 4]. Insulin resistance has key importance on chronic inflammation followed by endothelial dysfunction, formation and development of atheroma plaque [5, 6]. Endothelial dysfunction seen in diabetes is the most important factor that initiates and promotes the macroangiopathic and atherosclerotic process. Due to major role of normal endothelium on blood vessel homeostasis, it is known that endothelial dysfunction has major effects in pathophysiology of vasospasm, thrombus for- mation and diseases progressing with blood vessel proliferation [7, 8]. Today, atherosclerosis is considered to be an inflammatory disease. Many cells (endothelial cells, smooth muscle cells, macrophages) and proteins (inflammatory cytokines, adhesion molecules) play a role in this inflammatory process and development of the lesion [9].

Coronary angiography used to detect coronary artery disease only reveals the atherosclerotic lesions narrowing towards the blood vessel lumen. Coronary angiography do not provide with sufficient data regarding physiology of coronary blood flow or endothelial function. In recent years, transthoracic echocardiography (TTE) or measurements of coronary flow reserve (CFR) obtained with invasive coronary angiographic methods, have been drawing attention in demonstrating coronary arterial endothelial function and level of microvascular circulation. Based on the principle that inability of coronary arteries to vasodilate during metabolic need indicates endothelial dysfunction, CFR measurements can confidently determine the status of both epicardial coronary arteries and microvascular coronary circulation [10].

The aim of our study was to non-invasively determine dysfunction in epicardial coronary arteries and microvascular circulation with measurement of coronary flow reserve using transthoracic echocardiography in patients with type 2 diabetes despite absence of ischemic symptoms, and to demonstrate the amelioration in endothelial functions, glycemic control and insulin resistance along with increase in coronary flow reserve after 8 weeks of regular exercise.

Material and methods

Fourty patients diagnosed with type 2 diabetes in Istanbul Facuty of Medicine, Department of Diabetes, who were on follow-up for at least three years due to diabetes, without ischemic symptoms, on oral antidiabetics and who had sedentary lifestyles were included in our study. All patients were included in the study after receiving their written consents. For this study Istanbul Faculty of Medicine's Ethics Committee approval was obtained. Diabetic patients included in the study were divided into two groups. Patients in the first group were put under a regular exercise program of 5 times per week by the Department of Sports Medicine and were encouraged to exercise regularly in the remaining days. Patients in the second group were not given any exercise program nor any additional information about exercise. Exclusion criteria for patients were presence of untreated (uncontrolled) hypertension (systolic blood pressure >160 mmHg, diastolic blood pressure >90 mmHg), known or suspected coronary artery disease, rhythm disorder (chronic or permanent atrial fibrillation etc.), chronic diseases such as chronic kidney failure and liver disease, bundle block in basal echocardiography, lung disease such as chronic obstructive pulmonary disease (COPD) that would limit effort capacity and absence of appropriate physical conditions to exercise. Patients whose left anterior descending artery (LAD) flow tracings were not ideal or unable to be seen with pulse wave Doppler were excluded from the study. Moreover, in order to compare features of diabetic patients such as CFR and insulin resistance with the healthy population, twenty healthy participants with similar age and sex characteristics with the patient group were included in the study.

Before starting the exercise program, a Burdick model treadmill stress test machine was used to perform exercise stress test to diabetic patients who would be included in the exercise program. All patients and those in healthy control group were given cardiopulmonary exercise test by the department of sports medicine using "Quinton 65 treadmill", "Quinton 5000" effort test system, "Cortex Metalyzer 3B" metabolic assessment device and "Metasoft 2.7" software support. To assess metabolic parameters of the participants, "Rudolph Mask 2 way 7910" was used during testing. Patients in the exercise group received 5 days a week of exercise for a duration of 8 weeks.

To all individuals that participated to the study, routine transthoracic echocardiographic mea- surements in left lateral decubitus position were performed with a 3 MHz probe using VIVID 7 (GE, General Electric) device. M-mode echocardiography and two-dimensional measurements were done in accordance with methods stated by American Society of Echocardiography [14]. Left ventricular conventional echocardiographic measurements were performed in all individuals.

Investigation of coronary flow reserve was done using the same device and a 3 mHz probe. LAD mid-distal flow was imaged using color Doppler in left lateral decubitus position, at the point of intersection of midclavicular line with 4-5th intercostal space, in longitudinal apical 2 chamber view of the left ventricle, with optimal velocity of 12-15 cm/s. The cursor was placed on the LAD flow. First, basal value [PDV (peak diastolic flow velocity)] of the coronary flow velocity (CFV) was measured with pulsed- wave Doppler. Then, the subjects received 0.56 mg/kg of dipyridamole infusion for 4 minutes. In case of less than 10% of increase in heart rate compared to basal values, an additional 0.28 mg/kg of dipyridamole infusion for 2 minutes was given. 2 minutes after the dipyridamole infusion was over, hyperemic peak diastolic flow velocity was measured. CFR was calculated via the formula: hyperemic peak diastolic flow velocity/basal peak diastolic flow velocity. During dipyridamole infusion and until the procedures were over, patients were monitorized and their blood pressures were followed.

After 12 hours of fasting, morning plasma glucose and insulin levels, cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride, pro-brain natriuretic peptide (pro-BNP), highly sensitive C-reactive protein (hs-CRP), HbA1c, C- peptide, fructosamine and fibrinogen levels of patients and control group were measured.

In our study, the first step was to compare values of the healthy control group and those of diabetic patients were statistically compared at first. Basal values before exercise of diabetic patient who did not exercise regularly. Values obtained after exercise of these patients were compared with values before exercise and those of diabetic patients who did not exercise. Parameters that ameliorated after exercise of diabetic patients enrolled in the exercise program were likewise compared with those of the healthy group.

Statistical Analysis

Continuous variables with parametric distribution were expressed as mean + standart sapma deviation. Categroical data were expressed as frequncies and their differences were analyzed using the Chi-square test. Variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Simirnov/Shapiro-Wilk's test) to determine whether they were normally distributed. Continuous variables were compared using Student's t test or the Mann-

Whitney U test as appropiate. The ANOVA test or Kruskall Wallis Test was used to compare basal basal peak diastolic velocity (BPDV), hyperemic peak diastolic velocity (HPDV), CFR values of the groups. Statistical analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical significance was taken as $p<0.05$.

Results

Comparison of basal blood chemistry values and physical features such as age, height and weight of healthy volunteers and patient volunteers who participated in the study is given in Table1.

Table 1. Comparison of basal values of the groups.

	Diabetics with exercise (n=20)	Diabetics without exercise (n=20)	Healthy group	p
Age (year)	56.45 ± 4.72	55.25 ± 3.44	54.4 ± 4.08	0.29
Weight (kg)	79.3 ± 10.8	81.2 ± 9.18	82.1 ± 8.9	0.77
Height (cm)	165 ± 5.2	166 ± 7.1	169 ± 7.4	0.70
Insulin (uU/ml)	8.17 ± 5.1	10.2 ± 3.07	6.26 ± 2.1	0.004
Fasting blood glucose (mg/dL)	151 ± 44.65	143.3 ± 32.13	84.8 ± 7.9	<0.001
Basal hsCRP (mg/L)	3.36 ± 1.25	3.2 ± 1.09	1.99 ± 0.9	<0.001
Basal HOMA-IR	3.93 ± 1.85	3.45 ± 0.62	<1.3 ± 0.4	0.001
Basal Pro-BNP (ng/ml)	65.7 ± 80.5	53.2 ± 52	31.05 ± 17.6	0.037
Basal C-Peptide (ng/ml)	2.38 ± 1.15	2.33 ± 1.49	-	0.90
Triglyceride (mg/dl)	210.6 ± 113.7	231.5 ± 51.09	-	0.61
LDL cholesterol (mg/dl)	117.75 ± 23.56	116.9 ± 20.59	-	0.90
HDL cholesterol (mg/dl)	40 ± 11.69	38.95 ± 8.12	-	0.83
Basal HbA1c	7.46 ± 1.2	7.32 ± 0.4	-	0.65
Basal fructosamine (mmol/L)	3.01 ± 0.6	3.25 ± 0.59	-	0.24
Basal fibrinogen (mg/dl)	409.4 ± 117.6	400.7 ± 118.8	-	0.81
Basal VO_2 max	24.1 ± 2.66	25.3 ± 2.25	32.6 ± 6.67	<0.001

HsCRP: high sensitive c reactive protein, HOMA-IR: Insulin resistance calculated via homeostasis model assessment method, LDL: low density lipoprotein, HDL: high density lipoprotein, HbA1c: hemoglobin A1c, VO2 max: maximal oxygen consumption- maximal aerobic capacity

Comparison of basal peak diastolic flow velocity, hyperemic peak diastolic flow velocity and coronary flow reserves of diabetic patients that followed an exercise program, diabetic patients who did not follow an exercise program and healthy adult group is given in Table 2. According to this, while basal peak diastolic flows did not significantly differ between the three groups, there was a statistically significant difference in hyperemic peak diastolic flow velocity and coronary flow reserve between healthy adults and both groups of diabetic patients (Table 2). There are 20 people in the group of those who exercise. Of the 20 participants, 15 (75%) were able to complete the exercise program. Values of 15 patients before and after exercise were evaluated.

Table 2. Comparison of basal BPDV, HPDV, CFR values of the groups

Coronary flow	Diabetics with exercise (n=20)	Diabetics without exercise (n=20)	Healthy group	Test value	P
Basal BPDV (cm/s) †	32.70 ± 8.298	32.65 ± 5.071	33.45 ± 7.373	F=0.081	0.922[a]
Basal HPDV (cm/s) †	54.75 ± 10.120	53.55 ± 7.112	75.15 ± 17.315	$\chi2$=23.467	0.0001[b]
Basal CFR (cm/s) †	1.68 ± 0.186	1.66 ± 0.239	2.25 ± 0.232	F=47.332	0.0001[a]

†: mean ± standard deviation.
a: ANOVA; b: Kruskal Wallis Test. BPDV: Basal peak diastolic flow velocity, CFR: Coronary flow reserve, HPDH: Hyperemic peak diastolic flow velocity.

Comparison of BPDV, HPDV and CFR values before and after exercise of the group of diabetic patients who exercise are given in Table 3; and HPDV and CFR values are statistically significantly higher after exercise compared to before. Blood chemistry values before and after exercise of the group under the exercise program is given in detail in Table 4, values before and after exercise of maximum oxygen intake (VO_2 max) were compared, and maximum oxygen intake was found to be statistically significantly lower before exercise than after (23.8 ± 2.9 vs 27.6 ± 2.9, p= 0.0001).

Table 3. Comparison of BPDV, HPDV, CFR values before and after exercise of the group of diabetics who exercise.

Coronary flow	n	Before exercise	After exercise	t	Pα
BPDV †	15	32.27 ± 9.384	34.80 ± 5.454	-0.881	0.393
HPDV †	15	54.27 ± 2.892	76.07 ± 13.771	5.261	0.0001
CFR †	15	1.69 ± 0.203	2.15 ± 0.253	6.082	0.0001

†: mean ± standard deviation.
BPDV: Basal peak diastolic flow velocity, CFR: Coronary flow reserve, HPDH: Hyperemic peak diastolic flow velocity.

