Evaluation and Treatment of Functional Constipation in Infants and Children: Evidence-Based Recommendations From ESPGHAN and NASPGHAN


ABSTRACT

Background: Constipation is a pediatric problem commonly encountered by many health care workers in primary, secondary, and tertiary care. To assist medical care providers in the evaluation and management of children with functional constipation, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition were charged with the task of developing a uniform document of evidence-based guidelines.

Methods: Nine clinical questions addressing diagnostic, therapeutic, and prognostic topics were formulated. A systematic literature search was performed from inception to October 2011 using Embase, MEDLINE, the Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials, and PsycINFO databases. The approach of the Grading of Recommendations Assessment, Development and Evaluation was applied to evaluate outcomes. For therapeutic questions, quality of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation system. Grading the quality of evidence for the other questions was performed according to the classification system of the Oxford Centre for Evidence-Based Medicine. During 3 consensus meetings, all recommendations were discussed and finalized. The group members voted on each recommendation, using the nominal voting technique. Expert opinion was used where no randomized controlled trials were available to support the recommendation.

Results: This evidence-based guideline provides recommendations for the evaluation and treatment of children with functional constipation to standardize and improve their quality of care. In addition, 2 algorithms were developed, one for the infants <6 months of age and the other for older infants and children.

Conclusion: This document is intended to be used in daily practice and as a basis for further clinical research. Large well-designed clinical trials are necessary with regard to diagnostic evaluation and treatment.

Key Words: children, constipation, encopresis, enema, evidence-based, fecal incontinence, fecal soiling, functional constipation, guideline, infants, laxative

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INTRODUCTION

Functional constipation is a common problem in childhood, with an estimated prevalence of 3% worldwide (1). In 17% to 40% of children, constipation starts in the first year of life (2). Constipation is often associated with infrequent and/or painful defecation, fecal incontinence, and abdominal pain; causes significant distress to the child and family; and has a significant impact on health care cost (3). Although constipation may have several etiologies, in most children presenting with this symptom no underlying medical disease responsible for the symptom can be found. The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition published a medical position paper in 1999, which was updated in 2006 (search until 2004) (4). Recommendations were based on an integration of a comprehensive and systematic review of the medical literature combined with expert opinion. In addition, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom developed a guideline in 2010, based on a best-evidence strategy, for children with constipation in primary and secondary care (5). To assist health care workers in the management of all of the children with constipation in primary, secondary, and tertiary care, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition elected to develop evidence-based guidelines as a joint effort. The present guideline provides recommendations for the diagnostic evaluation of children presenting with constipation and the treatment of children with functional constipation. It is intended to serve as a general guideline and should not be considered a substitute for clinical judgment or used as a protocol applicable to all patients. The guideline is also not aimed at the management of patients with underlying medical conditions causing constipation, but rather just for functional constipation.
METHODS

Literature Search and Grading the Articles for Quality of Evidence

The project started in September 2011 by formulating 9 clinical questions (Table 1). Seven questions were chosen based on the Dutch guidelines for functional constipation (6). In addition, 2 new questions were added to the present guidelines: questions 5 and 8. After the questions were formulated, the guidelines committee

<table>
<thead>
<tr>
<th>Question</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>What is the definition of functional constipation?</td>
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<tr>
<td>2</td>
<td>What are the alarm signs and symptoms that suggest the presence of an underlying disease causing the constipation?</td>
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<tr>
<td>3</td>
<td>In the diagnosis of functional constipation in children, what is the diagnostic value of: 3.1 Digital rectal examination? 3.2 Abdominal radiography? 3.3 CTT? 3.4 Transabdominal rectal ultrasonography?</td>
</tr>
<tr>
<td>4</td>
<td>Which of the following diagnostic tests should be performed in children with constipation in order to diagnose an underlying disease? 4.1 Laboratory investigations to diagnose (cow’s milk) allergy, celiac disease, hypothyroidism and hypercalcemia? 4.2 ARM or rectal suction biopsy to diagnose HD? 4.3 Use of barium enema to diagnose organic causes such as HD?</td>
</tr>
<tr>
<td>5</td>
<td>Which of the following examinations should be performed in children with intractable constipation to evaluate pathophysiology and diagnose an underlying abnormality? 5.1 Colonic manometry 5.2 MRI of the spine 5.3 Colonic full-thickness biopsies 5.4 Colonic scintigraphy</td>
</tr>
<tr>
<td>6</td>
<td>What is the additional effect of the following nonpharmacologic treatments in children with functional constipation? 6.1 Fiber 6.2 Fluid 6.3 Physical activity 6.4 Prebiotics 6.5 Probiotics 6.6 Behavioral therapy 6.7 Biofeedback 6.8 Multidisciplinary treatment 6.9 Alternative medicine</td>
</tr>
<tr>
<td>7</td>
<td>What is the most effective and safest pharmacologic treatment in children with functional constipation? 7.1 Which pharmacologic treatment should be given for disimpaction? 7.2 Which pharmacologic treatment should be given for maintenance therapy? 7.3 How long should children be receiving medical therapy?</td>
</tr>
<tr>
<td>8</td>
<td>What is the efficacy and safety of novel therapies for children with intractable constipation? 8.1 Lubiprostone, linaclotide, and prucalopride 8.2 Surgery (eg, ACE) 8.3 TNS</td>
</tr>
<tr>
<td>9</td>
<td>What is the prognosis and what are prognostic factors in children with functional constipation? 9.1 What is the prognosis of functional constipation in children? 9.2 What are prognostic factors in children with functional constipation?</td>
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</table>

ACE = antegrade continence enema; ARM = anorectal manometry; CTT = colonic transit time; HD = Hirschsprung disease; MRI = magnetic resonance imaging; TNS = transcutaneous nerve stimulation.
Using the GRADE system, the quality of evidence for therapeutic interventions (questions 5, 6, and 9) was graded as follows (10):

- High: Further research is unlikely to change our confidence in the estimate of effect.
- Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Very low: Any estimate of effect is uncertain.

See the online-only appendix for the quality assessment of all included studies (http://links.lww.com/MPG/A295).

