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REVIEW

Diagnosis and management of bladder bowel dysfunction in children with urinary tract infections: a position statement from the International Children's Continence Society

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Abstract
Background We present a consensus view from the International Children's Continence Society (ICCS) on the evaluation and management of bladder bowel dysfunction (BBD) in children with urinary tract infection (UTI). The statement aims to highlight the importance of BBD in the development and recurrence of childhood UTI and its management to reduce its associated morbidity and sequelae.
Methods A systematic literature search was done on PubMed, Embase, and Scopus databases until August 15, 2016. Relevant publications concerning BBD and its relationship with UTI among children were reviewed and aggregated for statements of recommendation. Discussion by the ICCS Board and a multi-disciplinary core group of authors resulted in a document available on its website for all ICCS members to review. Insights and feedback were considered with consensus and agreement reached to finalize this position statement.
Results BBD in children with UTI is summarized. Details regarding epidemiology, pathophysiology, and recommendations for general and family practitioners and pediatricians relating to the evaluation and management of this condition are presented.
Conclusions This document serves as the position statement from ICCS, based on literature review and expert opinion providing our current understanding of BBD in children with UTI.

Keywords Bladder bowel dysfunction · Urinary tract infection · Consensus statement

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Abbreviations

BBD	Bladder bowel dysfunction
BSFS	Bristol Stool Form Scale
DES	Dysfunctional elimination syndrome
DV	Dysfunctional voiding
DVSS	Dysfunctional voiding symptom score
LUT	Lower urinary tract
LUTD	Lower urinary tract dysfunction
PVR	Post-void residual urine
UTI	Urinary tract infection
VUR	Vesicoureteral reflux
VCUG	Voiding cystourethrogram
VUDS	Urodynamic and videourodynamic study
ACE	Antegrade continence enema
CIC	Clean intermittent catheterization

Introduction

Background

The association of lower urinary tract dysfunction (LUTD) with functional bowel dysfunction and incidence of urinary tract infections (UTI) among children has been increasingly documented in the past few decades. Failure to recognize the connection between the two conditions is a major risk factor when considering surgery or anticipating spontaneous resolution of vesicoureteral reflux (VUR) [1–3]. Recent reports support the relationship between functional bladder bowel dysfunction (BBD) and UTI that predisposes the child to recurrent infection, potentially causing renal scarring [4–7].

Terminology

The International Children's Continence Society (ICCS) discourages using terminologies such as dysfunctional elimination syndrome (DES), Hinman syndrome and dysfunctional voiding (DV), due to their connotation of a particular abnormality or condition [8]. BBD is recommended as an appropriate descriptive comprehensive term for a condition of combined bladder and bowel disturbance that does not explain pathogenesis but rather encompasses the parallel LUT and bowel dysfunction seen in children with neurologic conditions, yet has no identifiable or recognizable neurologic abnormality.

Scope and purpose

For this position statement, we only focused on the condition of non-neurogenic BBD in children with UTI. ICCS previously published the evaluation and management of children with neurogenic bladder dysfunction, which will not be discussed [9–11]. Details regarding definitions of various types of BBD as well as the management for bowel dysfunction (functional constipation or functional non-retentive fecal incontinence), dysfunctional voiding, daytime incontinence, nighttime incontinence (monosymptomatic or non-monosymptomatic enuresis) in children with LUT symptoms were reported in prior ICCS standardization documents [11–18]. For detailed definitions and full version of this position statement document please refer to http://i-c-c-s.org/standardisation-documents/.

We believe early recognition and appropriate management by primary care providers will produce the best outcomes; hence, primary care-givers, i.e., general pediatricians and family physicians, serve a very important role in the initial evaluation and management of BBD among patients with UTI. Proper knowledge in recognizing and managing BBD can reduce the number of UTI and prevent progression of associated morbidity and consequently renal damage. There is a lack of evidence-based information from randomized controlled trials on the management of children with BBD. The ICCS aimed to provide an up to date literature summary and highlight the importance of BBD in the development and recurrence of childhood UTI, and its management to reduce UTI-associated morbidity and sequelae.

