

Effect of constipation treatment on children with lower urinary tract symptoms

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ABSTRACT

Introduction: We aimed to evaluate the effects of constipation treatment on lower urinary tract symptoms (LUTS) in children presenting with both conditions.

Methods: A total of 60 children with LUTS and concomitant constipation were included. Constipation was diagnosed with the Rome IV criteria, based on clinical

history and validated assessment tools, including the Voiding Dysfunction Symptom Score (VDSS) and the Bristol Stool Form Scale (BSFS). All patients received oral lactulose treatment and were followed for one month. LUTS parameters were assessed subjectively and objectively through bladder diaries, uroflowmetry, postvoid residual (PVR) volumes, and symptom scores.

Results: The median age of the cohort was 90 months; 45% were male. Pre-treatment, 75% of patients demonstrated normal uroflow patterns, which increased to 93.3% post-treatment. Significant improvements were observed in maximum and minimum voided volumes from bladder diaries ($p < 0.001$ for both), as well as in uroflowmetry parameters, including maximum flow rate (Q_{max}), voided volume, and PVR ($p < 0.001$,

KEY MESSAGES

- Treatment of constipation results in significant improvement of LUTS in children.
- Both subjective symptom scores and objective urodynamic parameters improve after constipation management.
- Routine assessment and treatment of bowel dysfunction should be an integral part of pediatric LUTS management.

$p < 0.001$, $p = 0.001$, respectively). Symptom assessment, including VDSS, BSFS, and quality of life (QoL), also showed statistically significant improvements post-treatment ($p < 0.001$ for all). Subgroup analysis revealed significant differences in bladder diary and uroflowmetry parameters between treatment responders and non-responders. In multivariate logistic regression, only maximum voided volume from bladder diaries and voided volume on uroflowmetry were independently associated to treatment response.

Conclusions: Treatment of constipation in children with LUTS leads to significant improvements in both subjective and objective parameters. Comprehensive evaluation and management of bowel function should be considered a fundamental component in the care of paediatric patients with LUTS.

INTRODUCTION

Nearly half of the visits to paediatric urology outpatient clinics are due to LUTS [1]. These children may present with storage symptoms such as increased or decreased voiding frequency, urgency, nocturia; voiding symptoms such as hesitancy, straining, weak stream, intermittency, dysuria. In order to evaluate LUTS in children for treatment purposes, these symptoms must have been present for at least 3 months, and the child must be over the age of 5 [2].

The underlying causes of LUTS are frequently linked to dysfunctional voiding or overactive bladder (OAB) symptom complexes. In non-neurogenic cases, contributing factors can include behavioural issues, delayed cortical development, immature pontine control, and bladder and bowel dysfunction (BBD).

BBD is a frequently encountered yet often under-recognized condition in the paediatric population. It encompasses a wide range of LUTS that are commonly accompanied by gastrointestinal issues, particularly constipation and/or encopresis, and accounts for up to 40% of paediatric urology referrals [3]. The relationship between the bladder and bowel is well documented. Generally, increased rectal stool burden can interfere with bladder function with by exerting mechanical pressure, which reduces bladder capacity and may lead to urgency and urinary frequency, by altering the normal neural signalling pathways to the bladder and pelvic floor, which can diminish the sensation to void, cause bladder overactivity, impair bladder emptying, and result in elevated post-void residual (PVR) volumes [4]. International Children's Continence Society (ICCS) recommends that initial treatment for BBD should be focused on constipation and/or faecal incontinence [5].

Considering the relationship between LUTS with encopresis and constipation, as mentioned above, it is essential to include an evaluation of bowel function in the medical history of children presenting with LUTS. Addressing these defecation-related symptoms should also be an integral part of the treatment plan [5]. With this study, it was planned to comprehensively demonstrate the effect of constipation treatment on

LUTS such as enuresis, urinary incontinence, frequency, and urgency in paediatric patients who present with both constipation and LUTS, using symptom scores and lower urinary tract parameters.

METHODS

Children over the age of 5 who presented with LUTS such as enuresis, urinary incontinence, urgency, frequency and constipation lasting for at least 3 months were included in the study. Children were evaluated at our clinic between January and June 2024. Ethics approval was obtained from the local human ethics committee of the institution (Protocol No: 0819) for this prospective study.