Table 4. Comparison of biochemistry parameters before and after exercise of the group of diabetics who exercise.

	n	Before exercise	After exercise	t	p[a]
Insulin †	15	8.19 ± 5.715	8.38 ± 3.958	-0.231	0.820
C-Peptide †	15	2.09 ± 1.191	2.61 ± 1.792	-1.739	0.104
FBG †	15	150.67 ± 47.566	123.0 ± 31.173	3.126	0.007
HbA1c †	15	7.47 ± 1.406	6.88 ± 0.989	4.171	0.001
Fructosamine †	15	3.02 ± 0.736	2.66 ± 0.479	3.065	0.008
HDL †	15	40.73 ± 13.21	48.53 ± 14.784	-5.706	0.0001
Triglyceride †	15	210.40 ± 127.26	147.2 ± 63.493	2.367	0.033
LDL †	15	115.67 ± 26.161	97.73 ± 20.800	4.142	0.001
Fibrinogen †	15	410.80 ± 133.27	368.9 ± 117.62	2.617	0.020
CRP †	15	3.29 ± 1.39	2.49 ± 1.039	2.644	0.019
HOMA-IR †	15	4.20 ± 1.93	2.42 ± 1.208	3.714	0.002
Pro-BNP †	15	73.53 ± 91.	44.40 ± 32.758	1.818	0.091

†: mean ± standard deviation.
[a]: Paired Sample t-Test. FBG: fibrinogen, HbA1c: Hemoglobin A1c, HDL: high density lipoprotein, LDL: low density lipoprotein, CRP: C reactive protein, HOMA-IR: Insulin resistance calculated via homeostasis model assessment method, pro-BNP: pro brain natriuretic peptide

Discussion

It is known that diabetes leads to atherosclerosis, hypertension, coronary artery disease and certain problems in the heart free of valvular disease [11-13], that it increases cardiovascular mortality and that cardiovascular mortality in diabetic population is significantly higher compared to general population [14]. In our study, the positive effects of exercise on glycemic control, cholesterol panel, and inflammatory markers in

diabetic patients as well as its positive effect on endothelial functions were demonstrated by the CFR method. CFR values of diabetic patients were found to be lower than the healthy group in accordance with the literature.

In diabetes, aerobic exercise is as efficient as pharmacotherapy. Exercise not only attains glucose control, it also prevents cardiovascular complications of diabetes [15, 16]. According to duration and intensity of physical exercise, production of free radicals and activations of the antioxidant system can increase [17, 18]. Oxidative stress depends on the balance between production of free radicals and anti- oxidant activity. While excessively intense exercise plasma 8-hydroxyguanosine (8- OHdG) and serum malondialdehyde concentrations indicating oxidative stress; regular, conscious exercise decreases plasma levels of these oxdative stress markers. Effects of exercise on oxidative stress are shaped with duration and intensity of the exercise. Regular, conscious exercise is highly important in diabetic patients in order to achieve metabolic control and decrease oxidative stress [19, 20]. In a study by Nojima et al. [21] regular exercise for one year was shown to decrease oxidative stress leading to a visible drop in urinary 8- OHdG levels that indicate total oxidative stress.

It is known that oxidative stress disrupts glycemic control by causing insulin resistance and that it leads to micro and macrovascular complications [22]. Regular physical activity applied to diabetic patients improves glycemic control by decreasing oxidative stress. It decreases the frequency of complications encountered in diabetes. It mends endothelial dysfunctions seen in early stages of atherosclerosis: the most common and deadly complication of diabetes.

Endothelial dys- function in diabetic patients is directly associated with the duration and intensity of hypergly- cemia. In a study conducted by Yokoyama et al., longterm glycemic control was shown to signifi- cantly improve coronary flow reserve in patients with asymptomatic diabetes [23]. Nemes et al. [24] stated in their publication that there was a negative correlation between insulin resistance and CFR. Endothelial dysfunction was considered to be one of the reasons of insulin resistance in this study. In our study, we have observed that regular exercise leads to a significant decrease in insulin resistance. Decrease in insulin resistance brings on the improvement in endothelial functions. By decreasing insulin resistance, exercise ameliorates endothelial functions and increases coronary flow reserve. One of the mechanisms responsible for the improvement in endothelial functions in our patient group is the decreased insulin resistance in the physical activity and exercise group. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) values after regular and intense physical activity of patients in this group were significantly lower than initial HOMA-IR values of these patients and HOMA-IR values of 8 weeks after of the diabetic group that did not exercise.

In a study conducted by Ilercil et al. [25] patients with impaired glucose tolerance, association between left ventricle mass, left ventricle wall thickness and insulin resistance was investigated and an independent association between insulin resistance and increased left ventricle wall thickness was revealed. Similar to current literature, compared to healthy control group, left ventricle wall thickness in diabetic patients was likewise greater in our study. In a study by Sung et al., relation between increased left ventricle mass and endothelium dependent vasodilation in peripheral arteries was investigated and endothelium dependent vasodilation in peripheral arteries was found to be insufficient in those with increased left ventricle mass [26]. Davis et al. [27] stated in their study that increase in left ventricle mass was a component of metabolic syndrome and an important cardiovascular risk factor. There are much evidence supporting the existence of insulin resistance in pathogenesis of left ventricle hypertrophy.

It is known that diabetic patients do not have enough physical activities and that more than 80% of the diabetic patient population follows a sedentary lifestyle. Compared to general population, rate of having an inactive, sedentary lifestyle is higher in diabetic patients [28]. Within the lifestyle changes suggested to diabetic patients, along with diet, exercise is known to cause a significant decrease in morbidity and mortality [29]. It has been shown that regular exercise improves cardiac autonomic and contraction functions. Deficiency of insulin in diabetics leads to decreased activity of Na/Ca exhancer protein. With increased physical activity, in diabetic patients, insulin resistance decreases and intracellular calcium metabolism improves through the increase in the activity of Na/Ca exhancer protein. This is reflected as the increase in functional capacity in the clinical status of the patient. In our study, VO2 max values of the patients after 8 weeks of exercise showed significant improvement.

In diabetic patients, due to increased oxidative stress, endothelium is eroded and damaged. There is decrease in Nitric oxide (NO) dependent vasodilator system, increase in vasoconstrictor system along with a worsened ability of the coronary arteries to dilate due to endothelial dysfunction and decreased CFR values. CFR is a parameter with a prognostic value. Cortigiani et al. [30] followed 1130 patients with coronary artery disease, 270 of whom were diabetics, for a period of 16 months. Analyses regarding development of cardiovascular incidents showed that age ($p=0.02$), wall motion abnormalities ($p=0.05$), abnormal CFR value ($p<0.0001$) were the independent prognostic parameters. Compared to patients with CFR >2, those with CFR ≤2 had a significantly higher risk ($p<0.0001$) of having a cardiovascular incident regardless of being a diabetes status. In patients with normal CFR value, risk of having a cardiovascular incident was found to be 2.2% in diabetics and 2.0% in non-diabetics ($p=0.8$). While rate of cardiovascular incidents in diabetic patients with low CFR levels was 9.3%; annual rate of cardiovascular incidents in non-diabetic patients with low CFR levels was 5.1% [30].

In the current study, in accordance with the other studies in literature, comparison of control and diabetic groups CFR levels in diabetic patients' group were statistically lower compared to control group. After 8 weeks of exercise, there was significant improvement in coronary flow reserve of diabetic patients who exercised. Although initially there was no significant difference in coronary flow reserves between diabetic patient groups, at the end of 8 weeks, those who were not informed about physical activity had significantly lower coronary flow reserve than those who exercised. Comprehensive studies investigating the effects of exercise on CFR in diabetes arequite few. A study by Sebastian Sixt et al. [31] demonstrated that regular exercise improved coronary endothelial functions. Response of coronary arteries to acethylcholine after six months of exercise was invasively measured, and significant improvement in coronary endothelial functions was observed. In this study, coronary arteries of the patients were examined before and after exercise with an intravascular ultrasound, and no increase in coronary plaque burden with regular exercise was found. In our study, the argument that endothelial functions significantly improve in diabetic patients who exercise regularly was proven using transthoracic echocardiography, which is a non-invasive method easier to use in clinical practice. Endothelial dysfunction overlooked with coro- nary angiography or stress test can therefore be recognized with decrease in CFR, and detection of atherosclerosis in earlier stages will be possible.

The present study has the following limitations. First, our modest sample size obtained from a single center may make the

generalizability of the observed results difficult. Second, an assessment of additional markers of endothelial dysfunction besides CFR, which could have supported the study results, was not performed. Third, we did not perform coronary angiography on the patients. Fourth, is the absence of a long-term follow-up of the participants.

To summarize, regular exercise and physical activity are highly important in diabetic patients for primary and secondary protection against cardiovascular incidents. Physical activity increases insulin sensitivity in diabetic patients, and has many positive effects on glucose metabolism. In the current study we found that regular aerobic exercise improved CFR in patients with diabetus mellitus. In light of these findings, exercise should be highly recommended to diabetic patients and those with a risk of developing diabetes mellitus.

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Arch Clin Exp Med 2022;7(3):66-71. e-ISSN: 2564-6567

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Effects of surgical and medical treatments on stress urinary incontinence

Stres üriner inkontinans üzerine cerrahi ve medikal tedavilerin etkileri

Burçin Uğur Tosun [1], Özlem Altındağ [2], Gülhan Yılmaz Gökmen [3], Berkiye Kırmızıgil [1], Fettah Tosun [4]

Abstract

Aim: The aim of this study was to compare how surgical and medical treatments affect the quality of life, depression status and social participation of women with stress urinary incontinence.

Methods: The study included 32 women with diagnoses of stress urinary incontinence.

Among these women, 16 were designated as the medical treatment group, and the other 16 were designated as the surgical treatment group. Before the treatment and 8 weeks after its completion, the patients were evaluated with the International Consultation on Incontinence Questionnaire-Short Form, Incontinence Quality of Life Questionnaire, World Health Organization Quality of Life Instrument - Short Form, Beck Depression Inventory and Social Participation Questionnaire.

Results: The mean age of the subjects was 54.31±11.48 years in medical treatment group and 48.38±10.01 years in surgical treatment group. The mean body mass index values of the groups were respectively 27.56±2.79 and 26.56±2.25 kg/m^2. Following the treatment, statistically significant improvements were observed in urinary incontinence, depression, social participation and overall and disease-specific quality of life in both groups ($p<0.05$). Comparative analysis of the post-treatment changes in both groups showed statistically significant differences in the Beck Depression score, the total work activity and household activity scores in the Social Participation Questionnaire and the psychosocial subgroups of both World Health Organization Quality of Life Instrument and Incontinence Quality of Life Questionnaire ($p<0.05$).

Conclusions: Both treatments proved to be effective and usable to reduce the severity of stress urinary incontinence and depression, prevent social isolation and improve the quality of life.

Keywords: Quality of life, social participation, stress urinary incontinence, women

Öz

Amaç: Bu çalışmanın amacı, stres üriner inkontinans tanısı alan kadınlarda cerrahi ve medikal tedavilerin yaşam kalitesi, depresyon durumu ve toplumsal katılım üzerindeki etkilerini karşılaştırmaktır.

Yöntemler: Çalışmaya stres üriner inkontinans tanılı 32 kadın dahil edildi. Bu kadınlardan 16'sı medikal tedavi grubu, diğer 16'sı ise cerrahi tedavi grubu olarak belirlendi. Tedavi öncesi ve tedavi bitiminden 8 hafta sonra hastalar Uluslararası İnkontinans Sorgulama Formu - Kısa Formu, İnkontinans Yaşam Kalitesi Ölçeği, Dünya Sağlık Örgütü Yaşam Kalitesi Ölçeği - Kısa Formu, Beck Depresyon Ölçeği ve Toplumsal Katılım Anketi ile değerlendirildi.

Bulgular: Medikal tedavi grubunda olguların yaş ortalaması 54,31±11,48, cerrahi tedavi grubunda 48,38±10,01 idi. Grupların ortalama vücut kitle indeksi değerleri sırasıyla 27,56±2,79 ve 26,56±2,25 kg/m2 idi. Tedavi sonrası her iki grupta da idrar kaçırma, depresyon, toplumsal katılım, genel ve hastalığa özgü yaşam kalitesinde istatistiksel olarak anlamlı iyileşmeler görüldü ($p<0,05$). Her iki gruptaki tedavi sonrası değişikliklerin karşılaştırmalı analizi, Beck Depresyon skorunda, Toplumsal Katılım Anketindeki toplam iş aktivitesi ve ev aktivitesi skorlarında, Dünya Sağlık Örgütü Yaşam Kalitesi Ölçeği ve İnkontinans Yaşam Kalitesi Anketinin psikososyal alt gruplarında istatistiksel olarak anlamlı farklılıklar gösterdi ($p<0,05$).

