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Practice

Therapeutics

Laxatives for chronic constipation in adults

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Red flag features in chronic constipation

- Recent onset of constipation in older age (> 50 years)
- Obstructive symptoms
- Rectal bleeding
- Weight loss
- Family history of colon cancer
- Iron deficiency anaemia
- Haem positive stool

Summary of mechanism of action, dose, evidence for efficacy, and safety of individual laxatives

Agent	Mechanism of action	Dose	GRADE* quality assessment of evidence	Side effects occurring more frequently with active treatment
Psyllium	Bulk laxative (soluble fibre)	3.5 g twice daily	Very low	Abdominal pain
Bran	Bulk laxative (insoluble fibre)	20 g daily	Very low	Abdominal pain, flatulence, bloating
Lactulose	Osmotic laxative	15 mL twice daily (dose can be titrated up to maximum 90 mL daily)	Very low	No data

Polyethylene glycol	Osmotic laxative	17 g (1 sachet) once daily (dose can be titrated up to maximum 3 sachets daily)	Moderate	None
Bisacodyl	Stimulant laxative	Oral: 5-10 mg at night (dose can be titrated up to maximum 20 mg); rectal: 10 mg suppository	Moderate	Diarrhoea
Sodium picosulfate	Stimulant laxative	5-10 mg at night	Moderate	Diarrhoea
Docusate	Stool softener and stimulant laxative	500 mg daily	No data	No data

*Grading of Recommendations Assessment, Development and Evaluation (www.gradeworkinggroup.org/)

How well do laxatives work?

The main aim of treatment of chronic constipation is symptomatic relief. Our literature search identified no trials of stool softeners.

Bulk laxatives

A systematic review that examined the use of fibre for chronic constipation identified only six randomised controlled trials, four of which used soluble fibre, and two insoluble fibre. Only one trial was conducted in primary care. A formal meta-analysis was not done owing to concerns about the quality of the methods used in the identified studies. In each of the six trials (which used different endpoints) soluble fibre, when compared with placebo, led to significant improvements in overall symptoms, straining, pain on defecation, stool consistency, an increase in the mean number of stools per week, and a reduction in the number of days between stools. Whether these differences were of clinical significance is debatable. Evidence for any benefit of insoluble fibre was conflicting.

Osmotic laxatives

Six randomised placebo controlled trials of osmotic laxatives in chronic constipation were included in a recent meta-analysis. None were conducted entirely or partly in primary care, meaning that the findings may not be generalisable to patients consulting general practitioners.

Five randomised controlled trials (in 676 participants) reported dichotomous data for the efficacy of osmotic laxatives. Four of these trials used polyethylene glycol at a dose of 17 g once or twice daily for between two weeks and six months, and the fifth trial used 15 mL of lactulose once daily for three weeks. Overall, osmotic laxatives were superior to placebo, with a relative risk of symptoms failing to respond of 0.50 (95% confidence interval 0.36 to 0.63) (**fig 1**) and a number needed to treat of 3. The mean number of stools per week was significantly higher with osmotic laxatives than with placebo (weighted mean difference in the number of stools per week 2.51; 1.30 to 3.71) (**fig 2**).

Stimulant laxatives

The same meta-analysis identified only two randomised controlled trials of stimulant laxatives, but these recruited 735 patients. Both trials were conducted partly in primary care, and most patients enrolled were female. One trial used bisacodyl 10 mg once daily for four weeks, and the other sodium picosulfate 10 mg once daily for four weeks. These two laxatives are converted to the same active metabolite. The risk ratio for failure to respond to treatment was reduced with stimulant laxatives (0.54; 0.42 to 0.69) (**fig 1**), and the number needed to treat was 3. Both trials reported a significant increase in the mean number of stools per week compared with placebo (weighted mean difference 2.50; 0.93 to 4.07) (**fig 2**).

How safe are laxatives?

Bulk laxatives

In the systematic review cited above that examined the use of fibre for chronic constipation, only one randomised controlled trial reported the number of participants in each treatment arm who dropped out owing to adverse events (one of 104 participants randomised to psyllium and two of 97 receiving placebo). Another trial in the review reported on individual adverse events, with 18% of the participants who took psyllium experiencing abdominal pain compared with none of the placebo participants, although no differences in bloating or cramping were reported. Finally, one other trial in the review reported significantly higher combined symptom scores for side effects such as abdominal pain, flatulence, borborygmi, and bloating among the participants eating rye bread compared with those eating low fibre toast.

Osmotic and stimulant laxatives

Four trials identified by the meta-analysis cited above reported individual adverse events. No significant differences were detected in rates of abdominal pain, reported in all four trials containing 853 patients, or headache, reported in three randomised controlled trials containing 486 patients. Diarrhoea occurred more frequently in the two trials of stimulant laxatives (risk ratio 13.75; 2.82 to 67.14, number needed to harm 3). Despite concerns that osmotic and stimulant laxatives may cause fluid or electrolyte disturbances, and despite recommendations that stimulant laxatives be avoided in renal impairment, no evidence from the clinical trial literature supported these warnings. There is also no convincing evidence in humans that stimulant laxatives damage the myenteric plexus, which is often cited as a hypothetical concern,

although in practice the development of tolerance and increasing dose requirements have been noted.

What are the precautions?

All laxatives are contraindicated in intestinal obstruction. Avoid bulk laxatives, including psyllium, if faecal impaction is suspected, and advise patients taking these to maintain an adequate fluid intake. Lactulose should be used with caution in lactose intolerant patients (who may develop diarrhoea, as lactulose contains lactose) and is contraindicated in galactosaemia. Discontinue polyethylene glycol if symptoms suggesting fluid or electrolyte disturbance develop. In pregnancy, bulk laxatives should be used preferentially, and when these fail osmotic laxatives can be used.

If first line laxatives fail, it is important to ensure that another diagnosis has not been missed. In particular, pelvic floor dysfunction (paradoxical contraction of the pelvic floor muscles during attempts at defecation) should be considered and can be ruled out by doing a rectal examination (a “normal” finding is reassuring).

Given that most randomised controlled trials used at least four weeks of treatment, a reasonable trial of laxatives would be for at least a month. When possible, laxative doses should be reduced if symptoms allow.

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