Children with urinary tract infections (UTI), malignancy, neurogenic aetiology, anatomical abnormalities, faecal incontinence were excluded. Children with intestinal surgery or previous medical treatment for both voiding symptoms and constipation were also excluded. Only the primary cases of LUTS with constipation constituted the main study group. Patient selection is detailed in Figure 1.

The diagnosis of lower urinary tract dysfunction was based on mainly a history of enuresis, urinary incontinence, frequency, and urgency. All participants underwent clinical evaluation with uroflowmetry and ultrasonographic PVR volume measurement, 3-day bladder diary and Voiding Dysfunction Symptom Score (VDSS) [6]. Constipation was defined according to Rome IV paediatric criteria. Bristol Stool Form Scale (BSFS) and the VDSS were used as complementary tools to document stool form and symptom severity [7]. Also, BSFS was routinely obtained from all patients baseline and at the one-month control. According to the BSFS, types 1 and 2 were considered constipation [8].

Children presenting with constipation were routinely started on oral lactulose at a dose of 1–2 g/kg, administered once or twice daily. The dosage was titrated to achieve a target of 1–2 soft bowel movements per day [9]. In this study, lactulose was selected due to its greater availability and lower cost within our country's healthcare setting. Compliance with lactulose treatment was determined by evaluating parental statements and stool diaries at each follow-up visit. In addition, children received behavioural recommendations including dietary modification, adequate hydration, and regular toileting habits.

At the one-month follow-up visit, the presence or resolution of LUTS was subjectively evaluated by the child and/or their parent, with particular attention to the occurrence of dryness. Objective evaluation of LUTS was performed using the VDSS. Additionally, uroflowmetric parameters, PVR volume, 3-day bladder diary, and symptom scores were recorded and compared between baseline and post-treatment assessments to evaluate the impact of constipation management on urinary symptoms. Quality of Life (QoL) was assessed using the single parent-answered QoL question included in the VDSS. Expected Bladder Capacity (EBC) was calculated using the ICCS formula: $EBC (mL) = "30 \times age (years) + 1"$ [10]. Uroflowmetry and curve standardization was performed according to ICCS guidelines [2]. A minimum

acceptable voided volume for interpretation was set at 50% of EBC [2]. All measurements were performed using a self-calibrating autonomous uroflowmetry device (Aymed® Uroscan Plus) and pelvic ultrasound with PVR measurement (Siemens® Acuson X300). Uroflowmetries were carried out twice. PVR urine volumes were measured immediately after voiding using pelvic ultrasonography with the formula “anteroposterior diameter × oblique diameter × transverse diameter × 0.52” [11].

Treatment response was evaluated at the routine first month follow-up visit. Children were classified as responders if their bowel movement pattern improved to BSFS other than types 1 and 2. Patients who had BSFS type 1 or type 2 stool patterns before treatment and continued to demonstrate the same stool patterns at the 1-month follow-up were defined as non-responders.

The primary objective of this study was to evaluate the effect of a one-month lactulose regimen on LUTS in children with constipation. The primary endpoint was change in total VDSS at one month compared to baseline. Secondary endpoints included changes in uroflowmetry parameters, PVR, 3-day bladder diary variables, and parent-reported QoL.

Statistical analysis

The G*Power program was used for the power analysis. Since no previous study had investigated the use of oral lactulose in children, the study by Erickson et al., which evaluated the effect of polyethylene glycol treatment on lower urinary tract parameters in constipated children, was used as a reference [12]. It was calculated that at least 59 participants would be required to achieve 80% power ($d=0.37$, $\alpha=0.05$). Statistical analyses were conducted using IBM SPSS 25.0. Due to non-normal data distribution (Kolmogorov-Smirnov test), non-parametric tests were applied. Numerical data were presented as median (IQR), categorical data as counts/percentages. The Chi-square test analysed categorical data, while the Mann-Whitney U test compared groups. Wilcoxon tests assessed pre- and post-treatment differences. In addition to univariate analyses, exploratory multivariable logistic regression analyses were performed to identify independent predictors of treatment response and to adjust for potential confounders such as age, sex, and baseline symptom severity. Missing data were handled using listwise deletion, as the proportion of missing values was less than 5%. To minimize the risk of type I error, correlation analyses were restricted to clinically relevant variables. Statistical significance was set at $p<0.05$.

