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Intravesical botulinum-A toxin in children with refractory non-neurogenic overactive bladder

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Keywords
Overactive bladder; Urinary incontinence; Pediatrics; Botulinum toxins; Type A; Urotherapy; Refractory incontinence

Abbreviations
BTX-A, Botulinum-A toxin; EBC, Expected bladder capacity; FBV, Functional bladder volume; ICCS, International Children's Continence Society; IU, International units; MVV, Maximum voided volume; OAB, Overactive bladder; PVR, Postvoid residual; UDS, Urodynamic study; UTI, Urinary tract infection

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Summary

Introduction
Overactive bladder (OAB) with urinary incontinence poses a potentially significant impact on daily activities and quality of life. OAB can be unresponsive to specific urotherapy and antispasmodic medication. Due to its successful outcomes in the treatment of neurogenic bladder, intravesical botulinum-A toxin (BTX-A) became a possible solution for children refractory to treatment.

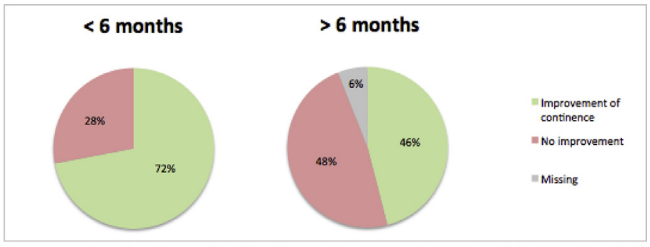
Objective
To analyse the outcomes of intravesical BTX-A injections on bladder volume and incontinence in children with refractory OAB.

Study design
The charts of children diagnosed with refractory non-neurogenic OAB who underwent BTX-A treatment in our centre since 2011 were retrospectively analysed. The functional bladder volume (FBV) is expressed as a percentage of the expected bladder capacity (EBC) for age. Dependent variables were compared using the Wilcoxon Signed Rank test. A multivariate logistic regression was used to identify predictors of the response on urinary incontinence.

Results
Fifty children (41 boys) with a median age of 9.9 years were included. In the short term, there was a significant increase in FBV after initial BTX-A treatment from a median of 52.9%–70% ($p = 0.000$). In the short (<6 months) and long term (6–12 months) 72% and 46% showed improvement of continence, respectively. Male gender and small baseline FBV predict a positive outcome on continence in the long term. The most prevalent complications were urinary tract infections occurring in five cases (10%).

Discussion
Although BTX-A injections serve as an effective therapy to increase bladder volume in non-neurogenic OAB children, the outcomes on urinary incontinence are highly variable. This may be a consequence of the multifactorial aspects of this condition. BTX-A will enable children to inhibit their bladder urgency. The effectiveness of post-BTX-A urotherapy training will therefore most probably be higher. We believe that BTX-A injections should be reserved for children refractory to both specific urotherapy and medication. An appropriate population seems to be children with severe OAB symptoms, confirmed detrusor overactivity in urodynamic study and reduced bladder volume.

Conclusion
In refractory OAB children, BTX-A injections are safe and effective in enlarging bladder volume and reducing OAB symptoms, particularly in the first six months after injection.



Response on urinary incontinence after initial BTX-A treatment in the short (< 6 months) and long term (6-12 months).

Summary Figure

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Introduction

Urinary incontinence is common in the paediatric population, frequently this is a result of an overactive bladder (OAB) [1]. According to the classification of the International Children's Continence Society (ICCS), OAB is characterised by symptoms of urgency and frequency, often accompanied by urinary incontinence [1]. It affects approximately 5—12% of the children aged 5—10 years. This condition poses a significant impact on daily activities and quality of life [2].

