Chronic Constipation Management in Adults

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Abstract: Constipation is a symptom characterized by defecation frequency less than three times a week or fecal impaction. Chronic constipation is characterized by a sense of rectal dissatisfaction, bowel movement difficulty, or both. This literature review will explain the latest pathophysiology of constipation, diagnosis based on international clinical criteria (ROME III), and national consensus of the Indonesian Society of Gastroenterology, as well as the selection of evidence-based therapy. Factors causing chronic constipation include mechanical, metabolic, neuropathic, myopathic and idiopathic. Diagnosis needs to be systematically evaluated from anamnesis, identification of alarm symptoms, physical examination and investigation. Management of chronic constipation depends on the type of constipation. It is performed comprehensively to restore normal physiological defecation function and evaluate constipation causes. Constipation treatment may be pharmacological and non-pharmacological. Constipation complications include pelvic organ prolapse, hemorrhoids, hemorrhoid bleeding, fissure ani, fecal impaction causing colonic or stercoraceous ulcer obstruction, resulting in bleeding/perforation and recurrent urinary tract infections due to ureter compression due to stool mass.

1 INTRODUCTION

Constipation is a chronic gastrointestinal problem affecting a patient's quality of life (McCrea et al., 2009; Sanchez and Bercik, 2011). The current pathophysiological mechanism shows a paradigm shift from idiopathic or functional to colonic neuropathology. Constipation by time is divided into acute less than 3 months and chronic constipation more than 3 months. This division is based on functional impairment of colon and anorectal function (Shah et al., 2008). The natural course of constipation has not been fully understood yet (Bharucha et al., 2013).

Constipation incidence increases with the development of gastrointestinal motility diagnostics. A randomized cohort study from Olmsted Country, USA evaluated 4,176 subjects and reported an overall constipation prevalence of about 16% (Chang et al., 2010). Colonoscopy data of Cipto Mangunkusumo Hospital, Jakarta, Indonesia in 1998-2005 showed that around 216 or 9% out of 2,397 patients, were indicated as having constipation. Constipation prevalence in Asia, including South Korea, China, and Indonesia, is estimated to occur 15-23% in women and about 11% in men (Thomsen, 2010).

The lack of pathophysiological knowledge becomes a major problem in constipation management. Instead of mechanical etiology, most societies consider chronic constipation a functional or idiopathic problem, including problems in the enteric nervous system. Constipation management needs thorough evaluation by anamnesis, physical examination and physiological tests (Gwee et al., 2013). This literature review will explain the latest constipation pathophysiology and diagnosis based on international clinical criteria (ROME III), national consensus of the Indonesian Society of Gastroenterology and the selection of evidence-based therapy.

2 DEFINITION

According to the American College of

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Gastroenterology, constipation is rectal dissatisfaction characterized by infrequent bowel movements of less than three times in 1 week, difficulty in passing stools, or a combination of both. The definition of constipation based on the World Gastroenterology Organization 2007 practice guidelines distinguishes constipation based on symptoms experienced by patients and clinical evaluation. The constipation criteria based on clinical judgment are divided into functional constipation and Irritable Bowel Syndrome (IBS) constipation according to ROME III criteria as shown in Table 1 (Longstreth et al., 2006; Sanchez and Bercik, 2011).

Table 1: Functional constipation based on ROME III (Longstreth et al., 2006)

Minimum three months of complaint (minimum six months of complaint)
Fulfilling minimum two criteria below: (minimum 25% of defecation process)
Straining
Lumpy stools
Unsatisfied feeling
Anorectal dysfunction
Manual maneuver to assist defecation (using fingers, support of pelvic floor muscle)
<3 bowel movements per week
Laxative use
Fulfilling IBS criteria

IBS is a recurrent pain or discomfort in the abdomen for at least 3 days per month in the last 3 months, and it is associated with two or more of improved defecation, onset associated with changes in bowel movement frequency, and onset associated with changes in stool shape. The symptoms occur during the last 3 months with symptom onset at least 6 months before the diagnosis (Camilleri, 2015).

