Slow transit constipation and lower urinary tract dysfunction

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Summary

Introduction

Many theories have been proposed for the coexistence of constipation and lower urinary tract dysfunction (LUTD), such as bladder compression from a distended rectum and stimulation of sacral reflexes from a full rectum. In these cases, successful treatment of constipation should result in resolution of bladder symptoms. Some children have refractory constipation and others respond well to treatment, but once treatment is discontinued most children relapse back into their constipation. This may indicate the existence of a defect in colon motility, with a persistent peristalsis problem. The existence of a common neuromuscular disorder should be the base for both bladder and bowel dysfunction (BBD).

Objective

To study colonic transit time (CTT) in children and adolescents with refractory constipation and lower urinary tract symptoms (LUTS).

Materials and methods

A total of 15 children (mean age 9.7 years) with refractory constipation and LUTS were evaluated with: standardized medical history; physical examination; bladder and bowel diaries; Bristol stool scale; Rome III criteria; Dysfunctional Voiding Scoring System (DVSS); ultrasound examination of the kidneys and urinary tract, and measurement of rectal diameter; urodynamic evaluation; and a CTT study using radiopaque markers.

Results

Urodynamic features were abnormal in 13 out of 15 children: 10 (66.7%) presented with detrusor overactivity (DO) and voiding dysfunction (VD), two (16.7%) had isolated DO, and one (8.3%) had a VD. The CTT study was abnormal in 12 out of 15 children: nine (60%) presented with slow transit constipation, three (20%) had outlet obstruction, and three (20%) had a normal CTT study. When comparing CTT and LUTD, nine (100%) children with slow transit constipation (STC) and three (50%) with no STC had DO (P = 0.04). Seven (77.8%) children with STC and three (50%) with no STC had VD (P = 0.29). The DVSS scores ranged from 6 to 21. The subgroup with STC had a DVSS score that was significantly higher than that of the subgroup with no STC (Figure).

Discussion

The present study showed a high prevalence of STC in children and adolescents with refractory constipation and LUTS. This was in accordance with previous studies that have demonstrated a rate of 50–60% of STC in children with refractory constipation. In addition, DO was found to be associated with STC, which raises the chance for the existence of a common neuromuscular disorder to be the base for both bladder and bowel dysmotility. The limitation of this study was the number of participants.

Conclusions

The present study demonstrated an association between DO and STC.

Figure

Children and adolescents with slow transit constipation had higher DVSS scores than those without slow transit constipation.

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Introduction

Coexistent bowel and bladder dysfunction have previously been noted in children [1,2]. In 1998, Koff et al. introduced the term Dysfunctional Elimination Syndrome (DES) in order to describe the association of lower urinary tract and bowel functional disorders. The spectrum of urinary disorders included urge syndrome, dysfunctional voiding, and enuresis [2]. The International Children Continence Society (ICCS) recently proposed the term ‘bladder and bowel dysfunction’ (BBD) to describe the combination of functional bladder and bowel disturbances and to replace the term DES. Despite various publications regarding constipation and lower urinary dysfunction, the exact pathophysiologic mechanisms are still not fully understood. Many theories have been proposed for the coexistence of constipation and lower urinary tract dysfunction, which include mechanical causes such as bladder compression from a distended rectum and stimulation of sacral reflexes from a full rectum [3]. In these cases, a successful treatment of constipation should result in immediate resolution of bladder symptoms. But some of these children have refractory constipation and others respond to treatment, but once treatment for their bowel issues is discontinued, most children will relapse back into their constipation. This indicates the existence of a defect in colon motility, with a persistent peristalsis problem, which leads to accumulation of stools. The existence of a common neuromuscular disorder should be the base for both bladder and bowel dysmotility [3]. The hypothesis of the present study was the association between slow transit constipation and lower urinary tract dysfunction (LUTD). The aims were: to analyze colonic transit time in children and adolescents with refractory constipation and lower urinary tract symptoms; to compare the subgroups of functional constipation with the subgroups of lower urinary tract dysfunction; and to evaluate the severity of LUTS among children with or without slow transit constipation.

