

# THE EFFECT OF INTRAVESICAL ONABOTULINUM TOXIN A TREATMENT ON QUALITY OF LIFE IN PATIENTS WITH OVERACTIVE BLADDER

# İNTRAVEZİKAL ONABOTULİNUM TOKSİN A TEDAVİSİNİN AŞIRI AKTİF MESANE HASTALARINDA YAŞAM KALİTESİ ÜZERİNE ETKİSİ

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### **ABSTRACT**

**Objective:** Overactive bladder (OAB) syndrome is common in women and negatively affects their quality of life. Our study aimed to evaluate the effect of intravesical onabotulinum toxin A injection on quality of life and urinary symptoms in patients with treatment resistant OAB syndrome.

Material and Method: The treatment records of 20 patients with treatment-resistant OAB were reviewed. The patients were injected with a 1:1 solution of saline and 100 units of onabotulinum toxin A at 20 different points on the body, avoiding the bladder trigon. The following survey instruments were used to determine the patient's quality of life before and after treatment: the King's Health Questionnaire (KHQ), the short-form Urodistress Inventory (UDI 6), the short-form Incontinence Impact Questionnaire (IIQ 7), the International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules (ICIQ FLUTS), the Female Sexual Function Index (FSFI), and the Pelvic Organ Prolapse/Urinary Incontinence Inquiry form (PISQ-12). The pre-and post-treatment results of the questionnaires were then evaluated.

**Result:** The uroflowmetry parameters indicated that the patients' maximum urine flow rate decreased significantly after treatment, as did their KHQ scores on all but one item. Evaluation of their FSFI scores indicated no significant change after treatment; however, the other quality of life questionnaires used (UDI-6, IIQ-7, ICIQ-FLUTS, and PISQ-12) revealed significant decreases, indicating an improvement in quality of life.

### ÖZET

Amaç: Aşırı aktif mesane (AAM), kadınlarda oldukça sık görülen ve hayat kalitesini olumsuz etkileyen bir sendromdur. Çalışmamızın amacı; tedaviye dirençli AAM sendromu olan hastalarda intravezikal onabotulinum toksin A enjeksiyonunun hastaların hayat kalitesine ve üriner semptomlarına olan etkisini değerlendirmektir.

Gereç ve Yöntem: Çalışmaya medikal tedaviye dirençli toplam 20 hasta dahil edildi. Hastalara 1:1 oranda salin ile sulandırılıp 100 Ünite onabotulinum toksin A kullanılarak 20 farklı noktaya, mesane trigonundan kaçınılarak enjeksiyon yapılmıştır. Hastaların yaşam kalitelerini belirlemek için kullanılan "King Sağlık Anketi (KHQ), Ürogenital Distres Envanteri kısa formu (UDI 6), İnkontinans Etki Anketi kısa formu (IIQ 7), ICIQ-FLUTS, Kadın Cinsel Fonksiyon Endeksi formu (FSFI), Pelvik Organ Prolapsusu/ Üriner İnkontinans Sorgulama formu (PISQ-12)" anketlerin tedavi öncesi ve tedavi sonrası sonuçları değerlendirilmiştir.

Bulgular: Tedavi öncesi ve sonrası üroflowmetri parametrelerinden maksimum idrar akım hızında anlamlı azalma izlendi. Tedavi öncesi ve sonrası yapılan KHQ skorlarının değerlendirilmesinde kişiler arası ilişkiler dışında tüm skorlarda anlamlı azalma izlendi. Tedavi öncesi ve sonrası FSFI skorları değerlendirildiğinde anlamlı bir değişiklik olmadığı izlendi. Ancak, diğer yaşam kalite anketleri olan UDI-6, IIQ-7, ICIQ-FLUTS ve PISQ-12'de anlamlı bir azalma olduğu ve yaşam kalitesinde olumlu değişim olduğu izlendi.

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**Conclusion:** When the patients' short-term results were evaluated, it was found that this therapy reduced their symptoms and complaints, thus improving their quality of life. Although none of the patients in the sample group experienced complications, in some cases catheterization is necessary due to infection and increased residual urine. Intravesical onabotulinum toxin A injection is a cheap and easy-to-administer treatment for OAB that has not responded to other treatments and does not cause serious side effects.