RESULTS

This study included 60 children. When the demographic data of these children were examined, the median age was 90 (71.5–145) months. Of the children, 27 (45%) were boys and 33 (55%) were girls. Patients with complaints of constipation, urinary incontinence was present in 65%, and enuresis was observed in 51.7% as accompanying LUTS. Before constipation treatment, the uroflowmetry patterns of the children were

analysed, and 45 (75%) had a normal pattern, while 15 (25%) had plateau, tower, intermittent, or staccato patterns. After constipation treatment, 56 (93.3%) children had a normal flow curve (Table 1).

When the pre- and post-treatment parameters were compared, a statistically significant difference was found in the maximum and minimum voided volumes obtained from bladder diaries ($p < 0.001$, $p < 0.001$, respectively). The median maximum voided volume before treatment was 200 ml, which increased to 210 ml after treatment. The minimum voided volume was 50 ml before treatment and increased to 75 ml post-treatment. Statistically significant differences were also found in Qmax, voided volume, and PVR values obtained from uroflowmetry before and after treatment ($p < 0.001$, $p < 0.001$, $p = 0.001$, respectively). The median Qmax value before treatment was 14 ml/s, increasing to 15 ml/s after treatment. The median voided volume before treatment was 130 ml and increased to 160.5 ml after treatment. The median PVR value remained 10 ml before and after treatment. When pre- and post-treatment symptom scores were compared, statistically significant changes were observed in the VDSS, and QoL scores ($p < 0.001$, $p < 0.001$, respectively) (Table 2).

Subsequently, the children were divided into subgroups based on their response to constipation treatment, and sub-group analysis was conducted. At the first month follow-up, 49 (81.7%) patients were classified as responders, while 11 (18.3%) patients were identified as non-responders based on the predefined BSFS criteria. Statistically significant differences were observed between the treatment-responsive and non-responsive groups in pre-treatment bladder diary maximum voided volume, Qmax, and PVR as well as in post-treatment bladder diary maximum voided volume, Qmax, and PVR ($p = 0.021$, $p = 0.032$, $p = 0.034$, $p = 0.028$, $p = 0.032$, $p = 0.024$, respectively) (Table 3) (Figure 2). None of the children who received oral lactulose for the treatment of constipation experienced any adverse effects related to this therapy.

The maximum and minimum voided volumes recorded in the bladder diary were compared between the groups that responded and did not respond to constipation treatment, based on the ratio to the EBC, both before and after treatment. A statistically significant difference was found between the groups in terms of the ratio of maximum voided volume to EBC before and after treatment ($p = 0.025$ and $p = 0.035$, respectively) (Table 3).

In the multivariate logistic regression analysis, treatment response to constipation therapy was defined as the dependent variable. Baseline bladder diary and uroflowmetry parameters were included in the model to evaluate their association with treatment response. Among the variables analysed, baseline maximum voided volume in the bladder diary and baseline voided volume measured by uroflowmetry were independently associated with treatment response. No other baseline demographic or clinical parameters showed a significant association (Table 4).

DISCUSSION

According to our results significant improvements were observed in voided volumes from bladder diaries, as well as in uroflowmetry parameters such as Qmax, voided volume, and PVR. VDSS and QoL also showed statistically significant improvements post-treatment. The statistically significant post-treatment changes observed in these parameters can be interpreted as a positive effect of constipation treatment. The changes in voided volume, Qmax, PVR, VDSS, and QoL were all highly significant. The clinical implications of these changes should also be considered. When examining the median values, symptom scores decreased, while voided volumes increased substantially after treatment. Although the increase in Qmax from 14 mL/s to 15 mL/s appears to be a minor positive change, the highly significant p-value ($p < 0.001$) suggests that this improvement was widespread across the study population. It may be speculated that greater changes could be observed with longer follow-up periods. Similarly, although the median PVR value remained 10 mL both before and after treatment, the narrowing of the distribution may have contributed to the highly significant result ($p = 0.001$).

Subgroup analysis revealed significant differences in bladder diary and uroflowmetry parameters between treatment responders and non-responders. Non-response to treatment despite a standardized protocol may be related to unmeasured individual differences in bowel motility. Additionally, the presence of a non-responder group may reflect to differences in the severity or duration of bowel dysfunction, or to additional underlying factors such as pelvic floor dysfunction, highlighting the need for individualized management and longer follow-up.