Methods

The present study was a prospective, descriptive study. Eighteen children with chronic constipation, who were refractory to conventional medical and behavioral treatment, were recruited from pediatric gastroenterology outpatient clinics from March 2013 to January 2014. The children were eligible if they had lower urinary tract symptoms and had been treated for constipation for at least 6 months. The exclusion criteria were: endocrine, metabolic or neurologic diseases; Hirschsprung disease; anorectal, spinal, urological or lower limbs orthopedic malformation. Three out of eighteen children were excluded due to the diagnosis of hypothyroidism, spinal malformation and renal malformation.

Ethical committee approval (project ID CAAE: 12673013.2.0000.5259) and written informed consent from all parents were obtained for the present study.

Protocol

The study was based on the following protocol: during the first visit, a standardized medical history, which included the initial diagnosis and previous treatment of constipation, fecal incontinence and LUTS, general health, growth and development, nutrition and family history, was carried out. A physical examination was performed with focus on the neurological system, back, lower limbs, abdomen, genitalia and digital rectal examination. The children were categorized as fitting into normal weight, being overweight, or obese, in accordance with the age-related body mass index (BMI) by WHO recommendations [4]. Constipation was defined by Rome III criteria [5]. The LUTS were classified in accordance with the ICCS terminology [6]. A validated version of the Brazilian Portuguese of Dysfunctional Voiding Scoring System (DVSS) was used to assess the severity of LUTS [7,8]. At the end of the first visit, parents were instructed to fill out a 3-day bladder diary with the frequency, voided volume, urgency and incontinence episodes recorded. In addition, they were asked to complete a 2-week bowel diary with the frequency of bowel movements, abdominal pain, evacuation difficulty and stool consistency. Stool consistency was assessed by the Bristol Scale [9]. All children underwent an ultrasound exam of kidney, bladder and rectum, as well as a urodynamic evaluation and a colonic transit time study. A follow-up was performed every month.

Ultrasound

The ultrasound (Toshiba Xario XL, SSA660A — Japan) was performed to evaluate the kidneys and urinary tract, and measure both post void residual (PVR) urine and rectal diameter. The PVR was measured less than 5 min after voiding and was considered to be abnormally elevated if a single PVR was >20 ml or 15% of bladder capacity (BC), or a repetitive PVR was >10 ml or 6% of BC [6]. A rectal diameter >3 cm was considered to be indicative of rectal impaction [10,11].

Colonic transit time

The assessment of total and segmental colonic transit time (CTT) was using radiopaque markers, as described by Metcalf et al. [12]. The children were instructed to maintain their usual diet, and discontinue the use of any medication that acts upon intestinal motility 5 days before the exam. They ingested a small capsule containing 24 radiopaque markers for 3 consecutive days. On the fourth day of the study, the children underwent plain abdominal radiograph in the supine position. One additional X-ray was performed on the seventh day of the study in case >80% of the markers had not been eliminated. The radiographs were performed with high kilovoltage, a high-sensitivity film and a high-luminosity screen in order to reduce radiation exposure. Localization of markers was based on the identification of body landmarks and gaseous outlines, as described by Arhan et al. [13]. Markers were counted in the right, left, and rectosigmoid regions, and mean segmental transit times were calculated according to a previously described formula [11,13]. Two medical radiologists independently counted the markers. Normal ranges for total and segmental transit time were based on the upper limits (means + 2 SD) previously described in healthy children:
Sixty-two children (38.7%) were G2P2, and three (30%) were G3P3. Three (30%) were G1P1, three (30%) were G2P1, one (10%) was G1P2, and one (10%) was G2P3.

Urodynamics

Urodynamic studies consisted of uroflowmetry with pelvic floor and abdominal electromyography (EMG) (Urostym, Laborie, Canada) and cystometry (Dynapack, Dynamed, Brazil). Initially, uroflowmetry was performed with EMG using surface electrodes. The children voided twice when they felt a strong desire to void. The diagnosis of voiding dysfunction (VD) was based on two consecutive uroflowmetries, with increased pelvic floor electromyography activity during voiding. To obtain abdominal and detrusor pressure, cystometry was performed using a urethral catheter and a rectal balloon catheter. The saline solution was infused between 5 and 10% of the expected bladder capacity per minute (without exceeding 20 ml/min) until the child needed to void. The results of the urodynamic evaluation were classified and described in accordance with the ICCS terminology. The urodynamic pattern was considered abnormal when the bladder had involuntary detrusor contractions, when the bladder capacity was smaller than expected for age, when the bladder pressure increased with filling to >10 cm H2O, when the bladder failed to have a sustained contraction during emptying, or if there was an incomplete voiding due to incoordination between the bladder and the external sphincter. The expected bladder capacity (EBC) for the age was calculated by the formula EBC = [age +1] × 30 ml. Detrusor overactivity (DO) was diagnosed by the occurrence of involuntary detrusor contractions during filling cystometry. The contractions could be phasic or terminal [6].

