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Baseline detrusor pressure and renal reserve as determinants of botulinum toxin a response in pediatric neurogenic bladder

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MAIN POINTS

- Intradetrusor botulinum toxin A (BTX-A) is a minimally invasive option for pediatric patients with medically refractory neurogenic bladder and can reduce storage-phase detrusor pressure.
- Achieving safe storage pressures (30–35 cmH_2O) is essential for upper urinary tract preservation, yet the response to BTX-A is heterogeneous.
- At 6 months after intradetrusor BTX-A, the reduction in pressure was modest, and only a minority of patients reached safe storage thresholds.
- Higher baseline p_det and preserved renal function (eGFR) were associated with a clinically meaningful response, defined as a decrease of $\geq$10 cmH_2O.
- Baseline p_det demonstrated fair discrimination in predicting response (AUC 0.72), which may support pressure-guided candidate selection (external validation is required).

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ABSTRACT

Aim: Pediatric neurogenic bladder (NB) represents a challenging condition that jeopardizes both lower and upper urinary tract integrity. This study aimed to evaluate the pressure-lowering efficacy of intradetrusor botulinum toxin A (BTX-A) in children with spinal-origin NB and to identify clinical and urodynamic predictors of treatment response.

Materials and Methods: In this retrospective cohort study, 38 pediatric patients with spinal-origin NB who received 100 IU of BTX-A between October 2023 and December 2024 were analyzed. BTX-A was injected cystoscopically at 20 detrusor sites, sparing the trigone. The primary outcome was the 6-month change in storage-phase detrusor pressure (Δp_det), calculated as p_det = p_ves − p_abd per ICCS standards. Secondary outcomes included an exploratory responder endpoint ($\geq$10 cmH_2O reduction in storage pressure) and attainment of guideline-based safe storage thresholds (<30 and <35 cmH_2O). Associations with demographic, functional, and renal parameters were examined using correlation, multivariable regression, and ROC analyses.

Results: Mean baseline storage-phase detrusor pressure was 59.9 ± 21.2 cmH_2O, decreasing to 52.5 ± 19.7 cmH_2O at six months (Δp_det = −7.4 ± 12.5 cmH_2O; $P < 0.05$). A $\geq$10 cmH_2O reduction in pressure was observed in 26.3% (10/38) of patients, and 10.5% and 13.2% achieved storage pressures <30 cmH_2O and <35 cmH_2O, respectively. In exploratory logistic regression, higher baseline p_det (OR = 1.05; P = 0.039) and preserved renal function (eGFR; OR = 1.04; P = 0.042) were associated with a $\geq$10 cmH_2O reduction, whereas etiology and age showed non-significant trends.

Conclusion: Intradetrusor BTX-A produced a modest but statistically significant reduction in storage-phase detrusor pressure, with only a minority of patients reaching guideline-defined safe storage thresholds. These findings support BTX-A as a clinically relevant pressure-lowering option within a multimodal, pressure-guided strategy --- particularly in children with high baseline pressures and preserved renal reserve --- rather than as a uniformly transformative stand-alone therapy.

Keywords: Pediatric neurogenic bladder, Botulinum toxin A, Detrusor pressure, Renal function, Spinal dysraphism

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INTRODUCTION

Neurogenic bladder (NB) in children is a chronic disorder that simultaneously threatens lower urinary tract function and upper urinary tract integrity, often leading to long-term morbidity when inadequately controlled. Contemporary guidelines highlight the central role of urodynamic assessment for diagnosis, risk stratification, and monitoring, recommending standardized terminology and methodology established by the *International Children's Continence Society (ICCS)* [1–3]. The principal therapeutic objective is to maintain safe storage pressures (<30–35 cmH_2O) and adequate bladder compliance to preserve renal function [1,4]. In this study, the term "spinal-origin neurogenic bladder" refers to neurogenic bladder dysfunction secondary to surgically treated myelomeningocele or other spinal dysraphism–related or spinal neurogenic conditions (including tethered cord, di-

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astematomyelia, and traumatic spinal lesions).

Conservative management—including clean intermittent catheterization (CIC), antimuscarinic agents, and behavioral therapy—remains first-line treatment. Yet approximately one-third of patients remain refractory, exhibiting persistently high storage pressures or poor compliance despite optimal conservative measures [1]. For these cases, intradetrusor botulinum toxin A (BTX-A) has emerged as a minimally invasive, reversible, and repeatable therapeutic option. By inhibiting acetylcholine release at the neuromuscular junction, BTX-A decreases detrusor overactivity and storage pressure, and improves bladder compliance and capacity [5,6].