First-line treatment for OAB is standard urotherapy. This implies bladder re-education or rehabilitation which aims to improve the filling and voiding function of the bladder-sphincter unit [3]. Comorbid problems, such as constipation, urinary tract infections and behavioural disorders, also need to be treated [1]. When standard urotherapy is not effective, the next step is specific urotherapy. This consists of pelvic floor biofeedback, cognitive behavioural therapy, psychotherapy and education [1,4]. In our hospital, if outpatient urotherapy is unsuccessful, children are offered inpatient urotherapy. This is a ten-day cognitive bladder training program and an intensive form of urotherapy reserved for therapy-resistant children, with a success rate of up to 75% [5]. In addition to specific urotherapy, pharmacological oral treatment with anticholinergic agents and/or mirabegron (hereinafter referred to as antispasmodic medication) can be added. Besides a lack of effect, not infrequently side effects, such as behavioural changes, dry mouth, constipation and blurred vision, cause medication cessation.

For children with refractory OAB unresponsive to specific urotherapy and oral medication, botulinum toxin is a possible solution [6]. Botulinum toxin is a potent neurotoxin produced by the Gram-negative, rod shaped anaerobic bacterium Clostridium Botulinum. Its efficacy is based on inhibiting calcium-mediated release of acetylcholine vesicles at the presynaptic neuromuscular junction in peripheral nerve endings, resulting in temporary flaccid muscle paralysis [6]. Injections are equally distributed into the detrusor muscle of the bladder. Successful outcomes in the treatment of neurogenic bladder by intravesical botulinum-A toxin (BTX-A) injections have been reported [7].

For non-neurogenic OAB, in contrast to adult study populations [8], studies on BTX-A in children are scarce and performed in small study groups. For example, Marte et al. [9] and Hoebeke et al. [10] reported the intravesical BTX-A treatment results of 21 and 15 children, respectively. Both showed a significant improvement in the urinary incontinence episodes after treatment, though objective urodynamic parameters were lacking. On the other hand, Al Edwan et al. [11] prospectively described a larger cohort of 46 children with idiopathic OAB receiving BTX-A injections. After 12 weeks, this group showed significant improvement of OAB symptoms. Improvement was seen in urodynamic parameters including involuntary detrusor contractions, compliance and bladder volume as well as quality of life. The deficit of long-term outcomes and small study cohorts demand for further research in this population of OAB children receiving BTX-A injections.

The aim of this study was to assess the outcomes of intravesical botulinum-A toxin injections in a representative cohort of children with refractory OAB. We hypothesized that treatment with BTX-A injections would significantly enhance the bladder volume enabling children to better inhibit bladder urgency.

Patients and methods

The institutional review board committee classified the present study as exempt of the Medical Research Involving Human Subjects Act. Data from medical charts have been retrospectively collected and anonymized. To be included in the study children must be diagnosed with OAB, unresponsive to urotherapy and antispasmodic medication and treated with intravesical BTX-A injections under the age of 18 years (between January 2011 and January 2020).

Exclusion criteria were a history of pelvic surgery, anatomical abnormalities, neurogenic bladder, syndromes that affect the bladder functions, previous treatment with BTX-A injections and an additional surgical intervention during the same procedure. Pre-operative data was collected including medical history, OAB symptoms (urgency, frequency and urinary incontinence), drug therapy, uroflowmetry and urodynamic study (UDS). High frequency is determined as a voiding frequency of eight or more times per day, according the ICCS-criteria. Expected bladder capacity (EBC) in milliliters (ml) is calculated by the formula: [age (years) + 1] × 30 ml [1]. The functional bladder volume (FBV) is computed with the maximum voided volume (MVV) expressed as a percentage of EBC for age.

Outcome measures

The primary outcome was the increase in bladder volume (FBV), computed with the MVV from bladder voiding diaries at the first postoperative outpatient appointment (± 6 weeks, see Appendix A). At this appointment, the post-void residual (PVR) was measured by ultrasonography of the bladder.

After initial BTX-A therapy, during outpatient follow-up, response is described as an improvement in urgency incontinence (short term; < 6 months vs long term; 6—12 months). Initial success was defined according the ICCS-criteria. Consequently, the following outcomes were obtained; complete response (100% improvement; achieving full continence during both the day and night); partial response (more than 50% reduction of symptoms) and no response (less than 50% reduction of symptoms).

