

Management of constipation in preventing urinary tract infections in children: a concise review

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ABSTRACT

Objectives: Constipation is a common problem in children. Chronic functional constipation (CFC) has been a claimed conditions that may increase the risk for urinary tract infections (UTIs). Dysfunctional voiding (DV) and lower urinary tract dysfunctions (LUTD) with chronic constipation are referred to dysfunctional elimination syndromes (DES). The aim of the present review is to look at the management of constipation in children with CFC or DES in reducing the risk of recurrent UTIs.

Methods: We performed a literature search on electronic databases (Pubmed and Scopus) for relevant clinical trials investigating the results of one or more treatments for children's constipation in the term of UTIs recurrence.

Results: The search strategy identified 20 valuable clinical trials. The studies are not homogenous but showed an improvement in UTIs occurrences in children managed for bowel dysfunction.

Conclusion: In conclusion, children referred to a pediatric nephrologist for UTIs should include an inquiry bowel habits and those with a positive assessment for bowel dysfunction needs the collaboration with a pediatric gastroenterologist with a multidisciplinary approach.

Keywords: Children, constipation, dysfunctional elimination syndromes, dysfunctional voiding, urinary tract infection

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Urinary tract infections (UTIs) are frequent in children. By seven years of age, 8% of girls and 2% of boys will have had at least one episode of UTI [1]. Prospective studies using 99mTc-labelled dimercaptosuccinic acid (DMSA) scintigraphy have shown that, after a febrile UTI, 30-40% of children will have renal scarring [2]. Follow-up data has established that long-term complications of UTIs with renal scarring include hypertension, proteinuria, pregnancy-related complications and even end-stage kidney failure [3]. Many predisposing factors to UTIs recurrence (vesicoureteral reflux [VUR], bladder and

bowel dysfunction [BBD], and genetic factors) have described in childhood [4, 5]. Both BBD and VUR are at high risk of developing recurrent UTIs than children with isolated VUR or children with isolated BBD [6]. There is still controversy about the role of chronic functional constipation (CFC) in predisposing children to UTIs [7].

Constipation is a common problem in children with a prevalence from 0.7% to 29.6% [8]. According to the Paris Consensus on Childhood Constipation Terminology (PACCT) Group, CFC as having at least two symptoms during the last eight weeks that include



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defecation frequency of less than three times, a fecal incontinence, frequency more than once, passage of large stools that clog the toilet, a palpable abdominal or rectal fecal mass, stool withholding and painful defecation [9]. CFC is chronic constipation without evidence of pathological conditions [10] and, at present, the most accepted definitions for CFC are the Rome III criteria [11]. In particular, sensation of anorectal blockage, straining during defecation and infrequent bowel movements are of great accuracy for the diagnosis of CFC [12]. Constipation may play a role in function and dysfunction of the urinary tract [13].

Dysfunctional voiding (DV), that refers to an intermittent and/or fluctuating uroflow rate due to involuntary intermittent contractions of the striated muscle of the external urethral sphincter or pelvic floor during voiding in normal individuals [14], and lower urinary tract dysfunctions (LUTD), that refers to patients with problems of bladder function [14], as dysfunctional elimination syndromes (DES) [15] with CFC [16]. DES and CFC increased the risk of UTIs in children [15, 17]. In agreement, it has observed recurrent UTIs in 25% of boys and 66% of girls among 180 patients with CFC [19], and in 62% of girls among 80 patients with DES [18].

Children with UTIs have more symptoms of constipation than without [20]. Wan et al. [21] suggested that up to 90% of children with UTI could have dysfunctional voiding or constipation habits. Although the degree of fecal loading, as seen on a plain abdominal radiograph, is not synonymous of constipation, there is a significant association between the degree of fecal loading and UTIs [22]. Decreased bladder filling, impression of the bladder wall provoking overactivity, and pelvic floor discoordination caused by withdrawal manoeuvres as a response to painful defecation can have an important clinical meaning [23]. Another hypothesis is that constipation can figure bacterial stasis with huge proliferation and translocation of the same bacteria into genitourinary apparatus. In fact, it has reported a correlation between intestinal bacterial stasis, methanogenic intestinal flora and UTIs [24].

The general approach to the child with functional constipation comprises dietary interventions (high fibre diet, hydration changes), behavioural change, regular toilet habits and laxatives to assure that bowel

movements occur at normal intervals with good evacuation [11].

The aim of the present look at to check if management of constipation in children with CFC or DES reduce the risk of UTIs recurrence.

METHODS

We performed a systematic literature search on electronic databases (Pubmed and Scopus) for relevant clinical trials published from January 1985 to June 2018, investigating the results of one or more treatments for children's constipation in the term of the resolution or amelioration of UTIs recurrence.