Consensus Meeting and Voting

Three consensus meetings were held to achieve consensus on and formulate all of the recommendations: September 2012, February 2013, and May 2013. Each subgroup presented the recommendations during the consensus meetings, wherein these were then discussed and modified according to the comments of the attendees. The consensus was formally achieved through nominal group technique, a structured quantitative method. The group anonymously voted on each recommendation. A 9-point scale was used (1 = strongly disagree to 9 = fully agree), and votes are reported by each recommendation (11). It was decided in advance that consensus was reached, if >75% of the working group members voted 6, 7, 8, or 9. The consensus was reached for all of the questions.

A decision was made to present 2 algorithms (Figs. 1 and 2). In contrast to the earlier guidelines, one pertains to the infant from birth to 6 months (instead of 1 year) and the other to the older child (7,8). This decision was based on the fact that defecation problems in infants <6 months old have different diagnostic considerations compared with older children, given the possibility of congenital problems and the influence of the different feeding and developmental issues. Both algorithms relate to any child presenting with constipation of at least 2 weeks’ duration and also include the evaluation and treatment options of the child with “intractable” constipation. The final draft of the guidelines was sent to all of the committee members for approval in May 2013.

Revision

This guideline should be revised every 3 to 5 years.

RESULTS

Question 1: What Is the Definition of Functional Constipation?

At present, the most widely accepted definitions for childhood functional constipation are the Rome III definitions (Table 2) (12,13). The Rome III definitions for functional constipation have been divided into 2 groups, based on the age of the patient. Infants

FIGURE 1. Algorithm for the evaluation and treatment of infants <6 months of age.
up to 4 years have to fulfill ≥2 of the criteria for at least 1 month, whereas those >4 years need to fulfill ≥2 of the criteria for at least 2 months, and to be included in the latter group children need to have a developmental age of at least 4 years and have insufficient criteria to fulfill the diagnosis of irritable bowel syndrome. Abdominal pain is a frequent associated symptom, but its presence is not considered a criterion for functional constipation. The role that constipation plays in children with predominant abdominal pain is not clear.

TABLE 2. Rome III diagnostic criteria for functional constipation

In the absence of organic pathology, ≥2 of the following must occur
For a child with a developmental age <4 years
1. ≤2 defecations per week
2. At least 1 episode of incontinence per week after the acquisition of toileting skills
3. History of excessive stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large-diameter stools that may obstruct the toilet
Accompanying symptoms may include irritability, decreased appetite, and/or early satiety, which may disappear immediately following passage of a large stool
For a child with a developmental age ≥4 years with insufficient criteria for irritable bowel syndrome
1. ≤2 defecations in the toilet per week
2. At least 1 episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large-diameter stools that may obstruct the toilet.

*Criteria fulfilled for at least 1 month. Adapted from Hyman et al (12).
†Criteria fulfilled at least once per week for at least 2 months before diagnosis. Adapted from Rasquin et al (13).
A subgroup of young children has defecation-related difficulties and has been categorized according to the Rome III criteria as having "infant dyschezia." This condition has been defined as occurring in an infant >6 months, with at least 10 minutes of straining and crying before successful passage of soft stools, in the absence of other health problems. Parents describe infants with dyschezia as straining for many minutes, screaming, crying, and turning red or purple in the face with effort. The symptoms persist for 10 to 20 minutes, until soft or liquid stools are passed. Stools are usually evacuated daily. The symptoms begin in the first months of life and resolve spontaneously after a few weeks. In the absence of any scientific literature evaluating this condition, infant dyschezia is not discussed in this document.

Not all of the children with defecation problems fulfill the Rome criteria, and other definitions have been proposed that are less stringent and have only included "difficulty with defecation for at least 2 weeks, which causes significant distress to the patient" (7). Although those definitions are more inclusive, they probably encompass a more heterogeneous group of patients. Several studies attempt to validate the Rome III criteria for functional constipation by comparing these criteria to other definitions. Boccia et al (14) compared the Paris Consensus on Childhood Constipation Terminology criteria (which are essentially the same as the Rome III criteria) with the Rome II criteria in 128 consecutive children presenting with disorders of defecation and found that the Paris Consensus criteria showed greater applicability than the Rome II criteria. Devanarayana et al (15) conducted a study in Sri Lanka comparing the Rome III and Rome II criteria for several functional gastrointestinal disorders and found that the Rome III criteria identified significantly more children with functional constipation. Finally, Burgers et al (16) investigated 336 children with defecation disorders and found that of the 6 Rome III criteria, 39% children had a defecation frequency ≤2/week, 75% had fecal incontinence, 75% displayed retentive posturing, 60% had pain during defecation, 49% passed large-diameter stools, and 49% had a palpable rectal fecal mass. According to the Rome III criteria, 87% had functional constipation compared with only 34% fulfilling criteria for different disorders of defecation based on the Rome II definitions.

The present document includes evidence related to patients diagnosed as having constipation using the established Rome III criteria or equivalent definitions at the time of the publication. Constipation is also a prominent symptom in children who have other underlying medical conditions such as prematurity, developmental delay, or other organic diseases, but the present guideline is not intended for those patients.

Given some evidence showing early treatment favorably affects outcome, we decided to use as an entry point in the algorithms children who fulfill the Rome III criteria for constipation, except for the duration (Fig. 1, boxes 1 and 7; Fig. 2, boxes 1 and 4). Based on consensus, the group agreed that the 2-month interval listed in the Rome III criteria for older children may unduly delay treatment in some children with constipation.

**Other Definitions Used in This Guideline**

*Intractable Constipation:* Constipation not responding to optimal conventional treatment for at least 3 months.

*Fecal Impaction:* A hard mass in the lower abdomen identified on physical examination or a dilated rectum filled with a large amount of stool on rectal examination or excessive stool in the distal colon on abdominal radiography.