Procedure

All interventions were performed under general anesthesia. Appropriate intravenous antibiotic prophylaxis was administered preoperatively. By rigid cystoscopy, a varying number of injections of the solution (Onabotulinum-A toxin, Botox®, diluted in normal saline 0.9%) were inserted in the detrusor muscle. Injections were equally distributed

over the bladder wall; in a few cases including the trigone. The total administered dose was determined by the surgeon, varying between 100 and 300 international units (IU). Dose was not based on any specific symptoms or urodynamic feature correlation, but rather on varying insights over the years and gained experience. Consequently, around 2011 a dose of 300 IU was administered due to successful outcomes on neurogenic patients. In these patients little side effects were seen. Over time, this dose has been reduced to 100 IU in non-neurogenic OAB-patients, consistent with recent literature [8].

In addition, children were offered postoperative guidance from an urotherapist. This was done under the conviction that children after BTX-A treatment will benefit from the increase in bladder volume during training and therefore are more likely to achieve continence.

Statistical analysis

The data sets were examined by descriptive analysis methods. Categorical variables were described by frequency and percentage, continuous variables were described by mean and standard deviation (if normally distributed) or median and interquartile range (IQR) (if skewed distributed). The Shapiro—Wilk test was used to determine whether the distributions of continuous variables were normal. Two dependent medians were compared by the Wilcoxon Signed Rank test. Univariate analysis was performed to identify differences in baseline characteristics between the responder and non-responder group, using Pearson chi-square or Fisher's exact test (when appropriate) for categorical variables. Independent factors influencing response after BTX-A treatment were examined by multivariate logistic regression analysis. In all tests the level of statistical significance was predefined at $p < 0.05$. Statistical analysis was performed using IBM SPSS Statistics 25.0.

Results

After exclusion, a total of 50 children were included (see Appendix B). Study characteristics are summarized in Table 1. The age at initial BTX-A injections ranged between 6.6 and 17.4 years (median 9.9) with female to male ratio of 1:4. The diagnosis was overactive bladder with urgency incontinence in all cases. Pre-operative UDS was performed in 44 children, with 37 (84.1%) showing detrusor overactivity and reduced bladder volume. Median treatment duration before BTX-A injections was 48 months (IQR 36—60). The treatment prior to BTX-A consisted of urotherapy (inpatient training program if feasible) mostly accompanied with anticholinergics and/or mirabegron. All included children have been refractory to this treatment or have experienced drug related side effects. Median complete duration of follow-up was 33.5 months (IQR 16.75—48.00).

Table 1 Overview of study characteristics.

Characteristic[a]	Frequencies (N = 50)
Gender:	
Boys	41 (82%)
Girls	9 (18%)
Age at initial BTX-A injections (years)	9.9 (8.3—11.8)
Urgency pre-BTX-A (N = 48)	47 (94%)
Frequency pre-BTX-A	43 (86%)
Urinary incontinence pre-BTX-A	50 (100%)
Duration of complaints (months)	48 (36.0—60.0)
Maximum voided volume pre-BTX-A (mL)	160 (128.8—200.0)
Functional bladder volume pre-BTX-A (%)	52.9 (48.4—63.6)
Post-void residual pre-BTX-A (mL)	0 (0.0—13.5)
Detrusor overactivity in UDS (N = 44)	37 (84.1%)
Previous constipation	26 (52%)
Previous UTIs	9 (18%)
of which girls	8 (88.9%)
Previous antispasmodic therapy	48 (96%)
Effect of antispasmodic therapy:	
Yes	23 (47.9%)
Doubtful	10 (20.8%)
Stopped because of side-effects	6 (12.5%)
No	9 (18.8%)
Previous dual therapy[b]	11 (22%)
Effect of dual therapy[b]:	
Yes	2 (18.2%)
Doubtful	1 (9.1%)
Stopped because of side-effects	1 (9.1%)
No	7 (63.5%)
Complete duration of follow-up time after BTX-A therapy (in months)	33.5 (16.8—48.0)
Repeated BTX-A treatment	12 (24%)
2 times	8 (16%)
3 times	3 (6%)
5 times	1 (2%)

Pre-BTX-A prior to BTX-A injections; *UDS* urodynamic study; *UTIs* urinary tract infections; *IQR* interquartile range.
[a] Median (IQR) for continuous variables with skewed distribution, and N (%) for categorical variables.
[b] Combination of anticholinergic agent and mirabegron.