3 RISK FACTORS

Factors causing chronic constipation include mechanical, metabolic, neuropathic, myopathic and idiopathic (functional). Mechanical causes can be detected through colonoscopy, such as tumors, intestinal strictures, anal fissures and intussusception. Metabolic causes include hypothyroidism, diabetes mellitus, hypercalcemia, hypokalemia and uremia. In addition, women, elderly, elderly pregnant women, lack of physical activity, low-calorie and fiber diet, low socioeconomic status, polypharmacy, physical and sexual violence, terminal stage, traveling, history of chronic constipation, psychological disorders and colonic inertia contribute to chronic constipation (Thomsen, 2010; Jamshed et al., 2011).

4 TYPES OF CONSTIPATION

Constipation by time is divided into acute constipation and chronic constipation. Furthermore, chronic constipation is divided into functional (primary) and secondary. Functional constipation, based on ROME III, is further classified into normal-transit constipation, slow-transit constipation and anorectal dysfunction or defecation (Basilisco and Coletta, 2013).

4.1 Acute constipation

Acute constipation has similar symptoms to chronic constipation, but with less than 3 months of complaint. This type of constipation is temporary due to psychological changes, dietary patterns, routine activities, opioid side-effects, postoperative, immobilization, colonic stricture and fecal impaction. Acute constipation is often asymptomatic without specific treatment (Rao SSC, 2016).

4.2 Chronic constipation

Chronic constipation is divided into primary and secondary. Primary constipation is further classified into normal-transit constipation, slow-transit constipation and anorectal dysfunction. No organic and biochemical abnormality is found in primary constipation. Factors affecting primary constipation are diet, impaired colonic motility, impaired absorption, motor anorectal, sensory function and psychological factors. The symptoms of primary constipation arise from the dysfunction between colonic regulation and stool movement, as well as the lack of anorectal neuromuscular coordination (Ghoshal, 2008).

Secondary chronic constipation generally has organic abnormalities or other conditions as the basic foundation. The causes of secondary chronic constipation include extrinsic factors, mechanical obstruction, metabolic abnormalities, myopathy, neuropathy and conditions inhibiting the digestive tract (Wald, 2003; Thomsen, 2010). On the other hand, factors influencing secondary constipation are anatomical abnormalities (anorectal, colon disease), diet, drugs (opioids), metabolic disorders and Parkinson's disease (Basilisco and Coletta, 2013).

4.3 Slow-transit constipation

This constipation is due to smooth colon's muscle activity dysfunction, neurotransmitter, impaired cell activity in the colon and colon reflex dysfunction that subsequently slow intestinal contraction. In addition, there is a decrease in colon motor activity, impaired gastrocolic reflex and decreased sleep-wake motor activity. These disorders will increase retrograde propulsion and nocturnal rectosigmoid motoric activity periodically that result in a deceleration of colonic propulsion process from the feces (Basilisco and Coletta, 2013).

Table 2: Possible disorders causing chronic constipation (Thomsen, 2010)

Extrinsic	Mechanical obstruction	Metabolic condition
Lack of fiber or water	Colon cancer	Diabetes mellitus
Intestinal flora imbalance	External compression of malignant lesions	Hypothyroidism
Ignoring urge to defecate	Stricture: diverticular/post-ischemic	Hypercalcemia
	Rectocele (if large)	Hypokalemia
	Postoperative abnormalities	Hypomagnesemia
	Megacolon	Uremia
	Anal fissure	Heavy metal poisoning
Myopathy	Other conditions	Neuropathy
Amyloidosis	Depression	Parkinson's disease
Scleroderma	Degenerative joint disease	Spinal cord or tumor trauma
	Autonomic neuropathy	Cerebrovascular disease
	Cognitive impairment	Multiple sclerosis
	Immobility	Aganglionosis (Hirschsprung's disease)

