

## Botulinum Toxin A in Pediatric Day-Time Lower Urinary Tract Conditions: A Single Center Experience

Krafft U, Hirner C, Hirner L, Darr C, Mahmoud O, Hadaschik B, Rehme C

<sup>1</sup>Department of Urology, University Hospital Essen-Duisburg Hufelandstr. 5545147 Essen, Germany

\*Corresponding author: Dr. Med. U. Krafft, Department of Urology, University Hospital Essen Hufelandstr. 5545147 Essen, Germany.

Citation: Krafft U, Hirner C, Hirner L, Darr C, Mahmoud O, et al. (2021) Botulinum Toxin A in Pediatric Day-Time Lower Urinary Tract Conditions: A Single Center Experience. J Urol Ren Dis 06: 1236. DOI: 10.29011/2575-7903.001236.

Received Date: 12 October, 2021; Accepted Date: 18 October, 2021; Published Date: 25 October, 2021

### Abstract

**Introduction:** To evaluate efficacy and safety of Botulinum Toxin A (Botox) injection in the detrusor for day-time lower urinary tract conditions with mainly overactive symptoms, we analyzed our uropediatric Botox-treated collective.

**Materials and Methods:** 21 Children who received a Botox treatment in our hospital between 2016 and 2020 for refractory day-time lower urinary tract conditions with mainly overactive symptoms with conclusive follow up were analyzed. In all cases we applied 100 IU Botox.

**Results:** Mean age of patients was 9,19 ( $\pm 3,0$ ). In 8/21 cases a preoperative urodynamic assessment was available. We reached a median follow up of 289 days (range 34-750). Mean bladder capacity increased from 157 ml ( $\pm 18,4$ ) to 213 ml ( $\pm 24,5$ ) ( $p = 0.001$ ). Mean voiding frequency decreased from 7.4 ( $\pm 0,61$ ) to 6.2 ( $\pm 0,55$ ) ( $p = 0.015$ ). 13/21 Patients (61.9%) encountered a partial or complete therapy response while 8/21 Children (38.1%) showed a therapy failure. Within the responder group, 8/13 Children (61, 5%) experienced an ongoing response. However, 5 Children relapsed on average in 176 days ( $\pm 45, 5$ ). 3 Children received a repeated injection of Botox. We observed no serious side effects.

**Discussion/Conclusion:** Even though pediatric Botox therapy still lacks standardization; our study indicates a safe and effective use for day-time lower urinary tract conditions with mainly overactive symptoms in children who are resistant to common treatments. Moreover, we found a one-time injection in most cases to be sufficient to improve symptoms in the long term.

**Keywords:** Overactive bladder; Pediatric incontinence; Botulinum toxin A; Pediatric day-time lower urinary tract conditions; Botulinum Toxin A; Incontinence

### Introduction

Symptoms of overactive bladder in the context of day-time lower urinary tract conditions (LUTC) in children is common and characterized by urinary urgency, usually accompanied by frequency, with or without urinary incontinence, in the absence of other obvious pathology. Affected children suffer from urinary urgency, pollakisuria and urge incontinence [1]. The treatment of LUTC involves a multimodal approach, beginning with mainly behavioral modification, urotherapy and therapy of potentially

complicating conditions such as constipation and UTIs. If these measures are ineffective anticholinergic medication is administered.

Intradetrusor injection of Botulinum toxin A (Botox) was first reported by Schurch et al. in patients with paraplegia using intermittent self-catheterization in 2000 [2]. Botox blocks the neuromuscular junction at the site of injection until new presynaptic nerve sprouts occur [3,4]. In adult patients with neurogenic bladder dysfunction, Botox represents a minimal invasive therapeutic option for neurogenic detrusor overactivity, detrusor-sphincter dyssynergia, non-neurogenic detrusor overactivity and chronic prostatic pain [5]. Furthermore, in the pediatric age group the use of Botox has been reported to be equally safe and effective

in children with overactive day-time LUTC [1,6]. However, only few trials investigated this topic [1,6-12]. No randomized controlled trials have been conducted to date. The European guidelines list Botox therapy as a promising treatment, but do not make a clear recommendation for this therapy [13]. Studies mentioned above examined sample sizes of 13 to 46 patients. However, therapy response differs considerably from approximately 30% to 70% [6,9]. It is also unclear which children benefit best from a Botox injection and which do not. In this retrospective analysis we aim to validate the efficacy of Botox in a single center cohort and try to explore characteristics of patients who are expected not to benefit from Botox therapy.