Complications of BTX-A injections

BTX-A injections resulted in some complications. Urinary tract infection (UTI) was noted in five children (all of which occurred > 14 days after injection). Hematuria occurred in one child directly after the procedure, requiring surgical intervention. In addition, one developed urinary retention up to 50% PVR after receiving 300 IU BTX-A, requiring prolonged intermittent self-catheterization. Finally, one child experienced systemic side effects after BTX-A. These side effects included listlessness, shortness of breath and behavioral changes (gloomy and quickly irritated). These adverse events resolved during the anticipated diminished temporal efficacy of BTX-A.

Bladder volume and response

MVV and FBV assessments (extracted from voiding diaries) after the BTX-A treatment were available in 47 out of 50 children. In the short term, a significant increase in FBV from a median of 52.9% (IQR 48.4–63.6%) to 70% (IQR 55.6–92.6%) ($p = 0.000$) was observed. OAB symptoms expressing in urgency and frequency persisted post-operatively in 10 (20%) and 14 (28%) children, respectively.

After initial BTX-A treatment, 13 of the 50 children (26%) achieved full continence after more than six months follow-up and nine children (18%) in the short term (Fig. 1a). Partial response was seen in 10 children (20%) in the long term, while 27 (54%) showed partial response in the short term. Univariate analyses on baseline differences are outlined in Table 2. In the long term, 22 out of 38 boys (57.9%) versus one out of nine girls (11.1%) had an improvement (complete and partial response combined) of continence. Furthermore, boys showed a greater response than girls to BTX-A treatment in the long term ($p = 0.023$). The male gender turned out to be a significant predictor of improvement in urinary incontinence ($p = 0.009$ Odds ratio [OR] 0.032) (Table 3). A small preoperative FBV came forward as significant predictor in the long term as well ($p = 0.030$ OR 0.935).

The coherence of outcomes on urinary incontinence and increase in FBV are displayed in Fig. 1b. There seems to be a relation between increase in FBV and initial success in the short term. However, the increase in FBV (ΔFBV) did not reach statistical significance as a univariate predictor for initial success ($p = 0.165$).

Antispasmodic therapy and response

There was a total of 23 children (47.9%) with a (temporary) favourable effect on antispasmodic therapy before BTX-A treatment. Of them, 18 (78.3%) had improvement of continence (complete + partial response) in the short term ($p = 0.640$). Eleven (50%) showed improvement in the long term.

Two out of 11 experienced an effect on previous dual therapy, meaning a combination of mirabegron with an anticholinergic agent. These two children also had a favourable response to BTX-A treatment in both the short and long term ($p = 0.155$ and $p = 0.252$). In fact, they achieved full continence in the long term.

Table 2 Univariate analyses on baseline differences between responders and non-responders on BTX-A treatment.

