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Review

Constipation in Children: Novel Insight Into Epidemiology, Pathophysiology and Management

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Constipation in children is a common health problem affecting 0.7% to 29.6% children across the world. Exact etiology for developing symptoms is not clear in children and the majority is considered to have functional constipation. Alteration of rectal and pelvic floor function through the brain-gut axis seems to play a crucial role in the etiology. The diagnosis is often a symptom-based clinical process. Recently developed Rome III diagnostic criteria looks promising, both in clinical and research fields. Laboratory investigations such as barium enema, colonoscopy, anorectal manometry and colonic transit studies are rarely indicated except in those who do not respond to standard management. Treatment of childhood constipation involves several facets including education and demystification, toilet training, rational use of laxatives for disimpaction and maintenance and regular follow-up. Surgical options should be considered only when medical therapy fails in long standing constipation. Since most of the management strategies of childhood constipation are not evidence-based, high-quality randomized controlled trials are required to assess the efficacy of currently available or newly emerging therapeutic options. Contrary to the common belief that children outgrow constipation as they grow up, a sizable percentage continue to have symptoms beyond puberty. **(J Neurogastroenterol Motil 2011;17:35-47)**

Key Words
Children; Constipation; Epidemiology; Management; Pathophysiology

Introduction

Constipation is one of the commonest digestive complaints in children, which has recently grown to quite a proportion in public health problem. Like many other functional disorders, its etiology, pathophysiology and prognosis are ill-understood. This results in strongly-held, believes-driven and self-introduced management strategies, which are blended with the culture of the country, sometimes even harmful to children. However, body of the scientific knowledge has grown both in depth and width during the last decade. This article focuses on current views on definition, epidemiology, clinical features, evaluation and management strategies of constipation in children.

Definitions

Constipation has long been considered a symptom, rather than a disease.[1] It is often perceived as infrequent motions or passage of hard stools. Some defined constipation as less than 3 bowel motions per week[2] or as difficulty in passing stools.[3] Approximately 0.5% of school children have defecation frequency less than 3 per

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week and 0.3% have fecal incontinence.[4] Furthermore, 20% of children also have at least 1 clinical feature of constipation.[5] Therefore, it is important to use diagnostic criteria based on multiple symptoms to define constipation.

In 1999, Rome II criteria were developed to diagnose defecation disorders.[6] Functional constipation was identified in infants and preschool children and functional fecal retention in older children. Subsequently, Rome II criteria were found to be too restrictive in diagnosing defecation disorders because they did not include cardinal features of constipation (fecal incontinence) as diagnostic criteria and demanded persistence of symptoms for at least 3 months.[7,8] Furthermore, division of functional constipation and functional fecal retention has no implications in clinical practice. However, the Rome process established a pathway to formulate universally acceptable diagnostic criteria for childhood defecation disorders through international collaboration.

The pediatric Rome III criteria were released in 2006 (Table 1). Functional constipation was recognized as a separate clinical entity by combining features of functional fecal retention and functional constipation. Furthermore, duration of symptoms was reduced to 8 weeks.[9] A recent community-based study comparing Rome II and Rome III criteria shows a 2.5-fold increase in prevalence of functional constipation.[10] The more inclusive nature of the Rome III criteria seems to have stemmed from including cardinal clinical features of constipation in the diagnostic criteria and necessity of shorter duration of symptoms.

Epidemiology

Global burden of childhood constipation is often underappreciated. This was mainly due to lack of data in this age group. In epidemiological studies, the definitions vary from accepted Rome criteria to proxy reports by parents. A recent systematic review in pediatric age group reported constipation in 0.7% to 29.6%.[11] Apart from differences in definitions, the variation in duration of symptoms needed to diagnose constipation, age distribution of the children studied and the method of data collection may also have an influence on the data. Studies that have used standard definitions like Rome II criteria have also showed wide ranges of prevalence.[12,13] Therefore, apart from varying definitions, several other factors seem to be responsible for the heterogeneity of epidemiological data, including environmental, socio-cultural and genetic factors.