Data analysis

Statistical analyses were performed with Statistical Package for the Social Science (SPSS), version 17 (SPSS Inc., Chicago, IL., USA). The Fisher’s test was used to compare data given as proportions. Other data were given as median values (range) and compared using the Mann–Whitney U-test; \( P < 0.05 \) was considered statistically significant. The lack of existing data on bowel physiology in the CTT of children with BBD prevented prospective power calculation. Thus, post hoc power calculation was provided.

Results

Fifteen children aged 7–14 years (mean age 9.7 years) were analyzed: 10 (66.6%) were male and five (33.3%) were female. The girls were aged from 7 to 11 years (mean age 8.6 years), four (80%) of whom were classified in pre-pubertal stages (M1P1), and one (20%) in the M2P2 stage. Ten boys aged 7–14 years (mean age 10.4 years) were analyzed: three (30%) were G1P1, three (30%) were G2P1, one (10%) was G2P2, and three (30%) were G3P3.

Eight out of 15 (53.3%) children were classified as having normal weight, three (20%) as being overweight, and four (26.7%) as being obese.

Eight (53.3%) out of 15 children had a history of constipation since their first year of life. Their previous treatment included diet, behavioral modifications, laxative drugs, and pelvic floor physiotherapy. A family history of constipation and LUTS were obtained in 13 (86%) and 11 (73%) children, respectively.

The most common bowel symptoms were: withholding behavior (93.3%); hard stools (93.3%); painful defecation (73.3%); abdominal pain (73.3%); fecal incontinence (66.6%); abdominal distension (66.6%); large diameter stools, which may obstruct the toilet (66.6%); blood in stools (66.6%); and a palpable rectal fecal mass (60%).

The most common LUTS were urgency (80%), daytime incontinence (60%), holding manoeuvres (47%), and straining for voiding (33%). Five out of 15 children had a history of febrile UTI. Three (60%) out of these five first had a UTI before the age of 1 year, and two (16.7%) presented with monosymptomatic nocturnal enuresis.

The urodynamic features were abnormal in 13 out of 15 children: 10 (66.7%) presented with detrusor overactivity and voiding dysfunction; two (16.7%) had isolated detrusor overactivity; and one (8.3%) had a voiding dysfunction with no detrusor overactivity.

The colonic transit time study was normal in three (20%) children, nine (60%) had STC, and three (20%) had outlet obstruction. Among the subjects with STC, three (33.3%) were female and six (66.7%) were male (\( P = 0.7 \)). Four (44.4%) were pre-pubertal and five (53.6%) were pubertal (\( P = 0.62 \)). The two subjects with monosymptomatic nocturnal enuresis had a normal urodynamic evaluation and a normal CTT, despite enuresis.

Table 1 shows the most common LUTS in children with STC and with no STC. Urgency and urinary incontinence were more common among those with STC. These differences were of statistical significance: \( P = 0.04 \) and \( P = 0.01 \), respectively. Detrusor overactivity was significantly associated with STC (Table 2). Voiding dysfunction was more common among children with STC than among those with no STC, but the difference was not statistically significant (\( P = 0.29 \)) (Table 3).

The DVSS scores ranged from 6 to 21, with no statistical significance difference between girls (6–21) and boys (7–21) (\( P = 0.3 \)). When using the Mann–Whitney U-test, the DVSS score was significantly higher in the subgroup with STC (median = 15.1) than in the subgroup with no STC.

<table>
<thead>
<tr>
<th>LUTS</th>
<th>STC n (%)</th>
<th>No STC n (%)</th>
<th>P-value</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgency</td>
<td>9 (100%)</td>
<td>3 (50%)</td>
<td>0.04</td>
<td>0.846</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>8 (88.9%)</td>
<td>1 (16.7%)</td>
<td>0.01</td>
<td>0.867</td>
</tr>
<tr>
<td>Holding manoeuver</td>
<td>6 (66.7%)</td>
<td>1 (16.7%)</td>
<td>0.08</td>
<td>0.527</td>
</tr>
<tr>
<td>Straining to void</td>
<td>2 (22.2%)</td>
<td>3 (50%)</td>
<td>0.28</td>
<td>0.201</td>
</tr>
<tr>
<td>STC, slow transit constipation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Table 2: Slow transit constipation (STC) and detrusor overactivity (DO).