Sonuç: Her iki tedavinin de stres üriner inkontinans ve depresyonun şiddetini azaltmada, sosyal izolasyonu önlemede ve yaşam kalitesini iyileştirmede etkili ve kullanılabilir olduğu kanıtlanmıştır.

Anahtar Kelimeler: Yaşam kalitesi, toplumsal katılım, stres üriner kontinans, kadın

[1] **Eastern Mediterranean University, Department of Physical Therapy and Rehabilitation, Famagusta, North Cyprus via Mersin 10, Turkey.**

[2] **Gaziantep University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Gaziantep, Turkey.**

[3] **Bandırma Onyedi Eylul University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Bandirma/Balıkesir, Turkey.**

[4] **Adana Medline Hospital, Urology Department, Adana, Turkey.**

BUT: 0000-0001-9919-2708
ÖA: 0000-0003-1119-2987
GYG: 0000-0002-0468-7036
BK: 0000-0002-2389-7880
FT: 0000-0001-8616-6674

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Sorumlu yazar / Corresponding author:
Burçin Uğur Tosun

Adana Gençlik ve Spor İl Müdürlüğü, Adana, Türkiye.
e-mail: burcnugur@yahoo.com
Tel/Phone: 0 507 772 1772

Introduction

According to the definition by the International Continence Society (ICS), Urinary Incontinence (UI) is an objectively demonstrable involuntary leakage of urine that creates social or hygienic problems [1]. Studies show that the prevalence of UI varies between 25 and 45% worldwide [1]. In Turkey, similar studies suggest a prevalence ranging between 23 and 57% [2, 3].

Among the risk factors for UI are sex, parity, race, menopause, smoking, constipation, obesity and history of gynecological surgery [4]. UI affects all age groups and negatively changes the quality of life through psychological, social and sexual problems. A constant feeling of wetness and irritation may cause emotional problems that can escalate to the point of depression [5].

The prevalence of UI increases with age. Nevertheless, the condition is not to be considered as part of the natural course of aging. As patients in Turkey avoid consulting a physician, the desired success rate is yet to be achieved due to consideration of UI as a normal process in aging, even though most patients are eligible for treatment [6]. Incontinence should be accepted as a health problem at all stages of life and treated with appropriate methods to improve quality of life [7].

The most common type of incontinence in women is Stress Urinary Incontinence (SUI) experienced as a result of actions that increase intra-abdominal pressure, such as coughing, laughing or lifting heavy objects [8]. The ICS defines SUI as leaking of urine resulting from the intravesical pressure exceeding urethral pressure without detrusor overactivity [5, 8].

SUI is not a life-threatening condition and even though it affects the quality of life negatively in individuals of both sexes in all ages, it affects women more often worldwide due to anatomical and hormonal factors [8]. SUI can be treated with surgical and non-surgical methods. Non-surgical methods may be further divided into pharmaceutical treatment and non-pharmaceutical treatment options. The latter group includes behavioral therapy, pelvic floor exercises, biofeedback and electrical stimulation therapy [9]. It is worth remembering that there is no single 'accurate choice' in SUI treatment. The treatment should be customized based on individual characteristics and circumstances such as symptoms, co-morbidities and intra-operative risk factors [10].

Contemporary, with the improved overall quality of life and prolonged life expectancies, increasingly more research is carried out for the diagnosis and treatment of incontinence. Therefore, the aim of this study was to determine how surgical and medical SUI treatments on women affect their quality of life, depression status and social particpation and comparatively evaluate the treatment methods in terms of their respective advantages and limitations.

Material and methods

Study Design and Participants

This was a prospective, non-randomized comparative, single-center study. A total of 32 female patients over the age of 18, who were newly diagnosed with SUI and had symptoms ongoing for over 6 months were included in the study. Cases were excluded if the individual had a vaginal or pelvic operation in the last 6 months, an active urinary tract infection or more than 3 urinary tract infections in the past year, a neurological or neuromuscular disease (cerebrovascular accident, Alzheimer's, spinal cord injury or dementia), kidney or liver failure or was illiterate or in a condition to prevent evaluation or communication. The treatment group (surgical or medical treatment) of patients who meet the inclusion criteria was decided together by the patient and the physician. 16 patients constituted the surgical treatment group and 16 patients constituted the medical treatment group. The sample size was determined with the G-Power 3.1 software (Universität Düsseldorf, Germany) [11]. A review of the literature showed that the effectiveness of medical treatment applied SUI on I-QOL was reported as Cohen's d = 0.75 (10.5±14-unit changes) [12]. The number of individuals in the groups was determined by calculation that at least 16 patients should be included in each group in order to detect a similar change within the group with a power of 80% and a confidence interval of 95% for the treatments that were applied. The study was approved in Turkey by the Cukurova University Institute of Health Sciences Non-Interventional Clinical Studies Ethics Committee, in the Meeting no. 70 summoned on November 10, 2017 and under the file no. 29. The study was performed in accordance with the Declaration of Helsinki. Both written and verbal information about the objective of the study and the treatments to be applied were explained to all participants and their written informed consent was requested. Before the start of the study, all permissions were obtained from the Urology department of the hospital where the study was conducted.

Assessments

The 32 female SUI patients considered eligible either for medical (n=16) or surgical (n=16) treatment by their physician and met the inclusion criteria of the study were assessed immediately before the treatment and 8 weeks after their medical/surgical treatment. The subjects in the medical treatment group received medication, while those in the surgical treatment group underwent the Transobturator Tape (TOT) procedure. All patient assessments were performed face to face by the same physiotherapist.

Sociodemographic Assessments: The patients' personal information (name, surname, address, telephone number, occupation, education and smoking status) and clinical characteristics (age, height, weight, body mass index [BMI], systemic disorders, drugs used, number of childbirths and marital status) were recorded on the patient evaluation form.

Assesment of Quality of Life: The patients' quality of life was evaluated by using 2 different scales.

a- Incontinence Quality of Life Questionnaire (I-QOL): The scale was developed by Wagner et al. [13] to determine the quality of life of urinary incontinence patients.

All items are evaluated on a Likert-type scale and converted to a value between 0 and 100. The scale makes it possible to evaluate 3 dimensions: restricting behavior, psychological impact and restricting social life. High scores indicate a better quality of life as opposed to low scores which indicate a poorer quality of life.

b- World Health Organization Quality of Life Instrument-Short Form (WHOQOL-BREF): The health-related quality of life scale was developed by the World Health Organization. The scale consists of 26 questions to measure physical, mental, social and environmental well-being. Each area is calculated with a score from 4 to 20. Higher scores indicate increased quality of life [14].

Evaluation of the Incontinence Status: The International Consultation on Incontinence Questionnaire - Short Form (ICIQ-SF) consisting of 6 questions was used to assess the severity, frequency, type of incontinence and its implications on quality of life. The possible scores on the scale are between 0 and 21. A score of eight is the cutoff point representing the beginning of uncomfortable to disruptive UI. As the score increases, the quality of life deteriorates [15]. The increasing score indicates the worsening in quality of life.

Evaluation of Depression

The depression status of the subjects was assessed with the Beck Depression Inventory (BDI). The purpose of using the scale in this study was not to diagnose depression, we aimed to determine the risk of depression and measure the severity of depressive symptoms. Developed by Beck [16], the scale consists of 21 self-assessment statements and provides 4-point Likert-type measurements. Each item is rated on a scale of 0 to 3 and the total score is obtained by adding the scores of all items together. The higher the score, the more severe is the depression.

Evaluation of Community Participation

The Social Participation Questionnaire was preferred to assess the extent the subjects actively took part in life activities and how active they were [17]. The Social Participation Questionnaire consists of 15 items. It is used to evaluate individuals' home and family life, as well as their social and work activities. Most of these 15 items range on a scale from 0 to 2. A score of 2 indicates more independence and integrity.

In previous studies, 3 sub-scores were obtained with a breakdown of 10 points for home activities, 12 points for social activities and 7 points for work activities. The total score is calculated in a range of 0 to 29.

Statistical Analysis

Statistical analyses of the study were performed with the 'Statistical Package for the Social Sciences' (SPSS) Version IBM Statistic 21.0 (SPSS Inc., Chicago, IL, USA). It was determined with the 'One Sample Kolmogorov-Smirnov' test that the variables were not normally distributed. "Wilcoxon Signed-Rank Test" was used to compare the data before and after the treatment of the groups and the contrast between the groups was performed with "Mann-Whitney U" test. The comparison of the categorical data was carried out using 'Chi-squared' test. The parametric variables are expressed as mean ± standard deviation (X±SD), whereas the descriptive variables are expressed in terms of percentage. The significance level was accepted as $p<0.05$ in all tests.

Results

The demographic and clinical characteristics of the cases and the comparison between the groups are shown in Table 1. While no statistically significant difference was found between the groups in terms of BMI and age ($p>0.05$), it was seen that the mean number of childbirths in the medical treatment group was significantly higher than that of the surgical treatment group ($p<0.05$, $p=0.02$).

Table 1: Comparison of groups in terms of demographic and clinical characteristics

	Medical Treatment Group (n=16)	Surgical Treatment Group (n=16)	P
Age (years) †, ‡	54.31±11.482 57 (34-73)	48.38±10.006 49.5 (28-66)	0.130
BMI (kg/m^2) †, ‡	27.56±2.79 27 (22.6-32)	26.56±2.25 26.5 (23-31)	0.227
Number of childbirths †, ‡	3.13±1.025 3 (2-5)	2.25±0.931 2 (0-4)	0.017

†: mean±standard deviation, ‡: median (min-max).
BMI: Body Mass Index.

Table 2 shows a comparison of the groups in terms of their baseline quality of life, UI and social participation scores. In the comparison of the groups, statistically considerable differences were observed except for the score of the general subgroup of WHOQOL-BREF ($p<0.05$). Moreover, there was a statistically significant difference between the baseline depression states ($p<0.05$). A comparative assessment of the baseline scores in the Social Participation Questionnaire showed that there was no statistically appreciable contrast between the subgroups of home activities and social activities in this regard ($p>0.05$).

However, p value was found to be significant between work activities and total scores ($p<0.05$). The baseline values of ICIQ-SF and I-QOL were similar across the groups ($p>0.05$) (Table 2).

Table 2: Comparison of the patients receiving medical and surgical treatment in terms of baseline values of quality of life, incontinence and social participation.

	Medical Treatment Group †, ‡	Surgical Treatment Group †, ‡	p
ICIQ-SF	16.87 2.47 16.5 (13-21)	17.69±3.01 18 (9-21)	0.20
WHOQOL-BREF			
Overall	27.34±16.59 25 (0-50)	22.66±14.59 18.75 (0-50)	0.36
Physical	40.62±15.36 41.06 (10.71-78.50)	29.46±10.95 30.35 (10.71-50.00)	0.02
Psychosocial	48.89±18.34 47.91(20.83-9.16)	33.98±11.53 33.33 (16.66-56.30)	0.02
Social	42.14±18.31 41.66 (8.33-66.66)	29.68±13.94 25 (16.60-50.00)	0.04
Environment	41.19±20.09 39.06 (6.25-71.83)	25.97±12.17 25 (3.12-40.62)	0.03
Total	40.85±13.52 40.27(16.66-2.03)	29.98±10.29 25.46 (18.50-55.00)	0.02
I-QOL			
Behavior	15.00±4.32 14 (10-23)	14.31±3.48 13 (10-22)	0.79
Psychological	19.06±4.04 19 (13-26)	16.56±3.67 15 (12-23)	0.08
Social	8.25±2.98 7 (5-14)	8.69±2.24 8 (6-14)	0.24
Total	42.25±9.75 39 (31-58)	39.50±8.41 36 (31±55)	0.27
Beck Depression Inventory	23.69±11.83 25 (6-42)	37.19±8.51 38 (18-50)	0.001
Social Participation Questionnaire			
Home activities	5.38±2.70 6 (0-10)	3.62±2.44 3 (0-10)	0.40
Social activities	6.19±2.04 6 (2-9)	4.94±2.26 5 (0-9)	0.12
Work activities	18.56±4.66 18.5 (10-26)	17.50±3.92 17 (13-27)	0.02
Total	14.06±5.39 12 (4-23)	10.00±4.84 10 (3-21)	0.03

†: mean±standard deviation, ‡: median (min-max).
WHOQOL-BREF: World Health Organization Quality of Life Instrument, Short Form, ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form, I-QOL: Incontinence Quality of Life Questionnaire, SP: Social Participation.

