Treatment of constipation in older people

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The prevalence of constipation rises dramatically with age, with some estimates approaching 50% among adults over 80 years of age. Up to 40% of seniors living in the community and 60% of those in institutions are affected. Lower socioeconomic class, non-white race, regular medication use, female sex, and symptoms of anxiety and depression have all been associated with increased prevalence of constipation among older people.

Consequences of constipation can be substantial. In susceptible older people who are frail, excessive straining can trigger a syncopal episode, or coronary or cerebral ischemia. Less acutely, constipation leading to fecal impaction can present with anorexia, nausea and pain associated with functional decline. Case reports have identified stercoral ulceration, perforation and death as consequences of fecal impaction. Quality of life also appears to be lower for older people with than without constipation, and long-term care facilities incur high costs managing the problem, estimated at US$2253 per year per resident.

Given the growing proportion of older adults in North America, effective management of constipation by health care professionals will be increasingly necessary. Randomized controlled trials (RCTs), mostly categorized as lower quality with some higher quality trials, exist for the treatment of constipation in older people. New agents, with different mechanisms of action, have been developed. In this article, we review the efficacy and safety of treatments for constipation in older people. A summary of the evidence used in this review is found in Box 1.

How is constipation defined?

Any complaint of difficulty passing stool, incomplete passage of stool or diminished frequency identifies the problem. Straining is the most commonly identified symptom by older adults, even though physicians tend to rely on bowel movement frequency to diagnose constipation. Additionally, patients tend to underestimate their frequency of bowel movements. Normal stool frequency can vary between 3 motions per day and 3 motions per week. Frequencies outside that range may also be normal if a change from baseline has not been observed and no other symptoms manifest. For patients with moderate to severe cognitive impairment, diagnosis usually depends on a caregiver’s report.

In research settings, the consensus-based Rome III criteria (Box 2) are frequently used to define chronic constipation and can be used to further characterize the problem in the clinical setting.

What causes constipation in older people?

The causes of primary, or idiopathic, chronic constipation, including the subtypes of normal transit, slow transit and dyssynergic defecation (i.e., related to neuromuscular dysfunction), remain unknown. Despite the aging colon displaying smaller and more tightly packed collagen fibres as well as a reduced number of myenteric plexus neurons, age-related changes in colonic anatomy and physiology are not considered to be major contributors to the development of constipation.

Secondary causes of constipation are more easily identified. Medications, metabolic abnormalities and disease states are common culprits and often coexist in older people. These causes...
should be identified and treated before applying a label of primary constipation. Opioid analgesics, calcium-channel blockers, oral iron supplements and anti-diarrheal agents are frequently used medications that have constipation as an adverse effect. Disease states such as hypothyroidism, hypercalcemia, stroke, Parkinson disease and colorectal carcinoma can cause symptoms of constipation in older people. Boxes 3 and 4 list medications and disease states commonly implicated in causing constipation.14

Are investigations required?

Evidence-based recommendations for the diagnostic work-up of chronic constipation in older patients cannot be made because of the absence of research addressing the issue. We suggest conducting a thorough history and physical examination to elicit symptoms and signs of secondary causes of constipation. Careful review of medications, with the possibility of reducing the dose or substituting with another medication that does not have constipation as an adverse effect should be considered if the benefits of the drug are not greater than the bowel symptoms. Clinical judgment should be applied when requesting laboratory tests to identify metabolic causes such as hypothyroidism and hypercalcemia. An abdominal radiograph can help to exclude fecal impaction in patients who are immobile or cognitively impaired. If alarm symptoms or signs are present (Box 5), local or national guidelines for colon cancer screening should be consulted.

What treatments are effective?

Evidence from RCTs supports the use of osmotic agents as an effective treatment of chronic constipation in older people. One RCT evaluating electromyographic biofeedback for dyssynergic defecation also revealed benefit. Evidence supporting the use of bulk agents, stool softeners, stimulants and prokinetic agents was lacking, limited or inconsistent. At the time of our literature search, lifestyle modifications had not been evaluated in RCTs. The evidence is summarized herein by treatment, and details of the supporting trials15–30 are summarized in Appendix 1 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.120819/-/DC1).

Oral therapy

Osmotic agents

Osmotic agents exert their effect by promoting the secretion of water into the colonic lumen to maintain isotonicity with plasma. Lactulose and polyethylene glycol are commonly used osmotic agents. Studies of salts of poorly absorbed cations and anions, such as magnesium- and phosphate-based agents, did not meet our inclusion criteria.