Methods

A literature search was performed in PubMed, Embase, and Scopus medical databases until August 16, 2016, with the following search terms for title/ abstract (bladder bowel dysfunction - dysfunctional elimination syndrome - elimination disorder) AND (UTI) AND (Pediatrics - children) filtered for human studies; however, language was not a restriction. Additional records were gathered by cross-referencing and inquiring from experts in the field. After excluding duplicate records, 216 publications were identified. Assessment of relevance was accomplished by reviewing abstracts; full-text articles were ordered and included for the summary of literature and formation of this position statement.

A variety of experts from several healthcare disciplines including urology, nephrology, gastroenterology, general and developmental pediatrics, nurses, psychology, and psychiatry formed a multidisciplinary core group comprising representatives from North and South America, Europe, Middle East, Africa, Australia, and Asia. Formal discussions of the initial draft and the current literature were undertaken. The final draft was placed on the ICCS website for members to review; insights and feedback were solicited and considered. Consensus and agreement was reached to finalize this position statement.

Results

Epidemiology of UTI (infants versus older children)

Occurrence of UTI among infants and young children compared with older children varies widely. The etiology and pathophysiology differs between age groups. UTIs in infants usually connote a genitourinary anatomic abnormality, suggesting early radiologic imaging [19–21]. Girls had UTI as the cause of their fever in 7.5% at <3 months of age, 5.7% at 3–6 months, and 8.3% at 6–12 months, with further decline to 2.1% at 12–24 months. Boys had a prevalence of 8.7% at <3 months of age, 3.3% at 3–6 months and 1.7% between 6 and 12 months [22]. The incidence of febrile UTI in older, prepubertal children is much less, approximately 1% of boys and 3% of girls, and highly related to BBD (approximately 50%) [23–26].

BBD in infants and younger children

LUT function and dysfunction Normal voiding patterns in neonates are characterized by physiological dyscoordination, i.e., detrusor overactivity, low bladder capacity, and high voiding pressures [27]. Voiding patterns in healthy neonates are characterized by small, frequent voids of varying volumes and interrupted voiding in 30% [27, 28]. Their voiding frequency is 10 to 15 times per day until almost 12 months of age; some have postulated normalization of urinary flow begins after the first year of life as urinary frequency decreases to 8–10 times per day at age 2–3 years [29, 30].

Bowel pattern and functional constipation Considering the link between bowel movements and voiding in neonates, Wen et al., described defecating simultaneously with voiding may promote bladder emptying in newborns, specifically boys [31]. Clarification is needed regarding assessment of stool frequency and threshold for management among infants. Stool frequency declined from a mean of 3.0 times/day [3rd centile 0.6, 97th centile 5.9] at 4 weeks, to 1.3 times/day [0.6, 2.7] at 42 months of age [32]. The prevalence of functional constipation in children <12 months is approximately 15% (range, 0.05–39.3%) [33]. Additionally, formula fed, in comparison to breastfed infants, may defecate less than once per day; they are not constipated and should not receive unnecessary treatments [34].

BBD in older children

LUTD and associated conditions Voiding patterns among older children correspond with increased bladder capacity over time, eventually becoming more adult-like at 4–6 times/day [30]. The prevalence of LUTD among children is approximately 20% [35, 36]. Factors that could be associated with LUTD in preschool and school age children include anxiety and/or depression symptoms, bullying, abusive maternal/paternal attitudes and attention-deficit/hyperactive disorders [37–40]. Van Batavia et al. determined the prevalence of UTI in 53% of girls, but only 5% of boys with LUTD, most often in association with urinary stasis, detrusor underutilization disorder and voiding dysfunction [25]. Recent studies have shown LUTD is associated with recurrent UTIs and has negative effects on family and social relationships, school performance and quality of life in children [41].

Bowel dysfunction and functional constipation The prevalence of constipation in older children varies from 5 to 27% [35, 42]. Approximately 90% with fecal retention are found to have functional constipation without an organic cause [42, 43]. The coexistence of constipation and LUTD, including urinary incontinence and recurrent UTI is well described [8]. Functional constipation significantly impacts quality of life and the physical and emotional well-being of the child and the family; thus, appropriate evaluation and management is recommended [44, 45]. Diagnosis of functional constipation and other bowel dysfunction conditions have recently been updated as ROME IV criteria [46]. The six criteria are similar. Symptom duration decreases from 2 to 1 per month (see supplementary material, Appendix 1).

