

Quality of life in patients with overactive bladder following botulinum toxin treatment: a preliminary report

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ABSTRACT

Objectives: The aim of the present study was to compare the subjective quality of life in patients with overactive bladder (OAB) prior to intravesical botulinum toxin injection and three and six months thereafter.

Material and methods: The study included 50 women diagnosed with OAB refractory to oral pharmacotherapy. The respondents completed four questionnaires, ICIQ-OAB, ICIQ-OABqol, ICIQ-LUTSqol and a dedicated clinicodemographic survey.

Results: Intravesical injection of botulinum toxin A contributed to the attenuation of OAB-related ailments and resultant improvement of the quality of life. The ICIQ-OAB scores at three and six months post-injection were significantly lower than at the baseline ($p < 0.001$), implying that the treatment reduced the severity of OAB manifestations. OAB ailments had, without a doubt, a detrimental effect on the quality of life, as shown by high ICIQ-OABqol and ICIQ-LUTSqol scores before the treatment. Administration of botulinum toxin A was associated with a significant decrease in scores for all domains of the ICIQ-OABqol and ICIQ-LUTSqol scales ($p < 0.001$).

Conclusions: Botulinum toxin is an effective treatment option in patients with OAB who failed to respond to anticholinergic therapy. Botulinum toxin injections contributed to a significant improvement in the quality of life during a six-month follow-up.

Key words: botulinum toxin; overactive bladder; urinary incontinence; quality of life; onabotulinum toxin A

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INTRODUCTION

According to the International Continence Society (ICS), overactive bladder (OAB) is defined as urgency, with or without urge incontinence, usually with frequency and nocturia, not accompanied by an underlying urinary tract infection or other established pathology [1]. The diagnosis of OAB is based primarily on patient-reported ailments. Those ailments may considerably deteriorate the quality of life and cause various social, work-related, psychological and sexual problems [2]. Research conducted in Europe and the United States showed that the manifestations of OAB were present in more than 10% of the general population, with the risk double in persons > 65 years of age [3]. The results of another

epidemiological study suggest that the symptoms of OAB may occur in up to 16% of persons aged 40 years or older [4]. Such a high prevalence of this disorder warrants research on novel therapies that effectively control the symptoms of OAB. Botulinum toxin has been recognized as an effective treatment for some diseases, the symptoms of which could not be sufficiently controlled with available therapies [5]. In 2013, botulinum toxin A was approved by the US Food and Drug Administration (FDA) for the management of OAB manifestations associated with urge incontinence, urgency and frequency in adult patients who did not respond adequately or were intolerant to anticholinergic agents [6].

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Objectives

The aim of the present study was to compare the subjective quality of life in OAB patients prior to intravesical botulinum toxin injection and three and six months thereafter. This report presents preliminary data regarding the quality of life in OAB patients treated with botulinum toxin. The study is ongoing, with the final number of participants expected to be twice as high as presented herein.

MATERIAL AND METHODS

Research instruments

The study was conducted with four questionnaires: 1) International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB), 2) International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module (ICIQ-OABqol), 3) International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life Module (ICIQ-LUTSqol), and 4) a dedicated survey to collect sociodemographic data and selected clinical characteristics of the respondents, developed by the authors. The ICIQ-OAB consists of four questions about frequency, nocturia, urgency and urinary incontinence. The higher the score for each item, the higher the severity of the symptom. In the present study, the items included in the ICIQ-OABqol questionnaire were grouped into four domains: 1) Coping, 2) Concern, 3) Sleep, and 4) Social Interaction. According to Coyne et al. [7], such a four-factor solution is most accurate and interpretable. The items included in the ICIQ-LUTSqol questionnaire were grouped into eight domains, as suggested by Hebbert et al. [8], based on the King's Health Questionnaire (KHQ). An additional response, "not applicable", was added in the case of three questions about relationships, sex life and family to enable the respondents to answer all questions included in the survey. Calculating the overall result for the ICIQ-LUTSqol instrument, the response "not applicable" to the questions about personal relationships was scored no points. Question no. 20 of the ICIQ-LUTSqol refers to the overall impact of lower urinary tract symptoms on everyday life, with the answers scored from 0 to 10. The scores for individual domains of the three instruments (ICIQ-OAB, ICIQ-OABqol and ICIQ-LUTSqol) were normalized to a 0 to 100 points system, so each domain had an equal contribution to the overall score. A post-treatment decrease in the domains' scores was interpreted as a beneficial effect of botulinum toxin treatment on the quality of life. The scale describing the overall impact of individual symptoms for the patient, included in the ICIQ-OAB and ICIQ-LUTSqol instruments, was not considered during the analysis since sufficient information in this matter could be obtained at <http://www.iciq.net>.

