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Review article

Chronic constipation: A critical review

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ABSTRACT

Chronic constipation is a very common symptom that is rarely associated with life-threatening diseases, but has a substantial impact on patient quality of life and consumption of healthcare resources. Despite the large number of affected patients and the social relevance of the condition, no cost-effectiveness analysis has been made of any diagnostic or therapeutic algorithm, and there are few data comparing different diagnostic and therapeutic approaches in the long term. In this scenario, increasing emphasis has been placed on demonstrating that a number of older and new therapeutic options are effective in treating chronic constipation in well-performed randomised controlled trials, but there is still debate as to when these therapeutic options should be included in diagnostic and therapeutic algorithms. The aim of this review is to perform a critical evaluation of the current diagnostic and therapeutic options available for adult patients with chronic constipation in order to identify a rational patient approach; furthermore we attempt to clarify some of the more controversial points to aid clinicians in managing this symptom in a more efficacious and cost-effective manner.

1. Introduction

Chronic constipation is a very common and heterogeneous condition characterised by unsatisfying defecation associated with infrequent stools, difficult stool passage, or both [1]. It has a prevalence of 14% in the general population [2], and a significant impact on patient quality of life [3,4], working productivity [5], and consumption of healthcare resources [6]. Over the last ten years, both old and new treatments with different mechanisms of action have proved to be effective [7], but their role in the therapeutic approach still needs to be optimised. The aim of this review is to perform a critical evaluation of the diagnosis and treatment of chronic constipation in adults, concentrating on the most controversial issues raised by the current availability of effective treatments. Take-home messages are included at the end of each section.

1.1. Definitions

There are various definitions of chronic constipation, and the apparently small differences between them need to be acknowledged as they create groups of patients with potentially distinct responses to treatments. One of the most widely used is based on the Rome III criteria (Table 1) [8]. Whether the combination of two or more different symptoms identifies different subsets of patients remains unclear [9,10], as whether a bowel diary is needed to overcome the discrepancy between recalled and recorded bowel habits [11,12].

An alternative approach is to define constipation on the basis of a patient's dissatisfaction with the frequency of defecation and stool passage [1]. This approach is underpinned by the concept that it is the patients' perceived degree of dissatisfaction that makes a symptom more or less relevant. There are no details as to how this should be measured, but the symptoms should be considered clinically important and treated when they are severe enough to impair the patient's quality of life [1], a variable that is also influenced by psychological factors [13]. Moreover, the challenge of a definition based on dissatisfaction is that many people have their own, possibly erroneous conception of what constitutes a normal bowel habit: for example, elderly patients with normal bowel frequency (>3 times/week) often regard themselves as being constipated and take laxatives [14].

A third definition used in clinical trials is a modified version of the Rome criteria in which abnormal bowel frequency (<3 bowel movements/week) is the necessary condition for inclusion [15–19]. This restriction makes the patients more uniform and provides an objective parameter for assessing treatment efficacy, but excludes the important subgroup of patients who feel constipated despite normal bowel frequency [11,14]. It might also limit the possibility of extrapolating clinical trial results to the general population and

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Table 1
Rome III functional constipation criteria.[a]

1. Must include at least 2 of the following:
   a. Straining during at least 25% of defecations
   b. Lumpy or hard stools in at least 25% of defecations
   c. Sensation of incomplete evacuation for at lest 25% of defecations
   d. Sensation of anorectal obstruction/blockage for at least 25% of defecations
   e. Manual manoeuvres to facilitate at least 25% of defecations (*e.g.* digital evacuation, support of the pelvic floor)
   f. Fewer than three defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for diagnosis of irritable bowel syndrome

[a] Criteria fulfilled for the previous three months with symptom onset at least six months prior to diagnosis.

Table 2
Classes of medications (examples) and diseases associated with secondary constipation [24,25].