**Keywords:** Overactive bladder, onabotulinum toxin A, urinary retention, urgency

Sonuç: Medikal tedaviye dirençli aşırı aktif mesane sendromu olan hastalarda; intravezikal onabotulinum toksin A enjeksiyonunun kısa dönem sonuçları değerlendirildiğinde hastaların semptom, şikayetlerini azaltmış ve hastaların hayat kalitelerini olumlu yönde arttırmıştır. Bizim hasta grubumuzda komplikasyon gelişmemiş olsa da enfeksiyon ve rezidü idrar artışına bağlı kateterizasyon görülebilmektedir. Medikal tedaviye yanıt alınmayan AAM tedavisinde intravezikal onabotulinum toksin A enjeksiyonu ucuz, kolay uygulanabilir ve ciddi yan etkisi olmayan bir tedavi seçeneği olduğu düşünmekteyiz.

**Anahtar Kelimeler:** Aşırı aktif mesane, onabotulinum toksin A, üriner retansiyon, aciliyet hissi

## INTRODUCTION

The International Continence Society defines overactive bladder (OAB) as a chronic urgency with or without urge incontinence, usually with increased frequency of urination and nocturia. The prevalence of OAB increases with age, and it is estimated to affect 16.6% of all women (1). Risk factors include age, overweight, metabolic syndrome, smoking, neurological diseases, and menopause (2,3).

A detailed anamnesis, followed by a complete physical and systemic examination, is required to diagnose OAB. If a patient has one or more neurological and/or orthopedic diseases that may cause incontinence, that should be noted. A urogynecological examination begins with a physical examination and patients undergo a stress test, a Q-tip test, a Marshall-Bonney test, a pad test, and a tampon test; they are also asked to keep a bladder diary (4-8). Patient's symptoms and quality of life assessment scales were also evaluated. In addition to the physical examination, which includes a pelvic floor muscle strength assessment, urodynamic assessment tests (cystometry, uroflowmetry, and a urethral pressure profile) are conducted. Diagnoses can be made clinically or urodynamically. Symptoms are specific and sensitive as urodynamic studies in diagnosis (9).

OAB symptoms significantly reduce these patients' quality of life (10). This condition negatively affects many physical and social activities of daily and professional life and can be detrimental to mental health (11). The loss of workforce and treatment costs caused by the disease causes serious economic problems. Decreased self-confidence, embarrassment, and helplessness generally affect social relations negatively; 44% of women diagnosed with OAB report experiencing depression, and 80% report a reduced quality of life due to limitations on their social life or physical activity (12,13).

The low efficacy and poor tolerance of the available therapies reduce these patients' compliance with their treatment. Side effects such as dry mouth, constipation, and blurred vision caused by antimuscarinic agents lead to the discontinuation of these drug treatments (14). Alternative treatment options such as magnetic and sacral nerve stimulation are not always suitable for patients because they require frequent hospital visits and are less successful (15.16).

Onabotulinum toxin A, a third-stage overactive bladder treatment, relaxes the patient's muscles by inhibiting neurotransmitter release from presynaptic nerve terminals such as motor and parasympathetic nerves (17). It inhibits the release of acetylcholine from presynaptic terminals in the detrusor muscle, thus reducing the involuntary contraction of the muscle (17). It also suppresses urgency by affecting the afferent pathway, which is thought to block the release of neurotransmitters such as the substance P and adenosine triphosphate and inhibits the expression of the P2X3 receptor and TRPV1 (18).

Our study aimed to evaluate the effect of intravesical injection of onabotulinum toxin A on the quality of life and urinary symptoms of patients with treatment resistant OAB syndrome. The literature supports the use of onabotulinum toxin A to treat OAB and reduce patients' urinary symptoms (19). In our study, we assessed not only urinary symptoms but also the patient's quality of life and sexual function.