Until recently, it was believed that constipation is a disease of the developed world, but studies from Asia have reported equally high prevalence of constipation. A survey in Sri Lanka using Rome III criteria reported constipation in 10.6% of 10-16 years old.[14] Similarly, prevalence of constipation in Japan was 18.5%.[15]

Gender specific prevalence of constipation also varies between studies. Some studies have reported no difference in prevalence of constipation between girls and boys,[3,12,16,17] while others found significantly higher prevalence in girls.[13] Another study found a clear negative correlation between prevalence of constipation and age.[18]

The available data indicate that constipation is on the rise. A recent analysis of longitudinal data in the USA beginning from 1979 showed nearly 4-fold increase in rates of constipation during the last decade. There was a surge in both outpatient clinic visits and hospitalizations due to constipation between 1992 and 2004, with more than a doubling of rates in diagnosing constipation from outpatient clinics and nearly 4-fold increase in rates of hospital discharge under the diagnosis of constipation. Furthermore, children under 15 years had the highest number of clinic visits for constipation.[19] In addition, 5.4 million prescriptions were filled for constipation in the USA in 2004. All these facts prove that constipation is a growing health problem among children worldwide.

Risk Factors

Several risk factors have been identified in association with pediatric constipation. The main risk factors for constipation are listed in Table 2.

Low consumption of dietary fiber has long been considered as one of the leading risk factors. Undigested fibers in the colon are thought to increase the colonic transit and increase stool output. Lee et al[20] found that kindergarten children with constipation took significantly low median dietary fiber than non constipated children. Furthermore, fruits and total plant food intake were significantly lower in the constipated group.[20] Two other studies among older children also noted that children with constipation consume significantly less amount of dietary fiber than controls.[21,22] Available studies from Asia also show that fiber consumption in Asian countries such as Hong Kong[20,23] and Maldives[24] is lower than the recommended values.

Few studies have demonstrated its relationship with psychological factors. Inan et al[25] has shown that physical or psychological trauma and personal health problems were associated with constipation in school-aged children. Furthermore, they have found that abnormal oral habits (which were considered as an in-

direct measure of psychological stress) also showed a significant association with constipation.[25] A study from Sri Lanka involving school children of 10-16 years old noted that school-related stressful events such as separation from best friend, bullying at school, failure of exam and family-related events such as severe illness of family member, parents' job loss and frequent punishment by parents were predisposing them to develop constipation.[26] Furthermore, children living in a war-affected area had high prevalence of constipation compared to non war-affected areas.[26] Psychological factors including emotional stress are likely to modulate colonic and rectal functions, through the brain gut axis, leading to constipation.

Cow's milk protein allergy is considered as a risk factor for constipation. Several studies have reported reduction of constipation by elimination of cow's milk from diet.[27,28] However further studies are needed to confirm this association and to introduce cow's milk-free diet to infants and children with constipation. Other demonstrated risk factors are extreme low birth weight,[29] positive family history[18,21] and living in urban areas.[18,30] High consumption of junk foods with low fiber content and sedentary life style might have contributed to higher prevalence of constipation reported in children living in urban areas.

Table 1. Pediatric Rome III Criteria for Constipation

Rome III criteria for neonates and toddlers
Must include 1 mo of at least two of the following in infants up to 4 yr of age: 1. Two or fewer defecations per week 2. At least 1 episode per week of incontinence 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.
The accompanying symptoms disappear immediately following passage of a large stool.
Rome III criteria for children and adolescents
Must include two or more of the following in a child with a developmental age of at least 4 yr[a] with insufficient criteria for diagnosis of irritable bowel syndrome: 1. Two or fewer 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

[a]Criteria fulfilled at least once per week for at least 2 mo before diagnosis.

Pathophysiology

The pathophysiology of constipation in children is multi-factorial and is associated with interactions of many risk factors. Many organic diseases cause constipation (Table 2). However, the majority of constipation patients secondary to organic conditions usually have other clinical features suggestive of the relevant underlying organic disease. Organic diseases presenting as isolated constipation are rather uncommon.