**Material and Method:**

A total of 23 children received Botox injections into the detrusor between January 2016 and December 2020 due to LUTC suffering from symptoms of overactive bladder at our hospital. 2 patients were lost to follow up. Thus, 21 patients were included in the study (Table 1). A total of 24 Botox injections were applied. Age, a general history of urogenital disorders and medication, baseline urodynamic studies' results, baseline sonographic examination results, voiding frequency, functional bladder capacity as percentage of age adjusted expected capacity, post-void residual urine volume, presence of diurnal and/or nocturnal incontinence episodes, subjective therapy success, amount of injected Botox, additional injection requirements, follow up and time to recurrence of symptoms were recorded.

<b>Patient characteristics and symptoms</b>			
<b>Demographic details</b>	<b>male n = 15</b>	<b>female n = 6</b>	<b>Total n = 21</b>
Mean age in years (SD)	8.67 (±2.9)	10.50 (±3.2)	9.19 (±3,0)
Mean bodyweight in Kg (SD)	35.33 (±15.7)	45.67 (±3.2)	38.29 (±20.9)
Mean BMI in kg/m <sup>2</sup> (SD)	17,7 (±4.0)	20.1 (±9.5)	18.4 (±6.1)
<b>Urinary symptoms</b>			
Duration of symptoms < 3 years	10 (66.7%)	2 (33.3%)	12 (57.1%)
Duration of symptoms >3 years	5 (33.3%)	4 (66.7%)	9 (42.9%)
Frequency	8 (53.3%)	2 (33.3%)	10 (47.6%)
Urgency	10 (66.7%)	5 (83.3%)	15 (71.4%)
Incontinence	15 (100%)	6 (100.0%)	21 (100%)
Previous UTI	0	4 (66.7%)	4 (19.0%)
Previous bowel dysfunction	3 (20.0%)	2 (33.3%)	5 (23.8%)
<b>Medications prior to Botox</b>			
Anticholinergics	15 (100%)	6 (100%)	21 (100%)
Anticholinergics effective	2 (13.3%)	1 (16.7%)	3 (14.3%)
Desmopressin	4 (26.7%)	2 (33.3%)	6 (28.6%)
Desmopressin effective	0	1 (16.7%)	1 (4.8%)
<b>Sonography</b>			
Bladder Wall Thickness > 3mm	5 (30%)	3 (50%)	8 (38.1%)
Botox-Injection			
Single Injection	14 (93.3%)	4 (66.7%)	18 (85.7%)
Repeat Injection	1 (6.6%)	2 (33.3%)	3 (14.2%)
Preoperative urodynamics	4 (26.7%)	4 (66.7%)	8 (38.1%)

**Table 1:** Patient characteristics and symptoms (original).

The study was approved by the ethics committee of the University Hospital Essen and the number of the ethics vote: (20-9721-BO).

Each parent was informed about the “off-label” character of the Botox therapy lacking an official approval. The standard treatment of LUTC with mainly overactive symptoms follows a stepwise approach in our hospital. Initially conservative treatments such as therapy of concomitant bowel dysfunction, voiding training and biofeedback are applied. In the next step medical therapy is started usually with oxybutynin or trospiumchloride and in case of failure or intolerance switched to either tolterodine or propiverine. Magnetic resonance imaging was performed to rule out a neurogenic cause of LUTC in patients highly suspicious of neurogenic detrusor over activity.

Three-day voiding diaries were collected at baseline and at the end of the 4<sup>th</sup> week after the procedure. Furthermore, we took a detailed history and performed a clinical and sonographic examination during the 4<sup>th</sup> week appointment.

In only 8/21 cases (38.1%) a preoperative urodynamic study was performed, due to refusal of this invasive diagnostic method by most patients and parents. In cases with a doubtful diagnosis of a LUTC with symptoms of overactive bladder an urodynamic testing was enforced.

### Injection technique

Two experienced pediatric urologists performed all procedures. Prior to the procedure a negative urine analysis was required. Injection was performed under general anesthesia and with antibiotic prophylaxis. Botox was diluted in 15 ml of normal saline per 100 IE. The detrusor was injected at 30 sites with 0.5 ml each under cystoscopic guidance (Wolf Cystoscope 12° 8.0'9.8 CH. NL: 150MM GL: 283MM) using a 3.7Fr Deflux® injection needle. Injection was performed homogeneously distributed over the entire urinary bladder except trigone and sphincter (Figure1). After injection the bladder was emptied. Following spontaneous voiding the patient was discharged.

