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RESEARCH ARTICLE

Evaluating the Efficacy of Intravesical Botulinum Toxin Treatment in Enhancing Quality of Life for Patients with Overactive Bladder and Moderate Functional Impairment

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Abstract

Objective: Overactive bladder (OAB) significantly impacts the quality of life, affecting individuals across various age groups irrespective of gender. While conventional treatments exist, they often fall short for patients with moderate functional impairment, marked by an Eastern Cooperative Oncology Group Performance Score (ECOG PS3). Intravesical botulinum toxin therapy has emerged as a promising alternative, especially for those unresponsive to traditional pharmacotherapy.

Material and Methods: In this retrospective study from 2020 to 2023, we analyzed data from patients treated with botulinum toxin therapy for OAB. ECOG PS3 patients with a bladder capacity of at least 200 milliliters were included. Data collected included medical histories, voiding diary, and quality of life scores (ICIQ-SF and I-QOL).

Results: The research featured 46 individuals and demonstrated a statistically substantial advancement in quality-of-life following treatment. The parameters of incontinence episodes and voiding diary scores exhibited statistically significant enhancements. Notably, there was no observable increase in residual urine or urinary tract infections subsequent to treatment.

Conclusion: Intravesical botulinum toxin therapy has demonstrated a marked improvement in the quality of life for patients suffering from OAB and exhibiting moderate functional impairment. Nevertheless, further research is required in multicenter randomized trials to substantiate the findings and maintain their credibility.

Keywords: botulinum toxins, type A, overactive bladder, quality of life, urinary incontinence, urinary retention

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INTRODUCTION

Overactive bladder is a condition defined by dysfunction in bladder storage capacity, leading to a substantial decline in the quality of life of those affected (1, 2). This condition can affect individuals of all ages, regardless of sex, and can be effectively managed with lifestyle modifications, medications, and pelvic floor exercises. Patients with OAB who exhibit anticholinergic resistance may not experience the desired treatment outcomes. Patients presenting with a moderate impairment in functional capacity (ECOG PS3) may experience OAB symptoms resulting from either idiopathic or neurogenic causes. Notably, the decrease in quality of life experienced by this particular cohort of individuals may prove to be more pronounced than others (3).

Although the Eastern Cooperative Oncology Group Performance Scale (ECOG PS) was developed to assess cancer patients, it can also be employed for non-cancer patients(4, 5). The ECOG Performance Status Scale assesses the influence on patients' daily activities, rating them from 0 to 5, with 0 signifying complete functionality and 5 denoting passing away. The ECOG PS3 classification indicates that the patient can perform limited self-care activities but mainly depends on a bed or chair for support. This indicates that patients spend more than half of their time in bed or seated(6). Individuals with moderate functional impairment are severely negatively affected in terms of quality of life when conditions such as OAB occur. It may be more difficult for these patients to access health services regularly parallel to their illness. More curative treatment modalities need to be energetically prioritized.

Urinary incontinence and other complications such as sleep disorders, psychological disorders, fractures, and injuries resulting from falls are among the potential complications associated with Overactive Bladder (OAB) syndrome(7-9). Restricting fluid intake, decreased mobility, and constipation are common issues faced by patients, which can exacerbate their existing problems. Undoubtedly, patients often resort to social isolation and seek remedies such as increased reliance on diapers, limitation of physical activity, and spending extended periods in bed as a means of alleviating their symptoms. Moreover, these difficulties can give rise to social problems that exacerbate caregivers' burdens. Alternative treatment methods should be considered to change the negative processes in both patients and caregivers (10, 11).

Intravesical BTxA injections have gained prominence as a novel approach for treating OAB. The efficacy and safety of intravesical Botulinum Toxin therapy in the treatment of OAB are well known, especially in anticholinergic refractory patients (12). Intravesical botulinum toxin therapy with minimally invasive methods can be used safely and effectively in the elderly and those with neurologic deficits(11).

BTxA injections have been recognized as a valid therapeutic approach for patients with OAB syndrome, including those with either non-neurogenic or neurogenic conditions. It is usually considered in patients unresponsive to anticholinergic treatments followed by behavioral and physiotherapies. Unsuccessful treatment attempts in patients with restricted mobility negatively affect the quality of life and create a feeling of helplessness and loneliness in patients. Thus, restriction of fluid intake leads to undesirable conditions such as increased dependence on the bed or chair, which worsens the patient's general condition.

This study investigated the impact of intravesical injection of botulinum toxin in patients with ECOG PS3. It had two objectives: first, to assess the effectiveness and safety of intravesical botulinum toxin, and second, to report any observations regarding improved quality of life in this group of patients.

