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RESEARCH ARTICLE

Efficacy of 200 IU OnabotulinumtoxinA (Botulinum Toxin Type A) in Patients with Idiopathic Overactive Bladder Resistant to Anticholinergic Treatment: A Retrospective Analysis

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Abstract

Objective: This study aimed to evaluate the efficacy and safety of 200 IU of onabotulinumtoxinA in patients with idiopathic overactive bladder (OAB) and urinary incontinence who had previously shown no response to anticholinergic treatment. This study also sought to examine the impact of a reduction in bladder wall thickness (BWT) on treatment outcomes.

Material and Methods: A retrospective analysis was conducted on patients treated between January 2016 and June 2022. Baseline symptoms and quality of life data were compared with those obtained six months post-treatment. Baseline ultrasound (US)-measured post-void residual urine (PVR) and BWT were recorded. Patients with a history of neurological disorders, anticholinergic-naive patients, those diagnosed with bladder cancer, and those with bladder outlet obstruction were excluded.

Results: This study included 60 patients (41 females and 19 males) with a mean age of 36.05 years. At six months, statistically significant improvements were observed in OAB symptoms, including average urination frequency, nocturia, and incontinence episodes ($p<0.001$). Noteworthy reductions in BWT were also observed (median and mean values decreased from 5.25 mm and 5.22 mm to 4.60 mm and 4.66 mm, respectively). Two patients experienced urinary tract infections, and none required clean intermittent catheterization (CIC).

Conclusions: OnabotulinumtoxinA demonstrated substantial improvements in symptoms and patient-reported outcomes in patients who previously failed to respond to anticholinergic treatment. BWT reduction may be a valuable parameter for evaluating treatment success, although further research with statistical analysis is necessary.

Keywords: botulinum toxin type A, onabotulinumtoxinA, overactive bladder, randomized controlled trial, urinary incontinence, bladder wall thickness

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INTRODUCTION

Overactive bladder (OAB) is commonly characterized by urinary urgency, frequency, and nocturia, which may or may not be accompanied by urge incontinence in the absence of a urinary tract infection. The International Continence Society (ICS) classifies OAB into two subgroups: neurogenic OAB and idiopathic (non-neurogenic) OAB (1). With an estimated prevalence of 12–19%, OAB significantly impacts the quality of life and is associated with a physical, psychological, social, and economic burden comparable to chronic conditions such as cancer, diabetes mellitus, and heart disease (2-5).

Initial management of OAB typically involves behavioral therapy and lifestyle modifications, as recommended by the American Urological Association (AUA) and European Association of Urology (EAU) guidelines (6). First-line pharmacotherapy—using antimuscarinic agents and β3 agonists—often follows; however, adverse effects and limited efficacy may necessitate alternative treatments (6, 7). In such cases, more invasive interventions, including intravesical botulinum toxin (BTX) injections, neuromodulation (pudendal or sacral), and augmentation cystoplasty, are considered. Among these, BTX injections are favored for their relatively minimally invasive nature and proven efficacy in reducing incontinence episodes and improving quality of life (8-12).

While previous randomized controlled trials support BTX doses of 100 IU for idiopathic OAB and 200 IU for neurogenic OAB (4, 13-15), no study to date has evaluated the impact of BTX on bladder wall thickness (BWT) in this patient population. Given that increased BWT—possibly due to fibrosis, edema, or inflammation—may correlate with OAB symptoms (16-18), the present study was designed to fill this gap.

The primary objective of this study is to assess the efficacy of 200 IU onabotulinumtoxinA in alleviating symptoms and improving quality of life in patients with idiopathic OAB and urge incontinence who are refractory to conventional medical therapy. The secondary objective is to evaluate the impact of BTX therapy on bladder wall thickness (BWT).

In addition, this study reveals a novel injection protocol in which 200 IU onabotulinumtoxinA is delivered via 20 injection sites rather than the manufacturer's recommended 30 points. This modified approach is examined to determine if it offers comparable or enhanced outcomes.