Pathophysiologic relationship of BBD, UTI, VUR, and renal scarring

Causative effect of BBD that leads to UTI

BBD plays a substantial role in development of recurrent UTI [6, 7]. LUTD with incomplete bladder emptying is an important risk factor for development and recurrence of UTI in children [47, 48]. Rectal distention can compress the adjacent bladder neck and trigonal region leading to detrusor overactivity and possibly bladder outlet obstruction [17, 49].

The correlation between constipation and UTI may be due to increased uropathogenic organisms in the gastrointestinal tract leading to recurrent infection [50]. Urothelial invasion by bacteria may explain some recurrences of UTI, and improvement in BBD may prevent the bacteria from adhering again once they break out of the quiescent intracellular reservoirs [51]. Of 50 children using enema therapy for constipation for at least 6 months, no recurrent UTI and complete relief of urinary tract symptoms were reported in 30 patients (60%) [52]. Of 234 children treated for chronic constipation, relief occurred in 52% with no UTI in those without urinary tract anomaly [53].

Significance of BBD on VUR and renal scarring

About half the children with VUR have BBD [1, 54]. Underlying BBD lowers the surgical success for VUR and increases the febrile UTI rate after anti-reflux or endoscopic injection therapy for reflux [3]. Consequently, renal scarring is more likely identified in the presence of VUR, UTI and BBD [7, 30]. A post-hoc review from two large cohort studies, RIVUR and CUTIE trials, found that children with both VUR and LUTD had higher rates of recurrent UTI [6]. While a later analysis on these two cohort studies' data further extrapolated that BBD (OR, 6.44; 95% CI, 2.89–14.38) is associated with new renal scarring [26]. These findings support the current view that BBD is an important predictor for spontaneous reflux resolution, susceptibility for pyelonephritis and renal damaging [55, 56].

Evaluation of BBD in infants and children with UTI

Medical history and physical examination

Table 1 summarizes key assessment of BBD in children with UTI. Once a UTI is confirmed, a comprehensive medical history is imperative. It should include information regarding prematurity, prenatal hydronephrosis, birth history, toilet training, current voiding, and defecation patterns. Voiding patterns, i.e., voiding frequency, timing of any urinary incontinence, associated symptoms of daytime incontinence and enuresis, should be documented. Delaying tactics, i.e., Vincent's curtsy, crossing one's legs and bending down from the waist, pinching the glans of the penis between fingers, are typical maneuvers used by children with urgency incontinence [57]. Finally, sensory neural or muscle weakness/atrophy involving the lower extremities should be considered as subtle neurologic conditions that might be a cause for recurrent UTI [9, 10].

Gastrointestinal parameters, i.e., stool firmness, frequency, pain with defecation and encopresis, must be reviewed [15, 45]. Information on functional constipation using ROME IV criteria should be sought from caregivers [46]. Identifying the presence of other gastrointestinal symptoms, nausea, vomiting, weight loss or failure to thrive, loss of appetite, and behavioral or psychosocial issues, may correlate with severe BBD [58, 59]. The school environment and toileting conditions should be explored as they may cause postponement maneuvers for bladder and/or bowel emptying [5].

Physical examination, specifically the genital area, is essential in identifying anatomical abnormalities possibly responsible for BBD. A meatal anomaly may be associated with non-neurogenic DV that could present as anterior deflected urinary stream [60, 61]. The presence of urine trapped inside the redundant prepuce or phimosis may cause glandular irritation, and labial irritation from adhesions and/or vaginal pooling of urine may lead to changes in voiding habits and potentially recurrent UTI [62–64]. Abdominal examination assessing fecal mass and perianal inspection for fecal soiling, hemorrhoids, fissures, scars, and erythema, indicating hard and/or large diameter stools or sexual abuse are likewise important for determining etiologies for BBD [15, 18]. Digital rectal examination can be performed to fulfill ROME IV criteria for constipation to confirm the presence of large fecal mass in the rectum, while also assessing the sphincteric tone as an important adjunct to the physical examination for ruling out neurologic issues [10, 15, 18]. Additionally, a neurologic examination with special attention to the sacrum and lower extremities to rule out a neurologic origin of bladder and bowel symptoms is necessary [9, 15].