Organization and flow of the study

The analysis of the quality of life after botulinum toxin treatment included 50 women aged between 32 and 77 years. The inclusion criteria of the study were: OAB unresponsive to oral pharmacotherapy, age ≥ 18 years, and written informed consent for participation. Patients were not eligible for the study if they had a history of botulinum toxin treatment within six months before the enrollment, presented with urinary tract infections and/or predominant stress incontinence, and/or underwent urogynecological surgeries. The characteristics of the study group are presented in Table 1.

The patients were recruited at the Department of Gynecology, Endocrinology and Gynecologic Oncology of the 1st Public Clinical Hospital in Szczecin, affiliated with the Pomeranian Medical University. The study was conducted between November 2017 and December 2020.

The study consisted of three stages. The first stage was conducted before botulinum toxin treatment. After providing written informed consent for participation, the patients were asked to fill in the ICIQ-OAB, ICIQ-OABqol and ICIQ-LUTSqol forms and the dedicated survey. Examination with the three validated scales was repeated three and six months following the treatment. The dedicated survey was filled in only once, before the botulinum toxin treatment. Each patient received 100 units of botulinum toxin A (Botox[®], Allergan Inc., Irvine, CA, USA), injected across 20 sites in the detrusor muscle (5 units in 0.5 ml solution per site), except the trigonum vesicae. Fosfomycin was used for antimicrobial prophylaxis on the treatment day and one day before and one day after the treatment.

The protocol of the study was approved by the Local Bioethics Committee at the Pomeranian Medical University in Szczecin (decision no. KB-0012/125/17).

Statistical analysis

Statistical analysis of the results was conducted with Statistica 13 package. The results are presented as descriptive statistics, *i.e.*, means, standard deviations, medians, frequencies and percentages. The normal distribution of the study variables was verified with the Shapiro-Wilk test. Friedman ANOVA was used to compare multiple dependent samples (before the treatment, three and six months after the treatment). The results were considered statistically significant at $p \leq 0.05$.

RESULTS

The intravesical administration of botulinum toxin A contributed to a significant attenuation of the OAB symptoms and resultant improvement of the quality of life. The results are presented in Tables 2 and 3.

Three and six months after the intravesical injection of botulinum toxin, the ICIQ-OAB scores were significantly

Table 1. Characteristics of the study group		
General characteristics		
Age [years], mean \pm SD; median		58.52 \pm 10.12; 60.50
BMI [kg/m ²], mean \pm SD; median		28.87 \pm 5.21; 28.44
Marital status	married	36 (72.00%)
	common law	2 (4.00%)
	divorced	4 (8.00%)
	widowed	6 (12.00%)
	unmarried	2 (4.00%)
Place of residence	city	37 (74.00%)
	countryside	13 (26.00%)
Education	vocational	9 (18.00%)
	secondary	19 (38.00%)
	higher	15 (30.00%)
	primary	7 (14.00%)
Occupational activity	health pension	7 (14.00%)
	retirement pension	26 (52.00%)
	occupationally active	16 (32.00%)
	unemployed	1 (2.00%)
Type of work	blue collar worker	18 (36.00%)
	white collar worker	31 (62.00%)
	blue/white collar worker	1 (2.00%)
Urinary bladder problems in close family members	no	35 (70.00%)
	yes	15 (30.00%)
Gravidity	0	5 (10.00%)
	1	9 (18.00%)
	2	21 (42.00%)
	3	11 (22.00%)
	4	4 (8.00%)
Parity	0	5 (10.00%)
	1	12 (24.00%)
	2	23 (46.00%)
	3	8 (16.00%)
	4	2 (4.00%)

SD — standard deviation; BMI — body mass index

lower than before the treatment ($p < 0.001$). Significant changes were observed for each ICIQ-OAB item, *i.e.*, frequency, nocturia, urgency and urinary incontinence. The most evident decrease in symptom severity score was observed in the case of urgency. The post-treatment decrease in the ICIQ-OAB scores implies that the manifestations of OAB attenuated after botulinum toxin injection. However, it needs to be emphasized that after an initial decrease by month 3, the severity of OAB symptoms increased significantly between three- and six-months post-injection.

