

# The Effect of Intravesical OnabotulinumtoxinA Injection on Women Sexual Function in Overactive Bladder Treatment: Observational Study

## Aşırı Aktif Mesane Tedavisinde Kullanılan İntravezikal OnabotulinumtoksinA Enjeksiyonunun Kadın Cinsel Fonksiyonu Üzerindeki Etkisi: Gözlemsel Çalışma

Erkan MERDER<sup>a</sup>, Mehmet Gökhan ÇULHA<sup>a</sup>, Ahmet ARIMAN<sup>a</sup>, Bahadır ERMEÇ<sup>a</sup>, Murat ÖZER<sup>a</sup>, Fatih ALTUNRENDE<sup>a</sup>

<sup>a</sup>Department of Urology, University of Health Sciences Prof. Dr. Cemil Taşcıoğlu City Hospital, İstanbul, TURKEY

The study was presented as an orally at the 6<sup>th</sup> National Functional Urology and Female Urology Congress on 2-6 October 2019, Antalya, TURKEY.

**ABSTRACT Objective:** To investigate the effect of intravesical onabotulinumtoxinA (Botox) injection on female sexual function in women with overactive bladder (OAB) and to evaluate its relationship with OAB symptoms. **Material and Methods:** Data from 56 patients with idiopathic OAB and who were resistant to medical therapy between January 2018 and July 2019 were evaluated. The patients were evaluated with an overactive bladder symptom score (OABSS) and female sexual function index (FSFI) before and after 100 IU Botox treatment. The changes in the symptom scores of the patients and the FSFI scores were compared. **Results:** A total of 38 patients completed the study. The mean age of the patients was 41.59±11.79 (31-56), and the mean body mass index was 30.02±4.77 kg/m<sup>2</sup>. Mean duration of complaints was 48,93±45,32 months and mean number of pads daily used was 3,92±2,39. For the treatment of idiopathic OAB, 100IU Botox application to each patient was performed in 20 regions. Significant improvement was observed in the OABSS scores of the patients 12 weeks after treatment (10,32±3,01 to 4,68±2,21; p<0,001). When the FSFI scores were examined, a significant improvement was observed in the FSFI-desire, arousal, satisfaction, and pain subgroups and total FSFI score 12 weeks after the procedure. In the post-treatment evaluation, 94,73% of the patients were satisfied with the treatment. Urinary retention occurred in two patients. **Conclusion:** As a result of our study, intravesical botox injections have been shown to improve sexual function in women with OAB. More extensive studies are needed to better evaluate the effects of botox injection on sexual functions.

**Keywords:** Overactive bladder; botox; female sexual function; urge urinary incontinence

**ÖZET Amaç:** Aşırı aktif mesane (AAM) semptomları kadın cinsel fonksiyonu üzerinde olumsuz bir etkiye sahiptir. Bu çalışmanın amacı, AAM'li kadınlarda intravezikal onabotulinumtoksinA (Botoks) enjeksiyonunun kadın cinsel fonksiyonu üzerindeki etkisini araştırmak ve AAM semptomları ile ilişkisini değerlendirmektir. **Gereç ve Yöntemler:** Ocak 2018-Temmuz 2019 tarihleri arasında idiopatik AAM tanısı olan ve medikal tedaviye dirençli 56 hastanın verileri değerlendirildi. Hastalar 100 IU Botoks tedavisi öncesi ve tedaviden 12 hafta sonra aşırı aktif mesane semptom skoru (OABSS) ve kadın cinsel fonksiyon indeksi [female sexual function index (FSFI)] ile değerlendirildi. Hastaların semptom skorlarındaki değişiklikler ile FSFI skorları arasındaki değişiklikler karşılaştırıldı. **Bulgular:** Çalışmayı 38 hasta tamamladı. Hastaların yaş ortalaması 41,59±11,79 (31-56), beden kitle indeksi ortalaması 30,02±4,77 idi. Hastaların şikâyet süreleri ortalaması 48,93±45,32 ay, günlük ped kullanımı ortalaması 3,92±2,39'du. İdiopatik AAM tedavisi için her hastaya 100IU Botoks uygulaması 20 bölgeye yapıldı. Tedaviden 12 hafta sonra hastaların OABSS skorlarında anlamlı iyileşme izlendi (10,32±3,01'e 4,68±2,21; p<0,001). FSFI skorları incelendiğinde işlemden 12 hafta sonra FSFI-istek, uyarılma, doyum ve ağrı alt grupları ile toplam FSFI skorunda anlamlı iyileşme olduğu izlendi. Tedavi sonrası değerlendirmede hastaların %94,73'ü tedaviden memnundu. İki hastada idrar retansiyonu gerçekleşti. **Sonuç:** Çalışmamız sonucunda, intravezikal botoks enjeksiyonlarının AAM'li kadınlarda cinsel fonksiyonu iyileştirebileceği gösterilmiştir. Botoks enjeksiyonunun cinsel fonksiyonlar üzerine etkilerinin daha iyi değerlendirilmesi için konu ile ilgili daha geniş çalışmalara ihtiyaç vardır.