Bladder bowel diary, frequency volume chart and 4-h voiding observation in infants

A bladder and bowel diary supplements information obtained from history and physical examination. Diaries provide reliable and accurate bladder bowel elimination patterns [10, 18, 65, 66]. While assessing infants and pre-toilet trained children, caregivers may determine frequency of voiding by 4-h voiding observation along with bladder ultrasonography; weighing diapers before and after each void allows calculation of voided volume [27, 67, 68]. Frequency volume charts are useful to monitor treatment progression and intervention response.

BBD or LUTD questionnaires

Severity of the BBD can be assessed via several validated questionnaires. Dysfunctional voiding symptom score (DVSS) (Appendix 2) [69], is the most commonly adapted validated tool evaluating and monitoring treatment progress. Other evaluation tools have been developed and validated; i.e., DV and incontinence scoring system, DES assessment tool/symptom score, Bladder/Bowel Dysfunction Questionnaire and Incontinence Symptom Index-Pediatric [70–72]. Most of the assessment tools were determined to be equivalent for the evaluation of response to treatment [71]. We recommend clinicians adapt whichever tool they feel best fitted to their practice.

Bristol Stool Form Scale and Rome IV criteria of constipation

The Bristol Stool Form Scale (BSFS) consists of seven pictorials and stool form descriptors [73]. It allows children to express their bowel movement consistency. Aside from its descriptive function, accuracy of defecation history can be improved with its use in a 7-day bowel diary [15]. In children with recurrent UTI and constipation, maintaining a bowel diary with a BSFS and a frequency volume chart allows physicians and/or parents to monitor elimination habits and adjust treatment strategies [15, 59].

Table 1 Assessment of pediatric BBD

Evaluation	Essential information
Medical history	Obtain information about UTI occurrence
	Inquire about co-morbidities and other medical issues
	Elicit storage and emptying function and associated symptoms suggestive of BBD
	Inquire about observed neurologic symptoms
	Glean information on gastrointestinal symptoms
	Identify presence of other associated symptoms, behavioral or psychological issues
Physical examination	Genital examination
	Perineal examination
	Digital rectal examination, if indicated
	Neurologic examination
Bladder diary or 4-h voiding observation	48-h frequency volume chart for toilet trained children
	4-h voiding observation with the aid of bladder ultrasound for pre-toilet trained children
BBD or LUTD Questionnaires	Several validated questionnaires available for assessment and follow-up of BBD
Bristol stool form and Rome IV criteria of constipation	7-day bowel diary with description of stool forms
Ultrasound (transabdominal)	Imaging kidneys and urinary bladder
	Transverse rectal diameter
Abdominal scout film	Radiograph for fecal loading, spinal bony abnormality
Voiding cystourethrogram (VCUG)	Indicated for recurrent febrile UTI ± renal parenchymal abnormalities, i.e., scarring, cortical thinning, increased echogenicity, reduced corticomedullary differentiation, poor renal growth and/or dilatation of renal pelvis, calyces and ureters
Uroflowmetry and PVR	Uroflowmetry and post-void residual in toilet trained children
Invasive study	Voiding cystourethrography for febrile UTI - VUR and dysfunctional voiding
	Urodynamics or videourodynamics for detailed bladder/sphincter function

****UTI** urinary tract infection, *BBD* bladder bowel dysfunction, *LUTD* lower urinary tract dysfunction, *PVR* post void residual, *VUR* vesicoureteral reflux

Ultrasound (kidney, bladder and rectum) and abdominal scout film

In children with BBD, transabdominal ultrasound provides valuable information regarding the bladder (wall thickness, bladder volume and post-void residual urine (PVR)), kidney, and upper urinary tract assessment [8, 74, 75]. Renal anomalies may lead to concentrating defects and increased urine production. Further assessment such as serum electrolyte, glucose, C-reactive protein, and preferably procalcitonin level may be warranted to identify upper tract involvement and discriminate uncomplicated from complicated UTI [21, 24, 76–78].

Ultrasonic measurement of the transverse rectal diameter can delineate the degree of fecal matter behind the bladder; it is a simple but reliable technique to demonstrate fecal loading [15, 45, 79]. Although an abdominal scout film (KUB) is widely used to evaluate childhood constipation and assessment of fecal loading, there is insufficient evidence to support its routine diagnostic use [79].