The analysis of the quality of life measured with the ICIQ-OABqol scale demonstrated that botulinum toxin treatment contributed to significant changes across all domains compared with the baseline ($p < 0.001$). The most evident improvement in the quality of life, whether at three- or six-months post-treatment, was found in the Coping domain. Notably, no significant changes in the ICIQ-OABqol scores were documented between three- and six-months post-injection, implying that the quality of life improved significantly within the initial three months and then remained unchanged by month six.

The scores for all domains of the ICIQ-LUTSqol scale decreased significantly after botulinum toxin treatment ($p < 0.001$). The most evident improvement, both three- and six-months post-injection, was observed for the Physical Limitations domain. Detailed analysis of the ICIQ-LUTSqol scores showed that after an initial decrease, the impact of OAB-related ailments on the quality of life increased between three- and six-months post-injection. However, the change was significant solely for two domains, Personal Relationships and Sleep/Energy.

During the study, three (6%) patients reported adverse events of botulinum toxin treatment, namely urinary tract infection after the injection ($n = 2$, 4%) and urinary retention that required clean intermittent catheterization (CIC) ($n = 1$, 2%).

DISCUSSION

OAB manifestations, without a doubt, exerted an unfavorable effect on the quality of life of our patients, as shown by high ICIQ-OABqol and ICIQ-LUTSqol scores at the baseline. The present study showed that the quality of life in OAB improved significantly after botulinum toxin injection. This observation is consistent with published data about the outcomes of botulinum toxin treatment in patients with OAB.

Our study demonstrated that botulinum toxin injection contributed to a decrease in the frequency of urinary incontinence (UI) episodes associated with OAB. Similar findings were reported previously by Hamid et al. [9], who observed a substantial reduction in UI episodes per day from baseline to weeks 1 and 12 after onabotulinum toxin A injection. Moreover, those authors reported a reduction in urgency, nocturia and micturition episodes, which is also consistent with the results of our present study. Tamburro et al. [10] analyzed the quality of life in OAB at 12 weeks after onabotulinum toxin A injection using the 36-Item Short-Form Health Survey (SF-36), Overactive Bladder Screener and Treatment Benefit Scale questionnaires. In up to 87% of patients participating in that study, OAB-related ailments attenuated after the treatment, with the most evident improvement observed in the Emotional Role Functioning domain of the SF36. Our present study

Table 2. Comparison of scores for the International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ-OAB), International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module (ICIQ-OABqol) and International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life Module (ICIQ-LUTSqol) scales before botulinum toxin treatment and three and six months post-treatment

