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Reviewed and approved by specialists at IWK Health, NS, and the Janeway Children's Health and Rehabilitation Centre, NL

Clinical Practice Guideline on the Prevention and Management of Constipation in Children with Cancer

APPHON/ROHPPA supportive care guidelines have been developed by appropriate Atlantic Provinces health professional specialists (physicians, pharmacists, nurses and other health professionals) using evidence-based or best practice references. Format and content of the guidelines will change as they are reviewed and revised on a periodic basis. Care has been taken to ensure accuracy of the information. However, any physician or health professional using these guidelines will be responsible for verifying doses and administering medications and care according to their own institutional formularies and policies and acceptable standards of care.

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BACKGROUND:

There is a paucity of studies addressing the issue of constipation in children on chemotherapy. Approximately 60% of children experience clinical constipation while receiving chemotherapy for cancer. In a recent survey conducted in children with cancer, 43% of parents reported constipation as a major/significant problem (Pashankar, 2011). Several chemotherapy agents can cause constipation, but the combined use of vincristine and opiates is associated with high incidence of constipation. As vincristine is a chemotherapy agent used frequently in most types of cancers, many children receive this agent repeatedly throughout their treatment. Also, many children receive opiates for pain throughout their treatment. Multiple other factors may contribute to constipation in these patients, including abdominal surgery, altered diet, altered routines, and physical environment including privacy. It is therefore not surprising that a large number of children receiving cancer treatment experience constipation. After several days without a bowel movement, patients may experience abdominal distention with cramps and become irritable. Untreated constipation can lead to complications including hemorrhoids, anal fissures, paralytic ileus, peritonitis, fecal impaction, and life-threatening conditions of bowel obstruction, perforation and sepsis (Philips, 2008).

Constipation can be a significant problem that decreases quality of life of children with cancer and requires pre-emptive and prompt management.

DEFINITION OF CONSTIPATION:

Normal bowel movements range from 3 times a week to 3 times a day of formed stool. Changes in individual bowel frequency may be indicative of constipation (Tabbers, 2014).

Acute Constipation:

The North *American Society of Pediatric Gastroenterology, Hepatology, and Nutrition* (NASPGHAN) criteria. Constipation is defined as a delay or difficulty in defecation for 2 or more weeks and sufficient to cause significant distress to the patient. This may include harder, smaller stool, less frequent stooling, straining, etc.

Chronic Constipation:

The Rome III Functional Constipation Diagnostic criteria:

Diagnostic criteria must include one month of at least two of the following or two or fewer defecations per week in infants up to 4 years of age:

- At least one episode/week of incontinence after the acquisition of toileting skills.
- History of excessive stool retention.
- History of painful or hard bowel movements.
- Presence of a large fecal mass in the rectum.
- History of large-diameter stools which may obstruct the toilet.
- Accompanying symptoms may include irritability, decreased appetite, and/or early satiety. The accompanying symptoms disappear immediately following passage of a large stool

Diagnostic criteria* must include two or more of the following in a child with a developmental age of at least 4 years with insufficient criteria for diagnosis of IBS:

- Two or fewer defecations in the toilet per week.
- At least one episode of fecal incontinence per week.
- History of retentive posturing or excessive volitional stool retention.
- History of painful or hard bowel movements.
- Presence of a large fecal mass in the rectum.
- History of large-diameter stools which may obstruct the toilet.

* Criteria fulfilled at least once per week for at least 2 months prior to diagnosis

Causes of Constipation in Children with Cancer are Multifactorial and include:

- Drugs: Opioids, chemotherapy, phenothiazines, anticholinergics, antacids (aluminium, calcium), calcium channel blockers, tricyclic antidepressants, diuretics, antiemetics (ondansetron, aprepitant), vinca alkaloids (can slow GI transit time)
- Metabolic – hypothyroid, hypokalemia, hypophosphatemia, hypercalcemia, hypomagnesaemia
- Change in eating habits and decreased appetite
- Lack of exercise
- Stress
- Decreased fiber and fluid in diet
- Decreased motility
- Ileus – acute illness, electrolyte abnormality
- Mechanical obstruction – tumour, rectocele, hernia, adhesions
- Autonomic dysfunction – longstanding diabetes, renal failure, advanced cancer
- Spinal cord compression

MANAGEMENT:

Goals: Achievement of normal prediagnosis pattern or minimum of a soft formed bowel movement every 2 to 3 days. Protect integrity of rectal mucosa, especially in leukopenic or thrombocytopenic patients.

