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Review of management of refractory constipation: What lies ahead

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Abstract: Childhood constipation is a prevalent issue globally. Certain children experience persistent constipation and soiling, either as a result of surgical repair of anorectal malformations or underlying medical conditions that present management challenges. These refractory cases of constipation significantly affect the psychological well-being of both patients and their families. The available treatment options for refractory constipation are not clearly established. However, prompt and appropriate management of constipation contributes to an enhanced health-related quality of life. This article explores the current modalities available for treating children with challenging constipation and examines their impact on health-related quality of life.

Keywords: Quality of life; Constipation; Refractory.

1. Introduction

Childhood constipation is a common problem worldwide. The prevalence of childhood constipation in the general population ranges from 0.7% to 29.6% [1]. Chronic childhood constipation is associated with impaired quality of life. Strategies for early identification and optimal treatment of constipation with regular follow-up, adjustment of medications, and lifestyle changes may prevent chronic refractory constipation and its negative impact. Many children with refractory idiopathic constipation or soiling are resistant to regular intensive medical management, posing a major challenge worldwide [2]. There are groups of children, especially those with neurodisabilities, autism, postoperative anorectal malformation, or challenging behavior, whose constipation is difficult to manage. In this article, we will discuss this group of children whose constipation is difficult to treat and its impact on health-related quality of life. The article also focuses on current modalities and treatment options available for those who fail intensive medical management.

2. Constipation and Special Circumstances

Autism spectrum disorders (ASD) appear to predispose individuals to functional constipation with or without fecal incontinence. Children with ASD and functional constipation tend to be older and experience longer durations of symptoms compared to children without ASD [3]. Managing constipation in children with ASD is further complicated by selective eating, oral sensory processing issues, and difficulties in administering medications.

Similarly, children with attention deficit/hyperactivity disorder (ADHD) also suffer from functional constipation and fecal incontinence. The mechanism behind the association between ADHD and functional constipation is not clear, but it may involve atypical sensory processing, disregarding sensory stimuli, or other factors that interfere with normal toilet training progress [4]. Behavioral problems, such as oppositional behavior, poor attention span, and high activity level, contribute to poor adherence to medication or behavioral programs. These patients and their families may benefit from individual or group psychotherapy and a more

rigorous behavioral approach [5]. For example, clinical practice frequently encounters improvements in the behavior of children with autism after evacuation of retained feces [6].

In children with neurodisabilities, there is often a delay in recognizing and providing appropriate treatment for constipation. Symptoms are often present for months or years before receiving proper treatment. Such delays are particularly problematic in children with disabilities, either because constipation is accepted as an inevitable consequence of their neurological impairment or due to a higher priority given to other aspects of medical management, such as convulsion or postural deformity treatment. Children with disabilities often struggle to express the discomfort caused by constipation, and communication difficulties further hinder problem recognition. Abdominal pain is a frequently encountered symptom of chronic constipation and significantly contributes to the adverse effects on their quality of life. Adequate treatment of constipation in these cases provides relief for the child and can lead to improvements in appetite and behavior [6].

Fecal incontinence is common in patients who have undergone surgery for anorectal malformations. The use of enemas, laxatives, and medications in an indiscriminate manner, without demonstrated benefits, is a common approach. Implementing a systematic diagnostic approach and a bowel management program can provide assistance to such patients [7].

3. Management of Constipation

What are the challenges for refractory constipation? Children with refractory idiopathic constipation or resistant soiling pose significant challenges globally [2]. While the majority of children respond to medical and behavioral treatments, a considerable number of them continue to experience symptoms despite conventional therapy. Treatment failures often occur in patients with hypomotility, inadequate medication or premature discontinuation, and poor adherence [5].

Unfortunately, treatment options for children with constipation refractory to conventional approaches are limited [8]. Therapeutic decisions are guided by rectal biopsy to exclude Hirschsprung's disease, assessing motility through intestinal transit studies, anorectal/colonic manometry, and contrast rectal enema radiology to better understand the severity of megarectum and megacolon resulting from gut dysmotility or physiological overactivity of the anal sphincters [2]. Recent guidelines from European and North American pediatric gastroenterology societies recommend considering anal sphincter botulinum toxin injection, transanal irrigation, antegrade continence enemas (ACE), sacral nerve stimulation (SNS), and partial or total colonic resection for the treatment of intractable constipation [8]. Interventions for constipation is shown in Table 1.