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**Question 2: What Are the Alarm Signs and Symptoms That Suggest the Presence of an Underlying Disease Causing the Constipation?**

Although diagnosis of constipation is based on the history and physical examination, subjective symptom description is unreliable in infants and many children <8 years of age, and some purported symptoms of constipation in infants and children are nonspecific. The major role of history and physical examination in the evaluation of constipation is to exclude other disorders that present with difficulties with defecation and to identify complications (Figs. 1 and 2, boxes 2 and 3). The information that should be actively sought includes age of onset of symptoms, success or failure of toilet training, frequency and consistency of stools (preferably expressed according to existing stool scales such as the Bristol scale (17) or the Amsterdam infant stool scale (18) or the Lane scale, which is the modified Bristol Stool Form Scale for children (19,20)), pain and/or bleeding when passing stools, coexistence of abdominal pain or fecal incontinence (if present, whether it is also nocturnal), withholding behavior, dietary history, changes in appetite, nausea and/or vomiting, and weight loss. The age of the child when symptoms began is one of the easiest and most important pieces of information to obtain in the evaluation of the problem. Onset of symptoms in infants <1 month old raises the suspicion of the presence of an organic condition such as Hirschsprung disease (HD) (21). The timing of passage of the first meconium is especially relevant to the risk of having HD; delayed passage of meconium by 48 hours in a term neonate suggests the need for definitive testing to rule out the diagnosis. Although 99% of healthy term neonates pass their first meconium before 48 hours of life (22), 50% of children with HD also pass meconium within 48 hours of birth (23). Thus, the failure of passage of meconium within the first 48 hours of life, although suggestive of HD, does not establish the diagnosis.

The information should also be obtained regarding previous and present treatment. Ideally, based on expert opinion, a 3-day diary should be used to better evaluate dietary and fluid intake. Medication history should be collected, including the use of oral laxatives, enemas, suppositories, herbal treatments, behavioral treatment, and other medications.

The general development and psychosocial history, such as disruption of child or family life and activities, interaction with peers, and temperament, is also relevant. Family history should be carefully taken, searching for gastrointestinal diseases (HD, food allergies, inflammatory bowel disease, celiac disease, urinary bladder disease) and for abnormalities of organs such as the thyroid, parathyroid, kidneys, or systemic diseases such as cystic fibrosis. Physical examination should specifically focus on the growth parameters, abdominal examination (muscle tone, distension, fecal mass), inspection of the perianal region (anal position, stool present around the anus or on the undergarments, erythema, skin tags, anal fissures), and examination of the lumbosacral region (dimple, tuft of hair, gluteal cleft deviation, sacral agenesis, flat buttocks). Digital rectal examination evaluates the presence of an anal stenosis or of a fecal mass. The evacuation of explosive stools after withdrawal of
Based on expert opinion, we recommend using Tables 3, 4, and 5 for alarm signs and symptoms and diagnostic clues to identify an underlying disease responsible for the constipation. Voting: 7, 8, 8, 9, 9, 9, 9

**TABLE 3. Differential diagnoses of constipation in infants/toddlers and children/adolescents**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Definition</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Celiac disease</td>
<td>Autoimmune disorder affecting the small intestine</td>
<td>1%</td>
</tr>
<tr>
<td>Hypothyroidism, hypercalcemia, hypokalemia</td>
<td>Endocrine disorders affecting the thyroid and electrolyte balance</td>
<td>2%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Metabolic disorder affecting the blood glucose level</td>
<td>3%</td>
</tr>
<tr>
<td>Dietary protein allergy</td>
<td>Allergy to dietary proteins</td>
<td>4%</td>
</tr>
<tr>
<td>Drugs, toxins</td>
<td>Medication affecting the gut function</td>
<td>5%</td>
</tr>
<tr>
<td>Opiates, anticholinergics</td>
<td>Medication affecting the gut function</td>
<td>6%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Medication affecting the gut function</td>
<td>7%</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Medication affecting the gut function</td>
<td>8%</td>
</tr>
<tr>
<td>Heavy metal ingestion (lead)</td>
<td>Exposure to heavy metals affecting the gut function</td>
<td>9%</td>
</tr>
<tr>
<td>Vitamin D intoxication</td>
<td>Overdosage of vitamin D affecting the gut function</td>
<td>10%</td>
</tr>
<tr>
<td>Botulism</td>
<td>Neurotoxic effect of botulin affecting the gut function</td>
<td>11%</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Genetic disorder affecting the gut function</td>
<td>12%</td>
</tr>
<tr>
<td>HD</td>
<td>Hirschsprung disease</td>
<td>13%</td>
</tr>
<tr>
<td>Anal achalasia</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>14%</td>
</tr>
<tr>
<td>Colonic inertia</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>15%</td>
</tr>
<tr>
<td>Anatomic malformations</td>
<td>Abnormal anatomical structure affecting the gut function</td>
<td>16%</td>
</tr>
<tr>
<td>Imperforate anus</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>17%</td>
</tr>
<tr>
<td>Anal stenosis</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>18%</td>
</tr>
<tr>
<td>Pelvic mass (sacral teratoma)</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>19%</td>
</tr>
<tr>
<td>Spinal cord anomalies, trauma, tethered cord</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>20%</td>
</tr>
<tr>
<td>Abnormal abdominal musculature (prune belly, gastrochisis, Down syndrome)</td>
<td>Congenital anomalies affecting the gut function</td>
<td>21%</td>
</tr>
<tr>
<td>Pseudoobstruction (visceral neuropathies, myopathies, mesenchymopathies)</td>
<td>Anatomical obstruction affecting the gut function</td>
<td>22%</td>
</tr>
<tr>
<td>Multiple endocrine neoplasia type 2B</td>
<td>Genetic disorder affecting the gut function</td>
<td>23%</td>
</tr>
</tbody>
</table>

**Question 3: In the Diagnosis of Functional Constipation in Children, What Is the Diagnostic Value of the Following (3.1–3.4)**

**3.1 Digital Rectal Examination**

One study was included evaluating the value of digital rectal examination in diagnosing clinically defined childhood constipation. Beckman et al (24) aimed to determine whether clinical variables accurately identify children with radiographically proven constipation. In this study, the ability of the clinical examination to discriminate between radiographically constipated and nonconstipated children was evaluated in a cross-sectional study and reported a sensitivity of 77%, a specificity of 35%, and a likelihood ratio (LR, which means the likelihood that a given test result would be expected in a patient with functional constipation compared with the likelihood that that same result would be expected in a patient without functional constipation) of 1.2 (95% confidence interval [CI] CI 1.0–1.4). An LR of 1 indicates that a finding occurs as often in children with constipation as in children without constipation. A diagnosis of constipation as made by the clinician was not defined. None of the individual symptoms had a clinical relevant (LR ≥2 or ≤0.5) and statistically significant association with constipation. The best discriminator was “stool present on rectal examination” with an LR of 1.6 (1.2–2.0).

