
Approach to Patients with Refractory Constipation

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Abstract

A review of relevant publications revealed that the criteria for defining refractory constipation were ill-defined. Common treatment for constipation includes osmotic, stimulant, and enterokinetic agents. Prucalopride is a new enterokinetic agent that has been shown in clinical trials to produce significant improvements in bowel functions, gastrointestinal symptoms, and quality of life. Patients who fail pharmacological treatment should be referred to specialized centers for physiological laboratory evaluation like transit studies, balloon expulsion, anorectal manometry, and defecography. Potential pathophysiology of refractory constipation include physiological disturbances like pelvic floor dyssynergia and slow transit constipation. Physical defects such as rectocele and internal prolapse are uncommon. Psychological disturbances have been linked to persistent GI symptoms. Non-pharmacological treatments to consider include biofeedback and behavioral therapy. More studies are needed before surgery can be recommended. There is the possibility that a wider acceptance of the use of

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laxatives may substantially reduce the number of patients with refractory constipation.

Keywords

Constipation • Laxative • Biofeedback • Psychological • Surgery • Bowel

Introduction

Before embarking on the work-up and management of refractory constipation, the clinician must ask, what is refractory constipation? Situations where patients may be considered to have refractory constipation are when patients are subjected to clinical trials of new pharmacological agents or referred for total colectomy. A review of relevant publications revealed that the criteria for defining refractory constipation were ill-defined. The majority of studies reported duration of constipation, and simply that laxatives had been unsuccessful. No information was available to determine the type of laxatives, dosing, and duration of treatments. In a recent review by the Asian Neurogastroenterology & Motility Association, a pharmacological non-responder was defined as failure to respond to bisacodyl at 10 mg every night for at least 4 weeks, with consideration given to a total treatment period of up to 12 weeks if access to specialized centers is limited, or prucalopride at 2 mg daily for up to 12 weeks, and combining a stimulant or prokinetic agent with an osmotic agent may also be considered [1]. This is based on recent high-quality clinical trials which demonstrated improvement in quality-of-life scores in patients on daily treatment with either of these agents for 4 weeks (bisacodyl or picosulfate) to 12 weeks (prucalopride) [2–6]. Contrary to popular belief, patients who had received active treatment with bisacodyl were able to reduce their dosage with time [6].

Prucalopride is a new enterokinetic agent that has been shown in clinical trials to produce significant improvements in bowel functions, gastrointestinal symptoms, and quality of life, with improvements maintained on continued use for up to 24 months [2–4, 7]. Based on secondary endpoint analysis of data derived from the pivotal studies, it appears that prucalopride may be particularly effective at improving bloating [8].

Other treatments that may be explored in the future are lubiprostone and linaclotide, which belong to a new class of pharmacological agents known as colonic secretagogues. Table 7.1 serves as a guide to the feasibility of maximizing pharmacological agents before labeling a patient as having refractory constipation. The information on dosing ranges and treatment durations is based on those used in clinical trials of these agents. However, it is unclear if such an extended treatment can produce durable improvement.

Patients who fail pharmacological treatment should be referred to specialized centers for physiological laboratory evaluation (see Fig. 7.1).

Table 7.1 Summary of the various agents of chronic constipation

Category	Laxative	Population	Range of dosage	Duration of treatment
Osmotic	PEG	Adults	13–39 g/day	Up to 6 months
		Children	1–1.5 g/kg/day (disimpaction dose) 0.3–0.8 g/kg/day (maintenance dose)	Up to 7 days Up to 6 months
	Lactulose	Adults	15–60 ml	1–12 weeks
		Children (11–18 years)	15 ml twice daily	4 weeks
		Children (6–10 year)	10 ml twice daily	4 weeks
		Children (1–5 years)	5 ml twice daily	4 weeks
	Magnesium hydroxide	Elderly (>65 years)	25 ml/day	8 weeks
Stimulant	Bisacodyl/picosulfate	Adults	5–10 mg/day	4 weeks
		Children (6–14 years)	2.5–5 mg/day	No data ^a
Enterokinetics	Prucalopride	Adults (>65 years)	1 mg/day	12 weeks
		Adults (18–65 years)	2 mg/day	12 weeks