Several studies have demonstrated a quantitative decrease in interstitial cells of Cajal (Wang et al., 2008) and changes in the number of neurons in the myenteric plexus (Yik et al., 2011). The London classification reported hypoganglionosis, neuropathy inflammation, and degenerative leiomyopathy as some causes of slow-transit constipation (Knowles et al., 2010). The symptoms include the absence of contraction during defecation, abdominal discomfort, bloating and defecation frequency less than once per week. This type of constipation is most prevalent in young women, and causes colonic inertia complications. Management of slow-transit constipation includes aggressive laxatives, colectomy and ileorectal anastomosis (Wang et al., 2008; Meurette et al., 2010).

4.4 Anorectal dysfunction

Anorectal dysfunction is characterized by functional anorectal abnormalities and anorectal anatomy characterized by resistance during defecation, long time to defecate, requiring digital maneuvers for fecal evacuation and obstructive defecation of liquid stools. Anorectal dysfunction is caused by dyssynergia, rectal intussusception or prolapse, rectocele and descending perineum syndrome. Patients with dyssynergia cannot coordinate their pelvic floor muscles, abdominal muscles and recto-anal during defecation, resulting in hyposensitivity in the rectum (Rao, 2008; Basilisco and Coletta, 2013).

Anorectal dysfunction can be in the form of anorectal motor disturbance and sensory function, namely, a failure of external anal sphincter-puborectalis relaxation when attempting defecation also known as anismus; a hypertonic internal anal sphincter; inadequate rectal propulsion; rectal hyposensitivity and hypotonicity; anatomical anorectal alterations (large rectoceles/prolapse rectum); excessive perineal descent perineum; and the uncoupling of the sensory component or the urge to defecate and the normal pre-defecatory motor activity of the colon (Basilisco and Coletta, 2013).

5 DIAGNOSIS AND EVALUATION

Systematic evaluations, including anamnesis, alarm symptom identification, physical examination and supportive evaluation, are needed for diagnosis (Thomsen, 2010).

5.1 Anamnesis

Initial anamnesis evaluates dietary fiber adequacy, fluid intake of at least 2 liters/24 hours and physical activity or exercise. Afterwards, it evaluates the

onset and duration of constipation symptoms, constipation characteristics including frequency, rectal sensation, obstructive defecation, accompanying gastrointestinal symptoms, comorbidities, drug use, immobilization, excessive stroke, use of digital maneuvers and stool consistency assessment based on the Bristol scale to predict the transit time (Leung et al., 2011).

The alarm symptom signs in constipation include hematochezia, abdominal mass, a history of colorectal malignancy, family history of irritable bowel disease, significant weight loss, anorexia, chronic nausea and vomiting, first constipation and continues worsening, acute constipation in elderly and unidentified cause of anemia. Colonoscopy examination should be considered upon an alarm symptom sign (Thomsen, 2010).

5.2 Physical examination

Physical examination is systemically performed, starting with vital signs, nutritional status, abdominal examination, anorectal examination and neurological evaluation. The abdomen examination includes inspection of scar tissue, abdominal distension, palpation-percussion of abdominal mass, abdominal acute signs and auscultation in bowel sounds. Anorectal examination is conducted by inserting the index finger into the rectum to evaluate sphincter muscle condition, fecal presence and anorectal abnormalities such as stricture, hematoma, hemorrhoids, rectal prolapse, and tumor. Gynecological examination removes cysts or vaginal/uterus prolapse. Neurological examination is also necessary (Thomsen, 2010; Leung et al., 2011).