# **MATERIALS and METHOD**

# Patient selection and data collection

Patients treated at our clinic presenting with frequent urination, sense of urgency, nocturia, and/or urgent urinary incontinence between April 2014 and March 2018 were retrospectively assessed. In our study, 20 patients were included. All patients included in the study sample were over 18 years of age, diagnosed with treatment-resistant OAB syndrome following a urogynecological evaluation, had received at least two anticholinergic treatments over at least three months, and had been treated with onabotulinum toxin A. The patients in our sample discontinued their use of oral anticholinergic and ß receptor agonist drugs seven days before receiving the onabotulinum

toxin A injections. Patients who were under 18 years of age and those who had a history of neurological disease, stress urinary incontinence predominant mixed urinary incontinence, pregnancy, urinary retention, and/or with a postvoiding residue above 100 cc were excluded from the study. The study was approved by the Ethics Committee of the Istanbul Faculty of Medicine (Date: 21.10. 2022, No: 19).

# Preoperative evaluation and postoperative period

During the patients' urogynecological follow-ups, their urological symptoms, gynecological examination findings, stress tests, Q-tip tests, pelvic floor muscle strength evaluations, four-day bladder diaries, 24-hour pad tests, and urodynamic examinations before and after treatment were assessed. The urodynamic examination data included the maximum urine flow rate (Qmax), flow time, micturition volume, postvoiding residual urine volume, and maximum bladder capacity.

The pre-and post-treatment results of a series of instruments (the King's Health Questionnaire [KHQ], the shortform Urodistress Inventory [UDI6], the short-form Incontinence Impact Questionnaire [IIQ7], the International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules [ICIQFLUTS], the Female Sexual Function Index [FSFI], and the Pelvic Organ Prolapse/Urinary Incontinence Inquiry form [PISQ-12]) were used to determine the patient's quality of life. The patients' demographic data, urological symptoms, urogynecological evaluations, bladder diaries, pad tests, urodynamic examination data, treatments, and treatment results were recorded. Their cystometry, uroflowmetry, pad test, Q-tip test, stress test, and physical examination results were recorded before treatment; following treatment, they again underwent a uroflowmetry test and physical examination on the 15th day, and at postoperative 1st month a physical examination was conducted and the surveys were administered and a final physical examination at postoperative six months. The control results were recorded.

# Treatment procedure

Intravesical onabotulinum toxin A treatment was administered to patients over 18 years of age with idiopathic resistant OAB and whose symptoms persisted despite the use of two different anticholinergic treatments for at least three months in our clinic between April 2014 and March 2018. These patients were sedated, given local anesthesia, and injected with 100 units of onabotulinum toxin A diluted with saline at a ratio of 1:1 at 20 different points. These 20 points were randomly selected on the body of the bladder. Trigon and ureteral orifices were not injected. The procedures were performed with a rigid cystoscopy using a 22 G injection needle. Prophylactic antibiotic treatment was administered pre-and postop-

eratively to avoid the patients from developing a urinary tract infection (UTI).

The primary outcome of our study was the finding that onabotilinum toxin A was effective in treating OAB syndrome. The secondary result was the finding that this treatment positively affected the patients' social lives.

# Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 15.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Number and percentage distributions were used to evaluate the discrete data obtained from the patients. In our evaluation of the continuous data, we first used the Kolmogorov–Smirnov test to determine whether it had a normal distribution. The data obtained from the same individuals before and after the procedure were evaluated using the Wilcoxon signed-rank test. P values below 0.01 were considered statistically significant.

# **RESULTS**

Twenty patients were included in the study. The patients' mean age was 56.8±11.03 years (max: 73 years; min: 32 years). The patient's symptoms were frequent urination, sense of urgency, nocturia, and/or urgent urinary incontinence and/or stress urinary incontinence (Table 1). The mean number of births was 4.1±2.1 (2-9). One patient (5%) had never given birth; 17 (85%) had only vaginal deliveries; and 2 (10%) had both vaginal and cesarean section deliveries. The patients' mean body mass index (BMI) was 33.7±7.4. Fourteen patients (70%) were sexually active, while 6 (30%) were not. Four patients (20%) had no comorbidities while 16 (80%) had one or more, including hypertension (2 patients; 10%); only diabetes mellitus (DM; 1