In our study, multivariate analysis identified only maximum voided volume from bladder diaries and voided volume by uroflowmetry as independently associated with treatment response, while other baseline parameters did not show a significant effect. Importantly, these associations do not imply that bladder parameters predict constipation severity or treatment efficacy directly. Instead, they may serve as clinical correlates of response, highlighting the close functional interaction between bowel and bladder systems.

A review of the literature reveals numerous studies evaluating the relationship between LUTS and constipation [13, 14]. Sampaio et al. revealed that constipated children were 6.8 times more likely to have LUTS than those not constipated. Constipation was seen in 8.2% of children without dysfunctional voiding and in 35.2% of children with dysfunctional voiding. This relationship between dysfunctional voiding and constipation was calculated as strikingly significant ($p < 0.001$). They also pointed out that children with more severe constipation have more severe urinary symptoms [14].

Abreu et al. conducted another trial also documented the correlation between constipation and voiding symptoms. In this study, the VDSS was used to assess voiding dysfunction, while the Rome IV criteria were employed for the evaluation of constipation. However, unlike our study, this publication did not include a post-

treatment assessment. They showed that constipated children had higher constipation scores and voiding scores, with both scores increasing with the severity of functional constipation in 128 children with LUTS. They calculated a moderate correlation between the constipation score and the voiding dysfunction score. In the study by Abreu et al., the authors referred to “*voiding symptoms*”, which mainly describe bladder emptying phase symptoms. However, storage symptoms, such as overactive bladder, would also be expected to be considered in this context. Furthermore, the modified adult constipation score used in their study had not yet been validated at the time, which may limit the generalizability of their findings [13].

Shaikh et al. evaluated the prevalence of BBD in a well-characterized population of toilet-trained children with UTI and found a remarkably high prevalence of LUTS and constipation, affecting 54% of the study group. Interestingly, BBD was associated with an increased risk of recurrent UTI in the placebo subgroup. These findings suggest that BBD is not merely a clinical observation but may represent a pathophysiological interaction that predisposes to recurrent UTIs. Rectal distension due to functional constipation can exert mechanical and neural pressure on the bladder and urethra, impairing complete bladder emptying and increasing post-void residual volume, which provides a favourable environment for bacterial growth. Furthermore, the bladder and rectum share sacral neural pathways, and rectal fullness can inhibit bladder contractility, exacerbating LUTS. Chronic constipation may also lead to pelvic floor dyssynergia, further compromising bladder emptying and increasing UTI risk. These pathophysiological insights support the clinical recommendation by Shaikh et al. that early screening and management of BBD may reduce the risk of recurrent UTIs [15]. Borch et al. conducted study with 73 children. In this study, similar to our own, children presenting with both LUTS and constipation were treated with laxatives, and post-treatment outcomes were compared with pre-treatment findings. They showed that of the children with daytime urinary incontinence, 68% had at least a 50% reduction in number of daytime incontinence episodes by successful relief of constipation and 27% became completely continent during daytime. The authors recommend empirical treatment approach for bowel symptoms before intervening for bladder dysfunction in children with BBD. Therefore, the clinical approach of treating constipation in children with LUTS as the initial step is also justified in light of the results of this study [16]. Loening-Baucke et al. fulfilled larger trial on 234 children with chronic constipation, relief of constipation resulted in disappearance of urinary incontinence in 89% and nocturnal enuresis in 63% of patients all patients in 12-month follow-up. In this study, unlike ours, children were also evaluated for UTIs, and in addition to the significant improvements observed in LUTS following constipation treatment, a reduction in the rate of recurrent UTIs was also reported [17].

Erickson et al. demonstrated that aggressive treatment of the constipation provided cessation of infection in 44 patients and enuresis in 22 of 32 patients. In this study, unlike ours, polyethylene glycol 3350 was used for the treatment of constipation.