In conclusion, evidence does not support the use of digital rectal examination to diagnose functional constipation.

**3.2 Abdominal Radiography**

Demonstration of the presence or absence of fecal impaction has important therapeutic implications (Fig. 2, boxes 5 and 6).

One review was found (25). Five studies were included assessing the value of scoring fecal loading on abdominal radiography in diagnosing clinically defined childhood constipation. All studies evaluated the value of abdominal radiography to diagnose functional constipation, using as a reference the clinical definition of constipation. Barr et al (26) was the first to develop an abdominal radiography score to diagnose functional constipation. The Barr scoring system ranges from 0 to 25, with a total score of >10, indicating excessive fecal retention. Barr et al reported a sensitivity of 80% (95% CI 65–90) and a specificity of 90% (90% CI 74–98) using their scoring system. Benninga et al (27) also used the Barr scoring system and reported a lower sensitivity of 60% (95% CI 46–72) and a specificity of 43% (95% CI 18–71). Subsequently, Leech et al (28) developed a scoring system in which an abdominal radiograph is divided into 3 segments. Each segment is scored from 0 to 5, with a score range of 0 to 15. A total score of 8 to 15 indicated constipation. Application of this scoring system by Leech et al yielded a sensitivity of 76% (95% CI 58–89) and a specificity of 75% (95% CI 63–85). de Lorijn et al (29) also used the Leech scoring method (31). Fecal loading is scored on a scale from 0 to 5. They reported a sensitivity of 80% (95% CI 61–86) and a specificity of 59% (95% CI 42–75). Čayan et al (30) rated fecal loading on abdominal radiography defined by the Blethyn scoring method (31). Fecal loading is scored on a scale from 0 to 3. They reported a sensitivity of 70% (95% CI 35–93) and a specificity of 90% (95% CI 95–100). Among these studies, only the study by de Lorijn et al (29) presented an area under the curve (AUC). An AUC of 1 indicates perfect discrimination between children with and without constipation. An AUC of 0.5 indicates no discrimination at all. The AUC of 0.68 (0.58–0.80) in this study indicated poor discriminative value.

One additional study defined constipation based on colonic transit time (CTT) (32). The ability of scoring fecal loading according to Barr on abdominal radiography to discriminate between radiographically constipated (CTT > 60 hours) and nonconstipated children (CTT ≤ 60 hours) was evaluated and reported a best AUC of 0.84 (95% CI 0.79–0.89; scored by a consultant). The discriminative power was dependent on the level of experience of the radiologist (Barr scores of the junior physician and the student were poorer, with AUCs of 0.76 and 0.61 (95% CI 0.69–0.82 and 0.53–0.69).

In conclusion, evidence supports not using an abdominal radiography to diagnose functional constipation.

**3.3 CTT (Fig. 2, Box 25)**

Four studies were included evaluating the value of CTT in diagnosing clinically defined childhood constipation. Gutierrez et al...
(33) found that in constipated children the mean CTT was significantly prolonged compared with the control group (mean ± standard deviation [SD] 49.57 ± 25.38 versus 29.08 ± 8.3); CTT was inversely related to the number of defecations per week. Zaslavsky et al (34) found that in constipated children the mean CTT was significantly different from the mean in the control group (mean ± SD 58.25 ± 17.46 compared with 30.18 ± 13.15). de Lorijn et al (29) presented an AUC of 0.90 (range 0.83–0.96), indicating that CTT is a good discriminator between children with and without clinical constipation who were referred to a pediatric.
TABLE 5. Alarm signs and symptoms in constipation

- Constipation starting extremely early in life (<1 mo)
- Passage of meconium >48 h
- Family history of HD
- Ribbon stools
- Blood in the stools in the absence of anal fissures
- Failure to thrive
- Fever
- Bilious vomiting
- Abnormal thyroid gland
- Severe abdominal distension
- Perianal fistula
- Abnormal position of anus
- Absent anal or cremasteric reflex
- Decreased lower extremity strength/tone/reflex
- Tuft of hair on spine
- Sacral dimple
- Gluteal cleft deviation
- Extreme fear during anal inspection
- Anal scars

HD = Hirschsprung disease.

In conclusion, evidence does not support the routine use of colonic transit studies to diagnose functional constipation.

Comment: The working group concluded that demonstration of a normal CTT with the prompt passage of markers suggests either nonretentive fecal incontinence (a condition in which children have fecal incontinence without having functional constipation) or an unreliable medical history.

3.4 Transabdominal Rectal Ultrasonography

Four studies were included evaluating the value of transabdominal rectal ultrasonography in diagnosing childhood constipation. Bijos et al (35) calculated a recopal ratio by dividing the transverse diameter of the rectal ampulla by the transverse diameter of the pelvis. In children with functional constipation, the mean rectopal ratio was 0.22 ± 0.05 compared with healthy controls 0.15 ± 0.04. The difference was statistically significant in all age groups.

