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Chronic Constipation in Children: An Overview

by Ritu Walia, Nicholas Mulhearn, Raheel Khan, Carmen Cuffari

Constipation is a commonly encountered symptom in school-aged children. The symptoms may vary at presentation and may be complicated by fearful reactions to defecation leading to a stool withholding pattern resulting in encopresis. It is important that a combined approach including education of the patient and family, pharmacological management and behavioral training is utilized for effective treating and prevention of complications. This review summarizes the current evidence and aims to provide practical advice in primary care.

INTRODUCTION

G hronic constipation is one of the more common, yet challenging conditions encountered in pediatric practice. Approximately 3 percent of the general and 25 percent of the pediatric gastroenterology out-patient visits are due to constipation. Indeed, it is a cause of both emotional and economic burden amounting to health care costs of approximately \$6.9 billion annually.^{1,2}

Most often parents complain of either too hard, infrequent or pellet like stools that may or may not be accompanied with pain on defecation and rectal bleeding. Some of the common features associated with chronic constipation are listed in Table 1.

Beyond the neonatal period, the most common cause of constipation is functional. Parents, as well as children, are often reluctant to accept a behavioral modification approach to therapy and instead focus on finding an organic cause. This may lead to unnecessary testing and a delay in treatment. If left untreated over time, painful defecation in children can cause fearful reactions to develop, leading to fecal incontinence or encopresis^{2,3} Furthermore, it is estimated that over 80% of children with fecal incontinence suffer from chronic constipation and up to 30% of patients remain constipated until puberty. These numbers underscore the importance of a rapid diagnosis and early initiation of treatment to correct this learned behavior in children⁴

Table 1. Constipation and Pediatric Patients:Common Complaints

- 1. Difficulty in defecation, present for two weeks or more
- Infrequent of bowel movements (< 3 per week)
- 3. More than 1 episode of fecal incontinence per week
- 4. Large stools in the rectum or palpable on abdominal examination
- Passing of unusually large caliber stools, retentive posturing (stopping during play to squat or sit down)
- 6. Abdominal pain/discomfort, dyspepsia, increased gas
- 7. Withholding behaviors (such as not using restroom at school or other social events)
- 8. Potty dance sequence Due to pain associated with hard bowel movements children often withhold defecation by contracting their anal sphincter and gluteal muscles

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Table 2. Causes of Chronic Constipation

Inorganic

• Psycho- social issues

Organic Causes of Chronic Constipation Anatomic Malformations

- Imperforate anus
- Anal stenosis
- Anterior displaced anus
- Pelvic mass (sacral teratoma)

Metabolic and Gastrointestinal

- Hypothyroidism
- Hypercalcemia
- Hypokalemia
- Cystic fibrosis
- Diabetes mellitus
- Multiple endocrine neoplasia type 2B
- Gluten enteropathy

Neurologic Conditions

- Spinal cord abnormalities
- · Spinal cord trauma
- Neurofibromatosis
- Static encephalopathy
- · Tethered cord
- · Intestinal nerve or muscle disorders
- Hirschsprung's disease
- Intestinal neuronal dysplasia
- Visceral myopathies
- · Visceral neuropathies

Abnormal Abdominal Musculature

- Prune belly
- Gastroschisis
- Down syndrome

Connective Tissue Disorders

- Scleroderma
- · Systemic lupus erythematosus
- · Ehlers Danlos syndrome

Drugs

- Opiates
- Phenobarbital
- Sucralfate
- Antacids
- Antihypertensives
- Anticholinergics
- Antidepressants

Several studies have evaluated the consequences of persistent childhood functional constipation, all serving to further the notion that prompt treatment and prevention are beneficial to the child. For instance, in 2008 Chao and colleagues studied 2426 children with chronic constipation and demonstrated that this functional disorder was capable of retarding growth in children. In that study, the authors were able to show that with adequate therapy, patients with chronic constipation were able to achieve normal growth potential.⁵ In 2008, Boccia and colleagues correlated chronic functional constipation with functional dyspepsia. In these patients, the effective use of osmotic laxatives in children with functional constipation also helped improve symptoms associated with functional dyspepsia.⁶

Pediatric patients who suffer from chronic constipation tend to have a lower quality of life index as compared with healthy controls.⁷ Parents also reported low scores, thus reflecting the negative impact chronic constipation has on families.⁷ Thus, timely intervention in children with functional constipation may also prevent the development of co-morbid conditions.

Causes of Chronic Constipation

Childhood constipation is classified as either functional or organic. Functional constipation is a diagnosis of exclusion reserved for patients without anatomic or biochemical causes. In contrast to those with functional constipation, 5% of children are diagnosed with an identifiable organic cause⁸ (see Table 2).