Variables	< 6 months (N = 50)		*P*-value	6–12 months (N = 47)		*P*-value
	Response* N = 36 (72%)	No response N = 14 (28%)		Response* N = 23 (46%)	No response N = 24 (48%)	
Age at initial BTX-A injections			0.890[c]			0.191[a]
0–10 years	18 (50.0)	8 (57.1)		10 (43.5)	15 (62.5)	
> 10 years	18 (50.0)	6 (42.9)		13 (56.5)	9 (37.5)	
Gender			0.697[b]			**0.023****[b]
Boys	30 (83.3)	11 (78.6)		22 (95.7)	16 (66.7)	
Girls	6 (16.7)	3 (21.4)		1 (4.3)	8 (33.3)	
FBV pre-BTX-A			0.468[b]			**0.047****[c]
0–65%	26 (72.2)	12 (85.7)		21 (91.3)	15 (62.5)	
> 65%	10 (27.8)	2 (14.3)		2 (8.7)	9 (37.5)	
Duration of complaints			0.563[c]			0.853[c]
0–50 months	23 (63.9)	7 (50.0)		15 (65.2)	14 (58.3)	
> 50 months	13 (36.1)	7 (50.0)		8 (34.8)	10 (41.7)	
Dose of BTX-A			0.175[b]			1.000[c]
100–150 IU	22 (61.1)	12 (85.7)		15 (65.2)	16 (66.7)	
200–300 IU	14 (38.9)	2 (14.3)		8 (34.8)	8 (33.3)	
Detrusor overactivity in UDS pre-BTX-A (N = 44)			1.000[b]			0.668[b]
Yes	27 (84.4)	10 (83.3)		17 (89.5)	18 (81.8)	
No	5 (15.6)	2 (16.7)		2 (10.5)	4 (18.2)	
Effect previous antispasmodic therapy (N = 48)			0.640[a]			0.442[a]
Yes	18 (51.4)	5 (38.5)		11 (50.0)	11 (47.8)	
No	6 (17.1)	3 (23.1)		5 (22.7)	4 (17.4)	
Other	11 (31.4)	5 (38.5)		6 (27.2)	8 (34.7)	
Effect previous dual therapy (N = 11)			0.155[a]			0.252[a]
Yes	2 (40.0)	0 (0.0)		2 (33.3)	0 (0.0)	
No	2 (40.0)	5 (83.8)		4 (66.7)	3 (60.0)	
Other	1 (20.0)	1 (16.7)		0 (0.0)	2 (40.0)	

FBV functional bladder volume; *pre-BTX-A* prior to BTX-A injections; *UDS* urodynamic study.
*Response on continence after BTX-A treatment (complete response + partial response). **$p < .05$.
[a] Pearson's Chi-Square.
[b] Fisher's Exact Test.
[c] Continuity Correction.