To find relevant articles in these electronic databases, we used the keywords constipation OR dysfunctional elimination syndrome OR dysfunctional voiding AND urinary tract infection AND children.

Studies were qualified for inclusion if they were clinical trials (excluding observational studies, letters, case reports, conference abstracts, studies on animals and comments), searching for the role of one or more treatments for constipation in the term of the resolution or amelioration of UTIs recurrence.

First, we screened the list of titles and abstracts (total number identifies: 321); then we selected clinical trials and the articles of interest in their entirety. The strategy identified 20 clinical trials. We extracted the first author and year of publication, the number of cases, characteristics of constipation and treatment, and time of follow-up. We extracted information on the prevalence of constipation and UTI before and after the treatment.

RESULTS

Clinical trials

Twenty clinical trials (Table 1) involving patients with CFC or DES reported different treatment regimens for constipation (laxatives, enemas, high-fibre diet, biofeedback therapy, pelvic floor muscle exercises, sacral neuromodulation, regular voiding, pharmacotherapy etc.) [23, 25-43].

Studies that showed a significant reduction of UTIs related to DV [26-28, 40] or DES [29, 30, 32] or LUTD [42]. Other studies did not report if the results

Table 1. Characteristics and analysis of the included clinical trials

Clinical trials	n. (M/F)	Mean age (range)	Main pathology	Treatment	Follow-up	n. of patients with constipation before/after	n. of patients with UTI before/after
Chrzan 2008 [23]	50 (6/44)	9.6 (6.5-12) yrs	CFC, recurrent UTIs	Colonic washout enemas	6 mos	50/33 <i>p</i> = n.a.	50/20 <i>p</i> = n.a.
Kibar 2007 [25]	78 (8/70)	7.20 ± 2.04 (5-14) yrs	DV, vescico-ureteral reflux	Biofeedback, timed voiding	6 mos	9/2 <i>p</i> = n.a.	41/8 <i>p</i> = n.a.
Vesna 2010 [26]	86 (35/51) Group A 43 (15/28) Group B 32 (9/23)	7.1 ± 2.5 (3-13) yrs	DV	Group A) Standard urotherapy, pelvic floor exercises Group B) conservative treatment Laxatives; antibiotic prophylaxis if UTIs recurred in both groups	1 yr	Group A 15/0 <i>p</i> < 0.001 Group B 10/4 <i>p</i> < 0.05	Group A 19/6 <i>p</i> < 0.0001 Group B 15/9 <i>p</i> < 0.05
Vesna 2011 [27]	86 (35/51) Group A 43 (15/28) Group B 32 (9/23)	Group A 7.5±2.5 yrs Group B 6.7±2.5 yrs	DV	Group A) diaphragmatic breathing, pelvic floor muscles retraining plus group B treatment, Group B) regular voiding, hydration, posture, laxatives; antibiotic prophylaxis if UTIs recurred	1 yr	Group A 15/0 <i>p</i> < 0.0001 Group B 10/4 <i>p</i> < 0.05	Group A 19/6 <i>p</i> < 0.001 Group B 15/9 <i>p</i> < 0.05
Zivkovic 2012 [28]	43 (15/28)	7.5±2.5 (5-13) yrs	DV	Pharmacotherapy (11 anticholinergics, 11 desmopressin, 15 antibiotic prophylaxis); constipation treatment (education and laxatives); diaphragmatic breathing exercises; pelvic floor muscle exercises	1 yr	15/0 <i>p</i> < 0.0001	19/6 <i>p</i> < 0.0001
Kajbafzadeh 2011 [29]	80 (18/62) Group A 40 (8/32) Group B 40 (10/30)	Group A 8.5±2.7 yrs Group B 9±2.3 yrs	DES	Group A) animated biofeedback therapy and behavioral modification Group B) conservative therapy (only behavioral modification)	6 and 12 mos (4-37 mos) mean 13.3 mos	Group A 25/8/8 Group B 20/12/12 6 mos: <i>p</i> = 0.01 12 mos: <i>p</i> = 0.009	Group A 14/2/4 Group B 22/5/10 6 mos: <i>p</i> = 0.02 12 mos: <i>p</i> = 0.3
Humphreys 2006 [30]	23 (8/15)	(6-15) yrs	Severe DES	Sacral neuromodulation, medical therapy	(4-37 mos) mean 13.3 mos	15/3 <i>p</i> = 0.001	18/6 <i>p</i> < 0.0001
De Paepe 2000 [31]	20 (2/18)	M 4.5 yrs F 4.44 yrs	DV	Training program, biofeedback, antibiotic prophylaxis if UTIs recurred, drugs to relieve the impaction of encopresis	6-12 mos	8/3 <i>p</i> = n.a.	8/0 <i>p</i> = n.a.