**Anahtar Kelimeler:** Aşırı aktif mesane; botoks; kadın cinsel fonksiyonu; sıkışma tipi idrar kaçırma

**Correspondence:** Mehmet Gökhan ÇULHA

Department of Urology, University of Health Sciences Prof. Dr. Cemil Taşcıoğlu City Hospital, İstanbul, TURKEY/TÜRKİYE

E-mail: gokhan\_culha64@hotmail.com



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Overactive bladder (OAB), urinary incontinence, and sexual dysfunction are conditions that many women find difficult to come to the hospital because of embarrassment.<sup>1</sup> OAB is a symptom complex characterized by frequent urination, sudden urgency or urge-type urinary incontinence, without local, metabolic, or hormonal causes that explain these symptoms.<sup>2,3</sup> The most disturbing symptom of lower urinary tract symptoms (LUTS) is urge-type urinary incontinence, which can reduce patients' life quality.<sup>4</sup> Although urinary incontinence is a harmless condition, it creates psychological effects and affects the quality of life in women.<sup>5</sup> While the first-line treatment of OAB is usually conservative or pharmacological, invasive treatments (such as botox, sacral neuromodulation) are used in refractory patients.<sup>6</sup>

Studies have shown that OAB has negative effects on patients' sexual health. In the EpiLUTS study, it was reported that the sexual functions of women with dry and wet type OAB were affected.<sup>7</sup> Recently, some studies have evaluated existing treatments for OAB as having an effect on female sexual function. Positive results have been described in terms of improving sexual function in women undergoing sacral neuromodulation (SNM) or percutaneous tibial nerve stimulation (PTNS) for LUTS and/or other pelvic disorders.<sup>8,9</sup>

Botulinum toxin type A (onabotulinumtoxinA or Botox) is widely used worldwide for various reasons. It causes a temporary decrease in detrusor contraction by blocking the nerve activity in the detrusor muscles.<sup>10</sup> There have not been enough studies done to evaluate the effect on female sexual function after intravesical Botox injection. The aim of this study is

to investigate the effect of intravesical Botox injection on female sexual function in women with OAB and to evaluate its relationship with OAB symptoms.

## MATERIAL AND METHODS

The present study protocol was approved by the Institutional Review Board of University of Health Sciences Prof. Dr. Cemil Taşcıoğlu City Hospital (approval no: 351/2020, approval date: 25.08.2020). Informed consent was obtained from all subjects when they were enrolled.

Data of 56 sexually active female patients who were admitted to the urology outpatient clinic due to idiopathic OAB between January 2018 and July 2019 and did not benefit from medical treatments were retrospectively analyzed. No more patients were enrolled in the study due to the coronavirus disease-2019 pandemic. Patients with mixed urinary incontinence and stress urinary incontinence were excluded.

Detailed medical histories of all patients were taken. Overactive bladder symptom score (OABSS) and female sexual function scale (FSFI) forms were completed. Pelvic examinations were then performed. Residual urine amounts were measured by transabdominal ultrasound. 100 IU Botox (100 U, Allergan, Westport, County Mayo, Ireland) was injected to the patients who were eligible for botox treatment. Inclusion and exclusion criteria are given in Table 1.