Clinical studies and meta-analyses consistently demonstrate significant reductions in Δp_det and improvements in bladder compliance and capacity within 3–6 months after BTX-A, with excellent safety and tolerability [5–8]. Repeated injections have been reported to maintain efficacy without cumulative adverse effects [9,10].

Despite these encouraging outcomes, heterogeneity persists in injection protocols, dosing regimens, concomitant therapies, and follow-up durations. Recent systematic reviews reaffirm overall efficacy but emphasize the importance of identifying predictors of response, particularly the effects of elevated baseline storage-phase pressure and preserved renal function on treatment success [7,11,12].

Accordingly, the present study aimed to evaluate the six-month effects of intradetrusor BTX-A on Δp_det in children with NB secondary to spinal pathology, to determine clinically meaningful response rates (≥10 cmH_2O reduction and/or attainment of safe storage thresholds), and to explore baseline urodynamic predictors of outcome.

MATERIALS AND METHODS

Study design and setting

This retrospective cohort study included consecutive pediatric patients diagnosed with neurogenic bladder (NB) who underwent intradetrusor botulinum toxin A (BTX-A) injections at a tertiary pediatric urology center between October 2023 and December 2024. A total of 38 children were included (mean age: 7.8 ± 4.0 years); 20 were female (52.6%) and 18 were male (47.4%). The etiology of NB was operated myelomeningocele (MMC) in 25 patients (65.8%) and other spinal pathologies (diastematomyelia, tethered cord syndrome, or traumatic spinal lesions) in 13 patients (34.2%). Functionally, 17 children (44.7%) were ambulatory, and 21 (55.3%) were non-ambulatory. The mean estimated glomerular filtration rate (eGFR) was 118.0 ± 33.2 mL/min/1.73 m^2, and the mean age at initiation of clean intermittent catheterization (CIC) was 5.1 ± 4.0 years (see Table 1 for demographic characteristics).

Inclusion and Exclusion criteria

Inclusion criteria

- NB secondary to operated MMC or other spinal pathologies (diastematomyelia, tethered cord syndrome, or spinal cord injury) with CIC for ≥ 6 months;
- Availability of complete pre-procedure and 6-month follow-up clinical and urodynamic data.

Exclusion criteria

History of major urological reconstructive surgery (e.g., bladder augmentation or ureteral reimplantation) and/or missing baseline data.

Intervention (BTX-A protocol)

All procedures were performed under general anesthesia by the same pediatric urology team. A total of 100 IU of onabotulinumtoxinA (Botox®, Allergan Inc., Irvine, CA, USA) diluted in 10 mL of normal saline was injected intradetrusorally under cystoscopic guidance at 20 evenly distributed sites over the bladder dome, anterior, and lateral walls, sparing the trigone. Injection depth was standardized to 2–3 mm using a 4-mm injection needle. No intraoperative or postoperative complications (e.g., hematuria, fever, or urinary retention) were observed. All patients continued their baseline CIC and antimuscarinic regimens as clinically indicated.

All patients received a fixed dose of 100 IU of onabotulinumtoxinA, diluted in 10 mL of normal saline, and injected into 20 sites. This fixed-dose regimen reflects our institutional protocol, which is largely shaped by national reimbursement constraints: botulinum toxin A for the treatment of pediatric neurogenic bladder is not reimbursed by the social security system; therefore, families must cover the full cost. To limit the financial burden and to allow single-vial use across a broad weight range (10–35 kg), individual dose titration based on weight or capacity was not routinely feasible.

Variables and definitions

Urodynamic variables: Δp_det (cmH_2O) measured before and 6 months after BTX-A injection, cystometric bladder capacity, and bladder volume at 40 cmH_2O.

Detrusor pressure (p_det): Intravesical pressure (p_ves) and abdominal pressure (p_abd) were recorded simultaneously during urodynamic testing. Storage-phase detrusor pressure (p_det) was calculated, in accordance with ICCS standards, as the difference between the two measures (p_det = p_ves − p_abd). Throughout the study, the parameter previously referred to as "storage-phase detrusor pressure" represents storage-phase detrusor pressure (p_det). In pediatric NB, persistent storage-phase p_det > 40 cmH_2O is associated with vesicoureteral reflux, renal scarring, and progressive loss of renal function; accordingly, storage-phase p_det was selected as the primary urodynamic endpoint for evaluating bladder dynamics and treatment outcomes.

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Clinical/cohort variables: age, sex, ambulation status, etiology (operated MMC vs. other spinal pathology), and renal function (eGFR).

Renal function: eGFR was calculated using the updated Schwartz formula, adjusted for age, sex, and height, expressed in mL/min/1.73 m^2. Values below age-specific reference ranges were considered indicative of renal impairment.

Treatment-related variables: use and type of antimuscarinic medication, duration of CIC, and age at initiation of CIC.