Table 1: Patients' symptoms

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Patients' symptoms	Frequency	Percentage
Stress incontinence + urgent urinary incontinence	3	15
Stress incontinence + urgent urinary incontinence + nocturia	3	15
Stress incontinence + urgent urinary incontinence + frequent urination	4	20
Frequent urination+ sense of urgency + urgent urinary incontinence	5	25
Nocturia + urgent urinary incontinence	2	10
Frequent urination + sense of urgency + nocturia	3	15
Total	20	100

patient; 5%); both hypertension and DM (5 patients; 25%); only depression (1 patient; 5%); DM, hypertension, and a goiter (2 patients; 10%); DM, hypertension, and asthma (1 patient; 5%); endometrial cancer, depression, and a goiter (1 patient; 5%); DM, hypertension, a goiter, and asthma (1 patient; 5%); only bipolar disorder (1 patient; 5%); and DM and osteoporosis (1 patient; 5%) (Table 2). Three patients (15%) were smokers, while 17 (85%) were non-smokers. All but four patients had a history of at least one gynecological operation: 8 patients (40%) had undergone an abdominal hysterectomy, 1 (5%) patient had undergone a Lefort Colpocleisis and perineoplasty, 5 patients (25%) had undergone a repair of the anterior vaginal wall, 1 patient (5%) had undergone a transoburator tape procedure, and 1 patient (5%) had undergone a transoburator tape procedure, cystoscopy, and other abdominal operations. Ten patients (50%) had been diagnosed with urgent urinary incontinence, and 10 (50%) had been diagnosed with mixed urinary incontinence. The mean duration of incontinence was 3.4±0.8 years (2-4 years).

The mean weight of the 24-hour pad tests before the treatment was  $306\pm605$  g. The mean value of the Q-tip test before treatment was  $46\pm23.4^{\circ}$ . Seventeen patients (85%) had performed pelvic floor exercises for at least three months before their procedure. The remaining three patients (15%) did not want to exercise. In the pre-treatment cystometric analysis, the patients' mean maximum bladder capacity, abdominal pressure, and de-

Table 2: Patients' comorbidities

	Frequency	Percentage
Comorbidities		
No comorbidities	4	20
Hypertension	2	10
Diabetes Mellitus	1	5
Hypertension + Diabetes Mellitus	5	25
Hypertension + Diabetes Mellitus + Goiter	2	10
Hypertension + Diabetes Mellitus + Asthma	1	5
Hypertension + Diabetes Mellitus + Asthma + Goiter	1	5
Depression	1	5
Depression+ Goiter+Endometrial Cancer	1	5
Bipolar Disorder	1	5
Diabetes Mellitus + Osteoporosis	1	5
Total	20	100

trusor pressure were found to be  $250\pm123$  mL,  $118\pm45.7$  cmH<sub>2</sub>O, and  $61\pm34$  cmH<sub>2</sub>O, respectively. Among all patients, the first urine sensation was observed at  $109\pm65.4$  cmH<sub>2</sub>O pressure and the compression sensation was felt at  $161\pm94.5$  cmH<sub>2</sub>O pressure (Table 3).

Table 3: Patients' pre-treatment cystometry values

Cystometric results	Mean
Bladder capacity	250.6±123.3 (95–507) mL
Maximum abdominal pressure	118.2±45.7 (20–187) cmH <sub>2</sub> O
Maximum detrusor pressure	61.7±34 (21–148) cmH <sub>2</sub> O
First sensation of need to urinate	109±65.4 (17–288) cmH <sub>2</sub> O
First sensation of urgency	161.3±94.5 (31–376) cmH <sub>2</sub> O

The maximum total dose used in each application was 100 units. Five patients (25%) were re-injected with intravesical onabotulinum toxin A after their first procedure; 3 (15%) underwent two re-injections; and 2 (10%) underwent three re-injections. A comparison of the patients' daily bladder data before and after treatment revealed a significant decrease in the mean diuretic fluid intake and urinary incontinence frequency (p<0.05). Although the patients' sense of urgency, the number of nocturia incidents, and urination decreased after treatment, there were no statistically significant differences in these symptoms (Table 4, Figure 1).