Reproduced with permission from Gwee et al. [1]

^aFor children, bisacodyl/picosulfate was only used as part of preparation to cleanse bowel

Potential Pathophysiology of Refractory Constipation

Physiological Factors

The two main physiological disturbances associated with refractory constipation are pelvic floor dyssynergia (PFD) and slow transit constipation (STC). Pelvic floor dyssynergia (alternative terms are anismus or obstructed defecation disorder) refers to paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation; this is believed to be an acquired behavioral disorder of defecation. Slow transit constipation is also referred to by its old name of colonic inertia, and refers to the inability of the colon to modify stool to an acceptable consistency and move the stool from the cecum to the rectosigmoid area. An alternative definition is prolonged colonic transit time that cannot be normalized even by the consumption of large amounts of dietary fiber. There is a wide variability of methodology used to measure colonic transit times, and the reproducibility of these tests is not high, and especially so for slow transit times [9]. Studies of patients referred to tertiary centers in Korea and Thailand (for presumed refractory constipation), reported PFD in 30–35 %, STC in 13–20 %, and PFD combined with STC 11–27 %, but a substantial proportion had normal transit constipation (13–47 %) [10, 11]. Similar to studies from the west, these Asian

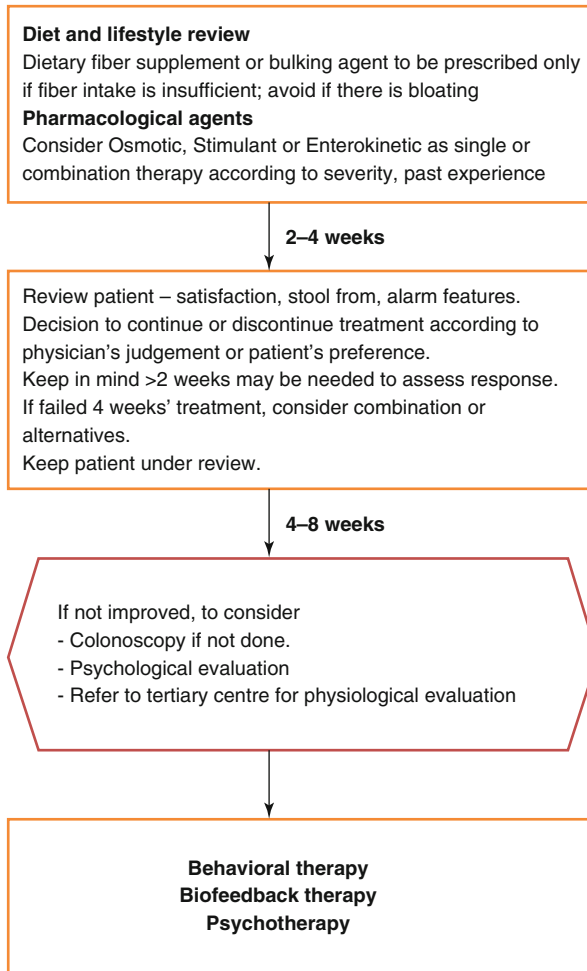


Fig. 7.1 Chronic Constipation Treatment Algorithm

studies suggest that symptoms alone cannot distinguish the different constipation subtypes.

Anatomical Factors

Physical defects such as rectocele (herniation of the rectal wall with retention of stool in the hernia after defecation) and internal prolapse are uncommon, reported in less than 1%, even in tertiary centers [12]. At least one study has reported that biofeedback can help more than half of these patients to overcome their constipation without the need for surgical repair [13].

Psychological Factors

An important aspect that is frequently overlooked is the psychological one. Numerous studies had shown the association of abuse history, in particular sexual and childhood abuse, with functional gastrointestinal diseases. Depression is not uncommon, especially in the elderly. In young women with severe constipation, the possibility of an eating disorder should be considered [14]. The possibility of a past history of sexual and physical abuse should be kept in mind [15]. In a referral-based clinic, Drossman et al. reported that of 206 women with functional gastrointestinal disorders, 44% reported a history of sexual abuse or physical abuse in childhood or later in life. However, only 17% had informed their doctors about the abuse. As these women may be psychologically predisposed to submit themselves to surgery, it is especially important for the physician to ask specifically for a history of abuse before contemplating a referral to a surgeon [15–17]. There is a strong possibility that psychological factors are a major reason for refractory constipation. Psychological disturbances have been linked to persistent GI symptoms and frequent health-seeking behavior as well as failure to respond to tertiary-level treatment [18, 19].