DIAGNOSIS

A thorough history and physical examination remains the single most important tool for the successful diagnosis and timely intervention for chronic constipation as depicted in Table 3.

There is conflicting evidence of the association between clinical symptoms of constipation and fecal loading on abdominal radiographs in children. Abdominal radiography should be reserved for patients, who are obese, refuse a rectal examination, or in whom there are other psychological factors that make the rectal examination traumatic. Additionally, abdominal radiography may be indicated in a child with a good history for constipation who does not have large amounts of stool on rectal examination.²

Scintigraphy can also be used to determine transit

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time and allows for the segmental evaluation of slow versus normal gastrointestinal transit time. Identification of the site of dysmotility in constipation may determine the cause and permit directed management. Images are taking incrementally between 2 and 48 hours after a bolus of radio-active material to provide a measure of intestinal transit and distinguish between slow transit constipation and functional fecal retention. Although, this technique is a simple quantitative measure of intestinal transit, its use should be reserved for cases refractory to typical medical therapy.^{8,9}

Anorectal manometry is a method of evaluating the response of the internal anal sphincter to inflation of a balloon catheter in the rectum. In children with Hirschsprung's disease, the internal sphincter does not relax in response to rectal distension, while in children without Hirschsprung's disease there is relaxation of the internal sphincter in response to rectal distension. Manometry can be useful in directing future therapy and can also be used to diagnose Hirschprung's disease.^{10,11} Positive findings on manometry may prompt a rectal suction biopsy (full thickness biopsy could also be used) for further determination of the diagnosis. In children < 1 year of age, the sensitivity and specificity of anorectal manometry is quite low and a rectal suction biopsy remains the gold standard in diagnosing Hirschsprung's disease. Confirmation of Hirschsprung's disease via rectal suction biopsy requires absence of ganglion cells in the submucosa on hematoxylin and eosin stain, and an elevation of hypertrophic neurofibers in the lamina propria on acetylcholine-esterase staining.¹¹

Colonic manometry is an invasive procedure that has been studied in patients with refractory constipation. Children with functional constipation show normal colonic motor activity with the presence of high amplitude propagating contractions and gastrocolonic response to meals; whereas children with rare colonic muscle disorders either have slow, weak colonic contractions or fail to demonstrate any altogether. The gastro-colonic response is absent in colonic neuropathy. During the evaluation of 375 colonic manometries, Villarreal et al reported colonic neuropathy in 130 and colonic myopathy in 14 patients, thus signifying the diagnostic validity of colonic manometry in the diagnosis of intractable constipation. Furthermore, the lack of peristaltic waves (high amplitude peristaltic contractions) on colonic manometry is considered a pathological marker in young children and may require

surgical intervention such as a diverting colostomy or ileostomy.¹²

TREATMENT

A four-step approach involving education, disimpaction, maintenance therapy and behavioral therapy is crucial to achieve complete resolution of symptoms.

Education

Educating the parents and patients is essential and any negative myths need to be dispelled. Dietary education, especially supplementation of fiber has become first line treatment of chronic functional constipation in children; however, the evidence is weak that diet plays a major role in childhood constipation. Fiber intake of 0.5 mg/day to 35 mg/day has been recommended by the American academy of pediatrics (AAP) in children.¹³ Loening-Baucke et al found glucomannan (a fiber gel polysaccharide from the tubers of the Japanese Konjac plant) to be beneficial in the treatment of constipation with and without encopresis in children in a doubleblind, randomized, crossover study. Significantly fewer children complained of abdominal pain and more children were successfully treated while on fiber as compared with placebo treatment, suggesting the increase in dietary fiber of constipated children with and without encopresis.¹⁴ A community-based survey on the prevalence of constipation in children ages 3-5years in Hong Kong reported approximately 30% of children suffering from constipation. Mean dietary fiber intake of these children was less than one-half of the dietary fiber intake recommended by the AAP and was significantly lower than their non-constipated counterparts.¹⁵ Another study conducted by Jennings et al, revealed a prevalence of 33% in children. Fluid and fiber intake was higher in children without constipation, therefore supporting the association of symptoms of constipation to low fiber intake.¹⁶ Some of the studies have conflicting data on the efficacy of supplementation of dietary fiber. There exists a need for more pediatric studies to show the beneficial effect of dietary fiber in the treatment of chronic childhood constipation.

Disimpaction

Hard stools palpated in the rectum on physical examination need to be removed by disimpaction. This can be achieved by oral and/or rectal medications.