**Table 4:** Data from patients' four-week bladder diaries before and after treatment

	Pre- treatment	Post- treatment	р
Bladder diary item	Mean	Mean	•
Average fluid intake (mL)	1842.6±714.2	1671±476.5	0.387
Diuretic fluid intake (mL)	777.2±444.8	515.2±215.6	0.013
Number of incidents of sense of urgency (n)	6.6±4.8	5.3±3.8	0.204
Number of incidents of urination	11±5.4	8.4±3.3	0.089
Number of incidents of nocturia	1.9±1.8	1.73±1.1	0.687
Number of incidents of urinary incontinence	3.4±2.8	1.4±1.3	0.009

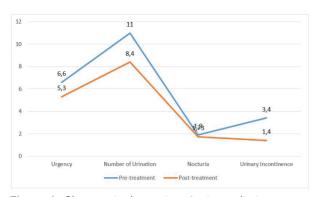


Figure 1: Changes in the patients' urinary diaries

Uroflowmetric examination revealed no significant difference before and after the procedure, except for the maximum urine flow rate (p>0.05). The maximum urine flow rate was observed to be statistically significantly lower after the procedure (p<0.05). There was no significant increase in residual urine volume (Table 5). The KHQ re-

**Table 5:** Patients' pre- and post-treatment uroflowmetry values

	Pre- treatment	Post- treatment	р
Uroflowmetry	Mean	Mean	
Maximum flow rate (mL/sec)	30.1±14.4	23.5±11	0.001
Average flow rate (mL/sec)	12.5±5.2	10.7±5.6	0.176
Residual urine volume (mL)	44.2±65. 6	33±32	0.896

**Table 6:** Patients' King's Health Questionnaire results before and after treatment

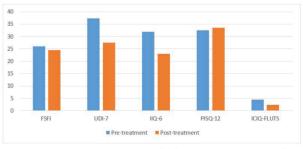
	Pre-	Post-	
	treatment	treatment	р
Questionnaire item	Mean	Mean	
Detection of general health	72.5±26.8	35.4±25	0.002
Incontinence effect	86.7±29.5	48.2±36.7	0.005
Role restrictions	80.8±35.0	40±37.6	0.002
Physical restrictions	72.5±34.7	42.4±40	0.005
Social restrictions	63.3±35.5	44.3±35	0.05
Interpersonal relations	20.8±31	22.5±34	0.575
Feelings	75.5±36.8	40.5±30.4	0.001
Sleep/energy	64.1±30.7	40.8±31.2	0.008
Intensity measurements	74.6±23.0	40.3±32.8	<0.001
Total score	611±161.8	369±235.4	0.002

vealed a statistically significant decrease in the patient's total scores before and after the procedure, and significant improvement was observed in all subgroups except interpersonal relationships (p<0.05, Table 6). There was no significant change in the patients' pre- and post-treatment FSFI scores, indicating that they did not experience any improvement in quality of life; however, their scores on the other quality of life questionnaires (UDI6, IIQ7, ICIQFLUTS, and PISQ-12) demonstrated that their quality of life did improve (p<0.05; Table 7, Figure 2).

**Table 7:** Patients' results for other questionnaires before and after treatment

	Pre- treatment	Post- treatment	р
FSFI			
Total	26.0±5.2	24.5±5.9	0.277
UDI-6			
Irritation/Urgency	48.8±13	32.5±13.5	0.02
Stress symptoms	35.9±10.6	31.2±14	0.013
Obstructive/ disturbing symptoms	27.3±14	19.1±15	0.021
Total	37.3±9.08	27.6±10.6	0.108
IIQ-7			
Total	32±13	23±15.4	0.04
PISQ-12			
Emotional	7.3±3	$6.9 \pm 3.5$	0.36
Physical	17±3.5	19±1.65	0.07
Partner- dependent	8.3±2	7.8±2.3	0.98
Total	32.6±5.3	33.6±5.8	0.24
ICIQ-FLUTS			
Total	4.56±3.3	2.4±2.3	0.04

FSFI: Female Sexual Function Index, ICIQ-FLUTS: International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules, IIQ-7: Incontinence Impact Questionnaire, PISQ-12: Pelvic Organ Prolapse/Urinary



**Figure 2:** Patients' quality of life survey results before and after treatment

FSFI: Female Sexual Function Inde, ICIQ-FLUTS: International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules, IIQ-7: Incontinence Impact Questionnaire, PISQ-12: Pelvic Organ Prolapse/Urinary Incontinence Inquiry; UDI-6: Urodistress Inventory

## DISCUSSION

Although OAB syndrome is a disease that entails serious financial and psychogenic losses for patients, the side effects of current medical treatments are detrimental to treatment compliance and reduce treatment success. Developments in the use of onabotulinum toxin A treatment and its positive results are promising for these patients.