Outcomes

Primary outcome: the change in storage-phase detrusor pressure (Δp_det = p_det,6-month − p_det,baseline).

Secondary outcomes: Secondary outcomes included (i) a reduction in storage pressure of ≥10 cmH_2O and (ii) attainment of guideline-based safe storage thresholds (<30 and <35 cmH_2O). The ≥10 cmH_2O cut-off is not a universally standardized value in the literature; rather, it was chosen a priori as a pragmatic, exploratory threshold to facilitate categorical interpretation of treatment response alongside the more clinically relevant pressure.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics version 29.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Paired comparisons between pre- and post-treatment values were performed using the paired t-test or Wilcoxon signed-rank test, as appropriate. Continuous variables were reported as means ± standard deviations (SDs), 95% confidence intervals (CIs), and effect sizes (Cohen's d_z). Associations between Δp_det and continuous covariates were evaluated with Pearson or Spearman correlation coefficients. Group comparisons were conducted using the Mann–Whitney U test for two-group comparisons and the Kruskal–Wallis test for multi-group analyses. Multivariable linear regression was used to identify independent predictors of Δp_det, whereas binary logistic regression was applied to determine predictors of a clinically significant reduction in pressure (≥10 cmH_2O). Receiver Operating Characteristic (ROC) curve analysis was used to determine the optimal baseline pressure cutoff for predicting a favorable response. A two-sided $P < 0.05$ was considered statistically significant. Because the continuous outcome (Δp_det) and the binary responder outcome (≥10 cmH_2O reduction) capture different aspects of treatment response, predictors may show divergent associations across models. Given the limited number of events (10 responders), logistic regression was prespecified as an exploratory analysis. The events-per-variable (EPV) ratio was below the recommended threshold; therefore, the logistic model may be unstable and prone to overfitting. These limitations were acknowledged when interpreting the results.

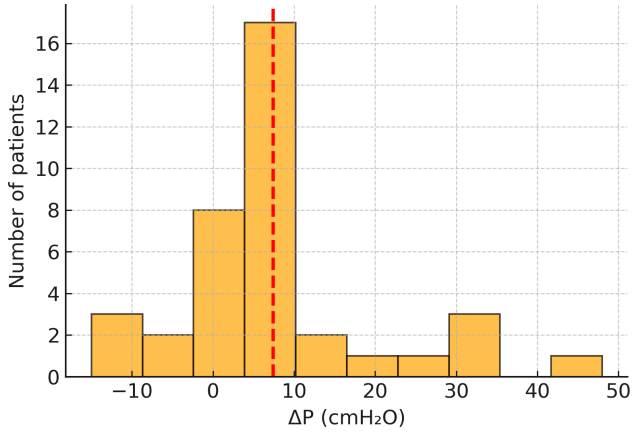

Figure 1. Distribution of storage-phase detrusor pressure change (Δp_det) following BTX-A injection. Most patients experienced a reduction in pressure, while a minority showed paradoxical increases.

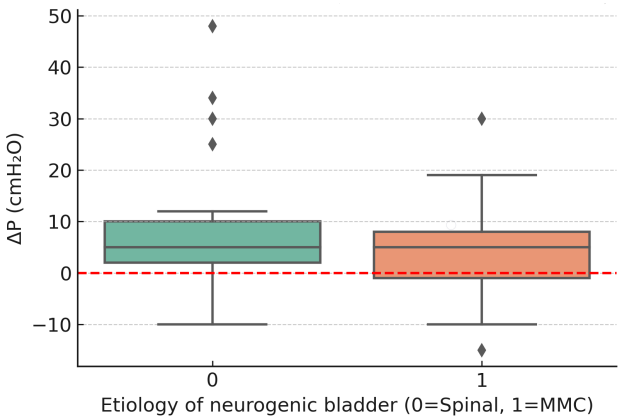

Figure 2. Detrusor pressure change (Δp_det) according to neurogenic bladder etiology (spinal vs. MMC). A greater reduction was observed in the spinal group, but the difference was not statistically significant (P > .05).

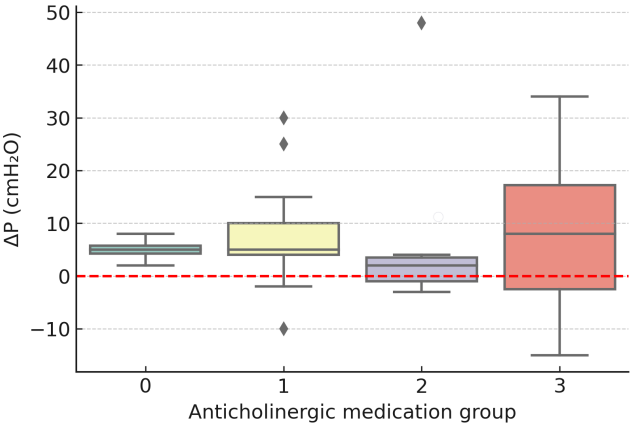

Figure 3. Detrusor pressure change (Δp_det) stratified by anticholinergic medication (0 = None, 1 = Oxybutynin, 2 = Tolterodine, 3 = Propiverine). No significant differences were detected between the groups.