Uroflowmetry and post-void residual (PVR)

In toilet-trained children, uroflowmetry and PVR are recommended as first line tests to recognize potential LUTD [8]. Normal uroflowmetry should be bell-shaped [80]. Repeat abnormal uroflow patterns and elevated PVR (defined as PVR >20 ml or 10% bladder capacity in children aged 4–6 years, and PVR >10 ml or 6% bladder capacity in children aged 7–12 years) are suggestive of LUTD [8, 47]. Few tools exist to evaluate BBD in infants and younger children. Measurement of bladder capacity and PVR using a bladder scanner or

transabdominal ultrasound supplementing a 4-h voiding observation can help to diagnose LUTD in infants and younger children [8, 27, 68]. High-grade VUR may be a common cause of incomplete bladder emptying and can confuse LUTD assessment using uroflowmetry with PVR; further assessment is therefore needed, especially among cases of recurrent UTI [47].

Voiding cystourethrogram (VCUG), urodynamic, and videourodynamic study (VUDS)

These studies may reveal abnormal bladder contour or spinning top urethra suggestive of DV or other related anomalies [81]. When high grade VUR is diagnosed or any aforementioned abnormal ultrasound finding, or decreased renal function/scarring on renal scintigraphy (DMSA), should prompt specialist referral for management and monitoring [24, 59]. Invasive studies, i.e., urodynamics or videourodynamics (VUDS) are not routinely recommended to diagnose BBD. Although formal urodynamic testing provides the greatest information regarding bladder storage, i.e., capacity, compliance, and contractility, VUDS can show detrusor overactivity, VUR, and dyscoordinated sphincter [82]. The specific patient population indicated for these invasive diagnostic procedures are patients with recurrent UTI with consideration of reflux, or neurologic conditions that are intended to be ruled out [9, 10, 24, 59].

Treatment for BBD

Figure 1 summarizes the algorithm and related reference for managing BBD in children with UTI. Treatment should first address the UTI according to guidelines depending on the suitable age group and local practice of the clinician. Evaluate and rule out congenital anomalies or neurogenic etiology of recurrent UTI with appropriate relevant management, followed by managing the bowel dysfunction and then LUTD [15, 24, 76, 83]. Daytime incontinence and related LUTD need management prior to enuresis therapy [13, 14, 16, 17].

Some suggest antibiotics in children with recurrent UTI when BBD is present [82, 83]. This is beneficial when initiating bladder training for VUR and BBD [7, 84, 85]. Despite concerns of increasing bacterial resistance with prolonged antibiotic exposure, antibacterial prophylaxis can help reduce recurrent UTIs; the risk and benefit juxtaposition must be analyzed [7, 86]. The step-wise treatment of BBD is recommended to start with conservative management of behavioral modification with regular monitoring aided by various clinical tools described in this text. Pharmacologic options may be offered depending on the patient's prominent presentation, which are discussed in the following sections. Surgical interventions are the last option with consideration of risk–benefit outcome of the intervention.

Conservative management

Multidisciplinary approach and urotherapy Table 2 summarizes various methods of conservative treatments for BBD. First-line therapy for BBD includes behavioral strategies to improve micturition and defecation [8, 11, 15]. Multidisciplinary approach involving at least pediatric subspecialists, urologist, gastroenterologist, and psychology professionals integrating urotherapy approaches