In the study by Singh et al (36), the impression of the rectum behind the urinary bladder seen as a crescent was measured; the median recopal ratio presented in children with constipation was 3.4 cm (range 2.10–7.0, interquartile range [IQR] 3.53) compared with 2.4 cm (range 1.3–4.2, IQR 0.72) in healthy controls. Cutoff values for constipation were not presented. In the study by Joensson et al (37), it was possible to visualize the transverse diameter of the rectum at least 3 hours after the last bowel movement in all of the included children. The children with constipation had a significantly larger rectal diameter than healthy children (mean ± SD 42.1 ± 15.4 vs 21.4 ± 6.0 mm). Using a cutoff value for constipation of 33.4 mm, 13 children would be misclassified. After laxative treatment, the rectal diameter of the children with constipation decreased significantly (from [mean ± SD] 42.1 ± 15.4 to 26.9 ± 5.6 mm). Klijn et al (38) found a statistically significant difference in mean rectal diameter between the constipated group (4.9 cm) and the control group (2.1 cm). The cutoff value was 3.3 cm, where >3.3 cm indicated constipation. The study by Singh et al (36) reported an AUC of 0.85 (0.79–0.90), indicating that measuring rectal diameter on ultrasound examination is a moderate-to-good discriminator between children with and without constipation.

In conclusion, evidence does not support the routine use of rectal ultrasound to diagnose functional constipation.
Routine allergy testing is not recommended to diagnose cow’s-milk allergy in children with functional constipation.

Voting: 7, 7, 8, 8, 9, 9, 9

Based on expert opinion, a 2- to 4-week trial of avoidance of CMP may be indicated in the child with intractable constipation.

Voting: 6, 6, 7, 7, 8, 8, 9
specific histologic abnormalities and the type of colonic dysfunction (52–54).

The search identified 50 studies. None of them fulfilled our inclusion criteria.

Comment: Although we do not recommend surgery just to obtain full-thickness colonic biopsies, a full-thickness biopsy may be appropriate in the context of the child receiving another intra-abdominal surgical procedure.

5.4 Colonic Scintigraphy

Nuclear scintigraphy provides information on colonic transit and may provide data also on gastric emptying and small bowel transit. It is considered to be useful in measuring colonic motility in children with slow transit constipation (55).

The search identified 263 studies. None fulfilled our inclusion criteria. No studies have assessed the diagnostic value of scintigraphy in children with functional constipation.

Question 6: What Is the Additional Effect of the Following Nonpharmacologic Treatments in Children With Functional Constipation?

For the role of CMP-free diet: see question 4.1 (Fig. 1, Box 24; Fig. 2, Box 21).

6.1 Fiber (Fig. 1, Box 8; Fig. 2, Box 9 “Education”)

The search identified 111 studies including 3 systematic reviews (9,56,57). Tabbers et al (9) performed a Clinical Evidence GRADE evaluation for most of the interventions. They, however, used different inclusion criteria and outcome measures compared with the present review. They found limited evidence that additional fiber improves constipation compared with placebo and that increased fiber intake is not as effective as lactulose. Pipers et al (56) included 2 studies concerning fiber and concluded that the pooled weighted standardized mean difference was 0.35 bowel movements per week in favor of fiber (95% CI: 0.04 to 0.74), which is neither statistically significant nor clinically relevant. The third and most recent systematic review concluded that studies were highly diverse with regard to the participants, interventions, and outcome measures; therefore, a meta-analysis could not be performed (57). Based on these 3 reviews, 3 studies fulfilled our inclusion criteria (58–60). After these reviews, 2 more RCTs were published that also fulfilled our inclusion criteria (61,62). Consequently, we included 5 studies concerning fiber according to our outcome measures: see GRADE evidence profiles in Appendix, question 6, http://links.lww.com/MPGA295.

In conclusion, evidence does not support the use of fiber supplements in the treatment of functional constipation.

6.2 Fluid (Fig. 1, Box 8; Fig. 2, Box 9 “Education”)

The search identified 166 studies including 2 systematic reviews (9,57). Both reviews concluded that based on 1 study, increasing oral fluid intake has not been shown to be beneficial (63). Young et al (63) investigated 108 children, 2 to 12 years with an unclear definition of constipation, comparing 3 groups: 50% increase in water intake, hypertonic (>600 mOsm/L) supplemental fluid, and normal fluid intake. This study has a high risk of bias: no information was provided about randomization, blinding, or the rate of loss-to-follow-up monitoring. No statistical assessment was conducted. The RCT found similar stool frequency at 3 weeks for the 3 groups. Because of the missing data such as means with SD, a GRADE evidence profile could not be performed.

In conclusion, evidence does not support the use of extra fluid intake in the treatment of functional constipation.

6.3 Physical Activity (Fig. 2, Box 9 “Education”)

There are no randomized studies that evaluate the effect of increased physical activity in childhood constipation.

6.4 Prebiotics

6.5 Probiotics

The present search identified 153 studies, including 4 systematic reviews (9,56,57,64). Tabbers et al (9) performed a GRADE assessment for most of the interventions. In the latter assessment, different inclusion criteria and outcome measures were used compared with the present review. No evidence was found supporting the use of prebiotics and probiotics (9). The other reviews included the same 2 RCTs concerning prebiotics but did not perform a GRADE evaluation (56,57). After these reviews, 3 more RCTs, fulfilling our inclusion criteria, evaluating the effect of probiotics, were published (65–67). It was, however, only possible to perform a GRADE evidence profile of 1 study owing to missing data in the other 2 studies (67). Therefore, we discuss these 2 studies. Guerra et al (65) carried out a crossover double-blind trial in 59 Brazilian children with functional constipation according to Rome III criteria. This study has a low risk of bias. The patients were randomized in 2 groups to receive either a goat yogurt supplemented with 10^9 colony-forming unit/mL Bifidobacterium longum daily or only the yogurt for a period of 5 weeks. The results were only graphically presented without reporting absolute numbers.

Coccorullo et al (66) performed a double-blind randomized placebo-controlled study in 44 formula-fed infants with a diagnosis of functional chronic constipation according to Rome III criteria. This study has a low risk of bias. The patients were randomized in 2 groups to receive either a goat yogurt supplemented with 10^9 colony-forming unit/mL Lactobacillus reuteri (DSM 17938) and the other group received a placebo. L reuteri was administered at a dose of 10^9 colony-forming units in 5 drops of oil suspension once per day for 8 weeks. Infants treated with L reuteri had a significantly higher defecation frequency than placebo after 2, 4, and 8 weeks of
treatment. The results were graphically presented without reporting absolute numbers with means and SDs, and there was no mean difference for outcome measures between the 2 groups.