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Choice of treatment is determined by a discussion between the patient and the caregiver. Polyethylene glycol (PEG) 3350, mineral oil, magnesium hydroxide, magnesium citrate, lactulose, sorbitol, senna, and bisacodyl are potential treatments available (see table 4).^{2,8,16} More recently, high dose PEG 3350 mixed in a commercially available sports drink given over a short period of time has been shown to be safe, effective, and tolerable in children as a bowel cleansing regimen prior to colonoscopy. This therapeutic solution is also gaining popularity amongst pediatricians and gastroenterologists for the treatment of chronic constipation and stool impaction across North America.¹⁷

Maintenance Therapy

Relapse is common, therefore adequate maintenance therapy is strongly recommended once disimpaction has been achieved. The duration of the maintenance phase needs to be individualized and may vary from months to years. Parents and children need to be counseled regarding the importance of this stage and should keep a regular bowel chart. Parents need to be advised on different alternatives in case the child does not pass stools on a regular basis. Close follow-up is important during the initial period of maintenance to avoid recurrence and ensure compliance.

Maintenance therapy may be achieved with behavioral modification, daily regimen of laxatives, good hydration, regular exercise and a balanced diet consisting of whole grains, fruits, and vegetables. However, there is not good evidence to support these recommendations. Pharmacological therapy has been used to prevent recurrence in children (see table 4).

PEG 3350 solution without added electrolytes is an odorless osmotic laxative, which has a very low risk of electrolyte imbalance. This powder mixes easily with juice or water and is absorbed only in trace amounts from the gastrointestinal tract. PEG 3350 without electrolytes is FDA approved for the treatment of chronic constipation in adults, but not in children. However, the therapeutic safety of this drug for the treatment of chronic childhood constipation and impaction has been demonstrated in many studies.^{18,19} In a prospective open labeled trial conducted by Pashankar et al, children with constipation and encopresis were treated with PEG 3350 for 2 months. PEG 3350 was administered at a dose of 1 g/kg/day mixed in a beverage of the patient's choice (17 g in 240 mL of fluid). The

Table 3. Enteral Formula Resources

History Including:

- · Duration of symptoms
- · Frequency of bowel movements
- · Caliber of stools
- · Abdominal pain
- Pain and rectal bleed while passing hard stool
- Fecal soiling
- · Withholding behavior
- · Change in appetite
- · Nausea or vomiting
- Weight loss
- Perianal fissures, dermatitis, abscess, or fistula

Complete Review of Systems

- Medication
- Dietary
- · Psychosocial and family history

Physical Examination

- Palpation of the abdomen for fecal mass
- Perianal examination for perianal soiling, fissures, hemorrhoids or streptococcal infections
- Digital rectal examination for hard stool and a patulous anus
 - A patulous anus is typically due to chronic fecal retention, but prior trauma or a spinal cord lesion need to be considered
- Back and spine examination
- Dimple
- Tuft of hair
- · Neurological examination
- Tone
- Strength

Table 4. Medications Used in the Treatment of Chronic Constipation and Disimpaction

Laxative	Dosage	Side effects
Usmotic Phosphate enema	2 yrs-6mL/kg up to 135 mL	 Hyperphosphatemia, hypocalcemia leading to tetany Mechanical trauma to rectal wall, abdominal distention or vomiting
Lactulose	1-3 mL/kg/day	• Flatulence, abdominal cramps
Sorbitol	1-3 mL/kg/day	• Flatulence, abdominal cramps
Magnesium hydroxide	1-3 mL/kg/day	 Infants may be susceptible to magnesium poisoning Overdose can lead to hypermagnesemia, hypophosphatemia and secondary hypocalcaemia
Magnesium citrate	> 6 years, 1-3 mL/kg/day; 6-12 years, 100-150 mL/day; 9-12 years, 150-300 mL/day	 Infants may be susceptible to magnesium poisoning Overdose can lead to hypermagnesemia, hypophosphatemia and secondary hypocalcaemia
PEG 3350	Disimpaction: 8 capfuls in 32 oz of Gatorade [™] 15 capfuls in 64 oz of Gatorade [™] Maintanence: 1 g/kg/day	 Nausea, bloating, abdominal cramps, vomiting
Polyethylene glycol electrolyte solution	Disimpaction: 25 mL/kg/hr (to 1000 mL/hr) by nasogastric tube until clear OR 20 mL/kg/hr for 4 hr/day	 Nausea, bloating, abdominal cramps, vomiting, and anal irritation
Mineral oil	Less than 1 year old– <i>not recommended</i> Disimpaction: 15-30 mL/yr of age, up to 240 mL daily Maintenance: 1-3 mL/kg/day	 Lipoid pneumonia if aspirated
Stimulants	2-6 years old: 2.5-7.5 mL/day; 6-12 years old: 5-15 mL/day Available as syrup, 8.8 mg of sennosides per 5 mL Also available as granules and tablets	 Idiosyncratic hepatitis, Melanosis coli, Hypertrophic osteoarthropathy, analgesic nephropathy
Bisacodyl	4-10 yrs: 5 mg 11-18 yrs: 5-10mg Rectal suppository > 2 yrs old: 0.5-1 suppository	 Abdominal pain, diarrhea and hypokalemia, abnormal rectal mucosa, and (rarely) proctitis Case reports of urolithiasis
Senna tablets (7.5 mg/tab)	1-2 tab	Abdominal pain, cramping, electrolyte imbalance
Glycerin suppositories	2-6 years: 1 - 1.7 rectally once > 6 years: 2-3g rectally once	