MATERIALS AND METHODS

This retrospective study analyzed 60 patients diagnosed with idiopathic OAB and urge incontinence for at least six months, all of whom had failed to respond to a minimum of two antimuscarinic agents and/or a β3 agonist over three months or more.

Patient Selection:

Inclusion Criteria:

- Diagnosis of idiopathic OAB with ≥6 months of urge incontinence
- Refractoriness to at least two antimuscarinic agents and/or a β3 agonist administered for at least three months

Exclusion Criteria:

- Neurological disorders
- Patients naive to anticholinergic therapy
- History of bladder cancer
- Bladder outlet obstruction

Non-neurogenic OAB was confirmed through a detailed clinical history, neurological examination, and, when indicated, imaging studies. Additionally, urodynamic tests were performed to differentiate non-neurogenic OAB from neurogenic bladder dysfunction. Patients with any neurological abnormality identified through clinical evaluation or imaging were excluded from the study.

Intervention:

Patients received 200 IU of onabotulinumtoxinA administered via cystoscopically guided injections at 20 sites (10 IU per site), differing from the manufacturer's recommended distribution of 30 injection points. Sedation or local anesthesia was provided, and cystoscopy was utilized to ensure that injections avoided the ureteral orifices and trigone, thereby minimizing the risk of complications.

Bladder Wall Thickness Measurement:

BWT was measured using a standardized ultrasound protocol. Patients were positioned in a seated position, and measurements were taken using a designated ultrasound

device with defined settings (e.g., probe frequency and measurement landmarks) to ensure reproducibility and accuracy.

Post-Procedure Care and Follow-Up:

- Patients were discharged on the same day following the procedure and prescribed oral ciprofloxacin (500 mg) for three days.
- Anticholinergic therapy was discontinued after BTX administration.
- Follow-up assessments were performed at 4 and 6 weeks post-procedure and included:
  - Bladder diaries to record urinary frequency and incontinence episodes
  - Quality of life questionnaires
  - Ultrasound evaluation of post-void residual (PVR) and BWT

Statistical Analyses:

Statistical analyses were performed using the SPSS software version 26. The variables were investigated using Kolmogorov-Simirnov/Shapiro-Wilk's test to determine whether or not they are normally distributed. Descriptive analyses were presented (using the table of frequencies for the ordinal variables) using medians and interquartile range (IQR) for the non-normally distributed and ordinal variables. Non-parametric tests were conducted to compare these parameters.

RESULTS

The present study comprised a sample of 60 patients, consisting of 41 females and 19 males, with a median age of 35 (IQR 25-45) years. The sample size afforded a comprehensive analysis and provided a representative sample of patients with idiopathic overactive bladder (OAB). The median body mass index (BMI) was 25.56 (IQR 23.28-28.08).

At the 6-month assessment, statistically significant improvements were observed in several OAB symptoms compared to the baseline. Specifically, there was a reduction in the average number of daily urination, nocturnal urination frequency, and incontinence episodes (P <0.001) (see Table 1).

Table 1. Here is the table summarizing the preoperative and postoperative 6th-month evaluation results:

Parameter	Pre-injection Median (IQR)	Pre-injection Mean (SD)	Post-injection Median (IQR)	Post-injection Mean (SD)	p-value
Nocturia	1 (0-2)	1.35 ± 1.56	0 (0-0)	0.20 ± 0.44	<0.001
Frequency	10 (8-10)	10.05 ± 2.22	4 (4-5.75)	4.62 ± 1.07	<0.001
Incontinence	1 (0-3)	1.42 ± 1.82	0 (0-0)	0 ± 0	<0.001
QoL	2 (1-2)	1.92 ± 0.74	4 (3-4)	3.52 ± 0.50	<0.001
Bladder Wall Thickness	5.25 (4.65-6.00)	5.22 ± 0.76	4.60 (4.20-5.15)	4.66 ± 0.58	<0.001
PMR	20 (0-34.25)	20.57 ± 25.47	20 (0-30)	18.10 ± 19.05	0.753
Qmax	30 (26-35)	30.98 ± 5.82	30 (26-35)	31.02 ± 5.80	0.317
Qave	18 (16-20)	18.03 ± 3.47	18 (16-20)	18.17 ± 3.47	0.317

This table provides a clear comparison of the pre-injection and post-injection values along with their statistical significance.