Table 1. Interventions for constipation: Indications, advantages, and disadvantages

	Indication	Advantage	Disadvantage
Botox injection	Physiological over activity of the external or internal anal sphincter. Idiopathic constipation	Safe and effective minimally invasive	Transient responders needs repeat injections
Sacral nerve stimulation	Non-neuropathic and Neuropathic CBBD In subjects with colonic inertia	Improvement in both symptoms and quality of life effective and long lasting	Invasive, expensive procedure
Solesta	Severe constipation and urinary incontinence in patients with spina bifida	Enhances the resting anal pressure minimally invasive	Chronic infection or migration
ACE	Megarectum neuropathic rectum after repair of anorectal anomalies	Improves quality of life child will be more independent	Pain at catheterization, skin excoriation/ granulomata, stomal leakage, stomal stenosis, surgical site infection, ACE revision from malfunction, stomal prolapse, post operative ileus, gut perforation, parastomal hernia and phosphate enema toxicity
Peristeen	Chronic idiopathic constipation	Decreased requirement for invasive surgeries	Discomfort rectal perforation
Colonic resection	Failure of medical treatment, megarectum, ACE failures	Improves quality of life, may be able to come off medications and enemas	Surgical procedure
Intestinal diversion	Idiopathic constipation	Alternate to ACE in less than 5 years	Colonic inertia and severe colonic distension, may lead to failure of procedure
Pelvic physiotherapy	Dyssynergic defecation in children whose comorbidities include anxiety and low-muscle tone	Fewer hospitalisations and colon surgeries safe, well-tolerated, and inexpensive	Not for children less than 5 years

4. Bowel Management Program

What is known? The term "bowel management" refers to a program implemented to maintain artificial cleanliness in the underwear of fecally incontinent patients. The program involves identifying the characteristics of each patient's colon, determining the specific type of enema that effectively cleanses the colon, and monitoring the process radiologically [9]. The goal of the bowel management program is to ensure a clean colon, taking advantage of the slow movement of stool from the right to the left colon, thereby keeping the patient completely clean in terms of fecal incontinence. The administration of a daily individually

designed enema is a key component of the program, allowing the patient to remain completely clean in the underwear for 24 hours between enemas [9]. When implemented appropriately, bowel management significantly improves the quality of life for children with fecal incontinence, surpassing the benefits of surgical interventions [9].

5. Botox Injection

Botulinum toxin is used for patients with physiological overactivity of the external or internal anal sphincter [2]. External anal sphincter BOTOX injection has shown markedly improved stooling patterns in patients, with a reduction in soiling episodes at 1-year follow-up [2]. It is speculated that BOTOX disrupts the vicious cycle of retentive stooling behavior, leading to functional recovery and a normal stooling pattern [10]. Injection of 160 units of BOTOX between the internal and external anal sphincter circumferentially (avoiding the urethra) may relax the sphincters and provide temporary or permanent relief [11]. A controlled study has also demonstrated good and excellent results with EAS needle-free Botox injection in children with idiopathic constipation, based on the concept that defecation is retentive and dyssynergic in such cases [10]. Botulinum toxin injection therapy can induce paradoxical contractions of the voluntary external sphincter, known as EAS dyssynergia [2]. If the response to botulinum toxin is transient, repeat injections or posterior myotomy or myectomy may be considered [10].

6. Sacral Nerve Stimulation

Sacral nerve stimulation is a promising and durable treatment for children with refractory constipation, particularly in decreasing fecal incontinence [8]. Childhood bowel and bladder dysfunction (CBBD), a retentive type of constipation, is commonly observed in cases of bowel dysfunction due to disorders like congenital spina bifida, cerebral palsy, transverse myelitis, tumors, trauma, etc.

Various tailored therapies, including cognitive-behavioral techniques, urotherapy, medication, biofeedback programs, clean intermittent catheterization, retrograde colonic enemas, injectable botulinum toxin, and in some cases, surgery, have been offered to children with CBBD (childhood bowel and bladder dysfunction) with varying success and adverse effects.

Sacral nerve stimulation has been a useful addition to management strategies for both non-neuropathic and neuropathic CBBD, although further high-quality evidence is required [12]. Sacral nerve stimulation prolongs colonic transit time by reducing antegrade transport in the ascending colon and increasing retrograde transport in the descending colon [12]. Previous studies suggest that sacral nerve stimulation is an effective treatment for constipation, believed to be mediated by the induction of propagating colonic pressure waves, which are defective in slow transit constipation. Thus, sacral nerve stimulation may have a particular advantage in subjects with colonic inertia. In addition to promoting colonic pressure waves, supraspinal and central effects have been observed. Despite extensive physiological research, the underlying mechanisms of action for sacral nerve stimulation remain unclear [13]. Sacral nerve stimulation has led to continued improvement in both symptoms and quality of life even at 2 years after treatment initiation, with particular improvement in concurrent fecal incontinence [8]. Sacral nerve stimulation is a minimally invasive and expensive procedure, but it has significant implications for the patient, as procedures like anal sphincter repair or colostomy are increasingly complex and carry significant morbidity [14–17]. A proper understanding of the mechanism of action of this therapy may significantly improve patient selection, treatment delivery, and subsequent outcomes [18–20].