Four placebo-controlled RCTs of osmotic agents (n = 250) all revealed statistically significant results in favour of active treatment.15–18 In one of the trials, polyethylene glycol improved stool frequency and resulted in improvement in Rome III criteria among 57 patients with Parkinson disease who had constipation (80% [16/20] in the treatment group v. 30.4% [7/23] in the placebo group, 95% confidence interval [CI] 23.9%–75.3% for the difference, \( p = \)
Two trials revealed benefit with lactulose. The first reported that patients given lactulose required less additional laxative use over 3 weeks than those in the placebo group (87% [47/54] v. 61% [30/49], \( p < 0.02 \)). The second trial, conducted over 12 weeks, reported a higher mean (± standard deviation) stool frequency per day with lactulose than with placebo (0.63 ± 0.31 lactulose v. 0.58 ± 0.30 placebo, \( p < 0.02 \)). The fourth trial showed that lactitol, another disaccharide similar to lactulose, increased stool frequency over 4 weeks (\( p < 0.001 \)), but no specific point estimate was reported.

Bloating, flatulence, abdominal pain and diarrhea are potential adverse effects from osmotic laxatives. These effects occur most often with lactulose because of its metabolism by colonic bacteria to carboxylic acids. Patients can also develop an aversion to the sweet taste of lactulose. Polyethylene glycol is metabolically inert and can be dissolved in other liquids.

Magnesium- and phosphate-based laxatives carry the risk of excessive absorption resulting in dose-dependent hypermagnesemia or hyperphosphatemia. More caution is advised in patients with renal impairment.

Bulk agents
Nonabsorbable, soluble dietary fibres, or bulk agents, exert their laxative effect by holding water in stool, thereby increasing stool weight, increasing colonic distension and improving frequency of bowel movements. There are natural, semisynthetic and synthetic varieties. Galacto-oligosaccharide is another nonabsorbable polysaccharide bulk laxative that has been evaluated in RCTs but is not readily available to consumers.

We found 7 RCTs (\( n = 254 \)) in which older people were randomly assigned to receive either dietary fibre or placebo. Two trials evaluating psyllium (\( n = 20 \)) did not show improvements in stool frequency. Results from 3 trials of galacto-oligosaccharide were mixed. Use of a mixture of fibre (guar gum and wheat bran) and the osmotic agent lactitol in yogourt resulted in increased stool frequency (5.9 ± 3.8/wk v. placebo 4.3 ± 1.8/wk, \( p < 0.05 \)) in 51 medical and surgical inpatients. It is unclear from this study whether the bulk agent or the osmotic agent was more responsible for the favourable result.
Fermentation of natural bulk agents by colonic bacteria can cause bloating and gas. Mechanical obstruction following consumption of bulk agents has been reported. Nonambulatory patients with low fluid intake may be at increased risk. Rare cases of allergic reactions to psyllium have also been described.

**Stimulants**

Stimulants exert their effect by increasing intestinal motility and colonic secretions. Anthranoids (senna, cascara) and diphenylmethane derivatives (bisacodyl) are commonly used stimulants.

Two trials involving patients in nursing homes (n = 182) compared stimulants with placebo and revealed significant benefit. In the first trial, use of an herbal mixture containing senna resulted in 4.14 more bowel movements on average over 4 weeks versus placebo (p = 0.017). The second trial studied an herbal formulation containing an anthraquinone combined with the osmotic agent magnesium oxide; however, the reported benefit (5.6 ± 2.0 spontaneous bowel movements/wk in the study group v. 4.6 ± 2.5/wk in the placebo group; p = 0.049) did not change a global assessment of efficacy by caregivers. Bisacodyl has not been evaluated in RCTs in older patients.

Abdominal pain, electrolyte imbalances and allergic reactions have been reported as adverse effects of stimulant laxatives. Regular use of anthranoids can cause pseudomelanosis coli, a benign and often completely reversible pigmentation of the mucosa of the large intestine. No definitive relation to myenteric nerve damage or carcinogenesis has been established with the use of stimulant laxatives. Regular use may lead to decreased efficacy over time.

**Stool softeners**

Stool softeners act as anionic surfactants, easing the interaction of water with solid stool. Intestinal motility and colonic secretions may also be increased. Stool softeners are generally well tolerated.

One trial of dioctyl sodium sulfofusinate conducted in 1968 showed 12 of 15 older inpatients to be less constipated than when they received placebo before active treatment (mean difference of 1.0 ± 0.29 stools/wk, p < 0.01).