They performed uroflowmetry and PVR measurements before and during treatment. The results documented that constipation resolution was associated with significant improvement in uroflowmetric parameters like our study. Particularly, the mean voided volume was almost doubled from 140 ml to 204 ml. They also observed a significant increase in Qmax from a mean value of 8.8 ml/s to 12.7 ml/s. Also, PVR value was remarkably decreased from 83 ml to 30 ml by constipation resolution. In our study, we observed similar findings in terms of uroflowmetry data by constipation resolution [12]. Our study has several limitations. First, the absence of a control group limits the ability to draw causal inferences regarding the observed improvements. Second, the follow-up period was relatively short, which may not fully reflect the long-term effects. Future studies with larger sample sizes, control groups, and longer follow-up periods are warranted to confirm these findings. Furthermore, future prospective studies, incorporating objective measures such as rectal diameter assessment or bowel diaries in addition to symptom scores may provide a more comprehensive evaluation of constipation. In our study, constipation severity was not quantitatively assessed, and all patients received standard-dose treatment; therefore, a potential dose-response relationship could not be evaluated. We believe that analyses focusing on this aspect in future studies will be beneficial in evaluating the effect of constipation treatment on LUTS. In addition, we think that it would be useful to show the effect of constipation treatment on urodynamic parameters with studies designed with children with treatment-resistant non-neurogenic and neurogenic LUTS who have indications for urodynamic studies.

CONCLUSIONS

We revealed that treatment of constipation in children with LUTS leads to significant improvements in both subjective and objective LUTS parameters. Comprehensive assessment and management of bowel function should be considered an essential component in the care of children with LUTS. Children with treatment-resistant LUTS may need to be re-evaluated for underlying intestinal dysfunction.

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FIGURES AND TABLES

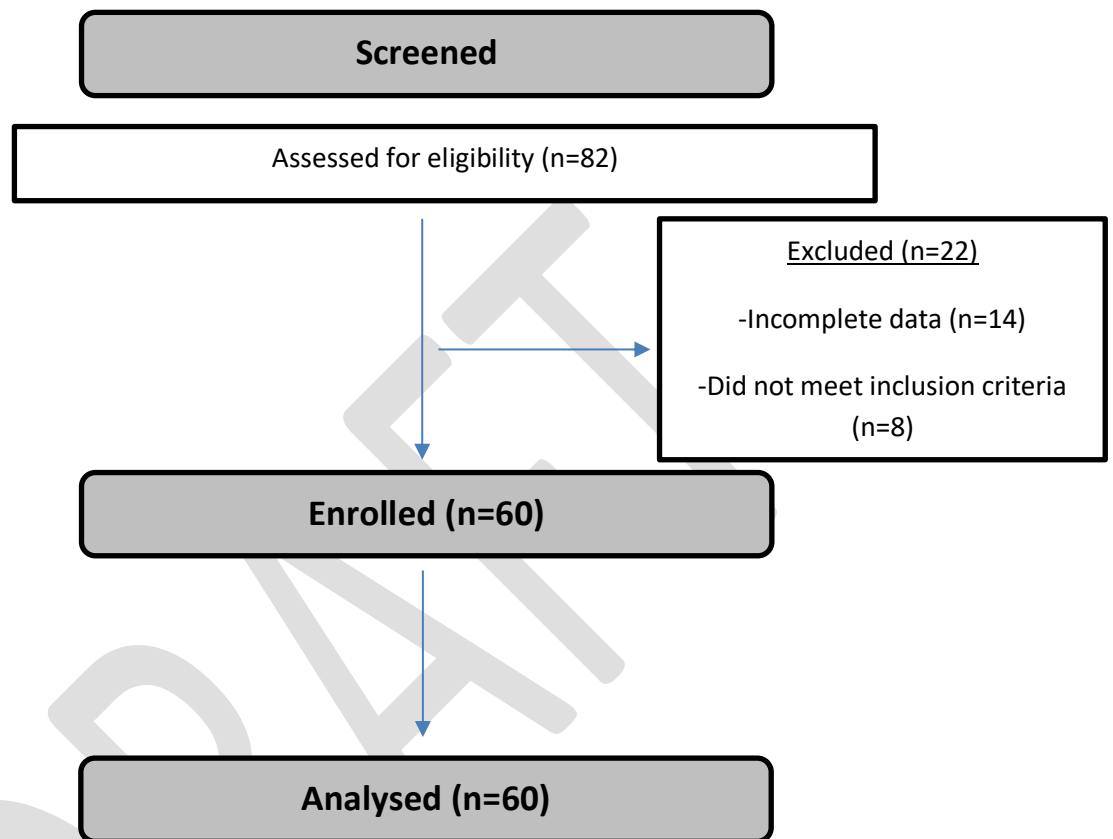
Figure 1. Patient flow diagram showing numbers screened, excluded (with reasons), enrolled and analyzed.