Antibiotic prophylaxis was started with a second generation cephalosporin during treatment. Under sedoanesthesia, the bladder was entered with a 22 fr Storz cystoscope. Botox was diluted with 10 cc 0.9%

**TABLE 1:** Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
- Non-pregnant, sexually active women over 18 years of age	- Stress urinary incontinence
- Idiopathic OAB symptoms	- Urinary tract infection
- Lack of efficacy (at least 2 drugs, each for ≥1 month)	- Bladder or pelvic tumors
or intolerance of antimuscarinic therapy and/or lack of efficacy	- Postvoid residual volume over 100 mL
	- Contraindications to onabotulinumtoxinA use
	- Previous onabotulinumtoxinA injections due to urological conditions

OAB: Overactive bladder.

NaCl and injected into the detrusor muscle at 20 points (5 IU per point) / 0.5 cc) with the help of a botox needle.

## QUESTIONNAIRE FORMS

OABSS is an inquiry form consisting of 4 questions. The frequency of urination during the day and night, urgency attacks in the last month and the frequency of urinary incontinence attacks are questioned in 2006.<sup>11</sup> Linguistic validation of this form was made by Culha et al. A total score of 3 and above and getting at least 2 points from the 3<sup>rd</sup> question confirms the diagnosis of OAB.<sup>12</sup> A score of 0-15 is taken from the questionnaire. High scores are related to the severity of OAB.

FSFI is a questionnaire form consisting of 19 questions and 6 subsections that question female sexual function.<sup>13,14</sup> In this form, six sub-sections of desire, arousal, lubrication, orgasm, satisfaction and pain, and female sexual function are examined. A total score below 26.55 indicates that there is female sexual dysfunction.<sup>15</sup>

Patients were evaluated with OABSS and FSFI before 100 IU Botox treatment and 12 weeks after treatment. In addition, patients were checked for side effects and satisfaction 1 week after the treatment. The changes in the symptoms scores of the patients and the changes between the FSFI scores were compared.

## STATISTICAL ANALYSIS

Statistical analysis was done using SPSS 20.0. The distribution of data was evaluated using the Kol-

mogorov-Smirnov test. Mann-Whitney U test and Wilcoxon test were used. A p value of <0.05 was considered statistically significant.

## RESULTS

A total of 38 patients completed the study. The mean age of the patients was  $41.59 \pm 11.79$  (31-56) years and the mean body mass index was  $30.02 \pm 4.77$  kg/m<sup>2</sup>. The average duration of complaints was  $48.93 \pm 45.32$  months, and the average daily pad use was  $3.92 \pm 2.39$ . Significant improvement was observed in the OABSS scores of the patients 12 weeks after the treatment (to  $10.32 \pm 3.01$ ,  $4.68 \pm 2.21$ ;  $p < 0.001$ ). When the FSFI scores were examined, a significant improvement was observed in the FSFI-desire, arousal, satisfaction and pain subgroups and the total FSFI score 12 weeks after the procedure. The most improvement after treatment was in the pain subgroup ( $p < 0.001$ ). There was no significant change in lubrication and orgasm subgroups ( $p > 0.05$ ) (Table 2).

While 29 patients (76.32%) had sexual dysfunction before treatment, 9 patients (23.68%) were found to have sexual dysfunction after treatment. A moderate negative correlation was found between the difference in OABSS symptom score and FSFI total score ( $p = 0.001$ ,  $r = 0.352$ ). In the post-treatment evaluation, 94.73% of the patients were satisfied with the treatment. Urinary retention occurred in two patients.

**TABLE 2:** OABSS and FSFI scores of patients before and 12 weeks after treatment.

	Pre-treatment		Post-treatment		p value
	Mean	SD	Mean	SD	
OABSS	10.32	2.208	4.682	3.0098	<0.001
FSFI desire	2.073	0.9208	3.491	2.1082	0.001
FSFI arousal	2.564	1.4063	3.218	1.2633	0.031
FSFI lubrication	3.545	1.8462	4.255	1.9279	0.116
FSFI orgasm	3.091	1.3866	3.564	0.7895	0.211
FSFI satisfaction	3.273	1.3614	4.073	1.0448	0.042
FSFI pain	1.891	0.8389	3.673	0.6250	<0.001
FSFI total	16.436	6.2616	22.273	6.3839	0.004

OABSS: Overactive bladder symptom score; FSFI: Female sexual function index; SD: Standard deviation.

