

celandine-aloe vera-psyllium or placebo (31). Capsules of 500 mg contained the active ingredients celandine, aloe vera, and psyllium in the ratio of 6:3:1. The initial dose was 1 capsule per day, taken with water at bedtime, and increased to 3 capsules per day depending on the response (31).

Benefits and harms. Based on the meta-analysis of data from 3 studies (29–31), the use of psyllium may lead to an increase in SBMs per week (MD 2.32, CI 0.86–3.79). Combined data from 2 studies showed that the use of psyllium may increase global relief symptoms (RR 1.86, CI 1.49–2.30), but there was little to no difference in stool consistency (MD –1.08, CI –1.33 to 0.83) (30,31). In absolute terms, psyllium was associated with 391 per 1,000 more individuals with global relief (from 223 more to 591 more). One study (30) examined withdrawal from the study because of diarrhea but with only 3 events; the summary estimate was too imprecise to make any conclusive statement (RR 0.47, CI 0.04–5.06); and no serious adverse events were reported in either arm. There were no data on CSBMs per week, responder rate, diarrhea, quality of life, or stool form.

Certainty in evidence of effects. The certainty of evidence for SBM, serious adverse events, and global relief was low and for diarrhea, was very low. We rated down certainty of evidence because of high risk of bias (concerns about methods of randomization and allocation concealment in 2 studies and high attrition in another study), indirectness, and imprecision.

Discussion

Fiber can be divided into soluble and insoluble fiber. Wheat bran, an insoluble fiber, is produced when the hard outer fiber of the wheat kernel is removed during the refining process. Inulin is a naturally occurring polysaccharide present in many plants and most often extracted from chicory. Inulin is a fructan and is considered both a soluble fiber and a prebiotic, meaning that it can stimulate the growth or activity of intestinal bacteria (32) that are believed to promote good gut health. Psyllium is also considered to be a soluble fiber and may also have prebiotic potential (33). Fiber has been recognized as important for normal laxation, primarily because it increases stool weight, and this has the secondary effect of reducing transit time. Fiber increases stool weight by its presence but also by increasing the water held by the fiber, as well as increasing bacterial mass from fermentation. However, inulin does not increase stool weight to the extent that wheat bran and psyllium do, but does undergo extensive fermentation (32).

Fiber is often recommended as a therapy to supplement dietary intake of fiber. However, as the studies above indicate, there are different formulations and types of fibers that have been evaluated and the included studies did not quantify the intake of dietary fiber. At least 2 studies were conducted with fiber that contained other ingredients such as milk or aloe vera that may additionally influence laxation. All studies are 30–40 years old, and the number of participants in the studies has been small and most are primarily conducted in women. Most of the included studies on fiber supplementation did not report on relevant patient important outcomes. The best data exist for psyllium, but even those are of low quality. In addition, wheat bran can exist as a finely ground powder that can decrease stool water content and harden stool (34). The chief side effect of fiber supplementation seems to be flatulence. In individuals with mild-to-moderate symptoms of constipation, especially who consume diets deficient in fiber, a trial of fiber supplementation is warranted because it is low-risk, low-cost, and easily accessible. In general, chronically constipated patients and nonconstipated

persons drink similar amounts of fluid on a daily basis. However, when individuals are placed in quartiles based on daily fluid intake, those in the lowest quartile for fluid intake are more likely to be constipated. Thus, efforts to increase fluid intake should be focused on those with low levels of fluid intake (35). Standard doses of fiber supplements are typically taken with 8–10 ounces of fluid (36).

OSMOTIC LAXATIVES

Recommendation 2: In adults with CIC, the panel recommends the use of PEG compared with management without PEG (strong recommendation, moderate certainty of evidence).

Implementation considerations

- A trial of fiber supplement can be considered for mild constipation before PEG use or in combination with PEG.
- Response to PEG has been shown to be durable over 6 months.
- Side effects include abdominal distension, loose stool, flatulence, and nausea.

Polyethylene glycol

Summary of evidence. Three randomized, placebo-controlled trials studied the effect of PEG on constipation (37–39). Two of these studies were multicenter trials conducted in Italy and enrolled participants aged 18–70 years with chronic constipation defined in accordance with the Rome criteria, that is, less than 2 bowel movements per week for at least 12 months or the presence of 2 or more of the following symptoms: <3 bowel movements per week, straining at defecation, sense of incomplete evacuation, and hard stools on at least 25% of occasions (37,38). In both trials, the treatment consisted of 17.5 g of PEG with electrolytes as a granular preparation or placebo dissolved in 250 mL of water taken twice daily. One study included 55 participants, and the treatment period lasted 8 weeks (38). The second study (37) included 70 participants and had 2 consecutive periods in which all participants received the active treatment, PEG for 4 weeks, and then those who responded were randomized to receive either PEG or placebo for 20 weeks. The third study was conducted in the United States and included 304 participants with chronic constipation based on modified Rome criteria, where participants reported <3 bowel movements per week for at least 3 months and one or more of the following: straining, lumpy or hard stools, and sensation of incomplete evacuation in >25% of defecations (39). Participants were randomized in a 2:1 ratio to PEG 3350 (n = 204) at a dose of 17 g or placebo (n = 100) mixed in 8 ounces of liquid once daily for 6 months.

Benefits and harms. PEG likely results in an increase in CSBMs per week compared with placebo (MD 2.90, CI 2.12–3.68), based on one study (39), and SBMs per week (MD 2.30, CI 1.55–3.06), based on meta-analyzed data from 3 studies (37–39). Across 2 studies, a higher rate of individuals met the responder definition, one study defined responder as normalization of bowel moments (37,38) and other defined based on the US Food and Drug Administration (FDA) end points (40), compared with placebo (RR 3.13, CI 2.00–4.89); PEG was associated with 312 more per 1,000 (from 146 more to 569 more). Diarrhea was noted more commonly in the treatment arm (158 more per 1,000, from 6 fewer to 896 more). A higher proportion of participants had global relief of symptoms with PEG compared with placebo with 454 per 1,000 in the PEG group (from 159 more to 948 more). There were no data for the following outcomes: stool form and quality of life. Two studies examined serious adverse events, but the number of