Sex: 19 males 41 females

Age: mean age 36.05 ± 11.72 years; median age: 35 (25 - 45) years

BMI: mean:25.73 ± 3.22 median 25.56 (23.28 – 28.08)

The following significant improvements in OAB symptoms were observed:

1. Urination Frequency: A statistically significant reduction in the average number of daily urinations was observed ($p<0.001$).
2. Nocturia: A statistically significant reduction in the frequency of nocturnal urination ($p<0.001$).
3. Incontinence Episodes: A statistically significant reduction in the number of incontinence episodes ($p<0.001$).
4. Bladder Volume Reductions: Median bladder weight (BWT) decreased from 5.25 mm (IQR 4.65-6.00) to 4.60 mm (IQR 4.20-5.15). (see Table 1).

Two patients developed urinary tract infections. Their post-void residual (PVR) measurements were 50 cc at week 4 and 60 cc during the early postoperative period. None of the patients required clean intermittent catheterization (CIC). Both patients with infections were prescribed antibiotics for two weeks and were symptom-free after treatment.

DISCUSSION

Previous studies have demonstrated that the use of 200 IU of onabotulinumtoxinA (BTX) leads to significant improvements in the quality of life and symptoms of overactive bladder (OAB) in patients who do not respond to anticholinergic medications. These results are consistent with previous research suggesting a link between bladder wall thickness (BWT) and OAB pathophysiology. However, this study did not investigate any disparities in BWT between men and women, which should be the focus of future studies. All patients were informed of the off-label use of BTX and provided consent prior to receiving the injections. Even though the study design was retrospective and the sample size was small, the findings were consistent with those of previous randomized controlled trials.

Comparisons with Previous Studies

The study results were reinforced by the analysis of larger datasets and more recent randomized controlled trials, offering further evidence of the effectiveness of the intervention. For instance, in a randomized controlled trial conducted by Tincello et al., 200 IU BTX was administered to 240 patients with idiopathic OAB, resulting in a significant decrease in the frequency of urge incontinence episodes from 6.20 to 1.67 at month 6 compared to baseline, which supports the findings of our study (15). Concurrent improvements in the urinary frequency were also consistent with our results. Another randomized controlled study involving 34 patients found improvements in the urinary frequency and frequency of urinary incontinence episodes after receiving 200 IU BTX injections, similar to our findings (11).

Quality of Life and Symptom Improvement

Our study findings indicate that the mean quality of life (QoL) score significantly improved from 1.92 ± 0.74 to 3.52 ± 0.50 ($p<0.001$) following the treatment, suggesting a positive impact on the participants' quality of life. To assess the quality of life of patients with OAB or urinary incontinence (UI), questionnaires such as the Incontinence Quality of Life (I-QoL) and Health-Related QoL (HRQoL) have been utilized in previous studies, reporting improvements similar to our study (4, 14, 17). Additional measures, such as the Overactive Bladder Symptom Score (OAB-SS) and Patient Global Impression of Improvement (PGI-I), have also shown comparable enhancements in patient outcomes (15, 16). Although our study participants reported improvements in their quality of life using a self-report 0–4 rating scale, future studies may benefit from incorporating both self-report and objective measures to obtain a more comprehensive understanding of the impact of interventions on QoL.