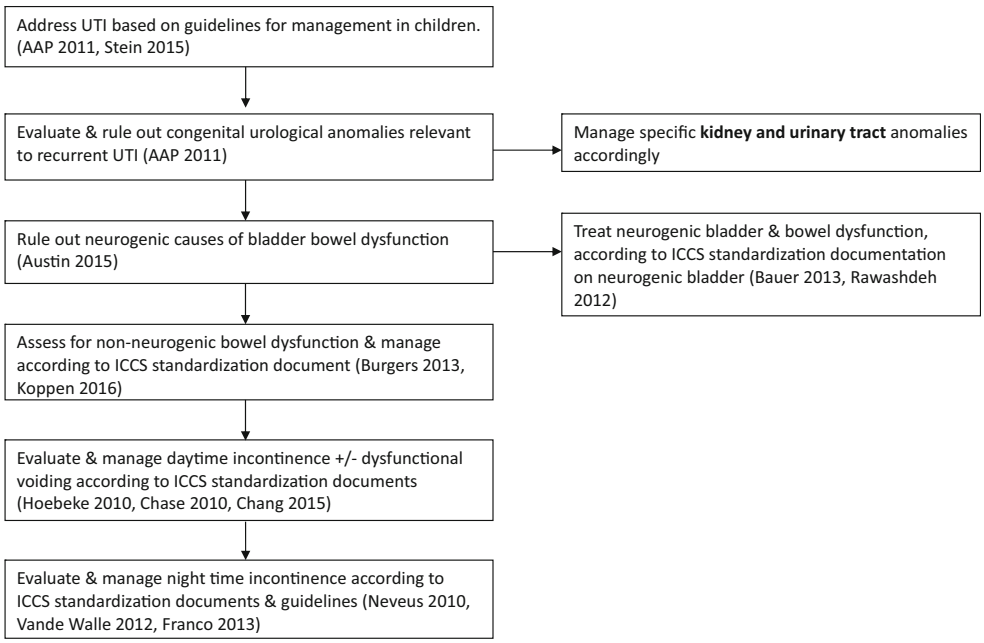

Fig. 1 Treatment strategy for children presented with urinary tract infection and bladder bowel dysfunction **UTI* urinary tract infection, *AAP* American Academy of Pediatrics, *ICCS* International Children Continence Society

Table 2 Conservative treatments for BBD

Methods	Details	indication
Urotherapy	Education and demystification Behavioral modification instruction Lifestyle advice Registration of symptoms and voiding habits Improvement in elimination habits Support and encouragement to patients and caregivers	All children
Early toilet training	Parental oriented toilet training method	May be beneficial in infants with elevated PVR
Bowel management	Education, fecal disimpaction, stool softeners, and fiber	All children with constipation
Biofeedback relaxation of pelvic floor	Using biological signals to enhance pelvic floor relaxation and facilitate micturition and defecation emptying	Children with dyscoordinated sphincter and/or pelvic floor muscles during voiding
Electroneurostimulation	Involving regulation of the cerebral cortex, spinal pathway and the target organ of pelvic floor muscles	Children refractory to conservative or pharmacological treatments
Clean intermittent catheterizations	Drain the bladder intermittently with clean urethral catheter	Children who fail conservative management and pharmacologic treatment

****BBD** bladder bowel dysfunction, *PVR* post void residual

yield better long-term success [5, 87, 88]. When behavioral abnormalities are present, appropriate psychiatric or psychological referral is warranted for additional evaluation and management [37]. Nurses, nurse practitioners, and/or urotherapists, who can advocate non-pharmacological and non-surgical approaches of management that involve education of both caregivers and children, are helpful in optimizing the outcome of behavioral modification. The allied healthcare professionals play a critical role in empowering treatment strategies by educating children and parents about normal urinary tract and bowel physiology, in addition to relevant aspects of treatment [5]. This has been successful in treating BBD among patients with UTI [15].

When managing these children, frequency/volume charts and bowel diaries help physicians and parents monitor voiding frequency and fluid intake. Bladder bowel diaries may reveal poor oral fluid intake that needs to be counterbalanced by adequate fluids. Normal spontaneous fluid intake not including the fluid content in food among healthy individuals is 65–160 ml/kg per day in young children, and 1.77 ± 0.57 l/day for older girls, and 1.79 ± 0.44 l/day for older boys [89, 90]. Variations in recommendations may be made depending on one's activity, body surface area, and climate.

Timed and double voiding maneuvers are advised for infrequent voiders to decrease urinary stasis time and to avoid bladder over-distension [8, 11, 30]. Good hygiene (wiping front to back, spreading labia and foreskin retraction) is a traditional belief and common practice that may prevent transference of colonic microbes to the UT. Good toileting posture and resting one's feet when sitting enables optimal relaxation of the pelvic floor muscle in 94%, and reduces DV and PVR compared to significantly higher EMG activity with unsupported legs [11, 91, 92].