Figure 2. Comparison of post-treatment bladder function parameters between responders and non-responders. Box plots compare post-treatment bladder function parameters between responders and non-responder groups, including (A) postvoid residual (PVR) volume, (B) voided volume measured by uroflowmetry, and (C) the ratio of maximum voided volume to expected bladder capacity (EBC). The central line represents the median, the box indicates the interquartile range (IQR), and the whiskers represent the minimum and maximum values excluding outliers. Between-group comparisons were performed using non-parametric statistical tests.

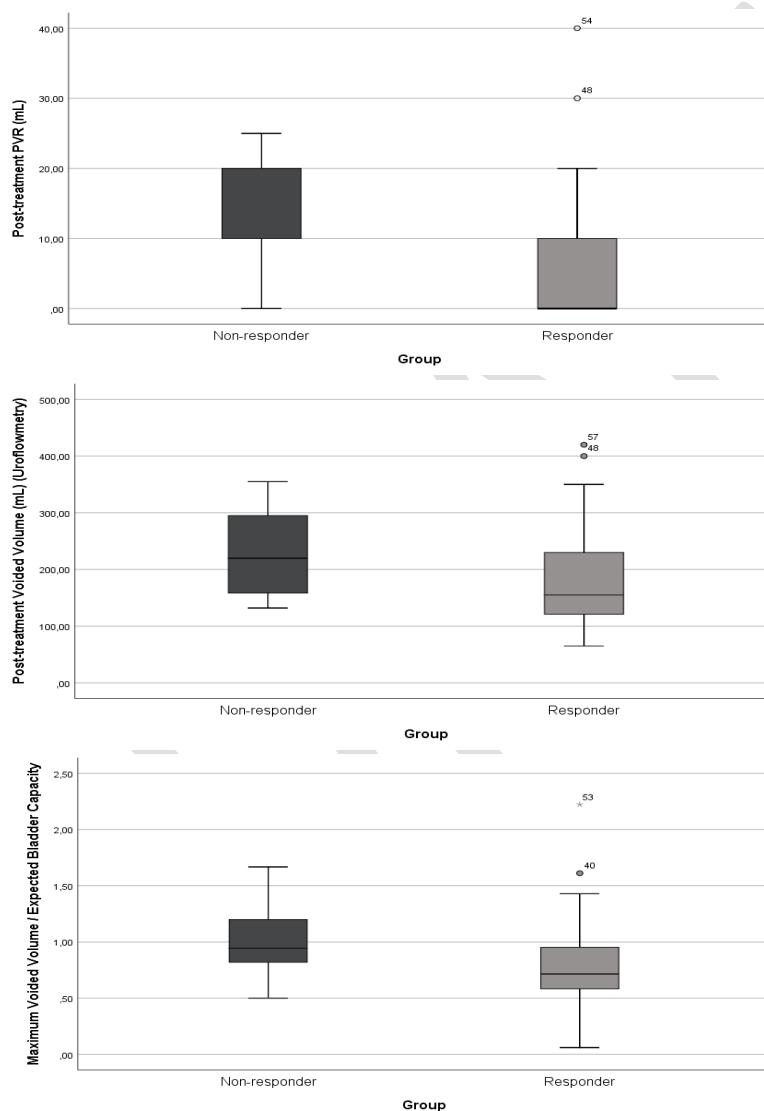


Table 1. Demographic analysis	
	(n:60)
Age, months, median (IQR)	90 (72.2–134.7)
Sex, male/female, (%)	27/33 (45/55)
Incontinence, n (%)	39 (65)
Enuresis, n (%)	31 (51.7)
Uroflowmetry curve, n (%)	
Pre-treatment	
Normal	45 (75)
Tower	1 (1.7)
Staccato	6 (10)
Intermittent	3 (5)
Plateau	5 (8.3)
Post-treatment	
Normal	56 (93.3)
Tower	0
Staccato	1 (1.7)
Intermittent	1 (1.7)
Plateau	2 (3.3)

IQR: interquartile range.