**Prokinetic agents**

Prokinetic agents act by stimulating 5-hydroxytryptamine-4 (5-HT₄) receptors in the intestine, which induces peristalsis. Two previous-generation prokinetics, cisapride and tegaserod, were removed from the market because of concerns about cardiac safety.

A newer agent, prucalopride, with less affinity for the human ether-à-go-go-related gene (hERG) protein and less anticipated cardiovascular effects than other prokinetic agents, has been tested. Three different doses of prucalopride were evaluated for 4 weeks in 300 older participants. Only the 4-mg dose, at one time point (wk 1), reached statistical significance for the primary outcome of 3 or more spontaneous and complete bowel movements per week. No differences in adverse effects were observed between the groups.

Concerns about a 9-year delay between the completion of a study evaluating prucalopride in adults with constipation and submission for publication have been raised. Prucalopride (Resprotran) was approved by Health Canada in 2011 for use in women with constipation in whom laxatives have failed. A recommendation for the use of prucalopride in older people cannot be made at this time.

**Enemas and suppositories**

We did not find RCTs that evaluated the use of only enemas and suppositories to treat chronic constipation in older people. In one RCT, 206 frail residents in long-term care facilities who had a history of fecal incontinence and impaction were randomly assigned to receive either lactulose alone or lactulose with a daily glycerine suppository and weekly enemas with tap water. Among the 123 participants remaining in the study after 5 weeks, episodes of incontinence and soiled laundry did not differ significantly between the study arms.

**Lifestyle modifications**

Our search did not identify RCTs of fluid intake or physical activity for constipation in older people. A retrospective cohort study involving 883 older volunteers did not find an association between chronic constipation and intake of fewer than 3 glasses, between 3 and 5 glasses, or 6 or more glasses of water per day (odds ratio [OR] 0.847, 95% CI 0.53–1.38). However, low fluid intake in a cohort of nursing home residents was found to be a risk factor for the development of constipation (OR 1.49, 95% CI 1.21–1.82).

Physical activity, in the form of resistance and functional-skills training, was evaluated in long-term care facilities but failed to show benefit over the control (a program involving discussions about topics of interest to older people, such as history, music and relaxation).

Appropriate physical activity should be encouraged for other health outcomes and may improve symptoms of constipation, but definitive evidence for improvement in constipation is...
lacking. Promoting fluid intake with the goal of improving symptoms of constipation is not supported by the literature.

**Biofeedback**

In dyssynergic defecation, a subtype of chronic constipation, musculature in the pelvic floor, particularly the puborectalis muscle and external anal sphincter, contract inappropriately during defecation, leading to difficulty passing stool and incomplete evacuation. Biofeedback is a method patients can learn to help gain control of relaxing these muscles during defecation.\(^3^\) The availability of biofeedback therapy is low.

A 4-week RCT of electromyographic biofeedback sessions twice weekly, conducted with 30 cognitively intact older people, reported an increase in stool frequency from 2 to 4 bowel movements per week compared with controls who received information on bowel functioning and counselling sessions twice weekly focused on the behavioural mechanisms involved in defecation \((p < 0.01)\).\(^3^\) Constipation was diagnosed based on Rome criteria, and efficacy was maintained up to 2 months after treatment. Adverse effects were not reported in this study.

**Comparison with studies involving younger adults**

We did not find reports of direct comparisons between younger and older adults. However, the results from studies presented in our review are similar to those reported in systematic reviews synthesizing data for adults irrespective of age. The American College of Gastroenterology provides a grade A recommendation for the use of polyethylene glycol and lactulose to improve stool frequency and consistency in adults. Psyllium, a bulk agent, received a grade B recommendation for improvement of stool frequency.