In summary, 1 study reporting the effect of prebiotics and 5 studies reporting the effect of probiotics fulfilled our inclusion criteria. It was possible to perform a GRADE evidence profile concerning the prebiotic study and 3 concerning probiotic studies.

**In conclusion, evidence does not support the use of pre- or probiotics in the treatment of childhood constipation.**

6.6 Behavioral Therapy (Fig. 2, Boxes 11, 27, and 35) and 6.7 Biofeedback (Fig. 2, Box 35)

The search identified 194 studies including 3 systematic reviews (9,57,68). All of the reviews concluded that behavioral therapy in addition to laxatives is not more effective than laxatives alone. Only 1 study (69) fulfilled our inclusion criteria: see Appendix, question 6, http://links.lww.com/MPG/A295. Concerning biofeedback therapy, 2 systematic reviews included the same studies with the same outcome measures (57,68). See GRADE evidence profiles in Appendix, question 7, http://links.lww.com/MPG/A295.

**In conclusion, evidence does not support the use of behavioral therapy or biofeedback in the treatment of childhood constipation.**

**Comment**: There may be benefit to refer children with constipation and behavioral abnormalities to a mental health provider (Fig. 2, boxes 11, 27, and 35).

6.8 Multidisciplinary Treatment (Pediatrician or Pediatric Gastroenterologist, Dietician, Psychologist, and Physical Therapist)

No RCTs were found.

6.9 Alternative Medicine (Including Acupuncture, Homeopathy, Mind-Body Therapy, Musculoskeletal Manipulations Such As Osteopathic and Chiropractic and Yoga)

No RCTs were found.

**Quality of evidence: very low.**

(21) A normal fiber intake is recommended in children with constipation.

*Voting: 6, 8, 9, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(22) Based on expert opinion, we recommend a normal fluid intake in children with constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(23) Based on expert opinion, we recommend a normal physical activity in children with constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(24) The routine use of prebiotics is not recommended in the treatment of childhood constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

**Quality of evidence: very low.**

(25) The routine use of probiotics is not recommended in the treatment of childhood constipation.

*Voting: 7, 8, 8, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(26) The routine use of an intensive behavioral protocolized therapy program in addition to conventional treatment is not recommended in childhood constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

(27) Based on expert opinion, we recommend demystification, explanation, and guidance for toilet training (in children with a developmental age of at least 4 years) in the treatment of childhood constipation.

*Voting: 7, 8, 8, 8, 9, 9, 9, 9*

**Quality of evidence: low.**

(28) The use of biofeedback as additional treatment is not recommended in childhood constipation.

*Voting: 7, 8, 8, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(29) Based on expert opinion, we do not recommend the routine use of multidisciplinary treatment in childhood constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

(30) Based on expert opinion, we do not recommend the use of alternative treatments in childhood constipation.

*Voting: 9, 9, 9, 9, 9, 9, 9, 9*

**Quality of evidence: low.**

**Question 7: What Is the Most Effective and Safest Pharmacologic Treatment in Children With Functional Constipation?**

The search identified 252 studies including 5 systematic reviews (9,56,70–72). Among the 5 systematic reviews, the review of Price et al (70) did not include any drug trial. Lee-Robichaud et al (71) performed a review to determine whether lactulose or polyethylene glycol (PEG) was more effective in treating chronic constipation and fecal impaction in adults and children. We included the 5 pediatric studies from that review in this guideline:
see GRADE evidence profiles for pooled outcome measures in Appendix, question 7, http://links.lww.com/MPG/A295 (73–77). Tabbers et al (9) investigated the effectiveness of most of the pharmacologic interventions but used different inclusion criteria and outcome measures compared with our guidelines. In separate reviews, both Candy et al (72) and Pijpers et al (56) concluded that because of the heterogeneity of the included studies with regard to participants, interventions, and outcome measures, statistical pooling of the results was not possible for most of the interventions. Nine studies fulfilled our inclusion criteria and were not already included by Lee-Robichaud et al (see GRADE evidence profiles in Appendix, question 7, http://links.lww.com/MPG/A295) (78–86).

No RCTs were found about the optimal dosages of the different medications (see Table 6 for recommended dosages of most frequently used oral and rectal laxatives).

7.1 Which Pharmacologic Treatment Should Be Given for Disimpaction? (Fig. 2, Boxes 6 and 11)

No placebo-controlled studies have evaluated the effect of oral laxatives or enemas on disimpaction. One study compared the effect of PEG to enemas but could not detect a difference in effect (85).

In conclusion, evidence shows that PEG and enemas are equally effective for fecal disimpaction.

Comment: High-dose PEG given orally is associated with a higher frequency of fecal incontinence during treatment of the fecal impaction compared with enema use; however, based on the argument that PEG can be administered orally, the working group decided to prefer PEG.