Over 90% of children with this condition have functional constipation.[31] Borowitz et al[32] reported painful defecation as the commonest factor for constipation. If there is pain during defecation, children usually withhold stools. During the withholding, rectal mucosa absorbs water from the fecal mass, which becomes harder and larger as the time passes and ultimately defecation becomes difficult. Therefore, when the desire to pass stools comes, children adopt retentive posture, hide from parents till the urge pass off. Passage of this fecal mass is painful and sometimes results in anal fissures which further aggravate pain and precipitate stool withholding. This sets up a vicious cycle of stool retention. Accumulation of stools in rectum causes gradual dilatation leading to megarectum resulting in loss of rectal sensation and urge

Table 2. Causes and Risk Factors of Constipation in Children

Intestinal causes	Hirschsprung disease
	Anorectal malformations
	Neuronal intestinal dysplasia
Metabolic/endocrine causes	Hypothyroidism
	Diabetics mellitus
	Hypercalcemia
	Hypokalaemia
	Vitamin D intoxication
Drugs	Opioids
	Anticholinergics
	Antidepressants
Other causes	Anorexia nervosa
	Sexual abuse
	Scleroderma
	Cystic fibrosis
Risk factors	Low fiber diet
	Psychological stress
	Cow's milk protein allergy
	Familial predisposition
	Prematurity
	Living in urban areas

for defecation. It had been shown that children with megarectum have high sensory threshold for rectal sensation.[33,34]

Other intestinal pathologies leading to chronic constipation surprisingly have not received much attention. Several studies have demonstrated slow colonic transit in 25%-69% children with constipation.[35-37] Furthermore, those with slow transit constipation had more severe symptoms including night time soiling.[35] Laparoscopic biopsies of the colon have shown deficiency of neurotransmitters such as substance P in some children.[38,39] Furthermore it was shown that number of antegrade pressure waves in the colon was significantly decreased in children with slow transit constipation.[40]

Clinical Features

The commonest symptoms of constipation are reduced stool frequency and passage of hard stools. The other symptoms include fecal soiling, passage of large volume stools, painful defecation and characteristic "retentive posturing." Straining at defecation, abdominal pain, anorexia, vomiting and bleeding per rectum are other associated features, although they are excluded from the diagnostic criteria.[16,18] Similarly constipation was the commonest cause of acute abdominal pain presenting to emergency department or primary care clinics.[41] The physical examination shows palpable fecal masses in the abdomen and fecal impaction in the rectum.

Evaluation

A detail history and thorough physical examination are the cornerstones in assessing a child with chronic constipation. These 2 steps would reveal the possible etiology and associated complications in the majority. Investigations are only needed in those who show clinical features of organic diseases and children do not respond to initial medical management.

Clinical History

History of meconium passage

Neonates pass meconium within first 48 hours. Delayed passage of meconium raises the possibility of short segment Hirschsprung disease and anorectal malformations.

Time of onset

A majority develop constipation around 2-4 years of age.[42] Significant intestinal pathologies such as anorectal malformations and neuronal intestinal dysplasia are common in children presenting with constipation very early in life. In some patients, the onset of symptoms is related to major stressful life events such as birth of a sibling or parental job loss.

Bowel habits and defecation behaviors

The majority of children with constipation have infrequent passage of stools. Hard and large caliber stools that can clog the toilet may lead to passage of blood with stools. Adaptation of withholding posture should be specifically questioned because sometimes parents interpret this as a genuine attempt to pass stools. Children stand on tip toes and often hold on to furniture till the desire for defecation is passed. Sweating and facial redness are also noted in this period. Leaking stools into the underwear without realizing indicates severe constipation.

Associated symptoms

Although non-specific, the presence of abdominal pain, nausea, and vomiting are associated with constipation. Most parents would complain the child has loss of appetite and fail to gain weight. History of urinary incontinence is also a feature.[43] Endocrine diseases which may cause constipation, such as diabetes mellitus would have features such as polyuria, polydipsia and weight loss. Furthermore, children with hypothyroidism may present with lethargy, poor school performances and weight gain.

Drugs

It is vital to take a history on current medications when assessing for constipation as certain drugs lead to constipation as adverse effects (Table 2).

Psychology

A detail history of psychological state is another important part in the assessment. It may reveal features of anorexia nervosa, depression and anxiety.

Risk factors

All other possible risk factors for the development of constipation are discussed above. General medical history, social details and the developmental history are also integral components in the assessment.

Physical Examination

Physical growth

Measurement of height and weight and comparison with the age appropriate centile charts gives idea about the physical growth. Hypothyroidism and other organic disorders may present as short stature or failure to thrive.

General examination

Young children with constipation often cling to their parents and look frightened during the consultation. Smell of the faeces

due to incontinence and general demeanor of the child are also important to note. Children with anorectal malformation and hypercalcaemia may sometimes show associated features. Young girls with anorexa nervosa often would show features of weight loss. Presence of scars, lipomas and haemangiomas on the lower spine would suggest the possibility of spinal dysraphism and underlying neurological abnormalities.