Medications:	Opiates (morphine), anticholinergic agents, tricyclic antidepressants (amitriptyline), antispasmodics (dicyclomine, mebeverine, peppermint oil), calcium channel blockers (verapamil, nifedipine), antiparkinsonian drugs, anticonvulsants (carbamazepine), sympathomimetics (ephedrine), antipsychotics (chloropromazine, clozapine, haloperidol, risperidone), diuretics (furosemide), antihypertensives (clonidine), antiarrhythmics (amiodarone), beta-adrenoceptor antagonists (atenolol), antihistamines, calcium or aluminium containing antacids, calcium supplements, iron supplements, antidiarrheal (loperamide), 5-HT3-receptor antagonists (ondansetron), bile acid sequestrants (cholestyramine), non-steroidal anti-inflammatory drugs (ibuprofen)
Organic stenosis:	Colorectal cancer; other intra- or extra-intestinal masses; inflammatory, ischemic or surgical stenosis
Endocrine or metabolic disorders:	Hypothyroidism, hypercalcemia, hyperparathyroidism, diabetes, porphyria, chronic renal insufficiency, pan-hypopituitarism, pregnancy
Neurological disorders:	Spinal cord injury, Parkinson's disease, cerebrovascular disease, paraplegia, multiple sclerosis, autonomic neuropathy, spina bifida
Enteric neuropathies:	Hirschsprung's disease, chronic intestinal pseudo-obstruction
Myogenic disorders:	Myotonic dystrophy, dermatomyositis, scleroderma, amyloidosis, chronic intestinal pseudo-obstruction
Anorectal disorders:	Anal fissures, anal strictures

the elderly, in whom the major complaints defining constipation are straining and hard stools rather than reduced bowel frequency [14,20].

Another debated point is whether irritable bowel syndrome with constipation (IBS-C) is a different entity from chronic/functional constipation. Some researchers consider the two conditions indistinguishable [1] because the abdominal pain and discomfort characterising IBS can also be associated with constipation [21,22]. Furthermore, although the Rome III criteria exclude IBS-C from the definition of functional constipation [8], if this requirement is not enforced, there is a large overlap between the two [23]. These observations suggest a continuum based on the severity of pain or discomfort [23], but do not exclude the possibility that the patients at the two extremes of the spectrum may benefit more from treatment aimed specifically at relieving abdominal pain or correcting the defecation disorder/colonic transit. In particular, the presence of abdominal pain in patients with chronic constipation is associated with a poorer quality of life and more frequent extra-intestinal somatic symptoms than in constipated patients with no abdominal pain [21].

Take-home messages (1)

The different definitions of chronic constipation create groups of patients with potentially distinct treatment responses.

Physicians prefer using objective and physical factors when defining constipation, whereas patient dissatisfaction may be unrelated to these factors.

Chronic constipation and irritable bowel syndrome with constipation often overlap.

2. Causes and pathophysiology

Most cases of chronic constipation are primary or idiopathic, but it is also necessary to acknowledge that a few cases may be *secondary* to a number of medications or diseases (Table 2) [24,25], because reducing or stopping the medications or treating the primary diseases may help to relieve the symptom. The long and heterogeneous list of conditions that induce constipation indicates that many pathophysiological mechanisms finally cause the same symptoms, which are often indistinguishable from those of the primary form.

The pathophysiology of *primary* chronic constipation is multifactorial and includes diet, colonic motility and absorption, anorectal motor and sensory function, and behavioural and psychological factors. Most studies have investigated the impact of only one factor at a time, whereas their multiplicity, overlapping nature, and bidirectional interplay should be taken into account in order to avoid oversimplification. Although it is conceivable that a better understanding of the pathophysiology of the condition might help in the planning of more rational therapy, the complex interactions of various pathophysiological factors suggest that therapeutic strategies based on only one of them should be considered with caution.

2.1. Diet

A fibre-rich diet accelerates transit time, softens stool and increases stool weight, but a diet that is poor in fibre can induce constipation [26]. However, the consumption of dietary fibre is no different between constipated and non-constipated subjects [27]. Increasing dietary fibre improves symptoms in patients with normal colonic transit and anorectal function, but not in constipated patients with delayed colonic transit and defecation disorders [28,29]. The latter are characterised by low stool weight and prolonged transit times regardless of the amount of fibre in their diet [26], which suggests that increasing their fibre intake does not normalise colonic transit and can even worsen their symptoms as a result of the gas produced by fibre metabolism.

2.2. Colonic motility and absorption

Delayed colonic transit is associated with small and hard stools [30] that are difficult to evacuate [31,32]. It has been found that faecal consistency and water content significantly correlate with colonic transit time [33], which suggests that prolonged colonic transit favours the time-dependent process of water absorption. Moreover, changes in colonic transit affect bacterial mass [34], and this may also influence colonic absorption and secretion.

Delayed colonic transit may be due to impaired colonic motor activity [35], but may also be secondary to voluntary stool retention [36], defecation disorders [37,38], or an inadequate caloric intake [39–41]. Studies of colectomy samples taken from patients with delayed colonic transit suggest that impaired motility might