Table 1 continued. Characteristics and analysis of the included clinical trials

Clinical trials	n. (M/F)	Mean age (range)	Main pathology	Treatment	Follow-up	n. of patients with constipation before/after	n. of patients with UTI before/after
Vasconcelos 2006 [32]	56 (18/62) Group 1 26 (9/17) Group 2 30 (10/20)	Group 1 10.8 ± 1.9 yrs Group 2 10.3 ± 2.6 yrs	DES	Group 1) 24 training sessions over a 3-month period Group 2) 16 training sessions over 2-month period	12 mos	Group 1 11/7 <i>p</i> = n.s. Group 2 11/9 <i>p</i> = n.s.	Group 1 8/1 <i>p</i> = 0.023 Group 2 13/3 <i>p</i> = 0.004
Yagci 2005 [33]	168 (16/152)	7.44 ± 2.24 (5-14) yrs	DV	Biofeedback, timed voiding, high-fiber diets, laxatives	6 mos and 2 yrs	26/7/9 <i>p</i> = 0.5	102/17/13 <i>p</i> = 0.125
McKenna 1999 [34]	41 (8/33)	7.2 (5-11) yrs	DV	Pelvic floor muscle retraining using interactive computer games, timed voiding, high-fiber diet	(3-15 mos) mean 7 mos	6 Improved: 66% Cured: 34% <i>p</i> = n.a.	22/3 <i>p</i> = n.a.
Barroso 2006 [35]	36 (n.a.)	7 (3-14) yrs	LUTD	Electrical stimulation and/or biofeedback training, behavioral training, antibiotic prophylaxis	(4-24 mos) mean 13.8 mos	12/3 <i>p</i> = n.a.	25/4 <i>p</i> = n.a.
Petronijevic 2007 [26]	9 (girls)	6.1 (3-11) yrs	DV	Botulin Toxin type A, standard urotherapy, education, regular toilet visits, dietary and hydration changes, laxatives	6 mos	2/1 <i>p</i> = n.a.	8/2 <i>p</i> = n.a.
O'Regan 1985 [37]	47 (girls)	8.2 ± 2.53 yrs	Recurrent UTIs, constipation	Enema regimen	12±2 mos	47/2 Encopresis 21/1 <i>p</i> = n.a.	47/3 <i>p</i> = n.a.
Loening-Baucke 1997 [38]	234 (176/58)	9 ± 3 (5-18) yrs	CFC, encopresis	Disimpaction (hypertonic phosphate enemas OR hyperosmolar milk-of-molasses enemas), fiber-rich foods, laxatives, education, prophylaxis if UTIs recurred	12 months (mean, 15 months)	234/112 <i>p</i> = n.a.	25/0 <i>p</i> = n.a.
Loening-Baucke 1989 [39]	97 (69/28)	9.0 (5-14.5) yrs	CFC, overflow incontinence	Laxatives, high fiber diet, bowel training	12 mos	97/43 (F>M)	n.a. (UTI in recovered 3/43, UTI in non-recovered 11/54; <i>p</i> = n.s.)
Khen-Dunlop 2006 [41]	60 (12/48)	8 (5-14) yrs	DV	Pelvic floor training, regular voiding	21 mos	25/n.a.	37/6
Amira 2013 [42]	72 (girls)	8 (7-10) yrs	LUTD	Standard and computer game assisted pelvic floor muscle retraining	(6-17 weeks) mean 11 weeks	36/n.a. <i>p</i> < 0.002	70/n.a. <i>p</i> < 0.001
Tugtepe 2015 [40]	45 (38 female)	8.5 ± 2.2 years	DV, refractory overactive bladder	Biofeedback therapy	3 months	8/1 <i>p</i> < 0.05	20/4 <i>p</i> < 0.001

Table 1 continued. Characteristics and analysis of the included clinical trials

Clinical trials	n. (M/F)	Mean age (range)	Main pathology	Treatment	Follow-up	n. of patients with constipation before/after	n. of patients with UTI before/after
Sarvari 2017 [43]	105 CFC (23.8% males) 104 controls (26% males)	CFC 4.38 ± 2.38 yrs Controls 4.43 ± 2.44 yrs	CFC	Lifestyle changes, child's family life style modification, increased physical activity, and pharmacotherapy	3 months	CFC 105/68	-3.8%

CFC = chronic functional constipation, DES = dysfunctional elimination syndrome, DV = dysfunctional voiding (urinary incontinence, hesitancy, straining, intermittency, weak stream), LUTD = lower urinary tract dysfunctions, n.a. = not available, n.s. = not significant

were different [23, 25, 31, 34-38, 43].