TABLE 6. Dosages of most frequently used oral and rectal laxatives

<table>
<thead>
<tr>
<th>Oral laxatives</th>
<th>Dosages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic laxatives</td>
<td>1–2 g/kg, once or twice/day</td>
</tr>
<tr>
<td>Milk of magnesia (magnesium hydroxide)</td>
<td>Maintenance: 0.2–0.8 g · kg⁻¹ · day⁻¹</td>
</tr>
<tr>
<td>Fecal disimpaction: 1–1.5 g · kg⁻¹ · day⁻¹ (with a maximum of 6 consecutive days)</td>
<td></td>
</tr>
<tr>
<td>2–5 y: 0.4–1.2 g/day, once or divided</td>
<td></td>
</tr>
<tr>
<td>6–11 y: 1.2–2.4 g/day, once or divided</td>
<td></td>
</tr>
<tr>
<td>12–18 y: 2.4–4.8 g/day, once or divided</td>
<td></td>
</tr>
<tr>
<td>Fecal softeners</td>
<td>1–18 y: 1–3 mL · kg⁻¹ · day⁻¹, once or divided, max 90 mL/day</td>
</tr>
<tr>
<td>Stimulant laxatives</td>
<td>3–10 y: 5 mg/day</td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>&gt;10 y: 5–10 mg/day</td>
</tr>
<tr>
<td>Senna</td>
<td>2–6 y: 2.5–5 mg once or twice/day</td>
</tr>
<tr>
<td>6–12 y: 7.5–10 mg/day</td>
<td></td>
</tr>
<tr>
<td>12 y: 15–20 mg /day</td>
<td></td>
</tr>
<tr>
<td>Sodium picosulfate</td>
<td>1 mo–4 y: 2.5–10 mg once/day</td>
</tr>
<tr>
<td>4–18 y: 2.5–20 mg once/day</td>
<td></td>
</tr>
<tr>
<td>Rectal laxatives/enemas</td>
<td>2–10 y: 5 mg once /day</td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>&gt;10 y: 5–10 mg once /day</td>
</tr>
<tr>
<td>Sodium docusate</td>
<td>&lt;6 y: 60 mL</td>
</tr>
<tr>
<td>&gt;6 y: 120 mL</td>
<td></td>
</tr>
<tr>
<td>Sodium phosphate</td>
<td>1–18 y: 2.5 mL/kg, max 133 mL/dose</td>
</tr>
<tr>
<td>NaCl</td>
<td>Neonate &lt;1 kg: 5 mL, &gt;1 kg: 10 mL</td>
</tr>
<tr>
<td>&gt;1 y: 6 mL/kg once or twice/day</td>
<td></td>
</tr>
<tr>
<td>2–11 y: 30–60 mL once/day</td>
<td></td>
</tr>
<tr>
<td>&gt;11 y: 60–150 mL once/day</td>
<td></td>
</tr>
</tbody>
</table>

PEG = polyethylene glycol.
Based on expert opinion, maintenance treatment with PEG with or without electrolytes is recommended as the first-line maintenance treatment. A starting dose of 0.4 g·kg⁻¹·day⁻¹ is recommended and the dose should be adjusted according to the clinical response.

Voting: 7, 7, 8, 8, 9, 9, 9. Two members (who had disclosed a COI with industry manufacturing PEG) did not participate in the discussion and did not vote.

The use of PEG with or without electrolytes is recommended as the first-line maintenance treatment. The use of milk of magnesia, mineral oil, and stimulant laxatives may be considered as an additional or second-line treatment.

Voting: 7, 7, 7, 9, 9, 9, 9

Quality of evidence: low.

Based on expert opinion, maintenance treatment should continue for at least 2 months. All symptoms of constipation symptoms should be resolved for at least 1 month before discontinuation of treatment. Treatment should be decreased gradually.

Voting: 7, 7, 8, 8, 8, 8, 9, 9

Based on expert opinion, the use of milk of magnesia, mineral oil, and stimulant laxatives may be considered as an additional or second-line treatment.

Voting: 7, 7, 7, 9, 9, 9, 9

Quality of evidence: very low.

8.1 Lubiprostone, Linaclotide, and Prucalopride

Lubiprostone, linaclotide, and prucalopride are drugs that have been found to be effective in constipated adults. To date, no randomized studies have been published in children.

8.2 Surgery (Fig. 2, Boxes 34 and 35)

The use of ACE has been reported as a successful therapeutic option for patients with long-lasting constipation when maximal conventional therapy is not successful. The antegrade delivery of cleansing solutions enables the patient to evacuate the colon at regular intervals, avoiding impaction of feces and reducing fecal incontinence.

No randomized studies were found.

Comment: Six open retrospective studies are available in children suggesting that ACE may be an option in children with intractable constipation (87–92). Potential complications (development of granulation tissue, leakage around the tube, tube dislodgment, skin infection, and stoma stenosis) should be thoroughly considered and discussed with parents and children. No data comparing different types of surgical procedures for the administration of antegrade enemas have been published.

8.3 Transcutaneous Nerve Stimulation (TNS) (Fig. 2, Boxes 34 and 35)

Transcutaneous electrical stimulation is a noninvasive and painless form of interventional therapy in which 4 surface electrodes are applied to the skin (2 abdominal, just below the costal margin; 2 paraspinal, over muscles between T9 and L2 spinal segments), which produce 2 sinusoidal currents that cross within the body (93).

See the GRADE evidence profile of 1 study in Appendix, question 8, http://links.lww.com/MPGA295 (94). In this RCT, investigators report a significant improvement of quality of life in children treated with TNS; however, the basal scores of quality of life in the 2 groups were not similar, thus precluding any valuable conclusion. In addition, in another report, TNS decreased transit time in treated patients but no data on stool pattern and frequency were reported (95).

In conclusion, evidence does not support the use of TNS in children with intractable constipation.

Quality of evidence: low.

Based on expert opinion, we do not recommend the routine use of lubiprostone, linaclotide, and prucalopride in children with intractable constipation.

Voting: 9, 9, 9, 9, 9, 9, 9, 9

Quality of evidence: very low.

The routine use of TNS in children with intractable constipation is not recommended.

Voting: 9, 9, 9, 9, 9, 9, 9, 9

Question 8: What Is the Efficacy and Safety of Novel Therapies for Children With Intractable Constipation?

Question 9: What Is the Prognosis and What Are Prognostic Factors in Children With Functional Constipation?
found that duration of symptoms <3 months before presentation had a positive effect on recovery.

Approximately 80% of the children adequately treated early in their course recovered without using laxatives at 6-month follow-up, compared with only 32% of the children with a delay in treatment. These data indicated that early adequate therapeutic intervention was more likely to be beneficial and contributed to successful outcome of constipation. Both high- and low-quality studies showed approximately 50% to 60% recovery rate after 1 year of intensive treatment. Prognostic factors could not be identified.

Data from tertiary care centers revealed similar recovery rates of 50% after 5 years of follow-up (101,111). Approximately 50% of children with constipation had at least 1 relapse within the first 5 years after initial recovery (105). This finding may explain similar success percentages between 1 and 5 years of follow-up. Thus, it seems of great importance to follow constipated children closely and restart medication promptly, if necessary. Furthermore, emphasis on recommended regimens for maintenance and how to reduce medication will help to improve the long-term outcome.