Increasing age is a risk factor for OAB. In a meta-analysis of 13 studies on OAB, it was found that the prevalence of urinary incontinence peaked in the fifth and eighth decades of life (18). In our study, the ages of the patients ranged from 32 to 73 years, with an average of 56.08±11.03 years, which is similar to the data reported in the literature. Smoking is one of the preventable risk factors for OAB. In a study of 11,678 patients conducted in Japan, 21.2% of the patients were smokers, and OAB was found to be significantly more common among smoking women (19). However, in another study conducted in the United States, the effect of smoking on OAB was not found to be significant (20). In our study, 17 (85%) of the patients did not smoke. Although we did not identify smoking as a definite predisposing factor, we think that spasms and the cholinergic effects of smoking in triggering conditions such as frequent coughing cause urinary leakage and play a role in OAB.

Vaginal birth is another risk factor for OAB. Although the rate of OAB and stress urinary incontinence after vaginal delivery is more common than delivery by cesarean section, this difference decreases as time and the number of births increases (21). Parazzini et al. found that vaginal delivery increased stress and mixed-type urinary incontinence, but did not significantly increase detrusor overactivity (22). In our study, all but one patient (5%) had given birth at least once, and all of the patients who had given birth had a history of at least one vaginal delivery. The fact that the majority of the patients we reviewed had given birth suggests that it may be a risk factor for OAB syndrome.

Diuresis is a risk factor for urinary incontinence in diseases such as DM, chronic obstructive pulmonary disease, and some neurological diseases. In patients with DM in particular, the duration of the disease and treatment and the presence of vascular complications is important. Brown et al. found an increase in the frequency of urinary incontinence in patients with impaired fasting glucose (33.4%) compared to the normal population (16.8%) (23). Eleven (55%) of the patients we reviewed had been diagnosed with DM. Neuropathy, which is one of the advanced complications of DM, may worsen OAB patients' symptoms.

Obesity, OAB, stress, urinary incontinence, and pelvic organ prolapse cause many urogynecological problems. In their study of 1,050 cases, Palma et al. compared patients with a normal BMI of 18.5–24.9 to those with high BMIs

and found that nocturia, sense of urgency, and urgent urinary incontinence were significantly more common in patients with a BMI>25 (24). The patients we reviewed had BMIs in the range of 33.7±7.4. We believe that increased intra-abdominal and intravesical pressure due to obesity exacerbates OAB symptoms.

We evaluated the patients' four-day bladder diaries and found no significant increase in the amount of fluid taken before and after the treatment (p>0.05). A significant decrease was observed in the number of reports of urinary incontinence compared to the period before treatment. The patients' diuretic fluid intake also decreased significantly after treatment. However, the sense of urgency was not significant, although the incidents of urination and nocturia decreased. These findings are not consistent with the literature (25,26). Although we think that this may be caused by genetic factors in response to Botox treatment and the experience of the practicing clinician, studies of larger sample populations are needed to draw definitive conclusions.

Hsieh et al. found that the effect of residual urine volume was a dose-dependent drug effect and that doses of >150 U were more common (27). They also emphasized that it was a temporary side effect, arguing that it peaked two weeks after injection with onabotulinum toxin A and then gradually decreased (27). Although increased residual urine volume after intravesical onabotulinum toxin A injection is a common complication, we did not find an increase in the post-treatment uroflowmetry results. When we compared the pre-and post-treatment uroflowmetry parameters, we found no significant change except for a decrease in the maximum flow rate, which we considered to be a natural result of onabotulinum toxin A treatment

Some studies conducted on patients who did not benefit from intravesical onabotulinum toxin A injection have reported that patients develop antibodies against onabotulinum toxin A in their serum, possibly due to frequent urinary infections (28). We routinely administer prophylactic antibiotic therapy to prevent pre- and postoperative UTIs, and we believe that this will both reduce the development of antibodies against onabotulinum toxin A and protect against UTIs.