Abdominal examination

The main aim of the abdominal examination is to assess the presence of palpable fecal mass. Usually it is found in the left iliac fossa or supra pubic region.

Perianal inspection and digital examination of the rectum

Inspection of the perianal region shows position of the anus, fissures, tags and inflammation. Children who had experienced chronic sexual abuse would show characteristic features. Repaired anorectal malformations would show surgical scars around the anus. Digital rectal examination assesses the anal tone and detects the presence of fecal mass. It is noted that the frequency of digital examination of rectum is unacceptably low in children with constipation.[44]

Neurological assessment

This will reveal neurological abnormalities in the lower spinal cord which may present as constipation.

Investigations

Laboratory investigations are rarely indicated in childhood constipation except in those with evidence of organic diseases from history and examination and in those who do not respond to adequate medical management. Otherwise, investigations are unlikely to reveal any additional information for the management.

Plain abdominal X-ray

Plain abdominal radiograph is performed to identify the degree of fecal loading in the colon and rectum.[45-47] It is considered to be useful in children who are not willing to undergo a rectal examination due to pain and fear.[5] However a systematic review shows that interpretation of the radiological findings is difficult, inconsistent and there is a poor correlation between clinical and radiological diagnosis.[48] The scoring systems for fecal loading are reported to have wide inter-observer and intra-observer variability, poor diagnostic accuracy, poor reproducibility and depend on the experience of the scorer.[49,50] Therefore, plain abdominal radiograph has a very limited value in clinical assessment of constipation.

Colonic transit studies

The transit time of the colon is studied using radio-opaque markers[51-53] and radionuclear scintigraphy.[54] The calculated total and segmental transit times allow to differentiate constipation due to delayed segmental and pan-colonic transit from constipation with normal transit.[51,55,56]

Several previous studies have reported delayed colonic transit times (segmental or total) in children with constipation.[36-38,49,57] de Lorijin and co-workers[57] reported delayed transit on rectosigmoid (48%) followed by descending and ascending colon (21%-22%). Another study showed slow transit constipation in 60% of the children with constipation and of them, 13% had pelvic floor dysfunction.[38] Children with slow transit constipation have lower defecation frequency and higher prevalence of day and night time soiling, painful defecation and palpable rectal or abdominal masses.[35,37,58] Therefore, colonic transit studies are beneficial in children with chronic treatment-resistant constipation to determine colonic transit abnormalities.

Anorectal manometry

Anorectal manometry is a collection of several tests that measure pressure changes in the rectum and the anal canal. It is often combined with surface electrode electromyography of the external anal sphincter and puborectalis muscle.[36] They provide details on rectal sensation, state of recto-anal inhibitory reflex, tone of anal sphincter and defecation dynamics.

Some studies have shown an increased threshold for rectal sensation in constipated children especially those with megarectum.[33,34] However probably the most important benefit of anorectal manometry in children with constipation is to exclude Hirschsprung disease. Generally, presence of recto-anal inhibitory reflex excludes Hirschsprung disease. However several studies have noted variable sensitivity, specificity, positive and negative predictive values in the diagnosis of Hirschsprung disease.[59-64] Furthermore, false positive results may occur due to immaturity of ganglion cells (in premature babies) and artefacts.[61] Therefore in cases with strong clinical suspicion of Hirschsprung disease, it is imperative to perform a suction biopsy to confirm or exclude the diagnosis.

Defecation dynamics are tested using anorectal manometry with integrated electromyogram of the external anal sphincter and puborectalis muscle. It is defined abnormal if there is increased manometric and myoelectrical activities in the sphincter complex during bearing down.[34] Pelvic floor dyssynergia was noted among constipated children in several studies.[65-67] Previous studies have shown that children with constipation have abnormally high rest-

ing anal tone.[65-67] In contrast, another study failed to show a difference in anal tone between constipated children and controls.[34]

Colonic manometry

Colonic manometry measures the intracolonic pressure using a multichannel manometry probe. It is useful in patients with intractable constipation. Children with functional constipation show normal colonic motor activity (presence of high amplitude propagating contractions and gastro-colonic response to meal). Children with rare colonic muscle disorders demonstrate absent or weak colonic contractions. The gastro-colonic response is absent in colonic neuropathy.[68]