7. Solesta

Solesta is an injectable and bulking agent dextranomer stabilized in hyaluronic acid that enhances resting anal pressure and improves fecal continence [3]. Injections of Solesta into the anus act as a filler to bulk up the tissue of the anal canal, helping to hold the stool [21]. Laparoscopic antegrade continence enema with antegrade bladder neck injection can be performed in the same setting and is a safe, efficacious, and minimally invasive approach for severe constipation and urinary incontinence in patients with spina bifida [3].

8. ACE

Patients with severe refractory constipation and incontinence may benefit from surgical intervention. As children grow older, they desire more independence and prefer not to rely on adults for their bowel management. The "continent appendicostomy" (also known as a Malone or ACE procedure) can be performed when a child becomes more independent and successful with bowel management. This procedure involves creating a small orifice in the umbilicus (belly button), allowing the patient to self-administer enemas using a small catheter while sitting on the toilet. It promotes independence and improves the quality of life for the child [9].

9. Peristeen

Peristeen is a transanal irrigation system that involves water irrigation of the large intestine using a disposable balloon catheter. It has been successfully used in the treatment of fecal incontinence, without requiring surgical intervention [13]. The Peristeen transanal irrigation system assists individuals with bowel dysfunction in flushing out the lower part of the bowel as part of their bowel management therapy [23]. Pediatric studies on Peristeen were non-comparative and consisted of observational case series. While the studies varied in quality and outcome measures, they generally indicated improvements in bowel management. However, evidence for children is weaker compared to adults, partly due to difficulties in obtaining valid patient-reported outcome measures (PROMs) for children [23]. The only potential complication is mild discomfort, and the risk of rectal perforation from rectal catheter irrigation is less than 1 in 100,000 cases [24].

10. Pelvic Physiotherapy

Dysfunction of the coordinated contraction and relaxation of pelvic floor and abdominal muscles during bowel movements may play a role in the onset and maintenance of functional constipation [25]. Children with functional constipation tend to strain their pelvic floor muscles and fail to relax the external anal sphincter during bowel movements, either consciously or unconsciously [26,27]. Reduced trunk stability can hinder the achievement of the posture and intra-abdominal pressure necessary for defecation [26,28].

Physiotherapy aims to improve the coordination between the abdominal and pelvic floor muscles [25]. Optimal results are expected with physiotherapy in children who recently developed symptoms [29]. The strength of physiotherapy lies in combining physical exercises with cognitive and behavioral elements, such as education and toilet training [30]. Pelvic physiotherapy, in conjunction with standard medical care, is more effective than standard medical care alone in constipated children. Pelvic physiotherapy may involve methods such as manometry (MT), myofeedback (electromyography feedback) (MFB), rectal balloon training (RBT), functional electric stimulation, flowmetry, and ultrasound scan [31].

11. Colorectal Resection

Permanent diversion is considered the last resort for refractory constipation [32]. It should be reserved for patients who do not respond to medical and surgical therapy. This procedure is primarily performed to alleviate the symptoms of constipation. Different techniques, such as segmental resection, subtotal colectomy, and total proctocolectomy, have varying outcomes. Segmental resection is indicated for children with a focal abnormality limited to a segment of the colon, such as a highly dilated rectum or rectosigmoid [32]. Subtotal colectomy is less common and less effective in children. Restorative total proctocolectomy with ileal pouch reconstruction is performed less frequently in constipated children but has been found to be effective [33].

12. Intestinal Diversion

Intestinal diversion, whether through ileostomy or colostomy, is an effective method for relieving symptoms of constipation. Permanent intestinal diversion is considered a last resort, but temporary diversion can benefit selected patients, such as those with significant pan-colonic dilatation and those unlikely to benefit from antegrade continence enema (ACE) therapy. Temporary diversion is an option for children under 5 years old, as ACE requires a cooperative and compliant patient [34]. Temporary diversion reduces colonic dilatation, improves colonic motility, and facilitates successful reanastomosis. While there are no studies

directly comparing ileostomy to colostomy in children, ileostomy is the safer choice when the site of colorectal dysfunction is unknown [33].

13. Conclusion

In conclusion, the current treatment modalities for refractory constipation in children have shown durable improvement in symptoms and quality of life. However, further studies are needed to evaluate predictors of treatment response, development of complications, and improvement in health-related quality of life. It is important to tailor the treatment strategy according to the individual patient's symptoms, factors, and response to treatment. There is no single surgery that represents the best practice for children with idiopathic constipation.

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