Table 2. Comparison of lower urinary tract system parameters			
	Pre-treatment	Post-treatment	p
Bladder diary			
Maximum voided volume (mL)	200 (112.5–247.5)	210 (150–297.5)	<0.001
Minimum voided volume (mL)	50 (30–97.5)	75 (50–120)	<0.001
Urination frequency (per day)	8 (6–10)	7 (7–9)	0.186
Uroflowmetry			
Qmax (mL/s)	14 (12–16)	15 (13–17)	<0.001
Voided volume (mL)	130 (90.7–204.2)	160.5 (132.7–243.7)	<0.001
PVR volume (mL)	10 (0–20)	10 (0–10)	0.001
VDSS	13 (9–15)	8 (5–11.7)	<0.001
QoL	2 (1–3)	1 (1–1)	<0.001

All continuous variables are presented as median (IQR). IQR: interquartile range; PVR: postvoid residual; Qmax: maximum flow rate; QoL: quality of life; VDSS: voiding dysfunction symptom score.

Table 3. Comparison of constipation treatment response			
	Responder group (n:49)	Non-responder group (n:11)	p
Age (months)	89 (71.5–130)	99 (73–145)	0.417
EBC (mL)	240 (195–345)	270 (210–390)	0.499
Pre-treatment			
Bladder diary			
Maximum voided volume (mL)	190 (100–215)	300 (165–320)	0.021
Minimum voided volume (mL)	50 (30–90)	60 (30–130)	0.454
Maximum voided volume (mL)/EBC	0.61 (0.47–0.86)	0.83 (0.66–1.25)	0.025
Minimum voided volume (mL)/EBC	0.2 (0.11–0.3)	0.25 (0.11–0.44)	0.406
Urination frequency (per day)	8 (6–10)	7 (6–10)	0.477
Uroflowmetry			
Qmax (mL/s)	14 (12–15.5)	15 (15–17)	0.058
Voided volume (mL)	123 (85–192.5)	183 (130–250)	0.032
PVR volume (mL)	10 (0–20)	20 (10–20)	0.034
VDSS	13 (9.5–15.5)	12 (6–15)	0.579
QoL	2 (1–3)	1 (1–2)	0.11
Post-treatment			
Bladder diary			
Maximum voided volume (mL)	200 (135–270)	290 (175–360)	0.028
Minimum voided volume (mL)	70 (50–120)	90 (45–190)	0.329
Maximum voided volume (mL)/EBC	0.71 (0.57–0.97)	0.94 (0.8–1.3)	0.035
Minimum voided volume (ml)/ebc	0.27 (0.2–0.38)	0.38 (0.16–0.57)	0.354
Urination Frequency (per day)	7 (7–9)	7 (5–9)	0.56
Uroflowmetry			
Qmax (mL/s)	15 (13–17)	16 (15–18)	0.337
Voided volume (mL)	155 (121–235)	220 (150–300)	0.032
PVR volume (mL)	0 (0–10)	10 (10–20)	0.024
VDSS	8 (5–11)	10 (8–16)	0.3
QoL	1 (1–1)	1 (1–2)	0.43

All continuous variables are presented as median (IQR). EBC: expected bladder capacity; IQR: interquartile range; PVR: postvoid residual; Qmax: maximum flow rate; QoL: quality of life; VDSS: voiding dysfunction symptom score.

Table 4. Multivariate logistic regression analysis of predictors of treatment response

Variable	OR	95% CI	p
Age (years)	0.960	(0.76–1.20)	0.731
Sex	0.946	(0.20–4.33)	0.943
Expected bladder capacity (mL)	1.021	(0.93–1.11)	0.659
Baseline voiding dysfunction symptom score	0.872	(0.74–1.01)	0.080
Baseline quality of life score	0.467	(0.19–1.11)	0.086
Baseline PVR volume (ml)	0.953	(0.89–1.01)	0.139
Bladder diary-maximum voided volume (mL)	0.985	(0.97–0.99)	0.036
Bladder diary-minimum voided volume (mL)	0.992	(0.97–1.01)	0.445
Bladder diary-urination frequency (n)	1.166	(0.92–1.46)	0.190
Uroflowmetry-voided volume (mL)	1.015	(1.00–1.02)	0.016
Uroflowmetry-Qmax (mL/s)	0.847	(0.63–1.13)	0.270

CI: confidence interval; OR: odds ratio; PVR: post-void residual; Qmax: maximum flow rate.