## DISCUSSION

As a result of our study, it was found that intravesical Botox treatment reduced OAB symptoms and significantly improved female sexual function in the desire, arousal, satisfaction and pain subgroups. In addition, it was observed that sexual function scores increased with the decrease in OAB symptoms.

Anticholinergic agents are frequently used as the second-line treatment method in the treatment of OAB. Common side effects of anticholinergics include dry mouth and dry eyes, although they do not have a negative effect on vaginal lubrication.<sup>16</sup> However, consistent results have not been obtained regarding the positive effect of anticholinergic therapy on sexual function.

OAB is a common symptom, especially in female patients.<sup>17,18</sup> OAB can affect the quality of life as well as sexual functions.<sup>19</sup> In recent years, anticholinergics used in the treatment of OAB have been found to improve sexual function.<sup>20</sup> However, there are also data where a significant relationship could not be found between studies.

One study using FSFI showed no benefit or improvement for the majority of participants (70%). Advanced treatment steps of OAB are interventional methods. On sexual function, PTNS has been shown to improve sexual function in women.<sup>9</sup>

A recent study by Musco et al. evaluated the change in sexual function of 33 women with OAB symptoms and undergoing PTNS.<sup>9</sup> As a result of this study, it was observed that PTNS produced significant increases in overall sexual function, desire and satisfaction scores (FSFI) in groups with and without female sexual dysfunction. Overall, significant improvements were found in all FSFI scores. OnabotulinumtoxinA 100 U dissolved in 10 mL of saline and injected in 20 points of the bladder wall above the trigone (0.5 mL per injection site) is licenced in Europe to treat OAB with persistent or refractory UUI in adults of both genders, despite the small number of males included in the registration trials.<sup>21</sup> Quality of life was substantially improved in the Botox, as shown by the more than 60% of positive responses

in the Treatment Benefit Scale questionnaire at week twelve.<sup>22</sup>

Botulinum toxin type A (onabotulinumtoxinA or Botox) shows a temporary decrease in bladder contractions. There are few studies evaluating the effect of this treatment on sexual function. Miotla et al. investigated the effect of intravesical BoNT-A injections on sexual function in women with OAB.<sup>23</sup> In this study, 56 women were evaluated using the FSFI questionnaire before treatment and 12 weeks after receiving the injections. Patients who received OnaBoNT-A injection showed significant improvements in all FSFI areas. FSFI scores increased significantly compared to the control group. In our study, significant improvements were observed in desire, arousal, satisfaction, pain subgroups and FSFI total score compared to before Botox injection.

In the study of Balzarro et al. assessed the effect of BoNT-A injection on sexual function in women with OAB, 32 women treated with Botox injection were evaluated for sexual function using FSFI before and 3 months after BoNT-A injection.<sup>24</sup> The study demonstrated significant improvement of most FSFI domains, except for desire and pain (no significant improvements). This study documented a significant correlation only between the reduction of episodes of urgency UI and improvement of FSFI. In our study, significant improvements were observed in desire, arousal, satisfaction, pain subgroups and FSFI total score compared to before botox injection. It was also observed that the improvement in FSFI scores correlated with the reduction of OAB symptoms.

The study has some limitations. The absence of a control group is the first of these. The small number of patients is another limitation. Lack of long-term follow-up is among the limitations of the study.

## CONCLUSION

While botox injection reduces OAB symptoms in women, it also improves sexual dysfunction due to LUTS. Moreover, the improvement in symptoms also leads to an increase in the improvement of sexual functions. In order to better evaluate the effect of Botox on female sexual function, a multi-center study

with more patients and long-term follow-up is required.

### Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or mem-

bers of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Erkan Merder, Mehmet Gökhan Çulha; **Design:** Mehmet Gökhan Çulha; **Control/Supervision:** Fatih Altunrende; **Data Collection and/or Processing:** Ahmet Arıman, Bahadır Ermeç; **Analysis and/or Interpretation:** Mehmet Gökhan Çulha, Murat Özer; **Literature Review:** Mehmet Gökhan Çulha, Bahadır Ermeç; **Writing the Article:** Ahmet Arıman, Bahadır Ermeç, Murat Özer; **Critical Review:** Fatih Altunrende, Mehmet Gökhan Çulha; **References and Fundings:** Fatih Altunrende; **Materials:** Murat Özer.

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