MATERIAL AND METHOD

Data Collection

This study included patients with moderately functional performance and OAB syndrome who underwent intravesical botulinum toxin treatment between 2020 and 2023. The study was conducted retrospectively, and data were generated through a retrospective review of patient files. The validated Turkish versions of the quality-of-life scale were used. Since urodynamic studies are not routinely performed in every patient, urodynamic results and data were not evaluated in this study. Figure 1 shows the flow chart.

Eligibility Criteria

All individuals in the study were part of the ECOG PS3 group, and their gender and age were not considered as selection criteria. The primary inclusion criterion was an ultrasonographic bladder capacity > 200 ml. Additionally, patients were required to have failed previous treatments with anticholinergic medications and/or beta-3 agonists.

A history of neurological disease or diabetes mellitus was not used as an exclusion criterion. However, patients with ongoing urinary tract infections or other acute urological conditions were excluded from the study. Those with mental or psychotic disorders who were likely to face difficulties during the follow-up were not included in the study. Furthermore, those whose residual urine volume after voiding, as determined by ultrasound, exceeded 100 cc were excluded from the study.

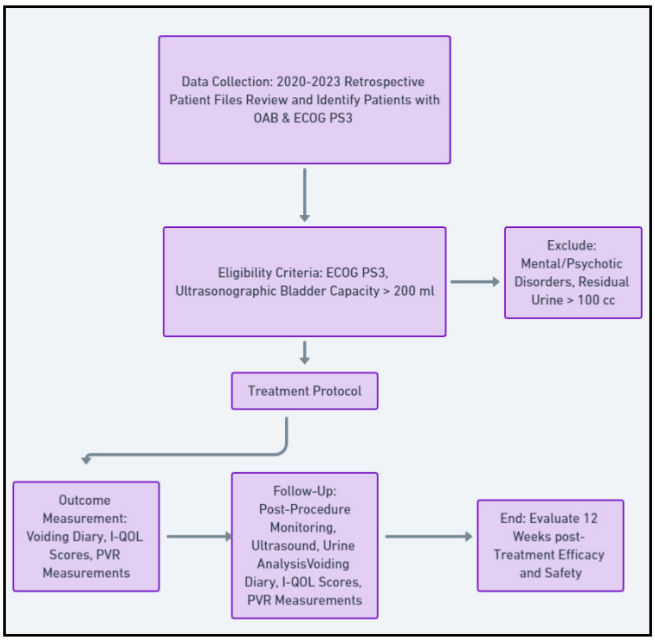

Figure 1. Flow Chart of Study

Data Analysis

The dependent samples t-test was used to compare the dependent variables across groups. Statistical significance was set at $p < 0.05$. The sample size was verified using G-Power software, with a power of 99.8 and an effect size of 0.8, as determined by Cohen's d. The tables provide a summary of the descriptive statistics. Categorical data are expressed as numbers (n) and percentages, while quantitative data are presented as mean ± standard deviation (SD). Regression and correlation tests were conducted to determine the factors influencing the treatment outcomes. Data analysis was performed using SPSS version 28.0 software.

Ethical Considerations

Before performing the procedure, informed consent was obtained from all patients, emphasizing the potential complications that may arise both during and after the intervention. This study followed the ethical guidelines established by the Declaration of Helsinki and was approved by the Ethics Committee of TRNC Burhan Nalbantoğlu State Hospital (project code 19/24).

Treatment and follow-up protocol

The surgical procedure was performed with sedation in the lithotomy position for all patients. The administration of third-generation cephalosporins serves as a prophylactic measure against infection. Patients diagnosed with idiopathic OAB received 100 IU of BTxA neurogenic component received 200 IU (13). Twenty bladder sites were injected using a rigid cystoscope. Following the procedure, an 18 Fr Foley catheter was inserted in all patients, and the urethral catheters were withdrawn three days after insertion. Voiding residual micturition controls, including ultrasound and urine analyses, were carried out one week after removal. After 12 weeks, the volume frequency charts, and quality of life questionnaires were assessed. Patients with pre-procedural or recurrent urinary tract infections were administered low-dose daily antibiotic therapy (trimethoprim) for three months as part of their treatment. Continuation rates for BTxA treatment sessions were tracked annually. After the initial BTxA application, patients were monitored to determine if they returned for second or third sessions as the effects of the initial treatment waned. The data on continuation rates was collected, enabling us to assess patient compliance and treatment effectiveness at various times.

RESULTS

A total of 46 individuals (16 men and 30 women) were evaluated in the study. The average age of participants was 69 years, with a standard deviation of 6.8 years. The participant's body mass index (BMI) ranged from 10.33 to 45.9, with a mean of 23.89 and a standard deviation of 6.25. The cause of OAB was idiopathic in 36 participants, while neurogenic bladder was the cause in 10 individuals. All patients with a neurogenic OAB had a history of intracranial embolism. Prior to administering BTxA injections into the bladder, the urine of 39 patients was found to be sterile, while infection was detected in 7 patients. Additionally, 12 patients reported experiencing constipation before treatment, whereas 34 did not. Among the study participants, 23 had hypertension, 8 had diabetes, 5 had COPD, and 13 had coronary disease. The patient characteristics are shown in Table 1.