Table 3 shows the intra- and inter-group comparisons of the general and disease-specific quality of life parameters before and after the treatment. After the treatment programs of both groups, there was a substantial change in all parameters of disease-specific I-QOL and WHOQOL-BREF ($p<0.05$). Following the treatment, a statistically appreciable increase in the psychosocial subgroup of WHOQOL-BREF ($p=0.04$) and the psychological subgroup of I-QOL ($p=0.04$) was observed in the surgical treatment group as opposed to the medical treatment group.

Table 3: Intra-group and inter-group comparisons of the pre- and post-treatment overall and disease-specific quality of life parameters

	Medical Treatment Group (n=16)				Surgical Treatment Group (n=16)				
	Pre-treatment mean±SD Median (Min-Max)	Post-treatment mean±SD Median (Min-Max)	Intra-group change (Δ) mean±SD Median (Min-Max)	p	Pre-treatment mean±SD Median (Min-Max)	Post-treatment mean±SD Median (Min-Max)	Intra-group change (Δ) mean±SD Median (Min-Max)	p	Inter-group difference (Δ) p
WHOQOL-BREF									
Overall	27.34±16.59 25 (0-50)	61.72±17.95 68.75 (25-87.5)	34.37±18.54 7.5 (0-75)	**0.001**	22.66±14.59 18.75 (0-50)	69.53±16.43 75 (37.5-87.5)	46.88±21.65 50 (0-75)	**0.001**	0.07
Physical	40.62±15.36 41.06 (10.71-78.5)	64.62±10.88 64.28 (46.42-87.5)	24.00±12.19 21.43 (7.14-46.43)	**0.001**	29.46±10.95 30.35 (10.71-50)	61.88±15.87 66.07 (15.00-82.14)	32.42±16.32 33.93 (0.72-71.43)	**<0.001**	0.17
Psychosocial	48.89±18.34 47.91 (20.83-79.16)	66.14±16.23 62.5 (37.5-100)	17.26±14.08325 12.50 ((-4.16)-54.17)	**0.001**	33.98±11.53 33.33 (16.66-56.30)	62.75±12.77 62.50 (33.33-83.33)	28.77±17.01 25.03 (0-62.5)	**0.001**	**0.04**
Social	42.14±18.31 41.66 (8.33-66.66)	62.49±13.26 58.33 (41.66-91.66)	2.50±2.28 3 ((-3)-7)	**0.001**	29.68±13.94 25 (16.60-50.00)	62.49±17.21 66.63 (16.66-91.66)	3.06±1.84 3 ((-1)-7.00)	**0.001**	0.55
Environment	41.19±20.09 39.06 (6.25-71.83)	60.55±12.17 59.37 (40.62-78.12)	19.35±14.95 15.63 (3.12-46.95)	**0.001**	25.97±12.17 25 (3.12-40.62)	53.32±19.35 51.56 (15.62-87.50)	27.34±21.72 23.45 ((-9.38)-62.50)	**<0.001**	0.24
Total	40.85±13.52 40.27 (16.66-62.03)	61.74±9.72 62.96 (49.07-86)	20.88±11.24 17.14 (4.63-38.89)	**0.001**	29.98±10.29 25.46 (18.50-55.00)	58.63±13.18 59.69 (29.25-77.77)	28.65±13.47 30.09 (7.4-55.55)	**<0.001**	0.11
I-QOL									
Behavior	15.00±4.32 14 (10-23)	33.50±5.34 34.5 (18-39)	18.50±8.37 21 ((-2)-29.00)	**0.001**	14.31±3.48 13 (10-22)	35.31±2.79 35.50 (31-40)	21.00±4.73 23 (12-27)	**<0.001**	0.48
Psychological	19.06±4.04 19 (13-26)	38.4375±5.253 17 40.5 (25-43)	19.38±7.42 20 (0-27)	**0.001**	16.56±3.67 15 (12-23)	40.69±2.98 42 (34-44)	24.13±6.05 26 (12-31)	**<0.001**	**0.04**
Social	8.25±2.98 7 (5-14)	21.56±3.83 23 (11-25)	13.32±6.15 (-2-20)	**0.001**	8.69±2.24 8 (6-14)	20.94±3.94 23 (8-25)	12.25±4.18728 14 (0-17)	**<0.001**	0.57
Total	42.25±9.75 39 (31-58)	93.50±13.65 98 (54-107)	51.25±20.42 57 ((-4)-74)	**0.001**	39.50±8.41 36 (31-55)	98.06±6.33 99.50 (87-106)	58.56±12.59 64.5 (35-74)	**0.001**	0.34

WHOQOL-BREF: World Health Organization Quality of Life Instrument -Short Form, I-QOL: Incontinence Quality of Life Questionnaire, SD: Standard Deviation, min: minimum, max: maximum.

Table 4 shows the intra and inter-group comparisons based on the ICIQ-SF, Beck Depression Inventory and Social Participation Questionnaire scores before and after the exercise training. After the treatment, a considerable decrease was observed in the ICIQ-SF values in both groups ($p<0.05$) but the comparison of changes across the groups were insignificant ($p>0.05$). The Beck Depression Inventory score decreased notable after both treatments, with the decrease in the surgical treatment group being remarkably higher than that of the medical treatment group. As for the assessment of Social Participation, the group that received medical treatment displayed a notable increase in the social activity and total scores, whereas the surgical treatment group showed a considerable increase in the home activity, social activity and total scores ($p<0.05$). Moreover, the comparisons between the groups showed a distinct improvement in the home activity, work activity and total scores.

Discussion

In this study, we performed a comparative assessment of female UI patients in terms of their severity of urinary incontinence, depression status, quality of life and social participation following 8-week surgical and medical treatments. It was found that the women who underwent surgical treatment significantly improved in the psychological parameters of depression, social participation and quality of life scores in comparison to the women in the medical treatment group.

The women with SUI often tend to deny their condition rather than seeking ways to solve their problem of incontinence. According to studies in Turkey, an average of 65% of women suffering from UI symptoms avoided physicians. The reasons for this may be listed as feelings of shame, negligence and not accepting the situation as a "health problem" [18]. When symptoms affect patients' quality of life to a moderate or high degree, they consult a physician and prefer conservative or medical treatment. Surgical treatment is considered only after all

Table 4: Intra-group and inter-group comparisons of the pre- and post-treatment parameters for ICIQ-SF, Beck Depression Inventory and Social Participation Questionnaire

	Medical Treatment Group (n=16)				Surgical Treatment Group (n=16)				
	Pre-treatment mean±SD Median (Min-Max)	**Post-treatment mean±SD Median (Min-Max)**	**Intra-group change mean±SD Median (Min-Max)**		**Pre-treatment mean±SD Median (Min-Max)**	**Post-treatment mean±SD Median (Min-Max)**	**Intra-group change mean±SD Median (Min-Max)**		**Inter-group difference**
ICIQ-SF	16.87 2.47 16.5 (13-21)	1.81±2.07 1 (0-5)	-15.06±3.06 -15 (-20-(-11))	**<0.001**	17.69±3.01 18 (9-21)	1.13±1.54 1 (0-6)	-16.56±3.24 -17 (-21-(-8))	**<0.001**	0.09
Beck Depression Inventory	23.69±11.83 25 (6-42)	7.13±8.72 3.5 (0-28)	-16.56±9.40 -15.5 (-40-(-6))	**0.001**	37.19±8.51 8 (18-50)	9.00±3.08 8.5 (5-14)	-28.19±9.52 -29.50 ((-41)-(-5))	**<0.001**	**0.00**
Social Participation Questionnaire									
Home activities	5.38±2.70 6 (0-10)	6.88±1.67 7 (3-10)	1.50±2.63 0.5 (-2-6)	0.057	3.62±2.44 3 (0-10)	7.44±2.39 7.5 (3-10)	3.81±1.91 4 (0-6)	**0.001**	**0.02**
Social activities	6.19±2.04 6 (2-9)	8.69±2.67 10 (2-12)	2.50±2.28 3 (-3-7)	**0.004**	4.94±2.26 5 (0-9)	8.00±1.75 8 (5-12)	3.06±1.84 3 ((-1)-7)	**0.001**	0.55
Work activities	18.56±4.66 18.5 (10-26)	3.00±2.06 2 (1-7)	4.50±3.37 4.5 (-2-10)	0.083	17.50±3.92 17 (13-27)	1.94±1.24 2 (1-6)	7.50±3.54 8 (0-14)	0.067	**0.03**
Total	14.06±5.39 12 (4-23)	18.56±4.66 18.5 (10-26)	4.50±3.36 4.5 ((-2)-(10))	**<0.001**	10.00±4.84424 10 (3-21)	17.5±3.92 17 (13-27)	7.5±3.54024 8 (0-14)	**<0.001**	**0.02**

ICIQ-SF: International Consultation on Incontinence Questionnaire-Short Form, SD: Standard Deviation, min: minimum, max: maximum

these potential solutions are exhausted [19]. When the baseline characteristics of the groups were examined in this study, it was seen that the quality of life, depression and social participation levels of those who preferred surgical treatment were lower than the levels of those in the medical treatment group, although there was no difference based on urinary incontinence. This suggested that patients endure SUI symptoms for a long time only to resort to surgical treatment as a final option.

UI is a high-prevalence condition in Turkey and in the world, affecting women's lives negatively in all areas and reducing their quality of life. Leroy et al. [20] evaluated the quality of life of in patients with and without incontinence using SF-36 and reported that incontinence decreased the quality of life in areas such as physical function, social function, pain, general health, energy status and mental status and cognitive function. Melville et al. [21] found that incontinent women were 3 times more likely to be affected by major depression, and the severity of incontinence was positively correlated with major depression and negatively correlated with quality of life. In another study with women who received an 8-week training course of pelvic floor exercises in addition to surgical treatment, better improvements were observed as per quality of life, as well as anxiety and depression levels [22]. In a study [23] evaluating the quality of life in women with SUI before surgical treatment and 6 weeks to 1 year after the treatment, significant improvements were found in both measurements after the treatment in comparison to the pre-treatment levels. It was also stated in the study that the long-term results were more significant than the short-term results. In our study, the women who were observed to have a very low quality of life before the treatment underwent medical or surgical procedures, and it was found that the urinary incontinence levels decreased to very low levels, and quality of life was improved in terms of both overall and disease-specific scores. It was noted, however, that the improvement rates were higher in the group that received surgical treatment. Our opinion is that elimination of incontinence as a health problem affecting people psychologically, physically and socially helps reduce its negative effects on women and improves their quality of life, regardless of whether it is achieved by medical or surgical treatment.