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Table 1. Patient demographics and clinical characteristics.

Parameter	Value
Age (years)	7.8 ± 4.0
Sex	Female: 20 (52.6%), Male: 18 (47.4%)
Etiology of neurogenic bladder	Operated MMC: 25 (65.8%), Other spinal pathology: 13 (34.2%)
Ambulatory status	Ambulatory: 17 (44.7%), Non-ambulatory: 21 (55.3%)
eGFR (mL/min/1.73m²)	118.0 ± 33.2
Age at initiation of CIC (years)	5.1 ± 4.0

Values are presented as mean ± standard deviation (SD) or number (percentage). Abbreviations: MMC, myelomeningocele; eGFR, estimated glomerular filtration rate; CIC, clean intermittent catheterization.

Table 2. Urodynamic findings.

Parameter	Value
Baseline intravesical pressure (cmH_2O)	59.9 ± 21.2
Post-BTX-A intravesical pressure (cmH_2O)	52.5 ± 19.7
Δ Pressure (cmH_2O)	−7.4 ± 12.5
Patients with ≥10 cmH_2O reduction (%)	10/38 (26.3%)
Patients achieving storage pressure <30 cmH_2O (%)	4/38 (10.5%)
Patients achieving storage pressure <35 cmH_2O (%)	5/38 (13.2%)

Values are presented as mean ± standard deviation (SD) or number (percentage). Abbreviations: BTX-A, botulinum toxin A; cmH_2O, centimeters of water.

Table 3. Multivariable linear regression analysis (predictors of ΔP).

Variable	β coefficient	95% CI	P value
Baseline pressure	−0.43	−0.69 → −0.17	.002
Bladder volume at 40 cmH_2O	+5.59	−0.80 → +11.98	.084
Other covariates	NS	--	>0.1

β = standardized regression coefficient; CI = confidence interval; NS = not significant. Abbreviations: ΔP, change in intravesical pressure; cmH_2O, centimeters of water.

Table 4. Univariable correlation analyses.

Variable	Pearson r	P value
Baseline pressure	−0.41	.011
CIC duration	−0.03	.84
Age at CIC initiation	−0.18	.28
Bladder capacity	−0.08	.63
Bladder volume at 40 cmH_2O	−0.06	.72
eGFR	+0.05	.75
Age	+0.03	.86

Pearson's correlation coefficients between intravesical pressure change (ΔP) and clinical variables. Abbreviations: CIC, clean intermittent catheterization; eGFR, estimated glomerular filtration rate; cmH_2O, centimeters of water.

Table 5. Logistic regression analysis (predictors of ≥10 cmH_2O reduction).

Variable	OR	95% CI	
Baseline pressure	1.05	1.00–1.10	.039
Etiology (MMC)	0.29	0.04–2.16	.227
Antimuscarinic use	1.28	0.49–3.33	.617
Age	1.34	0.99–1.81	.055
eGFR	1.04	1.00–1.09	.042

OR = odds ratio; CI = confidence interval; P < .05 was considered statistically significant. Abbreviations: MMC, myelomeningocele; eGFR, estimated glomerular filtration rate.

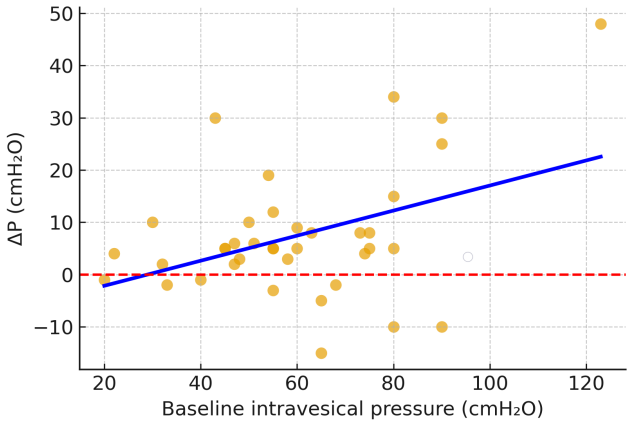

Figure 4. Correlation between baseline storage-phase detrusor pressure and pressure change (Δp_det) after BTX-A injection. Higher baseline pressures were associated with greater reductions (r = --0.41, P = .011).