There are studies in the literature showing an improvement in quality of life after intravesical onabotulinum toxin A injection (29,30). Twenty patients who received intravesical onabotulinum toxin A injections were included in our study. Of these, 5 (25%) required one subsequent re-injection, three required two subsequent re-injections, and two required three subsequent re-injections. When we reviewed the questionnaires administered to evaluate the patient's quality of life before and after treatment, we found a significant decrease in parameters other than interpersonal relationships in the KHQ. We found no significant

icant change in the patients' FSFI responses before and after treatment, but we did observe a significant decrease in scores for the UDI-6, IIQ-7, ICIQ-FLUTS, and PISQ-12, indicating a positive change in the patient's quality of life.

The fact that our study is retrospective is a limitation. Studies with larger sample populations, longer-term follow-up, and multicenter studies are needed to draw more precise conclusions about onabotulinum toxin A.

# CONCLUSION

In examining the short-term results of intravesical onabotulinum toxin A injection in patients with treatment-resistance OAB syndrome, we found that this therapy reduced the patient's symptoms and complaints and positively increased their quality of life. Although none of the patients in our sample population developed complications, catheterization may be needed in the event of infection and residual urine increase. We think that intravesical onabotulinum toxin A injection is an inexpensive alternative treatment for treatment-resistant OAB syndrome that is easy to administer and has no serious side effects.

Ethics Committee Approval: This study was approved by Istanbul Faculty of Medicine Clinical Research Ethics Committee (Date: 21.10.2022, No: 19).

Peer Review: Externally peer-reviewed.

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**Conflict of Interest:** The authors have no conflict of interest to declare.

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# **REFERENCES**

- Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the United States. World J Urol 2003;20(6):327-36. [CrossRef]
- Hsiao SM, Lin HH, Kuo HC. Factors associated with therapeutic efficacy of intravesical onabotulinum toxin A injection for overactive bladder syndrome. PLoS One 2016;11(1):e0147137. [CrossRef]
- Amundsen CL, Richter HE, Menefee SA, Komesu YM, Arya LA, Gregory WT, et al. Onabotulinum toxin A vs sacral neuromodulation on refractory urgency urinary incontinence in women: a randomized clinical trial. JAMA 2016;316(13):1366-74. [CrossRef]
- 4. Apostolidis A. Pharmacotherapy for overactive bladder:

- minimally invasive treatment—botulinum toxins. Expert Opin Pharmacother 2011;12(7):1029-39. [CrossRef]
- Chancellor MB, Patel V, Leng WW, Shenot PJ, Lam W, Globe DR, et al. Onabotulinum toxin A improves quality of life in patients with neurogenic detrusor overactivity. Neurology 2013;81(9):841-8. [CrossRef]
- Crystle CD, Charme LS, Copeland WE. Q-tip test in stress urinary incontinence. Obstet Gynecol 1971;38(2):313-5. [CrossRef]
- Liapis A, Bakas P, Christopoulos P, Giner M, Creatsas G. Tension-free vaginal tape for elderly women with stress urinary incontinence. Int J Gynaecol Obstet 2006;92(1):48-51. [CrossRef]
- Sutherst J, Brown M, Shawer M. Assessing the severity of urinary incontinence in women by weighing perineal pads. Lancet 1981;1(8230):1128-30. [CrossRef]
- Raju R, Linder BJ. Evaluation and treatment of overactive bladder in women. Mayo Clin Proc 2020;95(2):370-7.
  [CrossRef]
- Walsh JB, Mills GL. Measurement of urinary loss in elderly incontinent patients: a simple and accurate method. Lancet 1981;1(8230):1130-1. [CrossRef]
- Hellstrom AL, Andersson K, Hjalmas K, Jodal U. Pad tests in children with incontinence. Scand J Urol Nephrol 1986;20(1):47-50. [CrossRef]
- Raju R, Linder BJ. Evaluation and treatment of overactive bladder in women. Mayo Clin Proc 2020;95(2):370-7. [CrossRef]
- Humburg J. Die Urinin kontinenz der Frau: Einführung in die diagnostik und therapie [Female urinary incontinence: diagnosis and treatment] Ther Umsch 2019;73(9):535-40.
  [CrossRef]
- Malde S, Apostilidis A, Selai C, Rahnama'i MS, Marcelissen T, Cardozo L, et al. Botulinum toxin A for refractory OAB and idiopathic urinary retention: can phenotyping improve outcome for patients: ICI-RS 2019? Neurourol Urodyn 2020;39(13):104-12. [CrossRef]
- 15. Chen JL, Kuo HC. Clinical application of intravesical botulinum toxin type A for overactive bladder and interstitial cystitis. Investig Clin Urol 2020;61(1):S33-42. [CrossRef]
- Kim A, Lee KS, Jung R, Na S, Kim JC, Kim HG, et al. Healthrelated quality of life in patients with side effects after antimuscarinic treatment for overactive bladder. Low Urin Tract Symptoms 2017;9(3):171-5. [CrossRef]
- Chen LC, Kuo HC. Pathophysiology of refractory overactive bladder. Low Urin Tract Symptoms 2019;11(4):177-81.
  [CrossRef]
- Minassian VA, Drutz HP, Al-Badr A. urinary incontinence as a worldwide problem. Int J Gynaecol Obstet 2003;82(3):327-38. [CrossRef]
- 19. Madhu C, Enki D, Drake MJ, Hashim H. The functional effects of cigarette smoking in women on the lower urinary tract. Urol Int 2015;95(4):478-82. [CrossRef]
- Cheung WW, Borawski D, Abulafia O, Vincent MT, Harel M, Bluth MH. Characterization of overactive bladder in women in a primary care setting. Open Access J Urol 2011;3:29-34. [CrossRef]
- 21. Handa VL, Pierce CB, Munoz A, Blomquist JL. Longitudinal changes in overactive bladder and stress incontinence among parous women. Neurourol Urodyn 2015;34(4):356-61. [CrossRef]