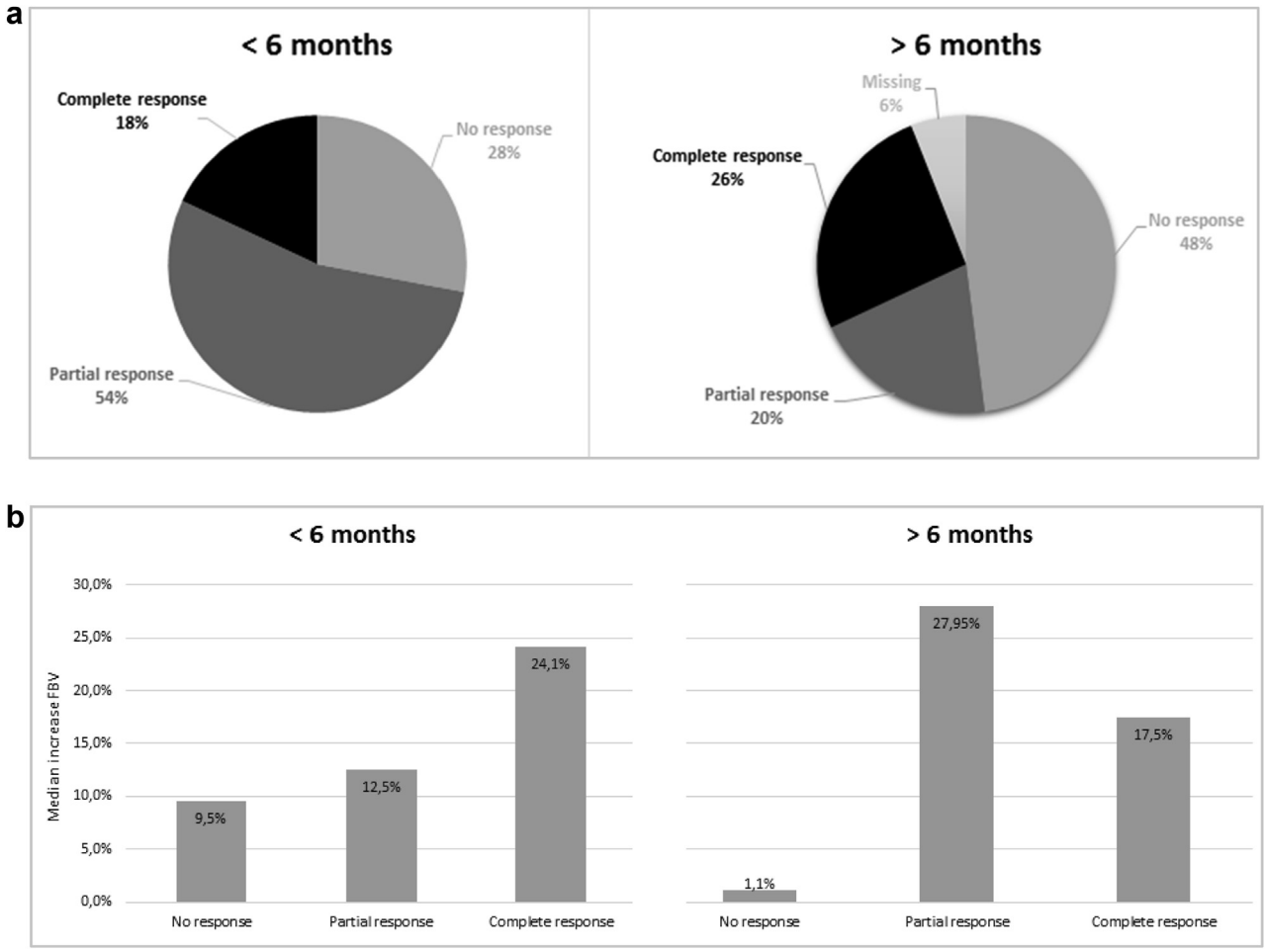

Fig. 1 (a) Response on continence (%) after initial BTX-A injection. Divided into short (<6 months) and long term (6—12 months) outcomes. *Complete response* (100% improvement; achieving full continence); *partial response* (more than 50% reduction of symptoms); *no response* (less than 50% reduction of symptoms). (b) Increase in median FBV (%) in no-, partial-, and complete-responder group. Short and long term outcomes. *FBV* functional bladder volume.

Dose of BTX-A

A group of 34 children (68%) received between 100 and 150 IU of BTX-A. Of them, 22 (64.7%) showed improvement of continence in the short term. Sixteen children (32%) received 200 or 300 IU, of which 14 (87.5%) had improvement. Therefore, a higher dose of BTX-A predicts a favourable response in the short term ($p = 0.042$ OR 1.020). Outcomes in the long term were similar between the two groups.

Postoperative uroflowmetry and UDS

After BTX-A treatment, in the available data of 41 children, a significant increase in PVR was seen from a median of 0 ml—12 ml (IQR 2.0—30.5) ($p = 0.042$). UDS was performed after the BTX-A injections in only eight cases (16%). Six of them showed no detrusor overactivity after BTX-A.

Multiple BTX-A injections

Due to the temporary effect of BTX-A injections, besides additional antispasmodic medication, 12 children (24%) received more injections. After the second BTX-A injection, nine children (75%) achieved full continence and seven (58.3%) showed improvement of voiding frequency.

Discussion

Overactive bladder and urinary incontinence pose a significant impact on daily activities and quality of life [2]. Primary treatment consists of urotherapy with bladder re-education or rehabilitation, mostly accompanied by antispasmodic agents [3]. When these interventions are ineffective, the next step is specific urotherapy. In our centre, we offer an inpatient urotherapy program for children refractory to this treatment [5]. After this, a small group still

Table 3 Multivariate logistic regression analysis for predicting the change of improvement of continence after BTX-A treatment.