Early toilet training A UK cohort study showed initiating toilet training after 24 months was associated with problems attaining and maintaining bladder control [93]. Some have empirically suggested early initiation of toilet training in children at risk of developing UTI [94]. Conversely, Yang et al. did not show a higher rate of LUTD among children toilet trained earlier [95]. Jansson corroborated that children had less bladder sphincter dyssynergia and lower PVR after toilet training [96, 97].

Fecal disimpaction, stool softeners, and fiber for bowel dysfunction Treating constipation leads to subsequent resolution of UTI and reduced pyuria, bacteriuria, and enuresis [1, 53]. Initiating an aggressive bowel regimen is important to prevent further infections in children with BBD and UTI. A four-step approach includes education and demystification regarding bowel physiology and dysfunction, fecal disimpaction with enema and laxatives, prevention of fecal reaccumulation with stool softeners such as polyethylene glycol, and behavioral therapy with follow-up [15, 42]. Maintenance therapy in treating constipation may be required for months to years afterwards [42, 43]. Dietary fiber and probiotics are helpful in managing functional constipation but their role and efficacy remain unclear [15, 45]. Chronic constipation may lead to UTI with concomitant sequalae [1, 24] in refractory cases lasting ~6 months, despite conventional therapy; this warrants referral to pediatric gastroenterology for further management [15, 45].

Biofeedback relaxation of pelvic floor and electroneurostimulation for BBD Biofeedback therapy helps to consciously modulate pelvic floor muscles with/without real time EMG feedback to achieve optimal uroflowmetry curves and low residual urine [11, 98, 99]. A current meta-analysis does not support the effectiveness of biofeedback in the management of BBD; however, earlier reviews with comprehensive analysis showed a pooled estimate of 83% improvement in recurrent UTI among patients with BBD [100, 101].

The mechanism of action for electroneurostimulation (ENS) is unclear, although studies show ENS involves regulation of the cortex, spinal pathway and pelvic floor muscles [102, 103]. Neurostimulation administered through a transcutaneous electrical nerve stimulation patch over sacral dermatomes/pudendal area, or percutaneous tibial nerve stimulation with needle and sacral implanted neuromodulator are considered as a treatment option for BBD, given that studies have shown that it may improve constipation, overactive bladder symptoms and fecal and urinary incontinence [18, 103, 104].

Clean intermittent catheterizations Increased PVR with urinary stasis leads to greater risk of UTI, persistent VUR, and consequently renal scarring [47, 105, 106]. The rationale for clean intermittent catheterization (CIC) to drain the bladder is to protect the kidney and its function. This is a viable option particularly among patients who were assessed to have non-neurogenic neurogenic bladder with persistent urinary retention and failed conservative management and pharmacotherapy [11, 30, 107]. Pohl et al. showed a fivefold reduction in symptomatic UTI and no febrile UTI after starting CIC in anatomically normal children [108]. These benefits must be balanced against the risk of discomfort, urethral stricture, and related cost [30].

Pharmacological treatment of BBD in children with UTI

Prophylactic antibiotics Pharmacological treatment of BBD in children with UTI is summarized in Table 3. The primary goal of addressing BBD is to minimize occurrence of UTI. Antibiotic prophylaxis is often maintained until patients show symptomatic improvement of LUTD and constipation [15]. Despite controversies regarding long-term use of prophylactic antibiotics [109], a subgroup of patients at high risk for recurrent febrile UTI, i.e., VUR, benefit from this treatment [85]. Current AUA guidelines recommend prophylactic antibiotics in patients with coincidental BBD and VUR, especially when renal cortical changes are noted [110].

Table 3 Pharmacological treatment of BBD in children with UTI

Types of medication	Indication
Prophylactic antibiotics	Coincidental BBD and VUR, particularly when renal cortical changes were noted and/or high-grade reflux is present
Alpha blockers	Primary bladder neck dysfunction (off label use)
Anticholinergic agents	Overactive bladder and urinary incontinence
Botulinum toxin A	Detrusor sphincter dyssynergia in patients refractory to conservative and pharmacologic therapies (off label use)

**BBD* bladder bowel dysfunction, *VUR* vesicoureteral reflux

Alpha-blockers Alpha-blockers (specifically doxazosin) have been advocated in the management of LUTD, specifically primary bladder neck dysfunction [111]. Alpha-blockers (doxazosin 0.5–1 mg nightly, or Prazosin 1 mg tablet daily in two divided doses) may lower PVR, severity of incontinence, and VUR grade, and improve DVSS and parental satisfaction among treatment-responsive children [112–114]. Their use is limited by a lack of safety data and 'off-label' status along with the risk of orthostatic hypotension [11, 111].