Dose-Response Relationships and Adverse Effects

While there is no definitive consensus on the optimal dose of botulinum toxin for treating idiopathic OAB or UI, a study by Dmochowski et al. investigated the relationship between dose response and adverse effects in both male and female patients. Statistically significant improvements in QoL scores and UI episodes were observed at doses of 150 IU or higher (14). These findings suggest that the optimal dose of BTX for the treatment of overactive bladder syndrome may be 150 IU or higher. However, higher doses are associated with an increased need for CIC. In our study, administering BTX at a dose of 200 IU resulted in significant improvements in UI symptoms and QoL without requiring CIC. The efficacy of the intervention was consistent with that of other studies, and the lower incidence of adverse effects may be attributed to the smaller sample size.

The most common adverse effects associated with botulinum toxin injections include the need for CIC due to increased

post-void residual (PVR) and urinary retention, followed by urinary tract infections (UTIs) (10). The incidence of these adverse effects is dose-dependent, with urinary retention rates ranging from 16% to 43% and UTI rates ranging from 8.6% to 44% in studies examining botulinum toxin injections at a dose of 200 IU (11,12,15,22). None of our patients experienced urinary retention or increased PVR necessitating CIC, while only two patients developed UTIs. This observation may be due to the small sample size, which limits the analysis of the adverse effects..

Injection Technique and Bladder Wall Thickness

Botulinum toxin is administered to the detrusor muscle while avoiding the ureteral orifices and trigones to prevent vesicoureteral reflux or urinary tract infections (2). A study advocating injections in regions rich in neurons, such as the trigone and floor of the bladder, indicated that this approach prevented an increase in PVR during the follow-up after treatment (23). In our study, the trigone and ureteral orifices were spared, and no cases of urinary retention or increased PVR requiring CIC were observed after the injections.

Bladder wall thickness is known to increase due to fibrosis, edema, or inflammation and plays a crucial role in the pathophysiology of OAB. Previous studies have utilized ultrasound as an affordable, noninvasive, and widely accessible diagnostic tool to measure bladder wall thickness and diagnose OAB. These studies have demonstrated statistically significant reductions in bladder wall thickness following anticholinergic therapy compared with baseline (16, 17, 24). In our study, we observed statistically significant reductions in bladder wall thickness at the month 6 visit after BTX injections. Comperat et al. reported a lower level of bladder fibrosis in patients who received BTX injections than in those who did not, consistent with our findings (18).

Limitations

The limitations of this study include its retrospective design, absence of a control group, small sample size, and reliance on self-reported measures of quality of life. Future research should incorporate prospective studies with control groups to validate these findings and examine the dose-response relationship. Additionally, investigations should incorporate longitudinal designs to understand the temporal dynamics of these relationships better and assess potential confounding variables that may influence observed outcomes.

CONCLUSION

The use of onabotulinumtoxinA has demonstrated promising results in improving the symptoms and overall well-being of patients who do not respond to anticholinergic therapy. Decreased bladder wall thickness may be a reliable indicator of treatment efficiency. To validate its effectiveness further, more substantial and comprehensive long-term clinical trials are necessary.

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Data Availability Statement: All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding authors.

Conflict of Interest: The authors declare no conflicts of interest.

Informed Consent: Written informed consent was obtained from all participants (or their parent/legal guardian/next of kin) to participate in this study.

Ethical Approval: Ministry of Health Hisar Hospital Medical and Ethical Advisory Board Date: 10.11.2023 Protocol: 23/54. This study was conducted in accordance with the Declaration of Helsinki of the World Medical Association.

Author Contributions: All authors contributed to the conception and design of this study. Material preparation, data collection, and analysis were performed by Ali Egemen Avci, Basri Çakıroğlu,Mehmet Gürkan Arikan, and Meftun Culpan. The first draft of the manuscript was written by Ali Egemen Avci, and all the authors commented on the previous versions of the manuscript. All authors have read and approved the final manuscript.

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