It is reported that, in Turkey, the rate of depression in patients with SUI is 24%, and the frequency of depression is higher in individuals with SUI [24]. Lack of control on urinary functions and the possibility that this can be noticed from the outside may lead to a loss of confidence in women. It was shown that the frequency of UI in middle-aged and elderly women is strongly associated with depression, and the severity of increased urinary incontinence is associated with increased depression and anxiety [25]. A review of the literature suggested that there is a plethora of studies on the prevalence of depression or the effects of depression in women with SUI but studies examining the effects of different treatment methods on depression in these women are inadequate in numbers. In a similar study [22], the effects of surgical treatment and pelvic floor exercises on women with SUI were examined. Evaluation of the patient groups before and 8 weeks after the treatment showed that the group which received surgical treatment experienced a superior improvement in terms of their anxiety and depression levels. In another study evaluating the 12-month results of surgical treatment in women with SUI with or without major depression, it was shown that, in the 12th post-operative month, 83% of the women with initial major depression completely recovered from it [26]. A limited number of studies on the effectiveness of treatment on depression showed that alleviation of incontinence severity in individuals with stress incontinence has a positive psychological effect and eliminates or decreases depression. Our study also showed significant improvements in the patients' depression status after both surgical and medical treatments, and a comparison of these two groups showed that the improvement in depression was more significant in the surgical treatment group. We are of the opinion that surgical treatment has a more positive effect on the psychosocial aspects, because treatment with medication and exercise requires a certain time to pass to show its effects.

Since incontinence is a condition that may cause feelings of shame, uncleanliness and inadequacy, it involves fear of being stigmatized. The perception of stigmatization has a negative effect

on the healing process as it leads to isolation and may drive the person to avoid social company, experience difficulties with friendships, thus resulting in poor social support [27]. In a study [28] which compared the effects of pelvic floor muscle training with and without the use of a resistance device in women suffering from UI, a decrease in the severity of incontinence and involuntary leakage of urine was found in both groups, as well as significant improvements in social participation. In our study, we evaluated social integration through a social participation questionnaire and found that participation in social life increased after treatment in both groups. Incontinence restricts individuals' lives in many areas, including social participation; therefore, its treatment is highly important to secure continued social participation.

Our study had certain limitations. As no long-term follow-up was conducted with the patients, we do not have information on the longevity of these short-term improvements. The diverse baseline values of the patients presented another limitation. However, since the evaluations were used before and after the treatment in intra- and inter-group changes (delta value) and comparisons, the results were not affected by the baseline values.

In conclusion, in the women with SUI, medical and surgical treatment improved the severity of urinary incontinence, quality of life, depression and social participation. The women who chose surgical treatment were in a poorer psychosocial condition before the treatment in comparison to the women who preferred medical treatment, but the former achieved a higher degree of improvement after the treatment. Both treatments proved to be effective and usable to reduce the severity of SUI and depression, prevent social isolation and improve quality of life. However, extensive research is required on the effects of SUI treatment methods on larger patient groups.

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Clinical and polysomnographic evaluation of morning headache in patients with obstructive sleep apnea syndrome

Obstrüktif uyku apne sendromu ve sabah baş ağrısı birlikteliğinde klinik ve polisomnografik değerlendirme

Şenay Yıldız Çelik [1], Özlem Özkubat [2]

Abstract

Background: The aim of the present study was to investigate the clinical and polysomnographic (PSG) characteristics in patients with PSG-verified obstructive sleep apnea syndrome (OSAS) with or without morning headache (MH) and to evaluate the response to nasal continuous positive airway pressure (n-CPAP) treatment.

Methods: Patients who were referred to the sleep laboratory due to suspected OSAS were prospectively evaluated and divided into two groups: with MH (group 1) and without MH (group 2). Age, sex, body mass index (BMI), Epworth Sleepiness Scale (ESS), Pittsburg Sleep Quality Index (PSQI), Hamilton Depression Scale (HDS), Hamilton Anxiety Scale (HAS), and PSG variables were compared. Patients in group 1 who received n-CPAP treatment were also evaluated for headache persistence.

Results: Seventy-eight patients with OSAS were included and 28 (35.9%) patients reported MH. Female gender and mean BMI were significantly higher in group 1 (43% vs. 20%, p=0.03; 33.1±4.9 vs. 30.6±4.8 kg/m^2, p=0.04, respectively). The ESS was higher in group 1 (10.8±4.4 vs. 8.4±4.1, p=0.02). PSQI score, HDS and HAS did not differ between the groups. Average SpO2 (90±3.64 vs. 92.4±2.88) and minimum SpO2 (78.1±10.7 vs. 83.2±6.8) were significantly lower in the MH group (p=0.02 and p=0.03). In addition, duration of SpO2 <90 was significantly higher in the MH group (17.98±17.67 vs. 11.07±12.37, p=0.04). Nineteen (86.4%) of the 22 patients who received n-CPAP treatment were headache free.

Conclusion: Minimum SpO2 levels and the duration of desaturation during sleep were associated with MH. The other risk factors were female gender and higher BMI. N-CPAP therapy is an effective treatment for patients with MH.

Keywords: Morning headache, sleep apnea headache, continuous positive airway pressure.

Öz

Amaç: Bu çalışmada polisomnografik olarak obstrüktif uyku apne sendromu (OUAS) tanısı konulan hastalarda sabah başağrısı (SBA) olan ve olmayan grupların klinik ve polisonmografi (PSG) sonuçları ile nazal pozitif basınçlı havayolu tedavisinin (n-CPAP) baş ağrısı üzerine etkileri araştırılmıştır.

Yöntemler: OUAS şüphesi ile uyku laboratuarına yönlendirilen hastalar prospektif olarak takip edilerek SBA olan (grup 1) ve SBA olmayan (grup 2) olmak üzere iki gruba ayrıldı. Yaş, cinsiyet, vücut kitle indeksi (VKI), Epworth uykululuk skalası (EUS), Pittsburg uyku kalitesi indeksi (PUKI), Hamilton depresyon skalası (HDS), Hamilton anksiyete skalası (HAS), and PSG sonuçları karşılaştırıldı. Grup 1'deki hastalardan n-CPAP tedavisi alanların son takipteki baş ağrıları değerlendirildi.

Bulgular: OUAS tanısı alan 78 hastanın dahil edildiği çalışmada hastaların 28'inde (%35,9) SBA vardı. Kadın cinsiyet ve ortalama VKI grup 1' de istatistiksel olarak fazla idi (sırasıyla %43 ve %20, p=0,03; 33,1±4,9 ve 30.6±4.8 kg/m^2, p=0.04). EUS sonuçları grup 1'de daha yüksek saptandı (10,8±4,4 vs. 8,4±4,1, p=0,02). PUKI, HDS and HAS iki grup arasında karşılaştırıldığında fark bulunmadı. Ortalama SpO_2 (90±3,64 ve 92,4±2,88) and minimum SpO_2 (78,1±10,7 ve 83,2±6,8) grup 1'de anlamlı düşük saptandı (p=0,02 ve p=0,03). Grup 1'de uyku süresi boyunca SpO_2 90'ın altında olduğu süre istatistiksel olarak daha yüksek idi (17,98±17,67 ve 11,07±12,37, p=0,04). n-CPAP tedavisi olan 22 hastanın 19'unda (86,4%) son takipte baş ağrısı saptanmadı.

Sonuç: Minimum SpO2 değerleri ve uyku sırasındaki desatürasyon süresi, kadın cinsiyet ve VKI SBA ile ilişkilidir. n-CPAP tedavisi SBA olan OUAS hastalarında etkili bir yöntemdir.

Anahtar Kelimeler: Sabah baş ağrısı, uyku apne sendromu, pozitif basınçlı havayolu tedavisi.

[1] **Department of Neurology, Beykoz State Hospital, Istanbul, Turkey**

[2] **Department of Pulmonary Medicine, Beykoz State Hospital, Istanbul, Turkey**

SYC: 0000-0002-7861-1018

OO: 0000-0001-5502-4892

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Sorumlu yazar / Corresponding author:
Şenay Yıldız Çelik

Adres/Address: Department of Neurology, Beykoz State Hospital, 34764 Istanbul, Turkey

E-mail: drsenayy@gmail.com

Tel/Phone: +905375585758

Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of partial or complete obstruction of the upper airway during sleep, often resulting in oxygen desaturation [1]. Sleep disruption may cause unrefreshing sleep, daytime sleepiness, fatigue, lack of energy, and intellectual deficit, and other common symptoms are snoring, nocturia, reflux, and morning headache (MH) [2]. The estimated prevalence of at least mild OSAS is 17%–33% in women and 34%–59% in men, while the prevalence of moderate or severe OSAS is 6%–13% in women and 13%–30% in men [3, 4].

Headache prevalence is high among patients, as evaluated using polysomnography (PSG) [5]; 29%–67% of patients with headache had OSAS using PSG [6, 7] while 32%–55% of OSAS patients had headache [5, 8]. The mechanism of the relationship between sleep and headache remains unclear. Patients with sleep disorders often complain of MH, and some studies have reported that MH is a non-specific clinical finding in sleep disorders [9-11]. It can also be encountered in primary or secondary headache disorders [12, 13] and mental disorders [14]. MH was reported more frequently among patients who were referred with a presumptive diagnosis of OSAS, and it is considered to be a common clinical finding of OSAS [15-17]. The prevalence of MH was reported to be 12%–18% in OSAS patients and 5%–8% in the general population [14, 18].

In the International Classification of Headache Disorders (ICHD) 3rd edition, MH associated with OSAS was classified as "sleep apnea headache," under the topic of "Headache attributed to disorders of homoeostasis" [13]. Some studies showed a relationship between MH and OSAS severity [15, 17] or MH and oxygen desaturation [17, 19], while other studies denied this relationship [5, 18]. Previous studies reported that effective use of nasal continuous positive airway pressure (n-CPAP) or uvulopalatopharyngoplasty (UPPP) could improve MH [15, 17, 20], which supports the association between OSAS and MH.

It is unclear whether the mechanism of MH in patients with OSAS is related to hypoxia, hypercapnia, or disturbance in sleep, and this requires clarification. The aim of the present study was to investigate the clinical and PSG characteristics in patients with PSG-verified OSAS with or without MH and to evaluate the response to n-CPAP treatment.

Material and methods

Patients with various sleep complaints were referred for suspected OSAS to the sleep laboratory of Beykoz State Hospital from April to September 2021 and were prospectively evaluated. Eighty-nine patients were diagnosed with OSAS. Eleven patients were excluded from study for the following reasons: four patients had other comorbid primary sleep disorders; four patients had poor signal quality on the recorded channels; and three patients had less than 3 hours of total sleep time. All participants provided written informed consent to participate in the study, in accordance with the standards of the Declaration of Helsinki. The study was approved by the ethics and Research Committee at the Umraniye Training and Research Hospital (B.10.1.TKH.4.34.H.GP.0.01/142.)

All patients underwent an 8-hour PSG that was supervised by a qualified technician. A Compumedics E series 44-channel device (MFI medical, San Diego, CA, USA) was used, and the recordings were performed in accordance with the American Academy of Sleep Medicine (AASM) criteria.

PSG data were evaluated by an experienced sleep physician, and the recordings were scored according to the AASM criteria (AASM-2020). OSAS was diagnosed on the basis of clinical evaluation and according to the criteria of International Classification of Sleep Disorders third edition (AASM ICSD-2014). The apnea–hypopnea index (AHI) was calculated as the number of apneas and hypopneas per hour during sleep, and the cut-off point for OSAS was ≥5/h. OSAS severity was classified using the AHI as follows: mild (5 to <15), moderate (15 to <30), and severe (≥30). The other PSG parameters that were evaluated were total sleep time (TST), sleep efficiency index, sleep stage percentages of TST (nonrapid eye movement [NREM] 1, 2, 3 and rapid eye movement [REM]), average oxygen saturation (SpO2), minimum SpO2, and duration of desaturation (SpO2<90).

The assessment for MH was performed using a headache questionnaire. If MH was present, headache features such as localization, frequency, duration, severity (visual analog score), and quality were recorded by the first author in a face-to-face interview. Sleep apnea headache have been distinguished from other neurological diseases using the International Classification of Headache Disorders (ICHD-3). The first two criteria to be met are as follows: MH is present on awaking after sleep with OSAS (AHI≥5); and includes at least two of following three criteria: 1) temporal relationship between headache onset and OSAS; 2) headache worsening or improving in parallel with worsening or improving OSAS; and 3) at least one of the following: 3.1) recurring on ≥15 days/month; 3.2) a duration of less than 4 hours; and 3.3) bilateral, pressing quality that was not accompanied by nausea, photophobia, or phonophobia. According to the definition of sleep apnea headache in the ICDH-3, the headache resolves with successful treatment of OSAS. Because some patients did not undergo CPAP treatment, we used the term MH instead of sleep apnea headache. If the patients were treated with n-CPAP, the frequency and severity of headache was compared with pre- and post-n-CPAP treatment.