Independent variables	< 6 months		6–12 months	
	P-value	OR (95% CI)	P-value	OR (95% CI)
Gender	0.589	0.612 (0.103–3.647)	**0.009****	**0.032 (0.002–0.430)**
Age at initial BTX-A injections	0.670	0.936 (0.692–1.268)	0.175	1.235 (0.911–1.674)
Duration of complaints	0.949	1.001 (0.970–1.034)	0.697	0.992 (0.952–1.034)
FBV pre-BTX-A	0.554	1.016 (0.965–1.070)	**0.030****	**0.935 (0.880–0.993)**
Dose of BTX-A	**0.042**	**1.020 (1.001–1.039)**	0.328	1.006 (0.994–1.019)

FBV functional bladder volume; *pre-BTX-A* prior to BTX-A injections; *OR* odds ratio; *CI* confidence interval. **$p < .05$.

remains refractory. Additionally, children cease medication due to drug related side effects. Moreover, the parents of children are often not satisfied with having their child on systemic daily medication. For these groups of children, intravesical BTX-A injections became a potential solution [6,7]. Literature has not proven that this off-label therapy is indeed safe and effective for children with non-neurogenic OAB.

To test its effectiveness, we examined the most direct, objective effect of intravesical BTX-A namely the increase in functional bladder volume. Due to the age-dependent growth of the bladder and variety of age in our study cohort, we corrected for the expected bladder capacity for age. As a secondary outcome, we analysed the achievement of urinary continence, which is the primary purpose of BTX-A treatment. Our primary and secondary outcomes were established in at least 47 of the 50 children.

This studies' complete follow-up period with a median of 33.5 months, 16.8 months minimum, shows the complexity of treatment in therapy resistant OAB children in our third line center. This shows us that treatment of children with OAB using intravesical BTX-A injections is not a simple, straightforward therapy in all OAB children.

Our study showed a significant increase in functional bladder volume after BTX-A treatment in a group of refractory OAB children in the third line. Of them, 72% and 46% showed improvement of continence in the short and long term, respectively. It is not sure whether long-term success is a direct result of the BTX-A injections. Pharmacologically the effectiveness of BTX-A diminishes after approximately six months. Achieving continence may be a consequence of maturation, environmental changes, additional urotherapy or problem-oriented attention during the follow-up time [3,12]. Due to the temporary effect of BTX-A repetitive treatment occurs. In the adult population with OAB receiving sequential BTX-A injections is very common. In our clinic we do not treat OAB children with ongoing BTX-A injections. We assume that in children due to the of short-term pharmacological effect of BTX-A, the child will be better capable to inhibit bladder urgency. Because of this the effectiveness of post-BTX-A urotherapy training will be higher [4,5]. The juvenile bladder might be more easily adaptable in gaining compliance after BTX-A. This study shows that 12 children (24%) did receive a second round of treatment. As a result, nine of these children (75%) initially achieved full continence. We believe that a second injection is only required in children with severe symptoms who have responded well to previous BTX-A treatment for a significant time period.

Our findings support the results of Al Edwan et al. [11], showing an improvement of OAB symptoms such as urgency and frequency in combination with an increase in bladder volume. Ingham et al. [13] also showed an increase in total bladder volume. Though in this study, as a result of concomitant rise in PVR, they found no improvement in FBV. Whereas Ringoir et al. [14] found a significant improvement in bladder volume of 23.1% after the first injection in a group of 257 children, which exceeds our rise of 17.1% of FBV.

There is limited data on long-term outcomes of BTX-A treatment. In the short term the complete response rate in this study is 18%. This is less than found in other studies, ranging between 28 and 66.7% [9,10,13–17]. In the study of Ingham et al. [13] and McDowell et al. [16] boys initially responded better than girls, whereas in our results this was more pronounced in the long-term response (57.9% boys vs 11.1% girls). Although our numbers are small, girls were more likely to have no response. This unfavourable outcome may be due to the etiology of OAB in girls [16], whereas in boys relative infravesical obstruction is the probably most common cause [18].