Non-pharmacological Treatments

Biofeedback and Behavioral Therapy

Biofeedback is a training technique which aims to teach patients to relax, instead of contracting, their pelvic floor muscles during straining at stool. There are several variations of the method; some involve the use of visual or auditory signals, from surface or electromyographic electrodes or anal probes, to inform patients whether they are performing the appropriate muscular action. In its most basic form, patients may also be trained to evacuate rectal contents by using a balloon, or even oatmeal porridge in the shape of a stool, introduced into the rectum to simulate defecation [20, 21]. Currently, biofeedback therapy is applied primarily to patients with PFD. Overall, biofeedback is a safe treatment which may produce durable improvement beyond the active treatment period. Randomized control trials in refractory chronic constipation patients with PFD have reported 70–80% success rates for up to 1 year [22–24]. Improvement was reported for constipation symptoms and overall symptoms, as well as dyssynergic pattern of defecation. However, the impact on quality of life or psychological state has not been fully assessed. As many as two-thirds of patients referred for biofeedback could have diagnosable psychiatric disorders, and those patients with a higher degree of quality-of-life impairment due to psychological distress are less likely to respond to biofeedback treatment [25].

Surgery

The scientific rationale for surgical treatments has not been clearly articulated. When contemplating a surgical referral, the following reservations should be

considered. Initially promising results with small numbers of highly selected patients may not be replicated when extended to larger series with longer term follow-up. Surgical treatments have not been evaluated to the same rigorous degree that modern pharmacological agents are subjected to. Non-destructive treatment approaches may become available or prove to be more effective. An example is that in the 1970s and 1980s an operation known as anorectal myectomy was advocated for adult patients with outlet obstruction. However, longer term follow-up revealed that in the majority of patients, the improvement was not sustained, and there was a high incidence of incontinence [26, 27]. In its place, biofeedback is now offered to patients with outlet obstruction. Similarly, for sub-total colectomy with ileo-rectal anastomosis, which is advocated for colonic inertia, initial series comprising 6–30 patients followed up for up to 6 years reported satisfactory results in 60–100%, but when one of these studies was extended for another 3 years and expanded to include 44 patients, the proportion of patients who were able to maintain normal bowel function fell to 50%, while 71% continued to experience abdominal pain, 39% required further surgery, and almost a quarter required psychiatric treatment for severe psychological disturbances [28–31]. A number of studies have also in the past demonstrated that when bisacodyl was instilled into the colon of patients classified as colonic inertia, as many as 60–90% achieved high amplitude propagated contractions [32–34]. This suggests that if high enough levels of the stimulant agent could be delivered, some of these colons could have been salvaged.

The possibility of a Munchausen phenomenon should be seriously considered in patients willing to subject themselves to an ablative procedure like colectomy. Patients with a history of sexual abuse had a ten-fold increased risk of surgery prior to their colectomy, and had a high probability of seeking medical care for abdominal complaints after their colectomy [35–38].

A number of recent studies found that the majority of patients with severe STC had evidence of small bowel motor abnormalities and are at risk of intestinal obstruction post-colectomy [39–43]. Our position is that any patient with functional constipation who is being considered for surgical intervention must undergo a formal psychiatric evaluation and an evaluation of GI motility with, at the minimum, measurement of small intestinal transit time.

Conclusion

The management of refractory constipation remains a challenge, not least because criteria for refractoriness has not been clearly defined. On the one hand, there is much prejudice regarding the use of laxatives that is not evidence based, while on the other hand, there is much uncritical acceptance of the effectiveness of fiber treatment that is poorly substantiated. There is the possibility that a wider acceptance of the use of laxatives may substantially reduce the number of patients with refractory constipation. The main challenge appears to be to identify and recognize the role that psychological disturbances play in refractory constipation. More attention to psychologically directed treatments, including biofeedback, with greater accessibility to these treatments, may help to reduce the number of patients who are driven to the treatment of last resort, ablative surgery.

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