RESULTS

Primary outcome

The mean baseline p_det was 59.9 ± 21.2 cmH_2O, decreasing to 52.5 ± 19.7 cmH_2O at 6 months, corresponding to an average change of Δp_det = −7.4 ± 12.5 cmH_2O (median −5; range −48 to +15 cmH_2O) (Tables 1 and 2). Most patients exhibited a post-treatment pressure reduction, although a small subset demonstrated minimal or paradoxical increases (Figure 1).

Secondary outcomes

A clinically significant response, defined as a ≥10 cmH_2O reduction in storage pressure, was observed in 26.3% (10/38) of patients, and only 10.5% and 13.2% achieved storage pressures <30 cmH_2O and <35 cmH_2O, respectively. Taken together,

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these findings indicate a modest overall pressure-lowering effect of BTX-A in this cohort, with a relatively small proportion of patients reaching guideline-recommended safe storage thresholds.

Subgroup and correlation analyses

Etiology: The mean pressure reduction was greater in patients with non-MMC spinal pathologies (−8.5 cmH_2O) than in those with myelomeningocele (MMC) (−5.3 cmH_2O); however, this difference was not statistically significant (P > .05) (Figure 2).

Under antimuscarinic therapy, Δp_det did not differ by drug type or treatment duration (P > .05; Figure 3). Although variable responses were observed within the propiverine subgroup, no clear superiority over other agents was demonstrated.

Functional status and CIC: Ambulatory children showed a larger mean reduction (−9.9 vs.−5.4 cmH_2O), which did not reach statistical significance (P = .19). Neither CIC duration nor age at initiation of CIC correlated with Δp_det (both P > .05).

Filling parameters: Δp_det was not significantly correlated with cystometric capacity (r = −0.08, P = .63) or bladder volume at 40 cmH_2O (r = −0.06, P = .72).

Renal function: No significant association was observed between baseline eGFR and Δp_det in univariable analysis (P > 0.05). Comprehensive univariable correlation results are summarized in Table 4.

Multivariable models

Linear regression (Δp_det as continuous outcome): Baseline storage-phase detrusor pressure emerged as an independent inverse predictor of Δp_det (β = −0.43, P = .002).

Bladder volume at 40 cmH_2O showed a borderline association (P = .084), while other covariates were not significant.

The model explained 36% of the variance (R^2 = 0.36; Table 3).

Logistic regression (≥ 10 cmH_2O reduction): Higher baseline storage-phase pressure (OR = 1.05; 95% CI 1.00–1.10; P = .039) and higher eGFR (OR = 1.04; 95% CI 1.00–1.09; P = .042) were independent predictors of a clinically significant response. MMC etiology and age showed nonsignificant trends (Table 5).

ROC analysis

To predict a ≥10 cmH_2O pressure reduction, baseline p_det yielded an AUC of 0.72, with an optimal cutoff of 58 cmH_2O (sensitivity 70%, specificity 65%) (Figure 4).

DISCUSSION

Overall efficacy

Intradetrusor botulinum toxin A (BTX-A) therapy produced a mean reduction of 7.4 cmH_2O in storage-phase detrusor pressure in children with neurogenic bladder (NB). This finding is consistent with previous systematic reviews and meta-analyses demonstrating significant short- and mid-term decreases in detrusor pressure after BTX-A injection [5–9, 12]. However, the magnitude of reduction in our cohort was smaller than the ~20–25 cmH_2O decreases reported in larger pediatric series. This difference may be attributed to our limited sample size, a high proportion of myelomeningocele (MMC) cases, and relatively low baseline pressures. Additional contributors likely include variations in injection technique, dose distribution, and concomitant antimuscarinic regimens [6, 9, 10].

Another factor that may have contributed to the modest and heterogeneous pressure response in our cohort is the use of a fixed 100-IU dose across a relatively wide weight range (10–35 kg). Due to national reimbursement restrictions and requirements for out-of-pocket payments, individualized weight- or capacity-based dose adjustments were not feasible in our setting. Prospective studies comparing fixed and weight-adjusted dosing protocols are warranted to better define the optimal BTX-A regimen in pediatric neurogenic bladder.

Although BTX-A significantly reduced storage-phase detrusor pressure at the group level, the magnitude of benefit in our series was modest, and only a minority of patients achieved either the predefined responder criterion (≥10 cmH_2O reduction) or the guideline-based safe storage threshold (<30–35 cmH_2O). In this context, our data support BTX-A as a clinically relevant but limited pressure-lowering option, rather than a universally transformative intervention for pediatric neurogenic bladder. The relatively low responder rate, compared with larger pediatric series, may reflect our small sample size, the predominance of myelomeningocele cases, relatively low baseline pressures, and the use of a fixed 100 IU dose across a broad weight range. Overall, these observations suggest that BTX-A provides a limited yet meaningful reduction in storage pressure in this high-risk cohort, and its role should be viewed as part of a multimodal, pressure-guided management strategy rather than as a definitive, stand-alone solution.