Mirabegron is a relatively new medicine for treating OAB, introduced in 2012. Although off-label in children, this medicine is being used more and more in pediatric urology. It can be combined with an anticholinergic agent. Dual therapy as compared to BTX-A injections clearly has the advantage of oral administration rather than a surgical intervention under general anaesthesia. However, in literature effects are still controversial [19]. Though, Morin et al. [20] studied a group of children with refractory OAB on dual therapy that showed a significant increase in bladder volume and favourable outcomes on continence. In this refractory group of OAB children, two out of 11 children that had received dual therapy experienced a beneficial effect.

Increase in PVR is an expected side effect of BTX-A because of the flaccid muscle paralysis [6]. High PVR is known to cause a higher risk for UTI and retention [3].

Ingham et al. [13] previously reported a PVR increase after BTX-A treatment from a median of 0—27 ml. In our study, postoperative PVR increased from a median of 0—12 ml. Even with this rise, PVR remains under the 10% of the median MVV (232 ml). Therefore, these outcomes raise no concerns about the use of BTX-A.

Our findings confirm the safety of intravesical BTX-A. The most prevalent complications were postoperative UTIs occurring in five cases (10%). Only one child developed urinary retention requiring prolonged intermittent self-catheterization. This low number is in accordance with other studies [15,17]. In our case the highest dose of 300 IU BTX-A was injected. Even though retention occurrence is scarce, because of the impact of the complication we continue to inform parents and children about the potential need for intermittent catheterization.

This study identifies the male gender and small baseline FBV as predictors for a favourable outcome of BTX-A on continence in the long term in a selected group of refractory OAB children. We believe that BTX-A injections are indicated in children refractory to both specific urotherapy and medication. An appropriate population seems to be children with severe OAB symptoms, confirmed detrusor overactivity in UDS, and reduced bladder volume. This calls for a more individualized approach in the treatment of OAB incontinence.

The limitations of our study include the selected study group of third-line refractory OAB children. The study design is retrospective, which results in some data deriving from interpretative documentations of the clinician and the absence of a control group. The timing of outpatient follow-up after BTX-A treatment varied. This might have led to determination of functional bladder volume in different stages. Symptom response assessment was subjective and thus, potentially, less accurate than in a research setting. In a prospective study suitable questionnaires could have been used. Furthermore, additional pharmacological therapy after BTX-A treatment has not been specified. On the other hand, we examined a large group of non-neurogenic OAB children within the pediatric urology in the literature. The follow-up covered a long period of time. Although retrospectively gathered, there was a low amount of missing data in our study.

Further research is needed to identify whether BTX-A injections have a long-term impact when treating OAB incontinence, as well as compared to dual therapy with antispasmodic medication. It is important to improve our understanding of which children are more likely to relapse after BTX-A treatment. Preferably this would be done in a prospective, placebo-controlled study design. Voiding diaries, efficacy questionnaires and planned uroflowmetry combined with UDS could then be employed.

Conclusion

For OAB children refractory to specific urotherapy and medication, BTX-A injections are an alternate option. Our study showed a significant increase in bladder volume in the short term after BTX-A treatment. Improvement of continence was seen in 72% of the children in the short term and in 46% in the long term. Boys with a small baseline FBV appear to respond better. Additionally, we confirmed the safety of this therapy with only few complications. An appropriate population for BTX-A treatment seems to be children with severe OAB symptoms, confirmed detrusor overactivity in UDS and reduced bladder volume. This calls for a more individualized approach in the treatment of OAB incontinence. This study does not provide the answer on whether or not BTX-A treatment should be repeated in children with OAB. Further prospective studies are necessary to determine its long-term efficacy as compared to dual therapy.

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Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpurol.2022.02.007.