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Review Article

### CONSTIPATION CAUSES AND MANAGEMENT

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**Abstract:**

**Introduction:** Chronic constipation is considered a common, persistent problem that affect several patients globally. In the US, it is estimated that the prevalence of constipation is about fifteen percent in the general population. This number is similar to the estimated global prevalence of about fourteen percent. Risk factors include but not limited to old age, female, and lower socioeconomic status. Almost fifty percent of people complaining of constipation report symptoms for more than five years. Chronic constipation affects the quality of life and the psychological well-being. Chronic constipation has a major economic burden and leads to significant healthcare utilization for patients. It is estimated that more than US\$800 million dollars were spent on laxatives by constipated patients in 2007. Moreover, constipation-related emergency room visits and inpatient admissions are increasing as well, particularly in a young age population. The definition of chronic constipation has changed over time to include more than a decreased number of stools per week. It involves a pattern of symptoms like excessive straining, a sense of incomplete evacuation, failed or lengthy attempts to defecate, use of digital manoeuvres for evacuation of stool, abdominal bloating, and hard consistency of stools. The wider definition of constipation has led to a more expansive therapeutic approach. Constipation is categorized into two types: primary and secondary types. Primary constipation is due to disturbed regulation of the neuromuscular components within the colon and anorectum as well as disruption in their corresponding ascending and descending pathways in the brain-gut axis. With the help of a symptom-based criteria and diagnostic testing, primary constipation can be additionally categorized into functional defecation disorder, slow-transit constipation (STC), and constipation-predominant irritable bowel syndrome (IBS-C). Functional defecation disorders include dyssynergic defecation and illnesses that may obstruct defecation such as rectal prolapse, rectocele, and descending perineum syndrome. Dyssynergic defecation is defined as paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation. STC is recognized as inadequate propulsive forces in the colon in the absence of dyssynergic defecation. Multiple underlying factors have been suggested for IBS-C, including genetic, environmental, social, biological, and psychological factors. It is important to consider that there is huge overlap between dyssynergic defecation, STC, and IBS-C. Greater than half of dyssynergic patients will exhibit delayed colonic transit. The opposite also holds true with greater than two-thirds of STC patients having concurrent dyssynergia. Secondary constipation could result from a variety of factors such as metabolic disturbances (hypercalcaemia, hypothyroidism), drugs (e.g. opiates, calcium channel blockers, antipsychotics), neurologic disorders (parkinsonism, spinal cord lesions, diabetes mellitus), and primary diseases of the colon (stricture, cancer, anal fissure, proctitis). **Aim of work:** In this review, we will discuss constipation causes and management. **Methodology:** We did a systematic search for constipation causes and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles. **Conclusions:** Constipation is a very common and complicated disorder, symptoms of which include more than decreased frequency of bowel movements. Over a detailed history and prospective stool diary, it is important to determine the severity and chronicity of symptoms and identify the presence of underlying secondary causes. Chronic idiopathic constipation, refractory to dietary and lifestyle changes and laxatives, should be assessed with proper testing to recognize underlying pathophysiology. Suspicion of dyssynergic defecation on a proper digital rectal examination should be verified with anorectal manometry and/or defecography and referred to centres with expertise in manometry-based biofeedback therapy. Colectomy should be reserved for patients with underlying colonic neuropathy identified on colonic manometry. Drugs for chronic idiopathic constipation in the pipeline, whether secretagogues, serotonergic agonists, or bile acid transporter inhibitors, are considered safe and effective, promising to give doctors more therapeutic alternatives in their arsenal. It continues to be seen where these newer agents will fit in the management guideline.

**Key words:** Constipation, pathophysiology, causes, management

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**INTRODUCTION:**

Chronic constipation is considered a common, persistent problem that affect several patients globally. In the US, it is estimated that the prevalence of constipation is about fifteen percent in the general population [1]. This number is similar to the estimated global prevalence of about fourteen percent [2]. Risk factors include but not limited to old age, female, and lower socioeconomic status. Almost fifty percent of people complaining of constipation report symptoms for more than five years [3]. Chronic constipation affects the quality of life and the psychological well-being [4]. Chronic constipation has a major economic burden and leads to significant healthcare utilization for patients. It is estimated that more than US\$800 million dollars were spent on laxatives by constipated patients in 2007 [5]. Moreover, constipation-related emergency room visits and inpatient admissions are increasing as well, particularly in a young age population [6].

The definition of chronic constipation has changed over time to include more than a decreased number of stools per week. It involves a pattern of symptoms like excessive straining, a sense of incomplete evacuation, failed or lengthy attempts to defecate, use of digital manoeuvres for evacuation of stool, abdominal bloating, and hard consistency of stools [7].