Few studies applied a randomization [26, 27, 29, 32]. In two studies by Vesna *et al.* [26, 27] divided the patients into two groups to compare different treatment regimens for DV; both groups had significant positive results in terms of amelioration of UTI recurrence and constipation. In another study, Kajbafzadeh *et al.* [29] randomized patients into 2 groups (biofeedback and conservative treatment) reporting a significant improvement of both constipation and UTI recurrence. Vasconcelos *et al.* [32], who compared two different treatments for DES, reported in both groups a significant improvement only in UTIs recurrences, because the prevalence of constipation had not decreased at follow-up compared to baseline.

Published studies involved a variable number of patients, from small cohorts of patients to a wide number (mean 71.4 patients, range 9-234), and often were only partial [41, 42].

A study of Loening-Baucke [38] is the one with the largest number of patients. The author observed that in 234 children with known CFC and encopresis which treatment of constipation could prevent UTIs in 10% of patients with recurrent UTIs. In a study by the same author [39], treatment of constipation resulted in amelioration of the CFC but reported no results in terms of UTI incidence. Khen-Dunlop *et al.* [41] reported the outcome only to resolve UTI recurrences and not for constipation. A recent study involving 209 children, CFC treatment did not show a significant (not stated) amelioration of UTIs recurrences [43]. In particular, this case-control study (105 CFC children

versus 104 controls) showed that the prevalence of UTI in case and control groups was 13.3% and 6.7% ($p = 0.17$), showing a large link between constipation and UTIs, but the prevalence of UTIs in case group decreased only to 3.8% after treatment of constipation [43].

A bias in the clinical trials [26-28, 31, 35, 38] was the association between antibiotic prophylaxis, used if UTIs recurred, and constipation treatment.

DISCUSSION

UTIs recurrence prevention in children is again a challenge question whether antimicrobial prophylaxis is still a matter of debate. It has conducted investigations to find optimal approaches to the assessment and management of UTIs and later interventions [44, 45].

Studies suggested a link between constipation and UTI recurrences in children. Guidelines for children with UTIs considered for investigate and managing of the bowel dysfunctions. The studies conducted so far reported a large reduction in UTIs occurrences in children managed for DES, DV or CFC [26, 28-30, 32, 33, 40].

American Academy of Pediatrics (AAP) published guidelines for the diagnosis and management of UTIs in febrile infants and young children younger than 2 years. No mention concerns evaluation and treatment of the associated constipation [46]. In the same way, the Italian Society of Pediatric Nephrology reports the recommendations for diagnosis and treatment of UTIs

in children younger than 3 years, but did not mention evaluation and treatment of constipation in affected ones [47]. The American Urological Association (AUA) guidelines recommended a continuous antimicrobial prophylaxis as management of a child >1-year-old with VUR, recurrent febrile UTIs, bladder and bowel dysfunction, or renal cortical anomalies. No mention regards the constipation in affected children [48]. The European Urological Association reported that if symptoms are suggestive of LUTD (urgency, incontinence, constipation, or holding manoeuvres), should do an extensive history and examination. No mention regarded constipation management in these children [49].

Only NICE clinical guideline (<https://www.nice.org.uk/guidance/qs36>) reported that constipation and DV are risk factors for UTIs and should as part of history and examination on confirmed UTI. A systematic review of 27 studies (1 RCT and 26 case studies) on the role of biofeedback in DES in paediatric patients showed a rate of improvement from 18% to 100% for constipation and of 83% in cases of UTI [50]. In children with severe constipation, a structured bowel management program decreases unplanned visits to the emergency department, hospital admissions, and costs for constipation-related health care for constipation-related morbidities (abdominal pain 39%, fecal impaction 17%, urinary retention 2.2%, urinary tract infections 14%) [51].

Limitations

Further studies are necessary to show the effectiveness of constipation treatment regimens in preventing recurrent UTIs in children. In fact, most clinical trials, investigating the results of one or more treatments for constipation in the term of the resolution or amelioration of UTI recurrence, lacking in randomization and controlled groups. The published study results often involved small cohorts of patients or were only partial.

CONCLUSION

In conclusion, constipation seems to be a predisposing factor for UTIs recurrence in children. Studies were not homogenous but showed an

improvement in UTIs occurrences in children managed for CFC or DES. Children referred to a paediatric nephrologist for UTIs should include an inquiry on bowel habits and those with a positive assessment for bowel dysfunction should by a paediatric gastroenterologist as a multidisciplinary approach.

Abbreviations

CFC = chronic functional constipation
 DES = dysfunctional elimination syndromes
 DV = dysfunctional voiding
 LUTD = lower urinary tract dysfunctions
 UTI = urinary tract infection
 VUR = vesicoureteral reflux

Conflict of interest

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