Rectal manipulations such as enemas and suppositories are contraindicated in patients with abnormal blood counts. They are discouraged for those on chemotherapy and/or with central lines even when counts are good.

All Healthcare professionals should be mindful of the signs and symptoms of constipation in children with cancer and start management immediately to prevent long-term complications.

An abdominal X-ray is not routinely done but may be required to confirm the extent of the fecal impaction.

Non-pharmacological Treatment:

- Ensure privacy for those who need it.
- Scheduled toileting: same time each day, ideally after meals.
- Position: try to get onto commode or at least sitting up with knees above level of pelvis (use a chair/bench if necessary). Provide smaller commode or toilet seat for

pre-school aged children with suitable arm support to hold on to.

- Encourage fluid intake, regular meals, daily exercise, respond to urge to move bowels, avoid straining.
- Add fiber to diet. The American Health Foundation (AHF) recommends a goal for minimal intake of dietary fiber for children and adolescents based on age. For patients aged 3- 20 years, the target amount is the age of the child plus 5 grams of dietary fiber. The American Academy of Pediatrics (AAP) recommends a daily dietary fiber intake of 0.5g/kg body weight per day, up to a maximum of age plus 10 g/day. The maximum recommended is 35 g/day after age 20 years. Increasing to or above the normal requirements should be done slowly to prevent cramping and fluid should be given with the fiber. Acceptable sources of fiber include fruit, vegetables, prune juice (can mix with orange juice to increase palatability or use strained prunes for babies).
- Avoid bulk agents like bran since 1) normalizes stool but not a good laxative, 2) need to use with a lot of water, 3) in debilitated patients, may precipitate obstruction by forming a viscous mass.

Pharmacological Treatment:

Do not use if suspect bowel obstruction.

NOTE: All children receiving Vincristine and/or an opiate should be prescribed an osmotic laxative prophylactically. Do not wait for a presentation of constipation.

Prophylactic Bowel Regimen:

a) Osmotic laxative daily with increased dose if no results.
b) Stimulant laxative if no bowel movement after 3 days while receiving osmotic laxative.
c) Continue osmotic laxative in addition to stimulant.

Opioids decrease the peristaltic contractions of the bowel and increase water absorption, causing stool to become excessively dehydrated. Patients may also experience an increase in anal sphincter tone and a decreased sensation to defecate, which can contribute to constipation. It is important to prevent constipation from occurring by prescribing a laxative early in the course of treatment with an opioid.

There are no published pediatric guidelines for the treatment of opioid-induced constipation. As such, clinicians may defer to the guidelines for the management of constipation in children recommendations of the North American Society of Pediatric Gastroenterology, hepatology, and nutrition 2014 (Tabbers, 2014). These guidelines recommend osmotic laxatives for the initial treatment of functional constipation in children, with the addition of stimulants for children with more resistant constipation.

Table I. Medications Recommended for the Treatment and Prevention of Chronic Constipation in Children

Type of Laxative	Medication
Osmotic Laxatives:	• Polyethylene glycol 3350 • Lactulose
Stimulant Laxatives:	• Bisacodyl • Senna • Pico-Salax (osmotic)

Osmotic laxatives *– draw water into the bowel lumen which increases bulk and stimulates peristalsis.*

Polyethylene Glycol (PEG 3350 NF granular): Give with adequate oral fluid

- Dose (infants and children older than 6 months):
  - Initial dose 0.4-1.5 grams/kg/24h PO once daily to BID
  - Some authors recommend a starting dose of 1gram/kg/24h
  - Typical max dose 17 grams/day, but can titrate beyond this if needed (but consider adding stimulant laxative if > 17 grams/day required)
- Dose (children more than 20 kg and adults):
  - Initial dose 17 grams/dose (1 heaping tablespoonful) PO once daily
  - Typical max dose 17 grams BID, but can titrate beyond this if needed (but consider adding stimulant laxative if > 17 grams BID required)