The wider definition of constipation has led to a more expansive therapeutic approach. Constipation is categorized into two types: primary and secondary types. Primary constipation is due to disturbed regulation of the neuromuscular components within the colon and anorectum as well as disruption in their corresponding ascending and descending pathways in the brain-gut axis. With the help of a symptom-based criteria and diagnostic testing, primary constipation can be additionally categorized into functional defecation disorder, slow-transit constipation (STC), and constipation-predominant irritable bowel syndrome (IBS-C) [8]. Functional defecation disorders include dyssynergic defecation and

illnesses that may obstruct defecation such as rectal prolapse, rectocele, and descending perineum syndrome. Dyssynergic defecation is defined as paradoxical contraction or inadequate relaxation of the pelvic floor muscles during attempted defecation. STC is recognized as inadequate propulsive forces in the colon in the absence of dyssynergic defecation. Multiple underlying factors have been suggested for IBS-C, including genetic, environmental, social, biological, and psychological factors [9]. It is important to consider that there is huge overlap between dyssynergic defecation, STC, and IBS-C. Greater than half of dyssynergic patients will exhibit delayed colonic transit [10]. The opposite also holds true with greater than two-thirds of STC patients having concurrent dyssynergia. Secondary constipation could result from a variety of factors such as metabolic disturbances (hypercalcaemia, hypothyroidism), drugs (e.g. opiates, calcium channel blockers, antipsychotics), neurologic disorders (parkinsonism, spinal cord lesions, diabetes mellitus), and primary diseases of the colon (stricture, cancer, anal fissure, proctitis) [11].

In this review, we will discuss the most recent evidence regarding Constipation causes and management.

**METHODOLOGY:**

We did a systematic search for constipation causes and management using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: Constipation, pathophysiology, causes, management

**Pathophysiology**

Dyssynergia is considered an acquired behavioural problem of defecation that is estimated to present in 2/3 of adult patients with difficult defecation, stemming from faulty toilet training, behavioural problems, or parent-child conflicts [12]. Most

patients with dyssynergic defecation have inability to synchronize the abdominal, recto-anal, and pelvic floor muscles during attempted defecation. Failure of recto-anal coordination involves paradoxical anal contraction, inadequate anal relaxation, or impaired rectal/abdominal propulsive forces.

Recently, 4 additional patterns have been identified, by location of impaired anal relaxation – puborectalis, external anal sphincter, or both<sup>13</sup>. The presence of dyssynergic defecation has been linked to excessive perineal descent [14], rectocele, and solitary rectal ulcer syndrome (Rao et al. 1998b). About thirty two percent of these patients have delayed gastric emptying (Yu et al. 2015) and 2/3 rectal hyposensitivity. This suggests that dysregulation of brain-gut axis may play a role. STC is a multifactorial disorder with a strong female prevalence and our understanding of the pathophysiology underlying this condition is evolving.

### Therapeutic Approaches

The management plan to constipation depends on the nature of the constipation, if it is a primary or secondary condition and whether it is acute (less than three months) or chronic (more than three months). Acute constipation is important to rule out secondary causes, particularly colorectal cancer. If faecal impaction is suspected, enemas, suppositories, large-volume polyethylene glycol solution (PEG), stimulant laxatives, or disimpaction with sedation may be needed. In the absence of faecal impaction and other secondary causes, the acute constipation is treated similar to chronic constipation. Management of secondary constipation is customized to tackling the underlying condition. In medication-induced constipation, most often opioid-induced constipation (OIC), the first step is to withdraw the inciting medication. If opioid withdrawal is not effective, pharmaceutical advances have been made to management OIC. The recent medication for OIC, naloxegol, is an oral peripherally acting mu-opioid receptor antagonist. Naloxegol was proved to be a safe and effective management for OIC in a large randomized placebo-controlled study of OIC patients with noncancer pain [15]. Naloxegol was superior to placebo in patients unresponsive to laxatives, even at decreased doses.

### 3.1 Dietary and Lifestyle Modifications

The beginning management approach to primary chronic constipation, irrespective of the cause, comprises of diet and lifestyle modifications such as sufficient fluid and fiber intake, regular exercise, and dietary modification. Fiber is a poorly digested,

complex carbohydrate that either acts by bulking stool by drawing fluid into stool residues in the colon as a bulk laxative or undergoes partial fermentation producing short-chain fatty acids, hydrogen, methane, and carbon dioxide<sup>16</sup>. Fiber help speed up colonic transit, increases biomass, and induces changes in colonic pH and intestinal microbiome, which will affect membrane permeability and inflammation [17]. Fiber could be recognized based on solubility and fermentability. Bloating, abdominal distension, flatulence, and cramping limit the use of insoluble fibers.