By analyzing 375 colonic manometries, Villarreal et al[69] found colonic neuropathy in 130 and colonic myopathy in 15 and signified the diagnostic validity of colonic manometry in intractable constipation. Another study noted 30% of 173 children to have colonic neuromuscular diseases.[70] Colonic manometry via appendicostomy has shown abnormal high amplitude contractions, increased retrograde propagating sequences and lack of increase in amplitude of propagating sequences normally induced by meals and waking.[40]

Therefore, it is an important investigation in children with chronic treatment-resistant constipation, who do not respond to maximum doses of combined laxative therapy. Significant manometric abnormalities in such clinical situations make the clinician to think about other management options such as antegrade colonic enemas or surgical interventions.

Other investigations

Fecoflowmetry evaluates pressure changes in the rectum and anal canal during infusion of saline and also evacuation rates of saline from the rectum using uroflowmeter. Previous study has shown abnormalities in pressure curves and fecoflowmetry curves in children with chronic constipation.[71] Pelvic ultrasonograpy has been used to measure the diameter of the rectum in children with chronic constipation. These studies have shown larger rectal diameter in children with constipation compared to controls.[72,73] Anal endosonography has also revealed abnormalities in the sphincter complex in children with chronic constipation.[74] However these investigations need further validation before using in routine evaluation of affected children.

Management

Management of constipation encompasses several facets. However, only few randomized controlled trials are available to assess therapeutic options currently being used in treatment. In addition, little is known of their optimum therapeutic dosages and long-term side effects. Therefore, management of childhood constipation is mainly based on individual experience.

In the management of chronic constipation, a trustworthy relationship between the patient, parents and clinician is of paramount importance. The key steps in management include education and demystification, treatment of fecal impaction, maintenance therapy and close follow-up. Steps in management of childhood constipation are illustrated in the Figure.

Education

The general public has various concepts on constipation which may interfere with proper clinical management. Therefore educating the parents and patients about pathophysiology and precipitating factors will help to alleviate anxiety, minimize accusations and increase their involvement in management. Approximately 15% of children with constipation improve with nonaccusatory education, demystification and toilet training.[75] It is also worth mentioning to parents that the progress of treatment is often irregular and is marked by periods of improvement alternating with deterioration. Therefore, the duration of maintenance therapy ranges from 6 to 24 months.[21,76]

Behavioral Therapy

Behavioral therapies for constipation are designed to regularize toilet routines, discourage stool withholding and improve understanding of defecation dynamics. Several protocolized behavioral programs has been used as therapeutic interventions.[77,78] The stepwise approach described by van Dijk et al[78] included several steps. Psycho-education is used as the first step to change behavior of parents and child towards constipation. Reduction of anxiety towards defecation using education and models is helpful to promote successful defecation. In the next step, child is taught of straining techniques such as relaxation of legs and feet, to take a deep breath and hold it and how to push down while holding one's breath. Finally the behavior is reinforced by motivation and reward system and develops toilet routine without avoidance.[78] A randomized control trial which compared conventional treatment alone and conventional treatment with added behavioral therapy failed to demonstrate significant difference in improvement of defecation frequency and fecal soiling.[79] In contrast to this, a web based behavioral therapy plus laxatives with conventional treatment showed reduced fecal soiling, increased defecation in the toilet, and increased unprompted trips to the toilet in study group.[80]