Response by etiology

Histopathological studies have shown that fibrotic remodeling of detrusor smooth muscle may attenuate BTX-A efficacy in MMC-related NB [11,12]. Although histological data were unavailable in our series, this explanation accords with prior evidence. In contrast, greater pressure reductions have been documented in patients with non-MMC spinal dysraphism or with traumatic etiologies [13]. Our cohort demonstrated a similar trend toward a greater reduction among non-MMC cases, although statistical significance was not achieved due to limited power. Multicenter studies have likewise indicated that underlying etiology influences BTX-A responsiveness [14,15].

A small subset of patients exhibited paradoxical increases in

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storage pressure after BTX-A injection. Several mechanisms may account for this phenomenon. First, detrusor–sphincter dyssynergia may increase outlet resistance during bladder filling, thereby elevating storage-phase detrusor pressure despite detrusor chemodenervation. Second, transient inflammatory changes or mucosal edema following injection may temporarily augment storage pressures. Third, in patients with spinal dysraphism, autonomic dysreflexia–related hypertensive bladder responses may contribute to abrupt physiologic pressure surges. Finally, insufficient intradetrusor diffusion of BTX-A in severely fibrotic or poorly compliant bladders may limit therapeutic effect and even provoke compensatory overactivity. These mechanisms may collectively explain the paradoxical findings observed in this cohort and should be considered when interpreting individualized treatment response.

Clinically meaningful outcomes and pressure targets

Maintaining safe storage pressures (<30–35 cmH_2O) remains the principal determinant of upper urinary tract preservation [1,4]. In our series, the rate of clinically meaningful response—defined as a ≥10 cmH_2O reduction—was 26.3%. This is slightly lower than the 30–50% response rates reported in prior meta-analyses [4–9, 12], likely reflecting the small sample size, MMC predominance, and relatively low baseline pressures. Differences in injection techniques and adjunctive medications could also play a role.

Multivariable analysis identified higher baseline p_det as an independent predictor of greater pressure reduction, thereby supporting earlier BTX-A intervention in high-risk patients [10,11,14].

Our ROC analysis confirmed that a baseline pressure ≥58 cmH_2O predicted a clinically meaningful (≥10 cmH_2O) response with an AUC of 0.72, a sensitivity of 70%, and a specificity of 65%. This threshold may serve as a pragmatic marker for selecting optimal BTX-A candidates within the pediatric NB population with elevated baseline pressures.

Although Δp_det was analyzed as a continuous variable, we also reported a ≥10 cmH_2O reduction as a clinically interpretable categorical endpoint. Nevertheless, aligned with EAU/ESPU and ICCS guidelines, the primary therapeutic goal remains to achieve safe storage pressures (<30–35 cmH_2O) (1–4). Attaining this threshold has been associated with reduced renal scarring and better preservation of glomerular filtration rate (eGFR) [15]. In our cohort, no renal deterioration was observed among children who achieved safe storage levels, further underscoring the clinical importance of pressure-targeted management.

Renal function

Although univariable analysis revealed no direct correlation between eGFR and Δp_det, multivariable logistic regression identified preserved renal function as an independent predictor of a clinically meaningful response. eGFR was consistently calculated using the Schwartz formula, thereby ensuring methodological reliability. These findings suggest that preserved renal reserve may enhance responsiveness to BTX-A. Consistent with this, Gillon et al. demonstrated that BTX-A helped maintain renal function in multicenter pediatric cohorts [15]. Hence, renal function may represent not only an outcome but also a determinant of treatment success.

Although baseline eGFR did not correlate with Δp_det in univariable analysis, it emerged as a significant predictor in the exploratory logistic regression model. This discrepancy likely reflects the analytical difference between modeling a continuous change (Δp_det) versus a binary responder outcome (≥10 cmH_2O reduction). Additionally, the logistic model was constrained by a low events-per-variable ratio (10 events per variable), increasing the risk of instability and overfitting. Therefore, the association between preserved renal function and categorical response should be interpreted cautiously and considered hypothesis-generating rather than confirmatory.

Antimuscarinic therapy and combination regimens

We found no significant association between the type or duration of antimuscarinic therapy and Δp_det, consistent with previous pediatric data showing no superiority among agents [16]. Current EAU/ESPU guidelines emphasize tolerability and side-effect profiles rather than efficacy differences when selecting antimuscarinics [4]. Thus, BTX-A responsiveness appears largely independent of prior or concurrent antimuscarinic use.