Lactulose Liquid 667 mg/mL:

- Dose (children):
  - 5-10 mL/day – double the daily dose until stool is produced
  - Given orally once daily to QID; (usually greater than 60 mL/day not required)
- Onset – 1 to 2 days; mix with water, milk or juice to improve flavour
- May increase as required to achieve desired bowel motion frequency (maximum 60 mL/day)
- Not effective in opioid induced constipation

Stimulant laxatives – *irritate the bowel and increase peristaltic activity by stimulating myenteric plexus.*

Bisacodyl (Dulcolax®):

- Dose (children):
  - 3-12 yr: 5-10 mg or 0.3 mg/kg/dose PO once daily
- Dose (adults):
  - 5-15 mg/day PO once daily (maximum daily dose 30 mg PO)
  - Onset – 6 to 10 hours
- Enteric coated tablets must be swallowed whole and not crushed or chewed (to avoid gastric irritation)
- Do not take within one hour of antacids or milk.
- Contraindicated in patients with intestinal obstruction.

Senna (8.8 mg/ 5 mL syrup and 8.6 mg tablet):

- Dose (children):
  - syrup: 1 month to 1 year: 1.25-2.5 mL at bedtime (maximum 5 mL/day)
  - 1-5 years: 2.5-5 mL at bedtime (maximum 10 mL/day)
  - 5-15 years: 5-10 mL at bedtime (maximum 20 mL/day)
  - Tablet: Over 27 kg: 1 tablet at bedtime (maximum 2 tablets twice daily)
- Dose (adolescents and adults):
  - syrup: 10-15 mL at bedtime (maximum 15 mL twice daily)
  - tablet: 2 tablets at bedtime (maximum 4 tablets twice daily)

If other treatments are not effective, in consultation with pediatric oncology/hematology or pediatric gastroenterology, may recommend:

Pico-Salax (sodium picosulfate, magnesium oxide and citric acid): Picosulfate (a pro-drug) is an osmotic/stimulant laxative active locally in the colon.

1-6 years: ¼ sachet
6-12 years: ½ sachet
12 years-adult: 1 sachet
Give each dose with at least 150 mL of water.
May repeat dose in 6-8 hours (avoid 6 hours prior to bedtime) and give for 2 days maximum. If no result, investigation for obstruction and ileus should be considered.

Management of Refractory Opioid Induced Constipation:

Opioids act on the central mu, delta, and kappa opioid receptors. They also act on the mu receptors located on the gastrointestinal tract smooth muscle, which can hinder gastrointestinal motility, resulting in constipation.

Methylnaltrexone (brand name Relistor) is an opioid receptor antagonist that can reverse opioid induced constipation without affecting analgesia. It exhibits inhibition of the peripheral mu receptors that are present in the gastrointestinal tract.

For patients who are receiving an opiate and receiving optimal doses of combined osomotic and stimulant laxatives for at least 3 days without a bowel movement, methynaltrexone may be recommended.

Methylnaltrexone is safe and effective when given subcutaneously as a single dose to children with cancer with opioid induced constipation. The dose can be repeated in 3 days if no response seen. Consult pediatric oncologist to discuss more frequent dosing if required.

Table II. Approved Methylnaltrexone Dosing for Patients as per Product Monograph[8]

Patient weight (kg)	Subcutaneous Dose
< 33	0.15 mg/kg
33 - < 38	6 mg
38 - < 62	8 mg
62-114	12 mg
115-126	18 mg
> 126	0.15 mg/kg

DEVELOPMENT AND REVIEW:

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External Review (anonymous):

An anonymous external review of this guideline was conducted throughout Atlantic Canada by APPHON/ROHPPA. Twenty-two health care professionals responded to the external review, including hematologists/oncologists, nurse manager ED, registered nurses, pediatricians, pharmacists and other health care professionals. One review was a multi-disciplinary team response.

The guideline was reviewed again in 2026 with minimal updates and was approved by a multi-disciplinary team including experts in gastroenterology and oncology.

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