Questionnaire		Before treatment	3 months	6 months	p	p1 vs p2	p1 vs p3	p2 vs p3
		mean ± SD; Me	mean ± SD; Me	mean ± SD; Me				
ICIQ-OAB	How often do you pass urine during the day?	64.50 ± 25.80; 75.0	17.00 ± 20.48; 0.00	25.00 ± 20.82; 25.0	<0.001	<0.001	<0.001	0.014
	During the night, how many times do you have to get up to urinate, on average?	73.00 ± 25.67; 75.0	38.50 ± 31.63; 25.0	45.00 ± 30.3; 50.0	< 0.001	< 0.001	< 0.001	0.033
	Do you have to rush to the toilet to urinate?	84.00 ± 22.45; 100.00	34.50 ± 26.19; 25.0	43.00 ± 26.75; 50.0	< 0.001	< 0.001	< 0.001	0.004
	Does urine leak before you can get to the toilet?	64.00 ± 25.83; 75.0	20.50 ± 23.52; 29.0	29.00 ± 24.93; 25.0	< 0.001	< 0.001	< 0.001	0.011
	Overall score	285.50 ± 65.68; 287.5	110.50 ± 84.38; 75.0	142.00 ± 79.45; 125.0	< 0.001	< 0.001	< 0.001	< 0.001
ICIQ-OABqol	Coping	68.20 ± 21.99; 71.25	27.30 ± 26.95; 20.0	32.30 ± 28.18; 26.25	< 0.001	< 0.001	< 0.001	0.221
	Concern	60.74 ± 22.39; 60.0	22.40 ± 23.03; 14.3	27.49 ± 26.27; 20.0	< 0.001	< 0.001	< 0.001	0.284
	Sleep	60.72 ± 22.94; 62.0	27.60 ± 25.49; 20.0	33.84 ± 26.14; 26.0	< 0.001	< 0.001	< 0.001	0.174
	Social Interaction	40.16 ± 26.22; 36.0	13.76 ± 19.71; 4.0	15.76 ± 20.72	< 0.001	< 0.001	< 0.001	0.738
	Overall score	229.82 ± 82.11; 228.4	91.06 ± 91.59; 52.93	109.39 ± 96.49	< 0.001	< 0.001	< 0.001	0.316
ICIQ-LUTSqol	Role Limitations	78.00 ± 23.68; 83.3	28.00 ± 32.02; 25.0	34.67 ± 28.34; 33.3	< 0.001	< 0.001	< 0.001	0.089
	Physical Limitations	81.67 ± 23.63; 83.3	30.67 ± 33.05; 16.7	37.00 ± 29.79; 33.3	< 0.001	< 0.001	< 0.001	0.095
	Social Limitations	54.33 ± 32.61; 58.3	17.67 ± 26.17; 0.00	18.67 ± 24.20; 0.00	< 0.001	< 0.001	< 0.001	0.936
	Personal Relationships	47.28 ± 35.17; 55.6	14.49 ± 24.55; 0.00	19.26 ± 26.10; 0.00	< 0.001	< 0.001	< 0.001	0.034
	Emotions	57.33 ± 27.25; 55.6	20.67 ± 24.80; 11.1	24.67 ± 25.03; 22.2	< 0.001	< 0.001	< 0.001	0.280
	Sleep/Energy	64.67 ± 25.56; 66.7	29.67 ± 25.49; 33.3	36.33 ± 27.08; 33.3	< 0.001	< 0.001	< 0.001	0.044
	Undertaking activities mentioned in the survey	72.17 ± 23.37; 75.0	33.83 ± 28.74; 25.0	42.00 ± 30.30; 41.7	< 0.001	< 0.001	< 0.001	0.005
	Embarrassment	67.33 ± 34.00; 66.7	27.33 ± 27.51; 33.3	31.33 ± 33.95; 33.3	< 0.001	< 0.001	< 0.001	0.535
	Overall score	519.94 ± 169.33; 545.8	201.17 ± 198.45; 145.83	242.00 ± 199.40; 187.5	< 0.001	< 0.001	< 0.001	0.153

Me — Median; SD — standard deviation; p1 — score before treatment; p2 — score at three months post-treatment; p3 — score at six months post-treatment

Table 3. Answers to question no. 20 of the International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life Module (ICIQ-LUTSqol) scale, scored from 0 to 10

Question	Before treatment	3 months	6 months	p	p1 vs p2	p1 vs p3	p2 vs p3
	mean ± SD; Me	mean ± SD; Me	mean ± SD; Me				
Overall, how much do urinary symptoms interfere with your everyday life?	8.88 ± 1.32; 9.0	2.74 ± 2.93; 2.0	3.42 ± 3.21; 2.0	< 0.001	< 0.001	< 0.001	0.109

Me — Median; SD — standard deviation; p1 — score before treatment; p2 — score at three months post-treatment; p3 — score at six months post-treatment

also showed a significant improvement in the Emotions domain of the ICIQ-LUTSqol, including such items as feeling depressed, anxious or nervous, and feeling bad about yourself. However, the most evident improvement was found in the other two domains, the Coping domain of the ICIQ-OABqol scale and the Physical Limitations domain of

the ICIQ-LUTSqol scale. It needs to be stressed that women participating in the study conducted by Tamburro et al. [10] tended to be obese; also, the participants of our study presented with excess body weight, with a mean BMI of 28.44 kg/m². Juszczak et al. [11] analyzed the effectiveness of botulinum toxin A treatment in women with idiopathic

OAB, determining the quality of life with the King's Health Questionnaire (KHQ) and OAB Symptom Scores (OABSS) scale. The study showed that the impact of OAB symptoms on the quality of life measured by most of the KHQ domains decreased significantly three and six months after botulinum toxin injection. However, although the difference was not statistically significant, the overall negative impact of bladder-related symptoms on the quality of life at six- and nine-months post-injection was slightly higher than at three months post-injection. A similar phenomenon was also observed in our present study. The last item of the ICIQ-LUTSqol scale describes the degree to which urinary symptoms interfere with the everyday life of the respondent. In our present study, the scores for this item increased between three- and six-months post-injection, but the difference was not statistically significant. Similar to our present study, Juszczak et al. also observed a significant decrease in the severity of OAB manifestations after the administration of botulinum toxin A. According to those authors, the severity of the ailments decreased up to nine months post-treatment and then increased insignificantly. The ICIQ-OAB scores for our participants at both three and six months after the intravesical injection of botulinum toxin were significantly lower than before the treatment, corresponding to a decrease in the OAB symptom severity. However, a statistically significant increase in the ICIQ-OAB scores was observed between months three and six, which implies that after an initial attenuation, the severity of the ailments tended to increase. Rechberger et al. [12] used the KHQ to compare the quality of life before botulinum toxin injection and three months after the treatment. The authors observed a significant decrease in the impact of OAB on the quality of life in most of the KHQ domains, except for Social Limitations and Partner Relationships.