Excessive daytime sleepiness was evaluated using the Turkish version of the Epworth Sleepiness Scale (ESS) [21], and sleep quality was assessed using the Turkish version of the Pittsburg Sleep Quality Index (PSQI) [22]. Seven components including sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleeping medication use, and daytime dysfunctions were evaluated. The Hamilton Depression Scale (HDS) and Hamilton Anxiety Scale (HAS) were used to evaluate the presence of depression or anxiety that may cause MH.

Patients were divided into two groups: with MH (group 1) and without MH (group 2). Groups were compared according to age, sex, body mass index, comorbid disease (hypertension, diabetes mellitus, or cardiovascular disease), smoking, ESS, PSQI, HDS, HAS, and PSG variables. Additionally, headache persistence was evaluated for patients in group 1 who received n-CPAP treatment.

Statistical Analysis

Statistical analysis was performed using SPSS version 12 (SPSS Inc., Chicago, IL, USA). Categorical data were reported as the frequency while continuous data were reported as the mean and standard deviation. Normal distribution was investigated using the Shapiro–Wilk test, and variance homogeneity was assessed using the Levene test. To compare the groups, chi-square tests were used for categorical data, and independent sample t-tests were used for continuous data. If needed, the Mann–Whitney U test was used for continuous variables that had a non-normal distribution. A P-value of 0.05 was used as the cut-off for establishing statistical significance.

Results

Seventy-eight patients with OSAS were included in this study. Among the 78 consecutive OSAS patients, 28 (35.9%) reported MH. The mean frequency of headache was 14.3 ± 10.3/month, and 42.8% of the patients had 15 or more headaches in a month. (Table 1).

Table.1 The characteristics of morning headache in 28 patients (Group 1).

	n	%
Frequency		
1-8/month	6	21.5
8-15/ month	10	35.7
>15/month	12	42.8
Duration		
<1 h	4	14.2
1-4 h	19	68
>4 h	5	17.8
Character		
pressing	20	71.4
throbbing	6	21.4
stabbing	2	7.2
Severity (VAS)		
mild	6	21.4
moderate	18	64.3
severe	4	14.3
Localization		
bilateral	22	78.5
unilateral	6	21.5

Vas: visual analog scale.

Mean age did not differ between the groups (49.5±8.1 years vs. 50.1±10.8 years, respectively), while there were significantly more women in group 1 compared to group 2 (43% vs 20%, p=0.03). The mean body mass index (BMI) was higher in group 1 (33.1±4.9 kg/m^2 vs. 30.6±4.8 kg/m^2, p=0.04). Additionally, 71.4% of patients in group 1 had a comorbid disease, while 48% of patients had a comorbid disease in group 2 (p=0.04) The most common comorbid disease was hypertension, and it was present 50% of the patients in group 1 and 38% in group 2. (Table 2).

Table. 2 Demographic and clinical characteristics of patients with and without morning headache.

	Group 1 (n=28)	Group 2 (n=50)	P
Age (year) †	49.5± 8.1	50.1± 10.8	0.78*
Female ‡	12 (42.9)	10 (20)	0.03**
BMI (kg/m^2) †	33.1± 4.9	30.6± 4.8	0.04*
Comorbidity ‡	20 (71.4)	24 (48)	0.04**
Smoking ‡	12 (43)	21 (42)	0.94**

†: mean ± standard deviation, ‡: n (%), BMI: body mass index.

The ESS, which evaluated excessive daytime sleepiness, was higher in group 1 compared to group 2 (10.8±4.4 vs. 8.4±4.1, p=0.02). There was no significant difference between the PSQI score and subgroup scores for sleep quality between the groups (p>0.05). Similarly, HDS and HAS were not significantly different between the groups (p=0.55 and p=0.74, respectively). Eleven patients had a cut-off value of >8 for HDS (39.3%) in the MH group, while 17 (34%) had this cut-off in group 2. Moderate depression (HDS 14–18) was detected in four patients in both groups, while an HDS of >18 was not found in any of the patients (Table 3).

The mean AHI was higher in the MH group, but this difference was not statistically significant (38.9±19.5 vs. 34.3±21.7, p=0.35). The incidence of MH was 29.4% in mild OSAS, 36% in moderate OSAS, and 38.9% in severe OSAS. The average SpO_2 (90±3.64 vs. 92.4±2.88) and minimum SpO_2 (78.1±10.7 vs. 83.2 ±6.8) were significantly lower in the MH group (p=0.02 and p=0.03). Additionally, the duration of desaturation was significantly higher in the MH compared to the non-MH group (17.98±17.67 vs. 11.07±12.37, p=0.04).

Table 3. Epworth Sleepness Scale, Pittsburg Sleep Quality Index, Hamilton Depression Scale and Hamilton Anxiety Scale in groups.

	Group 1	Group 2	p*
Epworth Sleepness Scale †	10.8±4.4	8.4±4.1	0.02
Pittsburg Sleep Quality Index †	7.7±3.8	6.7±3.07	0.18
Sleep quality †	1.68±0.90	1.52±0.73	0.40
Sleep latency †	1.04±0.96	0.84±0.79	0.33
Sleep duration †	1.36±0.95	1.38±0.83	0.91
Habitual sleep efficiency †	1.04±1.36	0.96±1.12	0.77
Sleep disturbance †	1.39±0.62	1.12±0.71	0.09
Use of sleeping medication †	0.11±0.56	0.12±0.48	0.91
Daytime disfunction †	1.07±1.52	0.74±0.96	0.17
Hamilton Depression Scale †	8.43±3.91	7.92±3.46	0.55
Hamilton Anxiety Scale †	8.6±3.9	8.3±4.6	0.74

†: mean ± standard deviation, *Independent t test

Total sleep time, sleep efficiency index, and the percentages of NREM 1, 2, 3 and REM sleep did not differ between the groups (Table 4).

Table. 4 Polysomnographic parameters of patients in groups.

	Group 1	Group 2	P
TST (min) †	367.3±73.7	345.9±78.3	0.24*
SEI (%) †	75.3±14	74.4±15.3	0.80*
REM (%) †	14.1±6.6	14.7±8.4	0.75*
NREM1 (%) †	9.8±5.2	9.1±6.6	0.61*
NREM2 (%) †	61.7±8.3	62.6± 10.9	0.71*
NREM3 (%) †	14.2±7.3	13.6± 8.8	0.73*
AHI †	38.9±19.5	34.3±21.7	0.35**
Average O_2 †	90.92±2.58	92.40±2.88	0.02*
Min O_2 †	79.60±7.92	83.26±6.83	0.03*
Sleep time with O_2 <90% (%) †	17.98±17.67	11.07±12.37	0.04*

†: mean ± standard deviation.
TST: Total sleep time, SEI: Sleep efficacy index, REM: Rapid eye movement, NREM: non-rapid eye movement, AHI: Apnea- hypopnea index, O2: Oxygen level
*Independent t test
**Mann-Whitney U test

Fourteen (63.4%) of the 22 patients who received n-CPAP treatment day 1, 16 (72.7%) at week 1, and 19 (86.4%) at the month 1 follow-up were headache-free. In three patients whose headache persisted, the frequency of pain decreased by ≥50%.

Discussion

The main finding in the present study was that hypoxemia was prominent in OSAS patients with MH compared to the group of without MH. While the average SpO2 and minimum SpO2 levels were significantly lower in the MH group, duration of desaturation was significantly higher compared to the non-MH group. However, other studies showed different findings regarding the role of nocturnal hypoxia in the development of sleep apnea headache or MH in OSAS patients. Koç et al. [19] found the mean and minimum SpO2 to be lower and the desaturation index higher (both TST and REM) in OSAS patients with MH compared to those without MH [19]. Göksan et al. [17] found the mean SpO2, minimum REM, and NREM SpO_2 levels

to be low and the AHI to be high in the MH group, but none of these were a determining factor for MH in the logistic regression analysis. Additionally, in some studies, no significant difference was found between OSAS patients with and without MH for respiratory parameters using PSG [8, 18, 20, 23].

In the present study, no relationship was found between OSAS severity and MH or the mean AHI in both groups. While some studies showed that the prevalence of MH increases with OSAS severity [15, 16, 17], other studies did not support this relationship [5, 9, 18, 19, 23]. Alberti et al. [15] and Loh et al. [16] revealed this relationship when they increased OSAS severity by one degree in the presence of oxygen desaturation out of proportion to their AHI, but that association was not confirmed when they defined OSAS severity based on only AHI. Consistent with our study, the relationship between oxygen desaturation levels and the occurrence of MH was revealed in these other studies, and the notion that hypoxia plays a role in the development of MH was supported.

Sleep fragmentation and architectural distraction were reported to be a possible reason for MH development in OSAS [12]. In a study comparing patients who were diagnosed with OSAS with and without MH the day after the PSG examination, sleep duration, sleep efficiency, and NREM sleep percentage were found to be low in the MH group [11]. Eren et al. [24] determined that sleep disturbance was common in the patients with pulmonary disease. In other studies, no difference was found between patients with or without MH in terms of sleep duration, sleep efficiency, or NREM and REM sleep percentages, which is in agreement with our results [8, 17, 19].

MH is known to be a common symptom in OSAS [25, 26]. While the prevalence of MH in OSAS was reported to be 12%–18% in population-based studies [14, 18], this ratio increased to 20%–48% in patients with sleep problems, especially respiratory problems, who underwent PSC evaluation [15, 20, 23]. The prevalence of MH in our study was 35.9%, which is similar to that of the abovementioned studies.

Spalka et al. [23] found a relationship between MH and hypertension in OSAS, but this relationship was not present for BMI. Koç et al. [19] reported that comorbid diseases were higher in OSAS, but no difference was found between the MH and non-MH groups. Epidemiological studies have reported that comorbid diseases are detected with a higher incidence in women with OSAS than in men [4, 27]. In our study, BMI and comorbid disease association were higher in the MH group. These results may be related to the greater number of female patients in the MH group.

In a population-based study, MH was reported to be significantly higher in patients with, compared to those without, depression and anxiety (28.5% vs. 5.5%) [14]. In another study, depression was high in OSAS patients with headache, but there was no difference between patients with and without MH [8]. Another study did not include OSAS patients with MH who had HAD >8 because depression may be the major etiology of headache [17]. No difference was found in depression and HAD scores between patients with and without MH in the present study, and this finding suggested that depression was not a major factor in the etiology of MH in our patients.

While some studies reported no difference between ESS in OSAS patients with and without MH [8, 20, 28] there are also studies that found a significantly higher ESS in the MH group, which is similar to our results [19]. Additionally, consistent with the results of Suzuki et al., the PSQI total score and subgroup scores were not different between groups with and without MH in the present study [20].

The results of a study evaluating the n-CPAP treatment response in OSAS patients with chronic headache were found to be insufficient (24% of patients' headaches improved) [6], while another study reported that OSAS treatment may be effective for headaches in many patients [7]. However, effective oxygenation with n-CPAP therapy can achieve 80%–92% pain elimination in OSAS patients with MH [17, 20]. Similarly, our study showed that 86.4% of the patients who received n-CPAP treatment were headache-free at the end of the month 1, and the frequency of headaches in the remaining three patients decreased by ≥50%.

The mechanism by which the development of MH and sleep apnea headache occurs in OSAS has not yet been clarified. In the MH group, average and minimum SpO_2 were significantly lower, and duration of <90% SpO_2 was significantly higher. Considering our PSG results and n-CPAP treatment responses, nocturnal hypoxemia may play a role in the development of MH.