Nevertheless, use of these non-invasive steps would enhance

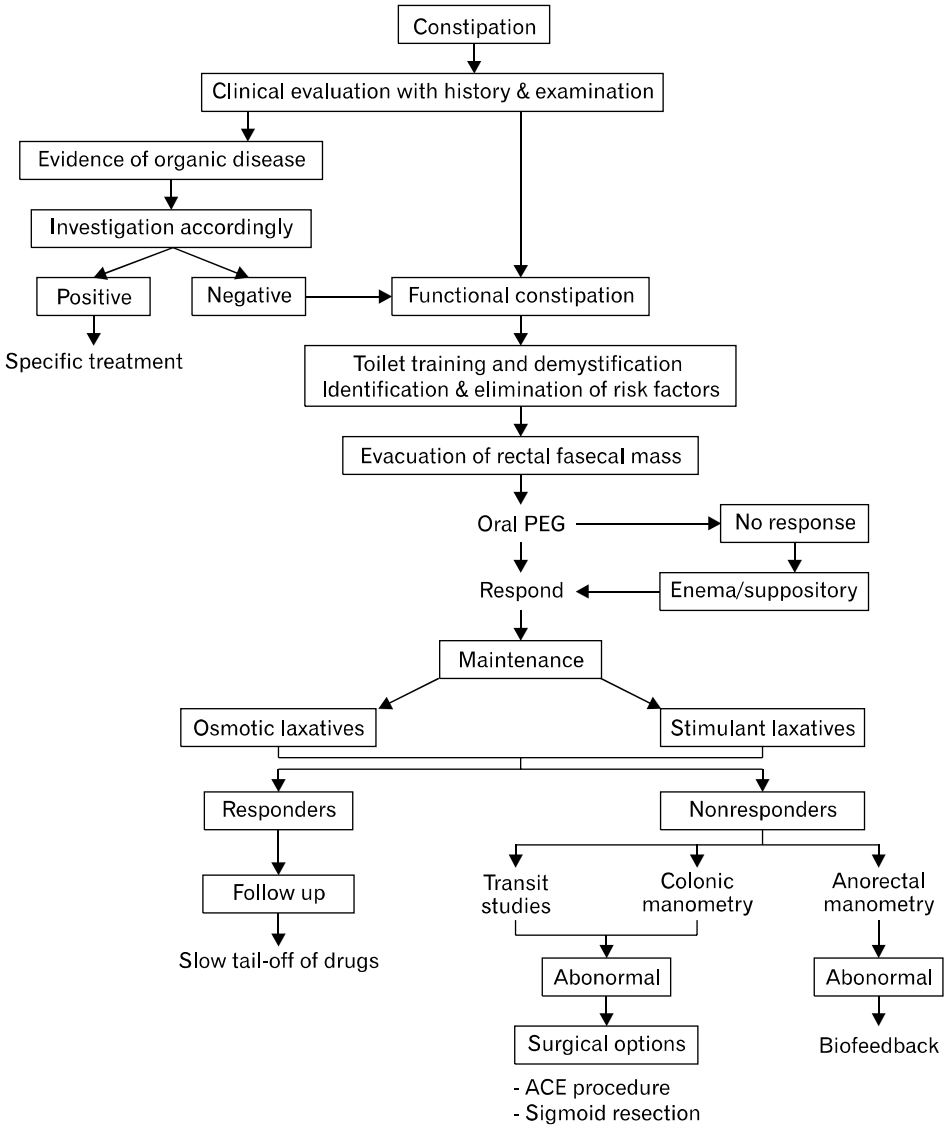

Figure. Algorithm of management of childhood constipation. PEG, polyethylene glycol; ACE, antegrade conlonic enema.

passing stools, improve strained family relationships and build a rapport between clinician and family. Therefore, behavioral therapy involving steps described above should be used in children presenting with chronic constipation.

Biofeedback Therapy

Biofeedback uses electrical or mechanical devices to increase the awareness of physiological functions of anal sphincter by providing the patient with visual, verbal and or auditory information and enhances self-control on body functions.[81] During biofeedback, patients are provided with visual graphs of their rectal pressure and electromyography of external anal sphincter and also taught to relax external anal sphincter with the rise of rectal pressure. This therapy is likely to be beneficial for the subgroup of patients with pelvic floor dyssynergia and enable them to relax their pelvic floor and external anal sphincter in achieving normal defecation. In agreement with this, several previous studies have shown the efficacy of biofeedback therapy in correcting abnormal defecation dynamics.[33,82,83] However, it failed to demonstrate an additional therapeutic value in clinical improvement of chronic constipation in children.[65] Therefore, at present, biofeedback therapy seems to be beneficial for only a small subgroup of children with chronic constipation who have pelvic floor dyssynergia.