Comparison with existing literature

Large observational series [4–6, 9–13] and meta-analyses [7–9, 12,14] provide robust evidence supporting the efficacy of BTX-A in pediatric NB. However, long-term renal outcomes and repeat-injection protocols remain underinvestigated. Zhou et al. [14] reported that repeated BTX-A injections can sustain a therapeutic benefit, albeit with diminishing magnitude over time. Other multicenter studies have shown that early BTX-A use in high-risk patients may aid upper tract preservation [15]. Collectively, these findings emphasize the importance of etiology, baseline pressure, and intervention timing in determining both short- and long-term outcomes.

General interpretation

Taken together, our results confirm that BTX-A significantly and safely reduces storage-phase detrusor pressure in pediatric NB. The magnitude of benefit varies according to baseline pressure, renal reserve, and underlying etiology, with patients with non-MMC spinal dysraphism showing a trend toward a greater response. These observations underscore the relevance of risk-stratified, pressure-targeted, and individualized management strategies, which constitute the cornerstone of contemporary pediatric neuro-urological care [1,10,15].

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Clinical implications

BTX-A is a safe and effective option for reducing storage-phase detrusor pressure in pediatric patients with neurogenic bladder.

Children presenting with higher baseline storage pressures and preserved renal function are more likely to achieve clinically meaningful improvement, highlighting the importance of these parameters for treatment timing and patient selection [10–15].

The observed trend toward greater responsiveness in non-MMC spinal dysraphism than in MMC suggests that etiology-specific management strategies may optimize therapeutic outcomes [11–14].

Incorporating BTX-A into the pediatric neurogenic bladder treatment algorithm can help restore safe storage pressures, preserve upper urinary tract integrity, and delay or even prevent the need for reconstructive surgery [1,4,15].

These findings reinforce the importance of a pressure-targeted, risk-stratified, and individualized approach in accordance with ICCS and EAU/ESPU guidelines and emphasize the role of standardized urodynamic assessment and early identification of high-pressure bladders to improve long-term renal and functional outcomes [1–4].

In the present study, we additionally reported the proportion of patients achieving a reduction of $\geq$10 cmH_2O as an exploratory categorical endpoint. This cut-off was not derived from formal consensus or guideline recommendations, but was selected as a pragmatic threshold to reflect a clearly perceptible change in storage pressure and to allow comparison with previous pediatric BTX-A series that reported similar magnitudes of decrease. Nevertheless, in line with ICCS and EAU/ESPU guidelines, our primary clinical interpretation remains focused on achieving safe storage pressures (<30–35 cmH_2O), which are more directly linked to upper urinary tract protection.

Limitations

This study has several limitations that warrant consideration. The retrospective, single-center design introduces inherent risks of selection and information bias, limiting causal inference. The sample size (n = 38) restricts the statistical power of subgroup analyses, particularly regarding etiology and renal outcomes. The follow-up duration (6 months) captures short-term efficacy but may not reflect the sustained effects observed in longer-term studies [4–9, 14]. Histopathological data were unavailable to clarify biological mechanisms underlying differential responses between MMC and non-MMC etiologies [11–13]. Lastly, although all procedures followed standardized ICCS criteria, variability in injection distribution and concurrent medical regimens could have introduced confounding effects. Future multicenter prospective studies with extended follow-up, larger cohorts, and additional urodynamic parameters (compliance, capacity, electromyography, lesion level) are needed to refine predictive models and establish evidence-based algorithms for BTX-A use in pediatric NB [3,7,10,14].

CONCLUSION

Intradetrusor BTX-A significantly reduced the storage-phase detrusor pressure over six months in children with neurogenic bladder ($\Delta p\_det = -7.4 \pm 12.5$ cmH_2O). Treatment response was independently associated with baseline p_det and renal reserve; etiology exhibited a nonsignificant trend favoring spinal dysraphism over MMC. None of the following correlated with outcomes: a history of antimuscarinic use, clean intermittent catheterization parameters, or cystometric capacity. These findings reinforce the role of BTX-A as a cornerstone in pressure-guided, individualized, and risk-adapted management of pediatric NB [3–5, 7–10, 14–16]. By targeting high-pressure bladders before irreversible detrusor fibrosis and renal injury occur, BTX-A offers a minimally invasive yet effective strategy to protect upper urinary tract integrity and improve long-term urological prognosis.

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Ethics Committee Approval: This study was approved by the Ethics Committee of Izmir City Hospital (Decision No: 338/2025, Date: August 13, 2025).