Some randomized controlled trials compared the outcomes in patients receiving botulinum toxin and placebo injections. While the present study included solely women treated with botulinum toxin A, without a control group, our findings are consistent with the results of published randomized trials, demonstrating that this neurotoxin is effective in the treatment of OAB. According to Chapple et al. and Nitti et al. [13, 14], the intravesical injection of 100 units of onabotulinum toxin A significantly reduced the severity of all OAB symptoms compared with the placebo in patients with OAB and UI who did not respond adequately to anticholinergic therapy. Moreover, unlike the placebo groups, patients receiving onabotulinum toxin A reported a clinically relevant and statistically significant ($p < 0.001$) improvement in all domains of the Incontinence Quality of Life (I-QOL) and KHQ scales at 12 weeks post-injection; this implies that botulinum toxin treatment had a beneficial effect on the quality of life. Our present study also showed

a significant improvement in the quality of life across all domains of the ICIQ-OABqol and ICIQ-LUTSqol scales.

The clinical benefits of onabotulinum toxin A injection were shown by Fowler et al. [15]. Those authors demonstrated that intravesical injection of botulinum toxin A contributed to an improvement in the health-related quality of life in patients with urinary incontinence associated with OAB, who did not respond adequately to conventional pharmacotherapy. The improvement in the quality of life was observed starting two weeks post-injection and persisted up to 36 weeks. In another study, Sahai et al. [16] showed that both the overall KHQ score and the scores for most of the individual domains improved substantially 12 weeks after the injection of onabotulinum toxin A compared with placebo ($p < 0.05$). The scores for the other two domains, Personal Relationships and Sleep Energy, also improved after the treatment, albeit not significantly. Our present study demonstrated a significant improvement across all domains of the ICIQ-LUTSqol scale, the King's Health Questionnaire adapted for use within the ICIQ structure. Sherif et al. [17] compared the outcomes of posterior tibial nerve stimulation (PTNS) and botulinum toxin A injection in patients with idiopathic OAB. While the botulinum toxin injections were more effective in OAB treatment, they were also associated with a higher number of adverse events.

Botulinum toxin injections were also shown to be effective in treating another form of OAB, neurogenic detrusor overactivity (NDO), not analyzed in the present study. In randomized placebo-controlled trials, botulinum toxin A injections (200 and 300 units) contributed to a significant reduction in UI episodes and improved urodynamic parameters in NDO patients [18–21]. Moreover, botulinum toxin injections were shown to exert a beneficial effect on the quality of life in NDO [22,23]. It is also worth mentioning that onabotulinum toxin A is well tolerated and effective in the treatment of NDO in children [24, 25]. Available evidence suggests that botulinum toxin is also effective in treating non-neurogenic OAB in children and adolescents [26, 27]. Finally, Christiansen et al. [28] found no differences in the duration of the beneficial effect of botulinum toxin treatment in patients with idiopathic and neurogenic OAB.

Analysis of correlations between the quality-of-life scales, ICIQ-OABqol and ICIQ-LUTSqol, and symptom severity scale, ICIQ-OAB, confirmed a link between OAB-related ailments and deterioration of the quality of life. Hence, a substantial attenuation of OAB symptoms was a principal contributor to the quality-of-life improvement in our patients.

Our study was not free from potential limitations. The long-term effectiveness of botulinum toxin injection cannot be evaluated based on a six-month follow-up. Nevertheless, Ginsberg et al. [29] reported a persistent, clinically-relevant improvement in the quality of life during a long-term (3.5-year)

observation of patients with OAB and UI receiving 100 units of onabotulinum toxin A.

CONCLUSIONS

Botulinum toxin is an effective treatment option in patients with OAB-related ailments who failed to respond to pharmacotherapy therapy. Botulinum toxin injections contributed to a significant improvement in the quality of life in patients with OAB symptoms during a six-month follow-up.

Article information and declarations

Conflict of interest

All authors declare no conflict of interest.

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