The present study also has some limitations. First, the number of the patients was relatively small. Second, we performed a regression analysis to evaluate the effectiveness of the n-CPAP therapy. Despite the limitations the study, this was a prospective study that contributes additional data about the relationship between MH and OSAS.

Mean and average SpO_2 levels and the duration of desaturation during sleep are the major risk factors for MH in women and OSAS patients with a higher BMI. N-CPAP therapy is an effective treatment for patients with MH.

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Evaluation of urological emergency cases admitted to emergency department

Acil servise başvuran ürolojik acil olguların değerlendirilmesi

Mehmet Gün [1], Fatih Çakmak [2], İbrahim İkizceli [2], Seda Özkan [2], Afşın İpekci [2], Serap Biberoğlu [2], Yonca Senem Akdeniz [2]

Abstract

Background: Especially in recent years, with the increase in the number of patients admitted to the emergency services the number of urological emergencies is increasing. Some of these require immediate attention. There are not enough studies on urological emergencies in our country. In this study, we aimed to investigate the demographic data of patients over the age of 18 who presented to the emergency department with non-traumatic urological emergency complaints.

Methods: This study was designed based on a 6-month prospective, cross-sectional study. After obtaining the approval of the ethics committee, patients over the age of 18 with urological emergency complaints were examined between 06.11.2019 and 06.05.2020.

Results: The ratio of urological emergencies to all patients was found to be 1.5%. 56.76% (n=231) of the patients were male and 43.24% (n=176) were female. In the study was found 44.7% of the patients to be urinary tract infection, 31.45% renal colic, 8.8% hematuria, 6.88% acute urinary retention. In our study, urology consultation was requested for 19% of urological emergency patients. Emergency intervention was applied to 21.13% of all urological emergency cases. Emergency operation was required for 1.47% of the patients. 10.81% of the patients required hospitalization.

Conclusion: As a result, urological emergencies are common. Among these cases, there may be diseases that require urgent intervention or surgery. It is very important for the patients the emergency physicians who evaluate the patient first to make a careful and meticulous evaluation and to make a urology consultation if necessary.

Keywords: Renal colic, urinary tract infection, urological emergency.

Öz

Amaç: Özellikle son yıllarda acil servislere başvuran hasta sayısının da artmasıyla ürolojik acil olguların da sayısı gün geçtikçe artmaktadır. Bunlardan bazıları acil müdahale gerektirir. Ülkemizde yeteri kadar ürolojik aciller ile ilgili çalışma yoktur. Bu çalışmada acil servise travma dışı ürolojik acil şikâyetlerle başvuran 18 yaş üstü hastaların demografik verilerini incelemeyi planladık.

Yöntemler: Çalışma 6 aylık prospektif, kesitsel araştırmaya dayanarak tasarlandı. Etik kurul onayı alındıktan sonra bir üniversite hastanesi acil servisine 06.11.2019 ile 05.06.2020 tarihleri arasında başvuran ürolojik acil şikayetleri olan 18 yaş üzeri hastalar incelendi.

Bulgular: Ürolojik acil hastaların tüm hastalara oranı %1,5 olarak saptandı. Hastaların %56,76 (n= 231)'sı erkek, %43,24 (n=176)'ü kadın olarak saptandı. Çalışmada hastaların %44,7'si idrar yolu enfeksiyonu, %31,45'si renal kolik, %8,8'i hematüri, %6,88'i akut üriner retansiyon, olarak saptanmıştır. Çalışmamızda ürolojik acil hastaların %19'una üroloji konsültasyonu istenmiştir. Tüm ürolojik acil olguların %21,13'ine acil girişim uygulanmıştır. Hastaların %1,47'sine acil operasyon gerekmiştir. Hastaların %10,81'ine servis yatışı gerekmiştir.

Sonuç: Sonuç olarak, ürolojik acil olgulara sık rastlanmaktadır. Bu olgular arasında acil girişim veya operasyon gerektiren hastalıklar olabilir. Hastayı ilk değerlendiren acil servis hekimlerinin dikkatli ve titiz bir değerlendirme yapması, gerekirse üroloji konsültasyonu istemesi oldukça önemlidir.

Anahtar Kelimeler: Renal kolik, idrar yolu enfeksiyonu, ürolojik acil.

[1] Department of Emergency Medicine, Tokat Turhal State Hospital, Tokat, Turkey.

[2] Department of Emergency Medicine, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Istanbul, Turkey.

MG: 0000-0003-3466-6014
FC: 0000-0002-8813-4139
II: 0000-0002-9825-4716
SO: 0000-0003-1835-8820
AI: 0000-0001-6125-4061
SB: 0000-0003-4709-3315
YSA: 0000-0002-4843-1155

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Sorumlu yazar / Corresponding author:
Fatih Çakmak

Adres/Address: Cerrahpasa Medical Faculty, Department of Emergency Medicine, Kocamustafapasa, Fatih, Istanbul, Turkey

E-mail: fatih.cakmak@istanbul.edu.tr
Tel/Phone: +905326539947

Introduction

Many patients apply to emergency department (ED) with urological problems. Especially in recent years, with the increase in the number of patients admitted to emergency services, the number of urological emergencies is increasing day by day. In a study conducted in Turkey, the ratio of urological emergencies admitted to the emergency service to all admissions was found to be 2.67% [1]. Some of these require immediate attention and are classified as urological emergencies. Urological emergencies can be classified as urinary tract infections (UTI), renal colic due to urinary system stone disease, acute urinary retention, hematuria, testicular torsion, Fournier's gangrene, postrenal occlusive conditions, epidymitis-orchitis and priapism. Among these, the most common ones are renal colic due to UTI and stone disease. Along with these, macroscopic hematuria, acute urinary retention, postrenal occlusive conditions, scrotal pathologies are common. Recognition of these diseases and timely correct intervention are very important in terms of morbidity and mortality of the patients [2, 3].

Hematuria can be defined as the appearance of red blood cells in the urine [4]. The frequency of admission to the hospital with the complaint of hematuria in the community varies between 2% and 31% [5]. It is clinically divided into two types as macroscopic hematuria and microscopic hematuria.[6]. Acute urinary retention (AUR) is one of the urological emergencies that is characterized by sudden onset of voluntary urination, frequent and dripping urination and painful bladder. It is mostly seen in older men. 10% of 70-year-old men and approximately 33% of 80-year-olds experience urinary retention at least once in their lifetime [7, 8].

Renal colic is one of the most common urological emergencies in ED with severe pain, which usually develops due to urinary system stone disease. The pain is typically felt as blunt and aching at the cost-vertebral angle [9,10]. Fournier's gangrene is a rare necrotizing fasciitis that affects the perineal, perianal or genital regions, with a high mortality rate. The mortality rate is high and requires early surgical treatment [11]. Clinical findings include fever, sudden onset pain with chills, edema, crepitation, and necrosis. The clinic may worsen rapidly and is accompanied by hypotension, general condition deterioration [12]. Testicular torsion is an emergency situation in which the blood supply of the testis is impaired as a result of the rotation of the spermatic cord around itself, and accordingly testicular ischemia occurs [13]. Priapism is defined as a prolonged erection that develops uncontrollably without sexual stimulation and cannot be terminated by ejaculation. It is a urological emergency because it may cause permanent erectile dysfunction and necrosis in penile tissue if early treatment is not initiated [14, 15]. Epididymitis and orchitis are defined as infection or inflammatory reaction of the epididymis and testis due to infection, local trauma or previous surgery. There is an underlying genitourinary anomaly or an infectious disease in the etiology. Fever, pain, and scrotal swelling are often present. Inflammation lasting longer than 6 weeks results in chronic epididymitis or orchitis [16, 17]. Postrenal acute renal failure(ARF) occurs after obstruction in the urinary tract. It can be caused by any stenosis in the renal pelvis, ureter, bladder, prostate, and urethra. The primary cause of urinary tract obstruction is benign prostatic hypertrophy (BPH) [18].

In this study, we planned to examine the demographic data of patients with non-traumatic urological emergencies who applied to a university hospital emergency department in a 6-month period between November 2019 and April 2020.

Material and methods

Our study was conducted as a 6-month prospective, cross-sectional study after the approval of the ethics committee dated 06/11/2020 and numbered 170623. Patients over the age of 18 who applied to a University Medical Faculty Emergency Service between 06.11.2019 and 06.05.2020 with urological emergency complaints were examined. The written informed consent was taken from the patients.

The subjects included in the study were age, gender, vital signs, presenting complaint (flank pain, burning in urine, blood in urine, darkening in urine, discharge, inability to urinate, testicular pain, inguinal pain, abdominal pain, fever), examination findings (suprapubic tenderness, CVAT), macroscopic hematuria, pyuria, testicular tenderness), laboratory examinations (WBC, CRP, platelet, urea, creatinine, aptt, INR, complete urine analysis), additional urological diseases, treatments (medical, emergency intervention, surgery) and recent conditions (discharge, hospitalization), were examined and recorded in the forms.

Patients who applied for hematuria only with the complaint of bleeding in the urine were included in the study. Patients with erythrocytes in laboratory urinalysis were not included in the study.

Patients under the age of 18, trauma patients, patients whose consent could not be obtained, and patients who left the hospital without permission without waiting for results were excluded from the study.

Statistical Analysis

IBM SPSS Statistics for Microsoft 22.0 (SPSS Inc, Chicago, United States of America) program was used for statistical analysis of our data. The Student-t test was used to compare the normally distributed quantitative data between the two groups, and the Mann-Whitney U test was used to compare the non-normally distributed quantitative data between the two groups. Fisher's exact and Pearson chi-square tests were used to compare qualitative data. When comparing three or more groups, the One-Way Anova test was used, and if the group variances were similar as post-hoc tests, Tukey-HSD; If group variances were different, Games-Howell tests were used.

Results

The study was conducted with 407 patients over the age of 18 who applied with urological emergency complaints and were accepted as urological emergencies. Of these patients, 56% (n=231) were male and 43% (n=176) were female. Compared to all applications, the rate of urological patients was found to be 1.5% in our study, while the rate of male patients was 0.80% and the rate of female patients was 0.65%. The ages, vital signs and laboratory parameters of the patients are shown in Table 1.

In our study, 181 of the patients were found to be UTI, 128 renal colic, 36 hematuria and 28 AUR, 36 hematuria, 13 epididymoorchitis and 6 post-renal ARF. In our study, hospitalization was provided for 3 patients with the diagnosis of Fournier's gangrene requiring emergency operation. UTI (0.67% of all cases and 44.47% of urological emergencies) and renal colic (0.47% of all admissions and 31.45% of urological cases) were found most frequently in urological emergencies.

Considering the examination findings of the patients included in the study, the most common examination finding in UTIs was tenderness in the suprapubic region in 56 patients (UTI rate 30.9%). Nine of the patients had tenderness in the lower quadrants of the abdomen. Pyuria was detected in 10 patients. Macroscopic hematuria was detected in all patients presenting with hematuria. Suprapubic tenderness was present in 27 of the patients with AUR.