patients reported an improvement in symptoms of fecal soiling, stool consistency and frequency without any side effects.¹⁸ The suggested initial dosage of PEG 3350 ranges from 0.2 to 1.5 mg/kg. This wide range exists since no randomized controlled trials to date have conclusively identified a single efficacious dose recommendation of PEG 3350.¹⁸ More recently a few retrospective studies have also evaluated the safety of PEG 3350 for the treatment of chronic constipation in children < 2 years of age. Of note, the dose of PEG 3350 varied in all three studies; yet the mean effective dose of 0.8 to 1.0 g/kg/d was similar in all these studies with very few reported side effects. These minor side effects were dose dependent and could be decreased with the change in dose.^{20, 21, 22}

Behavioral Modification and Biofeedback Therapy

Behavioral modification and education of the patient and family remains an integral part of maintenance therapy, most of which can be performed by the pediatrician. A daily toileting regimen should be followed with documentation of each bowel movement in a stool diary. This behavior can be motivated with a reward, positively reinforcing each successful defecation.²³ Colonic motor activity is more active within 2 hours of awakening, thus making this an optimal time for defecation. Also, immediately following meals there tends to be increased colonic motor activity making thirty minutes after meals an excellent time to attempt defecation. Difficult patients may need to be referred to behavioral specialists or counselors who may have specific, planned approaches.²³

Recently, the focus has shifted towards biofeedback therapy. 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. In > 50% of constipated children there is a paradoxical contraction rather than relaxation of the rectal muscles during defecation. Some studies have suggested that biofeedback therapy can help reverse this acquired behavior. Unlike adults, data with biofeedback therapy in the past has not shown favorable results in younger children and should be reserved for a subgroup of patients with pelvic floor dysnergia.^{24,25} The difference in responses among adults and children may be due to the higher cognitive processes involved in biofeedback training.

Emerging Therapies

Newer therapies have emerged for the treatment of chronic constipation, although the safety of these drugs in children still needs to be evaluated.

Selective Serotonin Uptake Agonists

Serotonin mediates peristalsis and stimulates secretions via 5HT-4 receptors in the gut wall. The Food and Drug Administration's (FDA) approval of Tegaserod in 2002 for the treatment of chronic constipation associated with irritable bowel syndrome offered a new and optimistic therapeutic approach to patients.^{26,27} Tegaserod acts by increasing small bowel transit and stimulates intestinal secretions and inhibits visceral afferent responses thus decreasing abdominal pain and bloating. However, Tegaserod was removed from US markets in 2007 after reports of serious cardiovascular side effects. Since the elimination of Tegaserod, several other 5-HT4 agonists such as prucalopride have been or are currently being examined by the FDA. Unfortunately, most of these compounds are not geared towards a pediatric population and thus their efficacy in children with constipation remains to be seen.

Chloride Channel Activator

One new therapy approved by the FDA in 2006 is a bicyclic fatty acid that acts as a selective chloride channel activator, known as lubiprostone. This drug has been shown to increase intestinal chloride and fluid secretion and facilitate defecation thus decreasing symptoms such as abdominal bloating, distention and severity of constipation.^{28,29} No current indications exist for pediatric patients.

Alvimopan

Alvimopan, a mu-receptor antagonist, is another investigational drug that awaits FDA approval for the treatment of chronic constipation. The polarity of the molecule limits the gastrointestinal absorption and penetration of the central nervous system.

Guanylate Cyclase Activators

Linactolide (previously MD-1100) is a fourteen amino acid peptide that acts locally in the intestine to stimulate the guanylate cyclase receptors increasing chloride and bicarbonate secretion thereby increasing the fluid secretion and motility. It has recently been studied in adults and has been shown to improve bowel habits and increase colonic transit.²⁹

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CONCLUSION

Chronic constipation remains a cause of great morbidity and emotional distress in pediatric patients and their caretakers. Recent technological advancements have been introduced to aid pediatricians in diagnosing chronic constipation refractory to treatment. However, in the overwhelming majority of cases, the only diagnostic evaluation necessary is a careful history and complete physical examination. Many new drugs are currently under investigation, albeit in the adult population. As more data become available from these studies, results and modifications may be extrapolated into the pediatric realm, with the hope of providing new, safe and effective treatment options for children suffering from chronic constipation. ■

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