- 22. Parazzini F, Chiaffarino F, Lavezzari M, Giambanco V. Risk factors for stress, urge or mixed urinary incontinence in Italy. BJOG 2003;110(10):927-33. [CrossRef]
- 23. Brown JS. Urinary incontinence: an important and underrecognized complication of type 2 diabetes mellitus. J Am Geriatrics Soc 2005;53(11):2028-9. [CrossRef]
- Palma T, Raimondi M, Souto S, Fozzatti C, Palma P, Riccetto C. Correlation between body mass index and overactive bladder symptoms in pre-menopausal women. Rev Assoc Med Bras (1992) 2014;60(2):111-7. [CrossRef]
- Herschorn S, Gajewski J, Ethans K, Corcos J, Carlson K, Bailly G, et al. Efficacy of botulinum toxin A injection for neurogenic detrusor overactivity and urinary incontinence: a randomized, double-blind trial. J Urol 2011;185(6):2229-35. [CrossRef]
- Dmochowski R, Chapple C, Nitti VW, Chancellor M, Everaert K, Thompson C, et al. Efficacy and safety of onabotulinum toxin A for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. J Urol 2010;184(6):2416-22. [CrossRef]

- 27. Hsieh PF, Chiu HC, Chen KC, Chang CH, Chou EC. Botulinum toxin A for the treatment of overactive bladder. Toxins (Basel) 2016;8(3):59. [CrossRef]
- 28. Schulte-Baukloh H, Herholz J, Bigalke H, Miller K, Knispel HH. Results of a BoNT/A antibody study in children and adolescents after onabotulinum toxin A (Botox®) detrusor injection. Urol Int 2011;87(4):434-8. [CrossRef]
- Kalsi V, Apostolidis A, Popat R, Gonzales G, Fowler CJ, Dasgupta P. Quality of life changes in patients with neurogenic versus idiopathic detrusor overactivity after intradetrusor injections of botulinum neurotoxin type A and correlations with lower urinary tract symptoms and urodynamic changes. Eur Urol 2006;49(3):528-35. [CrossRef]
- Game X, Khan S, Panicker JN, Kalsi V, Dalton C, Elneil S, et al. Comparison of the impact on health-related quality of life of repeated detrusor injections of botulinum toxin in patients with idiopathic or neurogenic detrusor overactivity. BJU Int 2011;107(11):1786-92. [CrossRef]