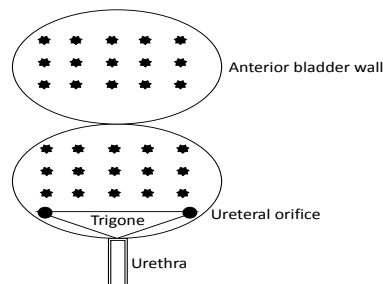


Figure 1:  
Intravesical distribution of Botulinum toxin A injections,  
asterisk symbol: injection points. (original)

**Figure 1:** Graphical visualization of the intravesical distribution of Botulinum toxin A injections.

We intended to repeat urodynamics after injection. However, a strong rejection of patients and parents against urodynamic evaluation was shown. Therefore, we considered a less invasive evaluation of therapy response via voiding diary plus detailed history and clinical as well as sonographic examination as sufficient.

We carried out follow-up examinations 4 weeks after the procedure and after that every 3 months or in case of relapse, side effects or complaints. All follow up examinations were carried out in our hospital. To better categorize therapy response, we called the absence of any symptoms a complete response, a reduction of at least 50% diurnal and nocturnal symptoms a partial response and everything else was called failure.

### Statistical Analysis

IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA) was used for statistical analyses. Average values were reported as arithmetic mean and standard deviation as a measure of variability. Paired t-test was performed to compare means. A p-value of at least 0.05 was considered to be statistically significant.

### Results

Between January 2016 and December 2020, 23 children underwent intradetrusor Botox injection in our hospital. Two patients were lost to follow-up, thus, we analyzed finally 21 cases with conclusive follow-up. Of 21 patients, 15 (71.5%) were male. The mean (SD) age and BMI (kg/m<sup>2</sup>) were 9.19 (±3,0) and 18.37 (5.96), respectively. Table 1 illustrates the patient baseline characteristics. 12 children suffered from LUTC symptoms for less than 3 years. All children reported diurnal incontinence, mostly associated with frequency and urgency. All patients had been previously treated with urotherapy and anticholinergics, but this therapy was partially effective in only 3 of them. 6 patients were characterized by a thickened bladder wall on sonographic examination. 18 patients received a single Botox injection, while 3 patients had repeated Botox treatments. The mean (SD) baseline bladder capacity was 157 ml (±18.4) ml. The dose of applied Botox in all cases amounted to 100 IE. Of 21 patients, 11 (52.3%) showed complete response after 1 month, the response was maintained for a mean (SD) of 295 (141) days. Two patients experienced recurrence of symptoms and received reinjection after 199 and 344 days. Two patients (9.5%) showed only partial response and symptoms recurred completely after 80 and 155 days. In the total group, the mean bladder capacity increased from 157 ml (±18.4) to 213 ml (±24.5) (p = 0.001), combined with a decrease in the mean voiding frequency from 7.4 (±0.61) to 6.2 (±0.55) (p = 0.015) (Table 2).

Parameter	Preoperative	Postoperative	P-value
Functional bladder capacity (SD, n = 21)	157 ml ( $\pm$ 18.4)	213 ml ( $\pm$ 24.5)	p = 0.001
Voiding Frequency (SD, n = 21)	7, 4 ( $\pm$ 0.61)	6, 2 ( $\pm$ 0.55)	p = 0.015

**Table 2:** Preoperative and postoperative parameters (original).

Preoperative and postoperative mean bladder capacity and mean voiding frequency (standard deviation as a measure of variability).

When comparing the preoperative characteristics of failure and response groups, non-responders had mean BMI and bodyweight of 15.6 kg/m<sup>2</sup> and 31kg. In contrast, responders were characterized by a mean BMI and bodyweight of 20, 2 kg/m<sup>2</sup> and 43kg. In Addition, non-responders had a preoperative functional bladder capacity of in mean 40.3% of the age-adjusted target capacity, whereas responders started with an adjusted bladder capacity of 49.3%. Furthermore, 87.5% of those with a poor outcome were male; in contrast, the responder group consisted of only 53.9% male patients. Interestingly, 7 of 13 responders showed a thickened bladder wall on sonography. This was in only 1 of 8 non-responders presentable (Table 3). We observed no serious side effects: 1 patient developed a urinary tract infection and 1 patient complaint about lower abdominal pain for 2 weeks before spontaneous disappearance of the symptoms. During the follow-up examinations at week 4 and every 3 months thereafter, we detected no post void residual (PVR) or need for clean intermittent catheterization (CIC) in any of the patients.