Anticholinergic agents and beta-3 agonists Anticholinergic agents, (i.e., oxybutynin (2.5–5 mg OD-TID), tolterodine (1–4 mg BID) and propiverine (5–15 mg OD-BID), are safe and effective in children with prominent symptoms of overactive bladder and urinary incontinence [115–117]. When treating LUTD, combined with behavioral modification, significant improvements in frequency, voided volume, incontinence, DVSS, and symptomatic BBD have been seen [118]. While evidence of symptomatic improvement exists in these children, the effect of anticholinergics on UTIs is unclear. Since anticholinergics may further aggravate bowel dysfunction, treating constipation before prescribing anticholinergics is indicated [30]. Beta-3 adrenergic agonists, such as mirabegron, improve bladder overactivity in adults and may also be useful in children [119]. However, current use of mirabegron in children is off-label.

Botulinum toxin A Botulinum toxin A (50-100 IU) injected into the external urethral sphincter may paralyze the muscle and its adjacent pelvic floor [120], thus playing a role in BBD patients with UTI [121]. One review concluded there was insufficient evidence to support botulinum toxin A for detrusor sphincter dyssynergia in children [122], but improvement in voiding parameters (flow rate and PVR), urinary continence, defecation and stool consistency in children refractory to conservative and pharmacologic therapies has been noted [123, 124].

Surgical treatment of BBD

Open and endoscopic surgeries for VUR and neonatal circumcision The role of surgical therapy in patients with BBD and UTIs is limited, as most children are initially managed conservatively with relatively high success [59]. Surgery for VUR may be indicated in children with BBD and recurrent

breakthrough UTIs, to avoid renal scarring and decreased function [24, 76, 110]. Open and endoscopic surgeries for VUR are recommended by the AUA guidelines in VUR patients with recurrent UTI and BBD [110]. BBD increases the risk of postoperative UTI. BBD should therefore be treated prior to VUR correction [110].

Circumcision is not recommended to prevent UTI [125]. Physiologic phimosis could be a factor for developing or having recurrent UTI [126, 127]. Its advocacy is limited to those boys at high risk of recurrent UTI, infants with posterior urethral valves and antenatal hydroureteronephrosis or recurrent balanitis [128–131].

Bladder augmentation, appendicovesicostomy (Mitrofanoff procedure), and antegrade continent enema (ACE) Bladder augmentation, Mitrofanoff continent stoma creation, and other surgical procedures are rarely indicated for children with BBD. However, those at risk for renal function deterioration due to severe BBD might benefit from augmentation cystoplasty with or without appendicovesicostomy (Mitrofanoff) when other measures fail [132, 133]. For severe cases of functional constipation, cecostomy tube and antegrade continence enema (ACE) that accesses the cecum either percutaneously or with an appendicostomy allows instillation of enema solutions to evacuate the colon and rectum [134]. Success rates range from 21 to 92% [30, 135]. However, due to related morbidities this treatment should be reserved for refractory cases where benefits outweigh risks [15, 136].

Prognosis in the UTI condition after management of BBD

Reports of 12-month efficacy for eliminating recurrent UTI using urotherapy in children with BBD vary between 40 and 68% [87, 99], while treatment of constipation resolves urinary incontinence and UTI with no sequae on renal function [4, 53]. Persistence of BBD after correction of VUR raises the risk of postoperative febrile UTI or recurrent UTI, indicating BBD is an important factor of UTI occurrence [137, 138].

Conclusions

This document served as an important, up-to-date literature summary for the management of pediatric UTI with BBD. Further randomized controlled trials are still needed to provide evidence-based management in this special group of patients.

When treating children presenting with febrile UTI, BBD should be sought and assessed. The ultimate goal of treatment for these children is reduction in associated UTI morbidity and its sequelae. It is paramount to weigh the risk–benefit ratio of each treatment modality; hence, treatment approaches should be undertaken in a step-wise fashion, starting with the least invasive options first.

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Compliance with ethical standards

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