<table>
<thead>
<tr>
<th></th>
<th>DO n (%)</th>
<th>No DO n (%)</th>
<th>Total n (%)</th>
<th>P-value</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>9 (100%)</td>
<td>0 (0%)</td>
<td>9 (100%)</td>
<td>0.04</td>
<td>0.846</td>
</tr>
<tr>
<td>No STC</td>
<td>3 (50%)</td>
<td>3 (50%)</td>
<td>6 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12 (80%)</td>
<td>3 (20%)</td>
<td>15 (100%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Voiding dysfunction (VD) and slow transit constipation (STC).

<table>
<thead>
<tr>
<th></th>
<th>VD n (%)</th>
<th>No VD n (%)</th>
<th>Total n (%)</th>
<th>P-value</th>
<th>Power</th>
</tr>
</thead>
<tbody>
<tr>
<td>STC</td>
<td>7 (77.8%)</td>
<td>2 (22.2%)</td>
<td>9 (100%)</td>
<td>0.29</td>
<td>0.201</td>
</tr>
<tr>
<td>No STC</td>
<td>3 (50%)</td>
<td>3 (50%)</td>
<td>6 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>10 (70%)</td>
<td>5 (30%)</td>
<td>15 (100%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The interaction between bladder and bowel function may be partly due to overlapping pathways involving the neural dorsal ganglia, the spinal cord and the brain, along with neurotransmitters and hormonal mechanisms that would result in a cross-talk between the bladder and the rectum [19]. In the peripheral nervous system, the same nerves innervate the bladder and the anal rectum. In the central nervous system (CNS), afferent nerve signals from these organs are processed in the same regions of the brain, and both bladder and bowel functions are controlled by the same supraspinal regions such as the anterior cingulate gyrus, the insular cortex and the prefrontal cortex region of the brain [20,21].

Benninger et al. first described STC in 1996 [15]. The possible pathophysiological mechanisms suggested for STC are primary dysfunction of the colonic smooth muscle (myopathy) – resulting in ineffective peristaltic contractions – or of its nerve innervations (neuropathy), with paucity of interstitial cells of Cajal (ICC), and secondary to dysynergic defecation [22–24]. The ICCs are known to play an essential role in lower gastrointestinal tract function, acting as pacemakers that initiate slow-wave contractile activity in adjacent smooth muscle cells and as mediators of signal transduction from neurons to smooth muscle cells [25]. Stanton et al. tested neuromuscular transmission in the colonic circular muscle of children with STC and found that changes could be related to a lack of transmitters, a defect in the release of transmitters, a lack of binding to receptors, an absence of nerve fibers, an absence of ICC, and an absence of receptors in the nerve, ICC, or muscle [26,27]. Interestingly, interstitial cells that resemble the ICCs in the gut were recently identified in the urinary tract [28]. New pathomechanisms of detrusor overactivity involving the ICC have been postulated as follows: the disturbance of spontaneous contractility caused by altered signal transduction of ICC between nerves and detrusor muscle cells, and the alteration in signal transduction between urothelium and afferent nerve endings via suburothelial ICCs [29]. The ICCs disturbances appear to be part of common pathomechanisms that link slow transit constipation and detrusor overactivity.

A limitation of this study was the small number of participants with refractory constipation and LUTD. Nevertheless, the association between detrusor overactivity and slow transit constipation was statistically significant and power calculation was >80%.

Conclusion

The present study provided the first systematic evaluation of colonic transit time in children with non-neurogenic refractory constipation and LUTD. The association between DO and STC suggests that some children with severe constipation may have a neuropathy affecting both the colonic and lower urinary tract system. Further studies are necessary to better understand the physiopathology and the optimal treatment for BBD subgroups.

Conflict of interest statement

None.
Funding source

This study has not received any grant or funding.

Ethical approval

Ethical committee approval (project ID CAAE: 12673013.2.0000.5259) and written informed consent from all parents were obtained for the present study.

References