### Table 1: Characteristics of treatments of chronic constipation in older people

<table>
<thead>
<tr>
<th>Category; mechanism</th>
<th>Treatment</th>
<th>Dose</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic agents</td>
<td>Polyethylene glycol</td>
<td>17–34 g/d</td>
<td>Bloating, flatulence, abdominal pain, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Lactulose</td>
<td>15–30 mL daily</td>
<td>Bloating, flatulence, abdominal pain, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Sorbitol</td>
<td>15–30 mL daily</td>
<td>Bloating, flatulence, abdominal pain, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Magnesium hydroxide</td>
<td>15–30 mg daily</td>
<td>Hypermagnesemia, bloating, flatulence, abdominal pain, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Sodium phosphate</td>
<td>10–25 mL with 350 mL of water</td>
<td>Hyperphosphatemia, hypocalcemia, hypernatremia and hypokalemia, bloating, flatulence, abdominal pain, diarrhea</td>
</tr>
<tr>
<td>Bulk agents</td>
<td>Psyllium</td>
<td>Up to 20 g/d</td>
<td>Bloating, flatulence; rarely cases of mechanical obstruction and allergic reactions</td>
</tr>
<tr>
<td></td>
<td>Methylcellulose</td>
<td>Up to 20 g/d</td>
<td>Bloating, flatulence</td>
</tr>
<tr>
<td></td>
<td>Polycarbophil</td>
<td>Up to 20 g/d</td>
<td>Bloating, flatulence</td>
</tr>
<tr>
<td>Stimulants</td>
<td>Sennoside</td>
<td>Up to 68.8 g/d in divided doses</td>
<td>Abdominal cramps, hypokalemia, pseudomelanosisis coli</td>
</tr>
<tr>
<td></td>
<td>Bisacodyl</td>
<td>5–10 mg/d orally or rectally</td>
<td>Abdominal cramps, hypokalemia, pseudomelanosisis coli</td>
</tr>
<tr>
<td>Stool softeners</td>
<td>Dioctyl sodium sulfosuccinate or docusate</td>
<td>100 mg twice daily</td>
<td>Abdominal cramps, diarrhea</td>
</tr>
<tr>
<td></td>
<td>Docusate calcium</td>
<td>240 mg twice daily</td>
<td>Abdominal cramps, diarrhea</td>
</tr>
<tr>
<td>Prokinetic agents</td>
<td>Prucalopride</td>
<td>2 mg/d</td>
<td>Nausea, vomiting, flatulence, headache</td>
</tr>
<tr>
<td>Enemas or suppositories</td>
<td>Phosphate-based enema</td>
<td>120 mL/d</td>
<td>Hyperphosphatemia and other electrolyte disturbances</td>
</tr>
<tr>
<td></td>
<td>Tap-water enema</td>
<td>500 mL/d</td>
<td></td>
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<tr>
<td></td>
<td>Glycerin suppository</td>
<td>Once daily</td>
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</tr>
</tbody>
</table>

Note: 5-HT = 5-hydroxy-tryptamine-4.

Source: Lembo and Camilleri.\(^4^\)

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Data were insufficient to recommend the use of other bulk agents, magnesium hydroxide, stool softeners and stimulants.\(^{39}\)

**Are there new pharmacotherapeutic options?**

Pharmacotherapies targeted at specific cellular receptors in the gastrointestinal tract have been developed and studied in adults. To date, they have not been approved for use in Canada.

Since 2006, lubiprostone has been approved for use in the United States. Lubiprostone activates type 2 chloride channels, enhancing the secretion of chloride-rich intestinal fluid. A meta-analysis of data from 3 RCTs (\(n = 610\)) comparing this medication with placebo in adults revealed a benefit in spontaneous bowel movements (risk ratio [RR] of failure to respond to therapy 0.67, 95% CI 0.56–0.80).\(^{40}\) (Two of the trials reported the proportion of participants aged 65 years or older [10% and 13.2%].) Diarrhea (RR 4.46, 95% CI 1.28–15.48) and nausea (RR 7.27, 95% CI 3.76–14.06) were more frequent with lubiprostone than with placebo.\(^{40}\) Self-limited shortness of breath following the first dose has also been observed.\(^{41}\)

### Table 2: Stepwise approach to the management of constipation in older people

<table>
<thead>
<tr>
<th>Step</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Identify the predominant symptom*</td>
<td>Frequency, straining, incomplete evacuation</td>
</tr>
</tbody>
</table>
| 2. Identify possible secondary causes of constipation* | • Medications (e.g., opioids, nondihydropyridine calcium-channel blockers, iron supplements and antidiarrheal agents)  
• Disease states (e.g., colon cancer, stroke and Parkinson disease)  
• Secondary causes of constipation are treated in the same manner as primary constipation  
• If alarm symptoms or signs are present (see Box 5), local or national guidelines for colon cancer screening should be followed |
| 3. Exclude fecal impaction* | • In a person who is bedbound or has severe dementia, an abdominal radiograph or a digital rectal examination† can be used to diagnose impaction  
• Manual disimpaction is often necessary to treat fecal impaction |
| 4. Optimize behavioural factors† | • The seated position, with knees at or above the level of hips, is advised  
• If the person has moderate to severe cognitive impairment, allow adequate time to toilet after the morning meal, to take advantage of the gastrocolic reflex |
| 5. Trial of dietary modifications (2–4 wk) | • Gradually increase fibre intake to 20–30 g/d from dietary (fruits, vegetables, legumes) or supplemental sources (psyllium, methylcellulose, calcium polycarbophil)  
• Not advised in a person who is immobile or bedbound, to avoid impaction or obstruction |
| 6. Trial of a previously preferred laxative agent (2–4 wk) | • The patient may prefer one agent over another from past experience |
| 7. Trial of a laxative agent supported by evidence from RCTs involving older people (2–4 wk) | • Polyethylene glycol 17–34 g/d  
• Lactulose 15–30 mL daily to twice daily |
| 8. Trial of another laxative agent or a combination of agents from different classes (2–4 wk) | • Magnesium hydroxide 15–30 mg daily to twice daily  
• Docusate calcium 240 mg twice daily§  
• Bisacodyl 5–10 mg/d orally or rectally  
• Sennoside, up to 68.8 g/d in divided doses  
• Enema or suppository |
| 9. Referral to a gastroenterologist or geriatrician |