Patient characteristics	Responder	Non-responder
n	13	8
Mean age (SD)	9.5 ( $\pm$ 3.38)	8.8 ( $\pm$ 2.6)
Mean bodyweight in kg	43	31
Mean BMI	20.2	15.6
Bladder capacity pre-botox (percent of age-adjusted target capacity)	49.3	40.3
Male sex	7	7
Bladder wall thickness >3mm	7	1

**Table 3:** Responder and Non-responder characteristics.

Baseline characteristics of the responder and non-responder groups (SD: Standard deviation, BMI: Body mass index) (original).

## Discussion

Botox has been used in Urology predominantly to treat refractory neurogenic detrusor overactivity. Efficacy and safety of Botox has been demonstrated in both idiopathic and neurogenic

overactive bladder syndrome in the adult age group [12,14,15]. Thus, experience concerning efficacy and safety profile became vast in adults. In contrast, data regarding treatment of children is still limited. First steps were made in successfully treating children with neurogenic detrusor hyperreflexia by intradetrusor Botox [16]. Since then, several studies demonstrated a safe and effective use of Botox in children suffering from neurogenic detrusor overactivity [2,17-23]. In 2006 the first use of Botox in LUTC with mainly symptoms of overactive bladder in the pediatric population was reported as safe and effective [6]. Subsequently, few studies have been carried out investigating the use of Botox in the pediatric population for LUTC [1,6-12]. In comparison to adult age studies, uropediatric studies on Botox in LUTC are more seldom and covered with smaller sample sizes. In addition, the proportion of patients showing a response to therapy is unclear and differs significantly in the literature mentioned above. Furthermore, the number of Botox injections necessary to achieve a long-term response is uncertain. Therefore, we see an unmet need to validate the efficacy and safety profile of this therapy analyzing our uropediatric collective.

Results of 57, 46, 33, 21 and 15 botox-treated LUTC children were reported by McDowell, Al Edwan et al., Bayrak et al., Marte et al. and Hoebeke et al. respectively [6,7,11,12,24]. All of them demonstrated significant reduction of incontinence episodes and an increase of functional bladder capacity with minimal side effects. Except for Al Edwan, none of them included objective urodynamic assessment as outcome measure. Interestingly, a Korean working group found no compelling relationship between post-treatment urodynamics and patient reported impression of improvement [25]. Accordingly, we found only 50% of urodynamically-proven detrusor over activity patients responding to Botox treatment. However, the results of the discussed works are not perfectly comparable. While Bayrak and Blackburn describe only changes in individual symptoms, all other authors define a categorized response (full or partial response vs. failure) [6-9,11,24].

However, the results of our study correlate well with results of the aforementioned works: We found an increase of mean bladder capacity from 46, 7% or 157 ( $\pm$ 18.4) ml to 62, 4% or 213 ml ( $\pm$ 24.5) (p = 0.001) and a significant reduction of mean voiding frequency from 7.4 ( $\pm$ 0.61) to 6.2 ( $\pm$ 0.55) (p = 0.015; from 7 to 5 times per day in median). In particular, 13/21 Patients (61.9%) encountered a partial or complete therapy response while 8/21 Children showed a therapy failure. Only 3/13 children from the responder group (23, 1%) needed one repeated injection during follow up period.



Despite a small sample size, we found a comparatively high rate of primary response, which, interestingly, in many cases resulted in long-term response. In particular, we recognized in most cases a one-time application as sufficient, which underlines the efficacy of Botox therapy.

While the Marte working group used a Botox dose of 12.5 IU per kg bodyweight with a maximum dose of 200 IU, Hoebecke and Bayrak injected 100 IU fix dose. In contrast, another working group applicated 50 to 100 IU bodyweight-dependent and showed a reduction of daytime wetting, increased bladder capacity and decreased detrusor overactivity in 12 children [10]. However, we decided to use a fix dose of 100 IU Botox. We chose this dosage, because the probability of systemic, Botox-mediated side effects is reported to be negligible at a dosage of 100 IU [16]. Despite the small sample size, our results could help characterize in future a population for which botox therapy is effective. In the responder group of our study, we found patients with higher BMI and body weight, more male patients, and more often a sonographically measured thickened bladder wall.