Supportive evaluation to establish constipation diagnosis is conducted based on indications and needs, including (1) Laboratory: complete blood, glucose, creatinine, calcium, thyroid hormone, serum electrolytes, complete urine and fecal analysis. (2) Endoscopy: sigmoidoscopy and colonoscopy for identifications of narrowed lesion, intestinal obstruction and tissue retrieval for biopsy. Colonoscopy indications include 50-year-old patients without colon cancer screening, with symptom alarm, or history of surgery with constipation complaint. (3) Radiology: plain abdominal images, barium enema, CT colonography, to detect fecal retention in the colon, megacolon and aganglionic abnormalities. (4) Colorectal physiological examination with a colonic transit test if there is a rare complaint of chronic and refractory deficiency against laxative therapy. Colonic transit time is the time for a stool to pass through the colon. Methods used include the study of radiopaque markers or scintigraphy for measuring colonic transit quantitatively. (5) Wireless motility capsules (WMCs) assess regional abnormalities including gastric emptying, transit time in the small intestine, measure colonic transit, or whole gut transit time. It is conducted when there are refractory complaints concerning laxatives. WMCs have a sensitivity and specificity comparable to radiopaque marker examination or scintigraphy. WMCs are tolerated well, do not use contrast, have good patient compliance rates and avoid the risk of exposure to radiation, but are expensive. (6) Defecography can detect anatomical and functional anorectal abnormalities such as enterocele and intussusception. Its shortcomings are that it is difficult to perform in elderly with motility issues since the patient is embarrassed, dependent on the operator and less reliable. (7) Motility examination is in the form of anorectal manometry, colon manometry and balloon expulsion tests. Anorectal manometry can assess the function of the anal sphincter and pelvic floor reflex at rest and defecation, so it can diagnose dyssynergia during bowel movements. Colon manometry can evaluate intraluminal colon-rectum pressure activity, motor motility of colonic motility. (8) Another test is a barostat test for detecting anal hyposensitivity but is not routinely performed (Thomsen, 2010; Leung et al., 2011; Bharucha et al., 2013).

6 MANAGEMENT

Management of chronic constipation depends on the type of constipation. It is performed comprehensively to restore normal physiological defecation function and evaluate the cause of constipation. Constipation treatment may be pharmacological or non-pharmacological including lifestyle modification and surgery. Treatment may be given if there is no symptom alarm, age <40 years, no abnormalities during rectal examination and no secondary etiology (Thomsen, 2010).

6.1 Non-pharmacological

Non-pharmacologic management of chronic constipation includes lifestyle modification with constipation education, dietary changes by increasing the consumption of high-fiber foods about 20-35 grams/day and drinking enough water at least 30-50 cc/kgBW/day for adult patients with normal activity, consuming probiotics

(*Bifidobacterium sp.*), increasing physical activity, regulating defecation habit such as avoiding straining, familiarizing defecation after meals to train post-prandial bowel movement reflexes, and avoiding drugs that cause constipation (Bharucha et al., 2013; Sbahi and Cash, 2015).

6.2 Pharmacological

Pharmacological therapy may be laxative and non-laxative. Laxative therapy includes bulk laxatives such as psyllium, plantago ovata, and methyl cellulose; osmotic laxatives such as saline laxatives, magnesium hydroxide, sodium phosphate; absorbed disaccharide such as lactulose, sugar alcohol (sorbitol, mannitol, and polyethylene glycol), stimulant laxatives such as bisacodyl, castor oil, sodium picosulfate, and stool softener: dioctyl sodium sulfosuccinate; rectal enemas/suppositories such as bisacodyl, enema phosphate; and intestinal secretagogues such as lubiprostone, linaclotide, and plecanatide.

Meanwhile, non-laxative treatments include prokinetics, bacteriotherapy or probiotics (lactobacillus and *Bifidobacterium sp*), and traditional therapy (Ford and Suares, 2011; Wald, 2016). Further explanation is presented in Table 3.