Note: RCT = randomized controlled trial.  
*Steps 1 through 3 should be undertaken concurrently.  
†Step 4 should be undertaken concurrently with each of steps 5 through 8.  
§A negative digital rectal examination does not exclude the possibility of impaction more proximally. If the suspicion is high, an abdominal radiograph should be obtained.  
§Docusate calcium and docusate sodium are generally considered to be mild laxatives.
Linaclotide is a minimally absorbed, 14-amino-acid peptide that binds to the guanylate cyclase C receptor on the luminal surface of intestinal enterocytes. Binding initiates a signal transduction cascade that activates the cystic fibrosis transmembrane conductance regulator. This action promotes the release of chloride and bicarbonate into the intestinal lumen, thereby increasing colonic secretion and intestinal motility. In a systematic review and meta-analysis, 3 RCTs (n = 1582) comparing linaclotide with placebo in adults revealed a greater response to linaclotide than to placebo (RR of failure to respond to therapy 0.84, 95% CI 0.80–0.87). Diarrhea was more common in the treatment group than in the placebo group (RR 3.08, 95% CI 1.27–7.48). Linaclotide is not approved for use in Canada.

Second, the baseline definition of constipation varied extensively between trials, and most studies did not adhere to a standardized definition such as the Rome criteria for inclusion of participants. The trial by Zangaglia and colleagues of polyethylene glycol in patients with Parkinson disease and the trial by Simón and Bueno of electromyography biofeedback are the exceptions.

Third, laxatives were not assessed in specific subtypes of chronic constipation. As with most geriatric syndromes, however, a single isolated pathology accounting for symptoms is less common than multiple contributing factors.

Conclusion

Constipation is highly prevalent in older people. It can be the result of multiple contributing factors such as medication use and underlying disease states as well as primary constipation. The symptoms can have a profound impact on quality of life and in certain circumstances may lead to functional decline. Physicians should educate their patients on the wide range of normal bowel habits and the potential benefits of dietary modifications to improve symptoms. RCTs involving older participants have revealed the benefits of osmotic laxatives, such as polyethylene glycol and lactulose. Evidence supporting the use of bulk agents, stool softeners, stimulants and prokinetic agents was lacking, limited or inconsistent.

How can this review be applied in practice?

Constipation is usually manageable without extensive investigation, and most therapies carry a low risk of adverse events (Table 1). Behavioural measures to increase the chance of treatment success include ensuring adequate time to toilet, positioning the knees at or above the level of the hips for mechanical advantage while defecating, and taking advantage of the gastrocolic reflex by guiding cognitively impaired individuals to toilet following a meal. Based on our review of the literature and clinical experience, a stepwise approach is presented in Table 2.

Gaps in knowledge

Our review highlights some deficiencies in the research on constipation in older people. First, the overall reported quality of the trials retrieved in our search was low. The mean quality score according to the Jadad scale was 2.6 out of a possible 5 points. Only 3 trials scored 4 or greater, which is generally considered high quality. Common sources of bias included inadequately described processes for randomization and concealment of allocation, lack of blinding and variable follow-up. Confidence intervals surrounding point estimates were not always reported, and outcome measures were inconsistent across trials, with some reporting spontaneous bowel movements and others using composite outcomes. These studies are therefore at high risk of bias. However, the results from studies assessing osmotic laxatives were consistent with well-designed studies involving younger adults and can be used to guide treatment decisions.

References

44. Corazza E, Badiali D, Bazzocchi G, et al. Long term efficacy, safety, and tolerability of low daily doses of isosmotic polyeth-