According to common manner, we performed a trigone and sphincter sparing injection method [6,7,12]. In accordance to literature, we observed only little side effects [6-9,12,15,16,25]. 1 patient developed a urinary tract infection and 1 patient complaint about lower abdominal pain for 2 weeks before spontaneous disappearance of the symptoms. Follow up examinations as described above revealed no post void residual (PVR) or need for clean intermittent catheterization (CIC). Therefore, despite the limited recommendation of the guidelines [13,26], we consider Botox therapy to be safe and effective in cases of therapy refractory day-time LUTC with mainly symptoms of overactive bladder.

The limitations of our study are the lack of follow up urodynamics, its nature as retrospective study and a small sample size despite being comparable with other published works in the pediatric age group.

The results of this single-center analysis indicate a safe and effective use of Botulinum-A toxin for day-time lower urinary tract conditions with mainly overactive symptoms in children who are resistant to common treatments. Moreover, we found a one-time injection in most cases to be sufficient to improve symptoms in the long term.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Statements

Statement of Ethics: The study was approved by the ethics committee of the University Hospital Essen.

**Funding Sources:** None

## Author Contribution

Krafft U: Conception and design, acquisition, analysis, interpretation, drafting, writing, final approval.

Hirner C: acquisition, analysis, interpretation, drafting.

Hirner L: acquisition, analysis, interpretation.

Kaspar C: acquisition, analysis, interpretation.

Darr C: acquisition, analysis, interpretation.

Mahmoud O: Conception and design, final approval, critical revision.

Hadaschik B: Conception and design, final approval, critical revision.

Rehme C: Conception and design, acquisition, final approval, critical revision.

## References

1. Léon P, Jolly C, Binet A, Fiquet C, Vilette C, Lefebvre F, et al. Botulinum toxin injections in the management of non-neurogenic overactive bladders in children. *Journal of pediatric surgery*. 2014; 49(9):1424-8.
2. Schurch B, Stohrer M, Kramer G, Schmid DM, Gaul G, Hauri D. Botulinum-A toxin for treating detrusor hyperreflexia in spinal cord injured patients: a new alternative to anticholinergic drugs? Preliminary results. *The Journal of urology*. 2000; 164(3 Pt 1):692-7.
3. Meunier FA, Schiavo G, Molgó J. Botulinum neurotoxins: from paralysis to recovery of functional neuromuscular transmission. *Journal of Physiology-Paris*. 2002; 96(1-2):105-13.
4. Simpson LL. Kinetic studies on the interaction between botulinum toxins type A and the cholinergic neuromuscular junction. *The Journal of pharmacology and experimental therapeutics*. 1980; 212(1):16-21.
5. Leippold T, Reitz A, Schurch B. Botulinum toxin as a new therapy option for voiding disorders: current state of the art. *European urology*. 2003; 44(2):165-74.
6. Hoebecke P, De Caestecker K, Vande Walle J, Dehoorne J, Raes A, Verleyen P, et al. The Effect of Botulinum-A Toxin in Incontinent Children with Therapy Resistant Overactive Detrusor. *The Journal of urology*. 2006; 176(1):328-31.
7. Bayrak O, Sadioglu E, Sen H, Dogan K, Erturhan S, Seckiner I. Efficacy of onabotulinum toxin A injection in pediatric patients with non-neurogenic detrusor overactivity. *Neurourology and urodynamics*. 2017; 36(8):2078-82.
8. Blackburn S, Jones C, Bedoya S, Steinbrecher H, Malone P, Griffin S. Intravesical botulinum type-A toxin (Dysport®) in the treatment of idiopathic detrusor overactivity in children. *Journal of pediatric urology*. 2013; 9(6):750-3.
9. Ingham J, Angotti R, Lewis M, Goyal A. Onabotulinum toxin A in children with refractory idiopathic overactive bladder: medium-term outcomes. *Journal of Pediatric Urology*. 2019; 15(1):32.e1-e5.
10. Lahdes-Vasama TT, Anttila A, Wahl E, Taskinen S. Urodynamic assessment of children treated with botulinum toxin A injections for urge incontinence: a pilot study. *Scand J Urol Nephrol*. 2011; 45(6):397-400.