Dietary Measures

It is a wide spread practice to instruct patients with con-

stipation to increase fluid and fiber intake. According to 2 studies, increased fluid intake only resulted in increased urine output and had no effect on stool output or consistency.[84,85] In agreement with this, another study showed that increased water intake by 50% did not improve stool frequency or consistency.[86]

Low fiber intake has been recognized as a risk factor for constipation. Adequate intake of dietary fiber (age + 5 in grams) reduces risk of constipation, but further increase in fiber has no proven therapeutic value. Previous clinical trials failed to show significant improvement of bowel habits after fiber treatment compared to placebo and traditional treatments such as lactulose.[87,88] In one study, a subgroup analysis showed that children with prolonged basal colonic transit times significantly increases number of bowel motions after administration of high fiber diet.[89]

Disimpaction

Evacuation of feces accumulated in the rectum is the key therapeutic step in successful management of constipation. Several studies have assessed the value of polyethylene glycol (PEG) in fecal disimpaction. One study proved that PEG 3350 without electrolytes has cleared fecal impaction in 75% of children with constipation and children using higher doses had more clearance than those using lower doses.[41] In agreement with this, Pashanker et al[90] showed that, after 8 weeks of treatment with PEG without electrolytes, children had less fecal soiling, painful defecation, fecal impaction and rectal dilatation.

Another study showed that PEG 3350 plus electrolytes is more effective in disimpaction compared to suppositories or rectal enemas.[91] In addition, health costs and hospital admissions were reduced when using PEG compared to enemas and suppositories.[91] Furthermore, PEG 3350 plus electrolytes was effective in clearing fecal retention in chronic treatment resistant constipation. In another study, 90% of children with treatment resistant constipation were successfully treated with PEG.[92]

Administration of enemas to relieve rectal fecal loading has long been practiced in management of childhood constipation. It is important that clinicians use the rectal route, only when oral drugs have failed. Insertion of rectal enema may be extremely disturbing to the child who might already have anal fissures. Therefore, it needs to be given under sedation to minimize pain and psychological effects. Otherwise it may disturb the good relationship and understanding between clinician and child, which is essential in the long term management.

Maintenance Therapy

After achieving disimpaction it is vital to start daily oral laxatives to keep the stool soft thereby to prevent re-impaction. The duration of the maintenance phase needs to be individualized and may vary from months to years. Parents and children need to be counselled regarding the importance of this stage and should keep a regular bowel chart. Parents need to be advised on different alternatives to use if the child does not pass stools on a regular basis. A close follow-up is crucial during the initial period of maintenance to avoid recurrence. The main pharmacological agents used for maintenance are osmotic and stimulant laxatives.[31,93] Table 3 gives recommended dosage of laxatives commonly used during this phase.

Osmotic laxatives

Lactulose. It is an unabsorbable, osmotically active carbohydrate which drags water into the gut, keeps the stools soft and facilitates passage of stools without pain. Two randomized controlled trials comparing lactitol and lactulose have found that both are equally effective in increasing stool frequency and normalizing stool consistency.[31,94,95] When lactulose was compared with senna in a crossover trial, both drugs were found to be effective in improving defecation frequency.[96]

Polyethylene glycol. PEG is a non absorbable compound and is not digested by colonic bacteria. Its mechanism of action is increasing osmotic load in the large intestine which results in expansion of stool volume.[97] In a prospective observational study, Pashankar et al[98] failed to find any side effects following PEG therapy. PEG has not altered the serum electrolyte, osmolality and albumin levels of plasma and liver and renal functions.[98] In a double blind randomized controlled trial, Candy et al[92] noted that PEG with electrolytes was more effective compared to lactulose in increasing defecation frequency in children with intractable constipation. Furthermore, children on PEG plus electrolytes had less fecal impaction and did not need rescue medication.[92] In a randomized, crossover study comparing PEG with lactulose, parents felt that PEG was more effective compared to lactulose, even though there was no difference in frequency of bowel motions, stool form or easy passage of stools between 2 groups.[99] Two other double blind randomized controlled trials failed to demonstrate a significant difference in stool frequency between PEG and lactulose.[100,101] Two studies comparing PEG without electrolytes with milk of magnesia found no difference between 2 drugs with regard to outcome.[102,103] Therefore current evidence shows no advantage of one osmotic laxative over the others dur-