9.1 What Is the Prognosis of Functional Constipation in Children?

Among patients referred to pediatric gastroenterologists 50% will recover (≥3 bowel movements per week without fecal incontinence) and be without laxatives after 6 to 12 months. Approximately an additional 10% are well while taking laxatives, and 40% will still be symptomatic despite use of laxatives. A total of 50% and 80% of the children are recovered after 5 and 10 years, respectively, with the vast majority of patients no longer taking laxatives. In patients referred to pediatric gastroenterologists, a delay in initial medical treatment for >3 months from symptom onset correlates with longer duration of symptoms.

9.2 What Are Prognostic Factors in Children With Functional Constipation?

See Table 7.

**TABLE 7.** Summary of evidence for any of the following factors being related to the prognosis of functional constipation (see Appendix for more details, [http://links.lww.com/MPG/A295](http://links.lww.com/MPG/A295))

<table>
<thead>
<tr>
<th>Diagnostic Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) The Rome III criteria are recommended for the definition of functional constipation for all age groups.</td>
</tr>
<tr>
<td>(2) The diagnosis of functional constipation is based on history and physical examination.</td>
</tr>
<tr>
<td>(3) We recommend using alarm signs and symptoms and diagnostic clues to identify an underlying disease responsible for the constipation.</td>
</tr>
<tr>
<td>(4) If only 1 of the Rome III criteria is present and the diagnosis of functional constipation is uncertain, a digital examination of the anorectum is recommended.</td>
</tr>
<tr>
<td>(5) In the presence of alarm signs or symptoms or in children with intractable constipation, a digital examination of the anorectum is recommended to exclude underlying medical conditions.</td>
</tr>
<tr>
<td>(6) The routine use of an abdominal radiograph has no role to diagnose functional constipation.</td>
</tr>
<tr>
<td>(7) A plain abdominal radiography may be used in a child in whom fecal impaction is suspected but in whom physical examination is unreliable/not possible.</td>
</tr>
<tr>
<td>(8) Colonic transit studies are not recommended to diagnose functional constipation.</td>
</tr>
<tr>
<td>(9) A colonic transit study may be useful to discriminate between functional constipation and functional nonretentive fecal incontinence and in situations in which the diagnosis is not clear.</td>
</tr>
<tr>
<td>(10) Rectal ultrasound is not recommended to diagnose functional constipation.</td>
</tr>
<tr>
<td>(11) Routine allergy testing to diagnose cow’s-milk allergy is not recommended in children with constipation in the absence of alarm symptoms.</td>
</tr>
<tr>
<td>(12) Based on expert opinion, a 2- to 4-week trial of avoidance of CMP may be indicated in the child with intractable constipation.</td>
</tr>
<tr>
<td>(13) Routine laboratory testing to screen for hypothyroidism, celiac disease, and hypercalcemia is not recommended in children with constipation in the absence of alarm symptoms.</td>
</tr>
<tr>
<td>(14) Based on expert opinion, the main indication to perform ARM in the evaluation of intractable constipation is to assess the presence of the RAIR. Rectal biopsy is the gold standard for diagnosing HD.</td>
</tr>
<tr>
<td>(15) We do not recommend performing barium enema as an initial diagnostic tool for the evaluation of children with constipation.</td>
</tr>
<tr>
<td>(16) Colon manometry may be indicated in patients with intractable constipation before considering surgical intervention.</td>
</tr>
<tr>
<td>(17) The routine use of MRI of the spine is not recommended in patients with intractable constipation without other neurologic abnormalities.</td>
</tr>
<tr>
<td>(18) We do not recommend obtaining full-thickness colonic biopsies to diagnose colonic neuromuscular disorders in children with intractable constipation.</td>
</tr>
<tr>
<td>(19) We do not recommend the routine use of colonic scintigraphy studies in children with intractable constipation.</td>
</tr>
</tbody>
</table>

**Therapeutic Recommendations**

(21) A normal fiber intake is recommended.

(22) A normal fluid intake is recommended.
We recommend a normal physical activity in children with constipation.

The routine use of prebiotics is not recommended in the treatment of childhood constipation.

The routine use of probiotics is not recommended in the treatment of childhood constipation.

The routine use of an intensive behavioral protocolized therapy program in addition to conventional treatment is not recommended in childhood constipation.

Based on expert opinion, we recommend demystification, explanation, and guidance for toilet training (in children with a developmental age of at least 4 years) in the treatment of childhood constipation.

The use of biofeedback as additional treatment is not recommended in childhood constipation.

We do not recommend the routine use of multidisciplinary treatment in childhood constipation.

We do not recommend the use of alternative treatments in childhood constipation.

PEG with or without electrolytes orally 1 to 1.5 g - kg⁻¹·day⁻¹ for 3 to 6 days is recommended as the first-line treatment for children presenting with fecal impaction.

An enema once per day for 3 to 6 days is recommended for children with fecal impaction, if PEG is not available.

PEG with or without electrolytes is recommended as the first-line maintenance treatment. A starting dose of 0.4 g · kg⁻¹ · day⁻¹ is recommended and the dose should be adjusted according to the clinical response.

Addition of enemas to the chronic use of PEG is not recommended.

Lactulose is recommended as the first-line maintenance treatment, if PEG is not available.

Based on expert opinion, the use of milk of magnesia, mineral oil, and stimulant laxatives may be considered as an additional or second-line treatment.

Maintenance treatment should continue for at least 2 months. All symptoms of constipation symptoms should be resolved for at least 1 month before discontinuation of treatment. Treatment should be decreased gradually.

In the developmental stage of toilet training, medication should only be stopped once toilet training is achieved.

The routine use of lubiprostone, linaclootide, and prucalopride in children with intractable constipation is not recommended.

Antegrade enemas are recommended in the treatment of selected children with intractable constipation.

The routine use of TNS is not recommended in children with intractable constipation.

REFERENCES