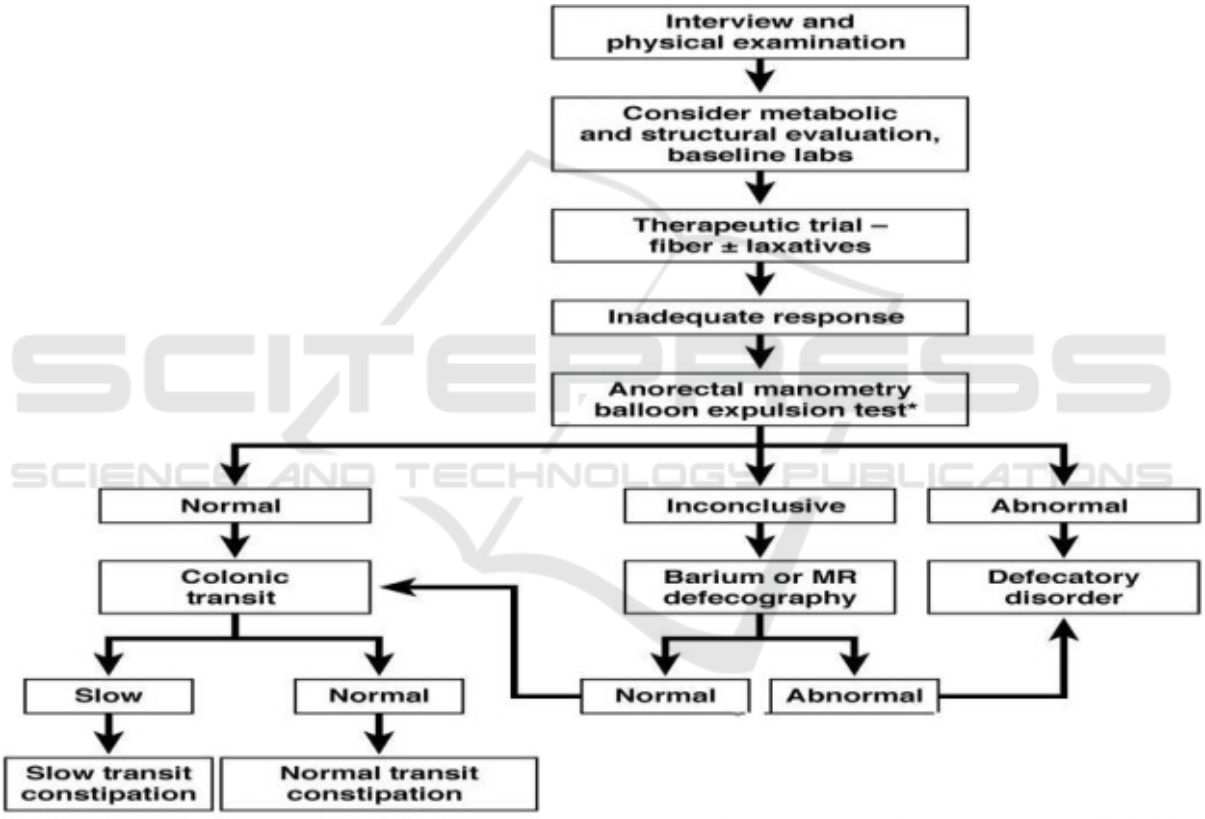

Figure 1: Constipation Diagnosis Algorithm (Bharucha et al., 2013)

Management of opioid-induced constipation has been growing because of increased use of opioids. The gastrointestinal effects of opioids may delay gastrointestinal transit times, stimulate non-propulsion motor activity, intestinal segmentation and increased tonus, increase fluid absorption by prolonging absorption time, and decrease electrolyte and water secretion into the intestinal lumen. This opioid effect works through three receptors, namely μ, κ, and δ. The main opioid mediation through μ receptors is found in the gut and central nervous system (Chey et al., 2014). Constipation therapy using opioid induction includes methylnaltrexone, alvimopan, and naloxegol (Siemens et al., 2015). Constipation management with a slow or normal transit time may be given a combination of stimulant and prokinetic laxative therapy (Bharucha et al., 2013).