Table 3. Drugs Commonly Used in the Management of Childhood Constipation

Drug class	Laxative	Dosage	Side effects
Osmotic laxatives			
	Magnesium hydroxide	3-12 yr, 5-10 mL/day 13-18 yr, 25-50 mL	Colics
	Lactulose	1-5 yr, 5 mL twice a day 6-10 yr, 10 mL twice daily 11-18 yr, 15 mL twice daily (1-3 mL/kg twice daily)	Flatulence, abdominal discomfort, cramps
	PEG 3350-4000 maintenance	0.26-0.84 g/day	Loose stools, bad taste, abdominal distension, abdominal pain, nausea
	PEG 3350 disimpaction	1-1.5 g/kg/day (3 to 4 days)	Loose stools, bad taste, abdominal distension, abdominal pain, nausea
Stimulating laxatives			
	Bisacodyl oral	4-10 yr, 5 mg at night 11-18 yr, 5-10 mg at night	Abdominal cramps, abdominal pain
	Bisacodyl rectal	2-10 yr, 5 mg in the morning 11-18 yr, 10 mg in morning	Abdominal cramps, anal irritation
	Senna tablets (7.5 mg per tablet)	6-12 yr, 1-2 tablets at night 13-18 yr, 2-4 tablets at night	Abdominal cramps, melanosis coli, electrolyte imbalance
	Senna granules (15 mg in 5 mL)	6-12 yr, 2.5-5 mL at night 13-18 yr, 5-10 mL at night	Abdominal cramps, electrolyte imbalance
	Sodium picosulphate	2-4 yr, 0.25 mg/kg at night 5-10 yr, 2.5-5 mg at night 11-18 yr, 5-10 mg at night	Abdominal cramps
	Docusate sodium	6 mo-2 yr, 12.5 mg, 3 times a day 3-12 yr, 12.5-25 mg, 3 times a day 13-18 yr, up to 500 mg daily in divided doses	Abdominal cramps
Stool softeners			
	Liquid paraffin	3-12 yr, 0.5-1 mL/kg (max 30 mL) twice daily	Anal irritation in prolonged use
		13-18 yr, 10-30 mL once daily	Granulomatous reaction caused by absorption

PEG, polyethylene glycol.

ing the maintenance phase of management.

Stimulant laxatives

Good quality clinical trials are lacking on effectiveness of stimulant laxative as maintenance therapy of childhood constipation and therefore it is difficult to draw evidence based conclusions. An open label randomized controlled trial comparing senna and lactulose showed no difference in bowel frequency. However, number of patients passing normal stools each day was significantly higher in patients receiving lactulose.[94] Sondheimer and Gervaise[104] noted that children using fecal softeners (mineral oil) had more daily motions and less fecal soiling than senna. Other stimulant laxatives such as bisacodyl, docusate sodium and sodium picosulphate have not been evaluated in randomized controlled trials.

New Therapeutic Options

Tegaserod

It is a serotonin receptor agonist which stimulates the peristaltic reflex, enhances intestinal secretions and decreases visceral sensitivity.[105] It also act as a prokinetic agent in the upper and lower gastrointestinal tract.[106] There are several trials of this drug in adults with constipation predominant irritable bowel syndrome and constipation. However the efficacy of this drug has not been evaluated in children.

Probiotics

A randomized control trial on the effectiveness of *Lactobacillus* GG as an adjunct to lactulose for children with constipation failed to show additional therapeutic benefit.[107] Another study

that compared the efficacy of probiotics containing *Lactobacillus casei rhamnosus* with magnesium oxide to a placebo, failed to show a significant difference in final outcome between probiotics and MgO.[108] More robust therapeutic trials are needed before recommending probiotics for routine management of constipation.

Surgery

Surgical options need to be considered only when medical therapy fails in long standing constipation. Children with loaded rectum who do not respond to enemas may need manual evacuation.[109] Sigmoid resection and removal of dilated megasigmoid is a successful surgical intervention in some patients with severe constipation.[110] Antegrade colonic enema via appendicocaecostomy is another surgical therapeutic option in severe functional constipation.[111,112] Possible complications of this intervention include stenosis of the cutaneous opening, leakage around the cecostomy tube and displacement of the tube.[113,114]

Prognosis

Van Ginkel et al[76] noted that 30% of children with constipation continued to have symptoms beyond puberty with several complications associated with it. A recent systematic review on prognosis of childhood constipation noted that the majority of them recover within 6-12 months of therapy and the recovery rate had no relationship with the age of onset, positive family history, defecation frequency and presence of fecal incontinence.[115]

Conclusion

Chronic constipation is a common pediatric problem affecting children worldwide. Exact etiology is unclear in the majority and is thought to be functional in origin. Constipation is a clinical diagnosis and investigations are rarely warranted, unless clues are found in the history or physical examination or poor response to therapy. Key steps in the management include education, rectal disimpaction, maintenance and follow-up. Approximately 30% of affected children will continue to have symptoms beyond puberty contrary to the common belief that children outgrow constipation.

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