Table 1. Characteristics of the Patients

Characteristic	Value
Total number of participants	n = 46
Gender - Males -Females	 16 30
Mean age (years) ± SD	69 ± 6.8
Mean BMI (kg/m²) ± SD	23.89 ± 6.25
BMI range (kg/m²)	10.33 - 45.9
Cause of OAB - Idiopathic - Neurogenic*	 n = 36 n = 10
Other health conditions - Hypertension - Diabetes - COPD - Coronary disease	 n = 23 n = 8 n = 5 n = 13

Note: BMI = Body Mass Index, SD = Standard Deviation, COPD = Chronic Obstructive Pulmonary Disease

The statistical analysis results indicated a substantial variation in the assessed parameters before and after treatment. The Wilcoxon Signed-Rank Test was used for data analysis due to the non-normal distribution of our post-treatment measurements, as confirmed by conducting the preliminary Shapiro-Wilk test. This decision was further supported by the paired nature of our pre- and post-treatment data comprising a total sample size of 46 participants.

Several key metrics exhibited statistically significant changes following treatment, as revealed by the Wilcoxon Signed-Rank Test: post-treatment voiding diary (VD) scores ($Z = -5.933$, $p < .001$), leakage incidents ($Z = -5.763$, $p < .001$), Incontinence Quality of Life questionnaire (I-QOL) scores ($Z = -5.842$, $p < .001$), and Post-void Residual (PVR) measurements ($Z = -3.874$, $p < .001$). The parameters evaluated before and after BTxA injection are summarized in Table 2.

The Spearman correlation test evaluated the relationship between various parameters given the non-normally distributed data. A strong positive correlation was identified between baseline and post-treatment ICIQ scores (pre-treatment ICIQ and post-treatment ICIQ) ($rho = .673$, $p < .001$), indicating a close relationship between quality-of-life measures before and after treatment. A significant positive correlation was also found between the pre-and post-I-QOL scores ($rho = .576$, $p < .001$).

A linear regression test was performed to determine the effects of the pre-treatment dependent and independent variables on post-treatment ICIQ and IQOL scores. Age, sex, body mass index (BMI), presence of urinary tract infection or constipation before treatment, pre-treatment post-voiding residual (PVR) amount, and number of urinary incontinence episodes demonstrated no impact on treatment outcomes.

Table 3. Shows annual retention rates for patients receiving BTxA treatments. The data indicate a decline in retention rates following the first session, suggesting a decrease in treatment adherence as the effects of the first BTxA session wane over time.

Table 2. Comparison of Parameters Before and After BTxA Injection

Parameter	Before Btx-A Injection (Mean ± SD)	After Btx-A Injection (Mean ± SD)	P-value
Incontinence Episodes	3±1.6	1±0.8	<0.01
Voiding Diary	15±1.29	10±1.28	<0.01
ICIQ-SF Score	16±3.16	6±5.17	<0.01
I-QOL Score	46±12.3	86±14.8	<0.01
PVR (% and n) <50ml 50-100ml >100ml	 100% (46/46) Nil Nil	 60.9% (28/46) 26.1% (12/46) 13.0% (6/46)	<0.01

Note: ICIQ: International Consultation on Incontinence Questionnaire, I-QOL: Incontinence Quality of Life, PVR: Post-voiding Residual Urine, SD: Standard Deviation, Min: Minimum, Max: Maximum, BTxA: Botulinum Toxin A

Table 3. Annual Continuation Rates for Patients Undergoing Sequential Intravesical BTxA Treatment Sessions

Year	Initial BTxA Application n (%)	Second BTxA Session n (%)	Third BTxA Session n (%)
2020	8(%100)	7(87.5%)	5(62.5%)
2021	12(100%)	10(83.3%)	6(50%)
2022	17(100%)	11(64.7%)	nil
2023	9(100%)	2(22,2%)	nil

BTxA; Botulinum Toxin A, n; Number

DISCUSSION

OAB syndrome, as defined by the International Continence Society, is a symptom complex comprising urinary urgency, usually accompanied by increased daytime frequency and/or nocturia, with or without urinary incontinence, in the absence of urinary tract infection (UTI) or other detectable diseases (13). Previous research has demonstrated the efficacy of BTxA in treating various medical conditions, although its impact on patients with an ECOG PS of 3 remains insufficiently documented. Our study supports using intravesical BTxA as an effective option for treating OAB in patients with ECOG PS 3 with empirical evidence.