6.3 Surgery

Surgical therapy is performed when neither a general therapy nor pharmacology response results. Surgical therapy includes colectomy and ileorectostomy. Subtotal colectomy with ileorectal anastomosis may improve chronic constipation complaints. The indication for subtotal colectomy is severe chronic constipation and does not respond to general or pharmacologic therapy; slow-transit constipation type of intestinal; no intestinal pseudo-obstruction; no pelvic floor dysfunction; no symptoms of dominant abdominal pain (Meurette et al., 2010; Sharma and Rao, 2017). Surgery is indicated if there are rectocele, intussusception and Hirschsprung, but persistent constipation symptoms (Sharma and Rao, 2017).

6.4 Biofeedback

Biofeedback is a form of constipation management to train the patient to perform pelvic floor muscle relaxation during straining to restore normal defecation function. This exercise is noninvasive. Biofeedback may be given to constipation patients as well as with fecal incontinence. Biofeedback has been shown to improve rectal coordination during the defecation process and reduce constipation symptoms (Sbahi and Cash, 2015).

7 COMPLICATIONS

Constipation complications include alvi incontinence, organ pelvic organ prolapse, hemorrhoids, hemorrhoid bleeding, fissure ani, fecal impaction causing colonic or stercoraceous ulcer obstruction resulting in bleeding/perforation, and recurrent urinary tract infections due to ureteric compression due to stool mass (Thomsen, 2010;

Table 3: List of Pharmacological Laxative Therapies (Ramkumar and Rao, 2005).

Laxative Class	Medications	Dosage	Time to onset of action (h)	Adverse effects	Mechanism of action
Bulk (fiber) Laxatives	Psyllium	1 tsp up to 3 times daily 2-4 tablets once daily	-	Flatulence, bloating, abdominal distension; rarely causing mechanical obstruction of esophagus and colon	Retaining water in stools, increasing stool bulk and improving consistency
	calcium polycarbophil	1 tsp up to 3 times daily 1 cup/day	- -		
	methylcellulose bran		-		
Stool softeners Or wetting Agents	Docusate sodium	100 mg twice daily	12-72	Intestinal cramping; irritation of throat (liquid formulation)	Promoting luminal water binding by detergent-like action, increasing stool bulk
	Sorbitol	15-30 ml once daily or twice daily.	24-48		
	Lactulose	15-30 mL once daily or twice daily	24-48		
	PEG	8-32 oz once daily	0.5-1		
Stimulant laxatives	Glycerin	Suppository, up to once daily 10 mg, suppositories or 5-10 mg orally up to 3 times/wk	0.25-1	Abdominal discomfort, rarely electrolyte disturbance, melanosis coli	Increasing intestinal peristalsis by acting on the myenteric nerve plexus, decreasing large intestinal water absorption
	Bisacodyl		0.25-1		
	Picosulfate anthraquinones Senokot	2 tablets once daily to 4 tablets twice daily.	8-12		
	Perdiem	1-2 tsp	8-12		
	Peri-colace	1-2 tablets once daily	8-12		
Saline laxatives	Magnesium	15-30 mL once daily or twice daily	1-3	Bloating, flatulence, abdominal cramping; in rare instances, electrolyte disturbance	Osmotic water binding
Enemas	Mineral oil retention	199-250 mL once daily	6-8		
	Tap water	500 Ml	5-15 min		
	Phosphate soapsuds	1 unit 1500 Ml	5-15 min 2-15 min		
Mixed laxatives	Dried plums			Flatulence, bloating	Stool bulking and osmotic action

(Leung et al., 2011).

8 CONCLUSION

Constipation is often found in everyday practice in all age groups, resulting in inhibiting activity. Constipation is a symptom characterized by defecation frequency less than three times a week or fecal impaction. Chronic constipation is characterized by a sense of rectal dissatisfaction, bowel movement difficulty, or both. The definition of constipation is based on ROME III, and clinicians should ensure adequate fluid intake, a high-fiber diet and adequate physical activity prior to management.

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