11. Marte A, Borrelli M, Sabatino M, Balzo B, Prezioso M, Pintozzi L, et al. Effectiveness of Botulinum-A Toxin for the Treatment of Refractory Overactive Bladder in Children. *European journal of pediatric surgery: official journal of Austrian Association of Pediatric Surgery [et al] = Zeitschrift für Kinderchirurgie*. 2010; 20:153-7.
12. Al Edwan GM, Mansi HH, Atta ONM, Shaath MM, Al Adwan R, Mahafza W, et al. Objective and subjective improvement in children with idiopathic detrusor overactivity after intravesical botulinum toxin injection: A preliminary report. *Journal of pediatric surgery*. 2019; 54(3):595-9.
13. Tekgul S, Stein R, Bogaert G, Undre S, Nijman RJM, Quaedackers J, et al. EAU-ESPU guidelines recommendations for daytime lower urinary tract conditions in children. *Eur J Pediatr*. 2020; 179(7):1069-77.
14. Anger JT, Weinberg A, Suttorp MJ, Litwin MS, Shekelle PG. Outcomes of Intravesical Botulinum Toxin for Idiopathic Overactive Bladder Symptoms: A Systematic Review of the Literature. *The Journal of urology*. 2010; 183(6):2258-64.
15. Dmochowski R, Sand PK. Botulinum toxin A in the overactive bladder: Current status and future directions. *BJU international*. 2007; 99(2):247-62.
16. Schulte-Baukloh H, Michael T, Schobert J, Stolze T, Knispel HH. Efficacy of botulinum-a toxin in children with detrusor hyperreflexia due to myelomeningocele: preliminary results. *Urology*. 2002; 59(3):325-7; discussion 7-8.
17. Ginsberg D, Gousse A, Keppenne V, Sievert KD, Thompson C, Lam W, et al. Phase 3 efficacy and tolerability study of onabotulinumtoxinA for urinary incontinence from neurogenic detrusor overactivity. *The Journal of urology*. 2012; 187(6):2131-9.
18. Greer T, Abbott J, Breytenbach W, McGuane D, Barker A, Khosa J, et al. Ten years of experience with intravesical and intrasphincteric onabotulinumtoxinA in children. *J Pediatr Urol*. 2016; 12(2):94 e1-6.
19. Peeraully R, Lam C, Mediratta N, Patel R, Williams A, Shenoy M, et al. Intradetrusor injection of botulinum toxin A in children: a 10-year single centre experience. 2019; 51(8):1321-7.
20. Reitz A, Stohrer M, Kramer G, Del Popolo G, Chartier-Kastler E, Pannek J, et al. European experience of 200 cases treated with botulinum-A toxin injections into the detrusor muscle for urinary incontinence due to neurogenic detrusor overactivity. *European urology*. 2004; 45(4):510-5.
21. Riccabona M, Koen M, Schindler M, Goedele B, Pycha A, Lusuardi L, et al. Botulinum-A toxin injection into the detrusor: a safe alternative in the treatment of children with myelomeningocele with detrusor hyperreflexia. *The Journal of urology*. 2004; 171(2 Pt 1):845-8; discussion 8.
22. Schurch B, Corcos JJCoiu. Botulinum toxin injections for paediatric incontinence. 2005; 15(4):264-7.
23. Schurch B, Schmid DM, Stohrer M. Treatment of neurogenic incontinence with botulinum toxin A. *The New England journal of medicine*. 2000; 342(9):665.
24. McDowell DT, Noone D, Tareen F, Waldron M, Quinn F. Urinary incontinence in children: botulinum toxin is a safe and effective treatment option. *Pediatric Surgery International*. 2012; 28(3):315-20.
25. Kim SW, Choi JH, Lee YS, Han SW, Im YJ. Preoperative Urodynamic Factors Predicting Outcome of Botulinum Toxin-A Intradetrusor Injection in Children with Neurogenic Detrusor Overactivity. *Urology*. 2014; 84(6):1480-4.
26. Gontard AV, Kuwertz-Bröking E. The Diagnosis and Treatment of Enuresis and Functional Daytime Urinary Incontinence. *Dtsch Arztebl Int*. 2019; 116(16):279-285.