Our findings align with the current literature, which suggests that botulinum toxin, particularly in patients resistant to or benefiting little from anticholinergics, can effectively alleviate overactive muscle symptoms(14). Nevertheless, concentrating on this particular patient group helps bridge the knowledge gap in this area. To evaluate the success rate of treatment for OAB, assessing the condition's impact on the patient's quality of life is essential, as it is a critical factor that influences treatment outcomes. Consequently, measuring the patient's quality of life using scales before and after treatment is a crucial component in determining the success rate of the treatment. As such, it should be considered an independent factor evaluated separately from other variables.

OAB has been shown to significantly negatively impact quality of life (2, 15). Our study indicates that OAB adversely influences quality of life during pre-treatment assessment; however, following treatment with intravesical botulinum therapy, quality of life scores improved.

One of the primary limitations of this study is its retrospective design, the absence of a control group, and the relatively small sample size. The retrospective nature inherently limits the ability to establish causal relationships, as the study relies on pre-existing data that may be subject to selection bias and lacks the randomization present in prospective studies. Additionally, without a control group, it is challenging to directly attribute the observed improvements in quality of life and symptom reduction solely to the intravesical Botulinum Toxin A therapy. These factors collectively limit the generalizability of our findings to the broader population of patients with overactive bladder (OAB).

Moreover, the small sample size may have limited our ability to detect less common complications or more nuanced treatment effects. The limited number of participants makes it difficult to generalize the findings to a larger population and may obscure the identification of rare adverse events. Therefore, while our results are promising, they should be interpreted with caution. Future studies with larger, multicenter prospective designs are necessary to validate our findings and to explore the full spectrum of treatment effects and potential complications. Such studies would provide a more robust understanding of the efficacy and safety of Botulinum Toxin A therapy in OAB patients.

We observed no significant increase in residual urine or the incidence of urinary tract infections (UTIs) following treatment with BTxA. However, it is crucial to recognize that the modest size of the study population may influence these findings. Smaller sample sizes can make it difficult to identify infrequent side effects or unique treatment effects in subgroups (16,17). Therefore, caution should be exercised when generalizing the results. Previous studies in larger patient groups have reported increased UTI frequency after BTxA treatment(18). Consequently, the inconsistency between our findings and those of previous studies might be attributed to the limitations of our sample size.

In addition, Botulinum Toxin A injections are not limited to patients resistant to anticholinergics but also have therapeutic effects on those who do not respond to beta-3 agonists or combination therapies. This broader applicability may indicate the need for further research to explore the potential of Botulinum Toxin A in the management of OAB in different patient subgroups.

Moreover, the lack of a control group precludes a comparison with other treatment modalities or with a placebo, which could have provided a more robust assessment of the therapy's efficacy. As such, while our findings are promising, they should be interpreted with caution, and there is a need for future studies with prospective designs and appropriate control groups to validate our results. These additional studies would help confirm the effectiveness of Botulinum Toxin A in improving the quality of life for OAB patients and better understand the potential placebo effects and other confounding variables that may have influenced our outcomes.

Increased post-voiding residual urine volume is a well-known complication in patients with intravesical BTx Administration and sometimes requires additional treatment modalities,

such as clean intermittent catheterization. However, although residual urine increased after voiding was observed in our study, no patients required additional treatment. Criteria, such as sample size or patient selection in the patient group, may be effective for these results.

The primary limitation of this study is that despite utilizing a statistically appropriate sample size, the small number of participants may have influenced the results and findings, particularly considering the scarcity of long-term and comprehensive follow-up data. The absence of long-term follow-up data precludes a thorough understanding of the sustainability of treatment benefits and potential delayed adverse effects. Future studies with extended follow-up periods are necessary to evaluate the durability of BTxA's therapeutic effects and to monitor for any long-term complications. Furthermore, the retrospective nature of the data collection, the absence of a control group, and the single-center conduct of the study were identified as significant weaknesses. Effective treatment protocols require a comprehensive assessment of the consequences of overactivity on quality of life.

Future research endeavors should explore comprehensive treatment methods integrating botulinum toxin therapy with other therapeutic interventions, such as behavioral modifications and physical therapy(9).

CONCLUSION

Intravesical BTxA therapy has been demonstrated to be both safe and effective in treating individuals with overactive bladder syndrome who experience moderate functional impairment. This treatment has been shown to enhance patients' quality of life. Nevertheless, our study suggests that further research is necessary in the form of controlled, multicenter studies with larger sample sizes to validate and extend the results obtained.

Abbreviations

OAB: overactive bladder syndrome, ECOG PS: Eastern Cooperative Oncology Group Performance Scale, ICIQ: International Consultation on Incontinence Questionnaire, I-QOL: Incontinence Quality of Life

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