Pathophysiology of Chronic Constipation

Subjects: Medicine, General & Internal

Contributor: Marcin Włodarczyk

Constipation is one of the major gastrointestinal disorders diagnosed in clinical practice in Western countries. Almost 20% of population suffer from this disorder, which means constipation is a substantial utilization of healthcare. Pathophysiology of constipation is complex and multifactorial, where aspects like disturbance in colonic transit, genetic predisposition, lifestyle habits, psychological distress, and many others need to be taken into consideration.

Chronic Constipation

1. Introduction

Constipation is one of the major gastrointestinal disorders diagnosed in clinical practice in Western countries. Worldwide prevalence is estimated from 12% to 19% [1][2][3]. Constipation is more frequent in North America and Europe in comparison with Asia, probably due to differences in culture, diet, or environment [2][4][5]. The definition of constipation points to a decreased number of defecations per week, as well as multiple other symptoms, such as sensation of incomplete evacuation, abdominal bloating, straining, elongated or failed attempts to defecate, hard stools, and necessity of digital disimpaction [3][6][7]. Constipation, due to its etiology, is commonly divided into two groups, primary and secondary. Primary constipation includes constipation predominant irritable bowel syndrome (IBS-C), functional constipation, slow transit constipation like myopathy, neuropathy, and functional defecation disorders. Secondary constipation may be a result of metabolic disorders (e.g., hypercalcemia), medications (e.g., calcium channel blockers or opiates), primary colonic disorders (e.g., cancer, proctitis) and neurologic disorders [3][5][8]. Constipation decreases life quality among patients, as they suffer from both physical symptoms and psychological distress. Many patients with constipation complain about dyspareunia, sexual dysfunction, and urine retention. Chronic constipation limits work productivity and social activities [4][5][9]. Diagnosing and treating constipation has a significant impact on economic burden, according to Sbahi et al. only testing for constipation costs almost $7 billion annually [4]. Commonness of this disorder, costs of medical care, and decrease in quality life cause constipation a serious issue for many specialists. The aim of this review is updating knowledge of chronic constipation and management in this disorder.

2. Pathophysiology of Chronic Constipation

The patients with chronic constipation may be divided into three groups according to the colonic transit [10]. Patients with normal colonic transit suffer from functional constipation, they are the most predominant subgroup. The second group consists of patients with rectal evacuation disorders, especially patients with dyssynergic

defecation [11]. Dyssynergic defecation, also known as anismus, obstructive defecation, pelvic floor dyssynergia, or outlet obstruction, is a result of incoordination between the abdominal wall and pelvic floor muscles, and the anal sphincters [10][11]. This incoordination may be a result of several mechanisms that include paradoxical anal contraction, impaired rectal contraction and inadequate anal relaxation. The least common type of chronic constipation is slow colonic constipation. Patients from this group usually present with dysfunctional retrograde colonic propulsion or postprandial motor activity. Pathophysiology of constipation is multifactorial, thereby it is problematic to match exact factor to one of the above groups.Positive family history of constipation and genetic predisposition seem to have a role in this disorder, since patients with functional constipation commonly have a positive family history, however there are no specific genes related to constipation.Diet is one of the most relevant factors of constipation. Insufficient fiber or fluid intake results in constipation in all age groups [6][12]. Murray et al. reported that 19% of their patients who were suffering from chronic constipation, were also diagnosed with eating disorders, therefore it should always be taken into consideration during diagnosis [13][14]. Moreover, many reviews, especially focused on cow's milk allergies in children, proved improvement in functional disorders after resignation from cow's milk.Another major factor of constipation is the lack of exercise. Inactivity may lead to obesity, what is yet another, commonly considered factor of constipation, nevertheless data about obesity and constipation are ambiguous [15][16].Clinicians also consider a connection between dysbiosis of gut microbiota and constipation. IBS-C patients have a decreased number of Actinobacteria in fecal samples and increased level of Bacteroides in their mucosal samples, also treatment with the use of synbiotics, probiotics, prebiotics, antibiotics, and fecal microbiota transplantation improves condition of patients with constipation. Moreover, in contrary to patients with normal transit, patients with chronic constipation presented methanogenic bacteria producing more methane, which slows colonic transit. This is a compelling evidence of the impact of dysbiosis on constipation [17][18][19]. As a consequence of growing popularity of probiotics, some patients use Bifidobacterium or Lactobacillus. Nevertheless, in some trials, probiotics are still as efficient as placebo [5][10][20]. What is more, Yarullina et al. recently reported a lack of motor activity disturbance or dysbiosis in chronic constipation, challenging previous theories and compromising the efficacy of conventional probiotic treatment. However, their study was based only on 20 patients, which means that additional experiments of this matter are needed [21].Efficient bowel movement depends on nerve endings of sensory neurons which react to the content of the intestine. Patients with constipation are frequently observed with colonic motor dysfunction, abnormal colonic sensation, and impaired defecation. The high-amplitude propagating contractions, that transfer content of the colon for the long distance, occur less frequently in patients with constipation [1][6][22][23]. Neuropathy and myopathy seem to be the most important causes of delayed colonic transfer. However, patients with neuropathy rarely receive satisfying treatment, whereas treatment of myopathic constipation is usually successful [5].Studies prove connection between constipation and psychological factors: constipation is more common in children with attention deficit disorders and autism, and constipated patients are more often observed with anxiety, stress, trauma, and depression [6][24][25][26]. In addition, experience acquired while toilet training in infancy, or even earlier, has a strong impact on developing chronic constipation in the future. Some toddlers hide during defecating—this behavior may be a consequence of parental reactions to feces and its negative connotation in their culture. Due to that, children may feel ashamed or embarrassed, thus the usage of a toilet or potty is more complicated for them later. Children who were hiding during the defecation are in high risk of developing later toilet training and constipation [27].Some patients with unpleasant associations of defecation, e.g.,

pain or social reasons try to avoid it through withholding the stool. That results in absorbing water by colonic mucosa from feces and leads to hard stools, what complicates the evacuation. Consequently, patients lose their regular urge to defecate [28]. Moreover, patients with normal colonic transit may develop symptoms of severe constipation, as a consequence of increased psychological distress [29].Constipation is also associated with age and female sex [2][30]. Polypharmacy, inadequate fiber or fluid intake, life situations disturbing regular bowel movements, and decreased physical activity may also increase prevalence of chronic constipation in elderly people. Moreover, sexual hormones during pregnancy slow down peristalsis, and also females are at high risk of injury of the pelvic floor during labor [2][3][5][8].Recently, more and more studies concerning chronic constipation focus on serotonin and its signaling role in the gut. Possible mechanisms involve a decrease in the number of Cajal cells or disruptions in the serotonin level. However, in the case of the latter it is still unclear whether the exact cause is in a decreased number of receptors and their function, or a decreased availability of serotonin at the receptors [31]. Nevertheless the serotonin signaling pathway is a target for multiple drugs used in the constipation treatment.Other possible mechanisms of constipation involve influence of proto-oncogenes, overexpression of progesterone receptors, infectious agents, autoimmunity, and tyrosine kinase C [31].

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