Table 1. Evaluation of age, vital signs and laboratory parameters of the patients included in the study by gender

	Gender		p
	Male	Female	
Age (year) †	51.65±19.99 20.00-95.00	44.84±19.80 18.00-104.00	0.001**
SBP (mmHg) †	139.38±24.86 88.00-237.00	132.14±21.85 83.00-212.00	0.002**
DBP (mmHg) †	83.61±16.80 52.00-159.00	81.09±14.38 52.00-137.00	0.111
MAP †	102.20±17.94 64.00-175.67	98.11±15.29 69.67-154.67	0.016*
Pulse (beats/min) †	87.85±18.52 48.00-190.00	88.94±16.00 53.00-153.00	0.533
Fewer (°C) †	36.48±0.84 26.50-40.00	36.43±1.55 16.70-38.00	0.675
SpO_2 (%) †	96.94±2.07 87.00-100.00	96.97±2.00 90.00-100.00	0.880
WBC ($x10^3/mm^3$) †	9.65±3.39 2.10-21.00	9.07±3.18 0.90-18.20	0.116
NEUT ($x10^3/mm^3$) †	6.87±3.39 1.30-19.10	6.41±3.10 0.20-16.40	0.205
HGB (g/dl) †	13.27±2.37 3.20-17.20	12.00±1.75 3.40-16.20	<0.001**
PLT ($x10^3/mm^3$) †	256.53±83.79 62.00-594.00	270.60±85.47 42.00-617.00	0.134
Urea (mg/dl) †	44.24±30.48 15.00-237.00	34.58±22.33 8.00-151.00	0.001
Creatinine (mg/dl) †	1.30±1.04 0.34-7.40	0.92±0.85 0.40-7.59	<0.001**
Potasium (mmol/l)	4.34±0.50 3.10-6.00	4.31±0.52 3.40-6.40	0.669
CRP (mg/l) †	38.31±79.55 0.30-498.00	28.87±59.72 0.10-481.00	0.235
Urine pH †	5.87±0.67 5.00-8.00	6.14±0.72 5.00-8.00	0.001**

†: mean±standard deviation, (min-max),
MAP = mean arterial pressure; SpO_2=oxygen saturation; SBP=systolic blood pressure; DBP= diastolic blood pressure; WBC=white blood cell; NEUT= neutrophil; HGB= hemoglobin; PLT=platelet; CRP= C-reactive protein.

In half (n=3) of the patients with post-renal ARF, the examination finding was CVAT and the examination finding was suorapubic tenderness in two of them. Considering that the most common cause of post-renal ARF is urinary calculus or urinary tract obstruction due to post-renal pathologies, the examination findings in our study support the diagnosis.

CVAT was detected in 108 (84.3% renal colic rate and 26.5% within-study rate) of 128 patients diagnosed with renal colic. Eighteen of the patients diagnosed with renal colic had tenderness in the lower quadrants.

Urology consultation was required for 78 of the 407 patients included in the study. Patients for whom urology consultation was requested constituted 19.1% of the patients included in the study. Urology consultation was required in 0.28% of the total ED patients who applied for a 6 months of period. Of the patients for whom urology consultation was requested, 63 were male and 15 were female. Male patients comprised 80.7% of the patients for whom urology consultation was requested. Emergency intervention was performed in 86 of the patients and emergency operation was required in six of them. Patients who underwent emergency intervention constituted 21.13% of all urological emergencies. Of the patients who underwent intervention, 74 were male and 12 were female. In total, 78 patients had a Foley catheter, four patients had a double-J catheter, 3 patients could not be inserted and suprapubic catheterization was inserted. Percutaneous nephrostomy was performed urgently in onr patient included in the study.

All of the six patients who needed surgery were male patients. Urology consultation was required in eight of 181 patients diagnosed with UTI. Urology consultation was required in 13 of the patients diagnosed with renal colic, in 21 of the patients presenting with hematuria, and in 13 of the patients presenting with AUR. The diseases requiring the most urology consultation were hematuria and AUR. Urology consultation was required in 5 of 6 patients with post-renal ARF.

The distribution of urology consultation, intervention and operation according to the diagnosis of the patients are shown in Table 2.

In our study, 10.81% (n=44) of 407 patients who applied to ED required ward admission. The remaining 363 patients were discharged from the ED. When the patients were examined according to gender, 34 of 44 patients admitted to the ward were male and 10 were female. In our study, it was determined that 19% (n=78) of urological emergency patients required urology consultation and 10.81% of them required service admission.

Considering the diagnoses, the highest number of hospitalizations was UTI with 17 patients. All six patients with post-renal ARF required hospitalization. Of the 36 patients who presented with hematuria, 8 were hospitalized and 28 were treated and discharged from the ED. The distribution of the patients according to their diagnosis and hospitalization or discharge is shown in Table 3.

Discussion

Urological emergencies constitute 51.87% of all cases. The most common urological emergency disease was found to be UTI with 51.74%. The rate of renal colic was found to be 27.68% and is similar to our study. In the same study, the rate of macroscopic hematuria was found to be 2%. Compared to the study of Kafkaslı et al. [2], the rate of hematuria was found to be higher in our study. While the patients requiring urology consultation in the study were 9.07% of all cases, this rate was found to be 19% in our study. In the same study, the rate of patients who underwent emergency urological intervention was found to be 6.14%.

In the study performed by Akıncı et al. [1], the ratio of urological emergencies to all cases was 2.67%. The most common urological emergency is UTI, followed by renal colic and acute urinary retention. The rate of UTI was 54.15% and renal colic was 33.1%, which is similar to our study. The rate of acute urinary retention is 7.97%, which is similar to the rate of AUR in our study. In the same study, 9.05% of the patients required urology consultation. 8.83% of the patients were treated as inpatients. In our study, hospitalized patients had similar rates with this study. In our study, the rate of patients requiring consultation was found to be higher. It is estimated that the reason for the high rate of urology consultation in our study is that our hospital is a 3rd level hospital and they were sent from another hospital for consultation. In the study of Akıncı et al. [1], the number of patients who underwent intervention was found to be 1.76% and it is similar to our study.

Table 2. Distribution of consultation, intervention and operation according to the diagnosis of the patients.

	Urology Consultation		Intervention		Operation	
	yes	no	yes	no	yes	no
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Urinary tract infection (n=181; 44.47%)	173 (42.51)	8 (1.97)	164 (40.29)	17 (4.18)	181 (44.47)	0 (0)
Renal colic (n=128; 31.45%)	115 (28.26)	13 (3.19)	125 (30.71)	3 (0.74)	128 (31.45)	0 (0)
Hematuria (n=36; 8.85%)	15 (3.69)	21 (5.16)	10 (2.46)	26 (6.39)	36 (8.85)	0 (0)
Acute urinary retention (n=28; 6.88%)	15 (3.69)	13 (3.19)	0 (0)	28 (6.88)	28 (6.88)	0 (0)
Epididymoorchitis (n=13; 3.19%)	7 (1.72)	6 (1.47)	12 (2.95)	1 (0.25)	13 (3.19)	0 (0)
Acute renal failure (n=6; 1.47%)	1 (0.25)	5 (1.23)	1 (0.25)	5 (1.23)	6 (1.47)	0 (0)
Other (n=15; 3.69%)	3 (0.74)	12 (2.95)	9 (2.21)	6 (1.47)	9 (2.21)	6 (1.47)

Table. 3 Hospitalization or discharge of patients according to their diagnosis.

	Gender		Outcome	
	Male	Female	Hospitalization	Discharge
	n (%)	n (%)	n (%)	n (%)
Urinary tract infection (n=181; 44.47%)	67 (16.46)	114 (28.01)	17 (4.8)	164 (40.29)
Renal colic (n=128; 31.45%)	77 (18.92)	51 (12.53)	4 (0.98)	124 (30.47)
Hematuria (n=36; 8.85%)	31 (7.62)	5 (1.23)	8 (1.97)	28 (6.88)
Acute urinary retention (n=28; 6.88%)	27 (6.63)	1 (0.25)	2 (0.49)	26 (6.39)
Epididymoorchitis (n=13; 3.19%)	13 (3.19)	0 (0)	1 (0.25)	12 (2.95)
Acute renal failure (n=6; 1.47%)	4 (0.98)	2 (0.49)	6 (1.47)	0 (0)
Other (n=15; 3.69%)	12 (2.95)	3 (0.74)	6 (1.47)	9 (2.21)

In a study by Talreja et al. [19], urological emergencies were examined among surgical admissions and urological emergencies were found to be 5.84% of all surgical emergencies. In our study, our results were found to be low because emergency applications were not divided into surgical emergencies and internal medicine. In the same study, the most common reason for admission was found to be renal colic with a rate of 24.17%. This result is similar to the rate of renal colic in our study.

In a study by Traore et al. [20], urological emergencies constitute 3.7% of all cases. This rate was found to be similar in our study. The most common urological emergency was found to be AUR with 48.28%. The rate of UTI was 19.92% and the rate of renal colic was 11.49%, which was lower than our study. The fact that the frequency of presentations varies according to studies may be evidence that urological emergencies vary according to the region. Their study was conducted in a hospital in Africa and our study was conducted in Europe. In the study of Bah and Diallo [21] in Guinea, the rate of AUR was reported as 73.9%. In the study of Ndiaye M et al. [22], the most common urological emergency was hematuria with a rate of 25.6%. The rate of AUR is seen in the second frequency with 21.6% and it was found to be higher than in our study. At the same time, the rate of UTI was found to be lower with 19% than in our study.

In the study of Topraktaş R. et al. [23], the rate of urological emergencies was found to be 2.19%, which is similar to our study. In the study conducted by Girgin R. et al. [24] to evaluate urological emergencies, the frequency of urological emergencies was found to be 0.39%. In the study, the most frequent application was evaluated as renal colic with 25.5% and it is close to our study. However, the rate of UTI was found to be 6.3% and it was found to be quite low compared to our study. In the same study, 15.5% of the patients required intervention. In the study, the frequency of AUR was found to be 10.6%, which was higher than in our study [23,24].

Renal colic is one of the most common urological emergencies, which is the reason for frequent admission to emergency services. In our study, it was found to be the second most common urological disease. In the USA, there are approximately 2 million applications for renal colic to emergency services annually [25]. Renal colic usually develops due to urinary system stone disease and the most common age range is male patients aged 20-50 years. Acute renal colic treatment is usually performed by ED doctors [2].

AUR usually occurs in male patients with BPH and its treatment is urinary catheterization. In the study of Fall et al. [26], the rate of AUR was reported as the most common urological emergency with a rate of 53%. In the study of Traore et al. [20], the most common urological emergency was found to be AUR with a rate of 48.28%. In the study of Girgin R. et al. [24], the frequency of AUR was reported as 10.6%. In this study, the rate of urethral catheterization was reported as 24.9% and the rate of percutaneous cystostomy (suprapubic catheterization) was reported as 4.89%. The results of our study are similar to this study [24].

Urinary system catheterization and percutaneous cystostomy are frequently performed interventions in emergency departments. Urethral catheter is usually inserted by emergency physicians. Percutaneous cystostomy may be required in patients in whom urethral catheterization cannot be performed. Fall et al. [26] reported the incidence of percutaneous cystostomy as 59.8% in their study. In the study of Topraktaş et al. [23], patients who underwent percutaneous cystostomy were reported as 22.3% of all cases. In our study, it was found that patients who underwent percutaneous cystostomy were lower than in other studies.

Macroscopic hematuria causes anxiety in patients and causes admission to ED. The important thing in the ED is the hemodynamic stability of the patient. In addition, considering that hematuria may cause urinary retention by forming a clot in the bladder, a catheter should be inserted and irrigation should be performed if necessary. In the study of Girgin R et al. [24], 30.8% of patients with hematuria were hospitalized. In the study of Fall et al. [26], the frequency of hematuria was reported as 7.1% [24]. In the study of Traore et al. [20], the rate of hematuria was found

to be 7.28%, and the rate of hematuria was found to be similar with our study.

Due to the COVID-19 pandemic in the world at the end of 2019 and in 2020, health institutions and especially the functioning of ED has changed in our country as well as all over the world. Since the beginning of the epidemic in Turkey in March, the number of patients admitted to the ER of our hospital, where we worked in the early days, has decreased considerably. In the 36-day study of Motterle et al. [27] in Italy in 2019 and 2020, on patients who underwent urology consultation during COVID-19, 287 urology consultations were reported in the same period in 2019, this number was 109 urology consultations during the COVID-19 epidemic period in 2020.

In the comparative study of Madanelo M. et al. [28] in 2019 and 2020 on urological emergencies of the COVID-19 epidemic, it was found that ED applications from urological emergencies were lower in the COVID-19 period.

In conclusion, urological emergencies are common. Among these cases, there may be diseases that require urgent intervention or operation. If the emergency physicians who first evaluate the patient in the ED should make a careful and meticulous evaluation, it is very important for the patient to make a urology consultation.

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