### 3.2 Over-the-Counter Laxatives

Laxatives are the core of drugs therapy for long-term therapy in patients who are resistant to lifestyle or dietary modification. Common types of laxatives include stool softeners, osmotic laxatives, and stimulant laxatives. Stool softeners are considered effective for hard stool consistency and straining during defecation. Osmotic laxatives, like lactulose, polyethylene glycol (PEG), or magnesium containing laxatives, draw fluid into the colonic lumen. Stimulant laxatives, like bisacodyl, sodium picosulfate, and senna, block colonic fluid absorption, induce secretion, and accelerate colonic transit. Osmotic laxatives are much better endured than stimulant laxatives, causing less abdominal cramping and pain [18].

### 3.3 Secretagogues

Secretagogues treat constipation through modifying epithelial ion channels to encourage colonic secretion and enhance colonic transit. The two FDA-approved secretagogues that are available for the management of chronic constipation and IBS-C include lubiprostone and linaclotide. Lubiprostone is an agonist of type 2 chloride channel (ClC-2), which is present on the apical membrane of the colonic epithelium. Activation of ClC 2 results in indirect activation of Na+K+Cl<sup>-</sup> co-transport and fluid secretion into the colonic lumen[19]. Lubiprostone, a bicyclic fatty acid derivative from prostaglandin-1, also interacts with basolateral prostaglandin E4 receptors to transport cystic fibrosis transmembrane conductance regulator (CFTR) anion channels to the apical membrane, thereby further increasing colonic secretion of chloride and water.

### 3.4 Serotonergic Prokinetic Agents

Serotonin, or 5-hydroxytryptamine (5-HT), is one of the most abundant neurotransmitter in the gastrointestinal tract and made by enterochromaffin cells. 5-HT receptors are G-proteincoupled receptors that play a major role in visceral sensation and GI

motility. The first 5-HT agonists, like cisapride and tegaserod, did not have selective affinity for 5-HT<sub>3</sub> and 5-HT<sub>4</sub> receptors, resulting in cardiac arrhythmias and ischemic events resulting in withdrawal [20]. Prucalopride, a wellabsorbed, highly selective 5-HT<sub>4</sub> receptor agonist with half-life of twenty hours and limited drug-drug interactions, has been shown to substantially increase the number of spontaneous bowel movements and improve constipation-related quality of life [21]. Adverse effects of prucalopride include headache, abdominal pain, nausea, and diarrhoea; But, till now, no cardiovascular adverse effects have been reported.

### 3.5 Biofeedback Therapy for Dyssynergic Defecation

Many randomized control trials (RCT) have demonstrated biofeedback treatment to be effective in treating dyssynergic in comparison to diet and lifestyle modifications, pharmacologic therapy, placebo, or sham biofeedback.

### 3.6 Surgical Consideration for Chronic Constipation

Patients with constant chronic constipation resistant to medical therapy could be referred to a specialized center for surgical evaluation of colectomy or cecostomy. Further evaluation of gastric emptying, small bowel transit, and colonic transit should be done prior to surgery. Surgery should be done only for refractory chronic constipation with severe colonic neuropathy in the absence of gastric and small bowel motility abnormalities. All other patients with chronic constipation should be treated with a medication only, which usually needs a multidisciplinary approach for these challenging cases. Cecostomy is usually recommended in institutionalized patients with neurologic lesions [22].

### CONCLUSION

Constipation is a very common and complicated disorder, symptoms of which include more than decreased frequency of bowel movements. Over a detailed history and prospective stool diary, it is important to determine the severity and chronicity of symptoms and identify the presence of underlying secondary causes. Chronic idiopathic constipation, refractory to dietary and lifestyle changes and laxatives, should be assessed with proper testing to recognize underlying pathophysiology. Suspicion of dyssynergic defecation on a proper digital rectal examination should be verified with anorectal manometry and/or defecography and referred to centres with expertise in manometry-based biofeedback therapy. Colectomy should be reserved for patients with underlying colonic neuropathy

identified on colonic manometry. Drugs for chronic idiopathic constipation in the pipeline, whether secretagogues, serotonergic agonists, or bile acid transporter inhibitors, are considered safe and effective, promising to give doctors more therapeutic alternatives in their arsenal. It continues to be seen where these newer agents will fit in the management guideline.

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