Informed Consent: Due to the retrospective nature of the study, informed consent was waived. No animal or invasive experimental procedures were performed.

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REFERENCES

1. Stein R, Bogaert G, Doğan HS, et al. EAU/ESPU guidelines on the management of neurogenic bladder in children and adolescents—Part I: Diagnostics and conservative treatment. *Neurourol Urodyn.* 2020;39(1):45–57. doi: 10.1002/nau.24211.
2. Bauer SB, Nijman RJ, Drzewiecki BA, Sillén U, Hoebeke P. International Children's Continence Society standardization report on urodynamic studies of the lower urinary tract in children. *Neurourol Urodyn.* 2015;34(7):640–647. doi: 10.1002/nau.22783.
3. Austin PF, Bauer SB, Bower W, et al. The standardization of terminology of lower urinary tract function in children and adolescents: Update report from the ICCS. *Neurourol Urodyn.* 2016;35(4):471–481. doi: 10.1002/nau.22751.
4. EAU Guidelines on Paediatric Urology. Arnhem (NL): European Association of Urology Guidelines Office. 2023. ISBN: 978-94-92671-19-1.
5. Wu SY, Chang SJ, Yang SS, Hsu CK. Botulinum Toxin Injection for Medically Refractory Neurogenic Bladder in Children: A Systematic Review. *Toxins (Basel).* 2021;13(7):447. doi: 10.3390/toxins13070447.
6. Badawi JK. Botulinum toxin therapy in children with neurogenic detrusor overactivity. *Turk J Urol.* 2020;46(1):2–12. doi: 10.5152/tud.2019.19070.
7. Panunzio A, Orlando R, Mazzucato G, et al. Response to Treatment with Botulinum Neurotoxin A (BoNT-A) in Children and Adolescents with Neurogenic Lower Urinary Tract Dysfunction and Idiopathic Overactive Bladder: A Systematic Review and Meta-Analysis. *Toxins (Basel).* 2024;16(10):443. doi: 10.3390/toxins16100443.
8. Zulli A, Paglia G, Raffaele A, Mosiello G. Intravesical Botulin Toxin-A injections for neurogenic bladder dysfunction in children: A decade update. *Toxins (Basel).* 2024;16(8):339. doi: 10.3390/toxins16080339.
9. Gamé X, Mouracade P, Chartier-Kastler E, et al. Botulinum toxin-A (Botox) intradetrusor injections in children with neurogenic detrusor overactivity/neurogenic overactive bladder: a systematic literature review. *J Pediatr Urol.* 2009;5(3):156-64. doi: 10.1016/j.jpurol.2009.01.005.
10. Schulte-Baukloh H, Knispel HH, Stolze T, Weiss C, Michael T, Miller K. Repeated botulinum-A toxin injections in the treatment of children with neurogenic detrusor overactivity. *Urology.* 2005;66(4):865–870. doi: 10.1016/j.urology.2005.04.054.
11. Hascoet J, Peyronnet B, Forin V, et al. Intradetrusor Injections of Botulinum Toxin Type A in Children With Spina Bifida: A Multicenter Study. *Urology.* 2018;116:161-167. doi: 10.1016/10.1016/j.urology.2018.02.033
12. Giannantoni A, Mearini E, Del Zingaro M, Porena M. Six-year follow-up of botulinum toxin A intradetrusorial injections in patients with refractory neurogenic detrusor overactivity: Clinical and urodynamic results. *Eur Urol.* 2009;55(3):705–711. doi: 10.1016/j.eururo.2008.08.048.
13. Schulte-Baukloh H, Michael T, Stürzebecher B, Knispel HH. Botulinum-a toxin detrusor injection as a novel approach in the treatment of bladder spasticity in children with neurogenic bladder. *Eur Urol.* 2003;44(1):139-43. doi: 10.1016/s0302-2838(03)00136-2.
14. Franco I, Hoebeke PB, Dobremez E, et al. Long-term safety and tolerability of repeated treatments with onabotulinumtoxinA in children with neurogenic detrusor overactivity. *J Urol.* 2023;209(4):774–784. doi: 10.1097/JU.0000000000003157.
15. He G, Shen N, Feng S. Botulinum toxin A for the treatment of neurogenic bladder in children: A systematic review and meta-analysis. *ANZ J Surg.* 2025;95(6):1115–1121. doi: 10.1111/ans.19309.
16. Madersbacher H, Mürtz G, Alloussi S, et al. Propiverine vs oxybutynin for treating neurogenic detrusor overactivity in children and adolescents: results of a multicentre observational cohort study. *BJU Int.* 2009;103(6):776-81. doi: 10.1111/j.1464-410X.2008.08093.x.

https://doi.org/10.5455/annalsmedres.2025.11.336