2.07–2.73) and PAC-QOL scores (MD 0.65, 95% CI 0.50–0.80) compared with placebo. Furthermore, the use of SPS leads to higher responder rates (RR 2.60, 95% CI 2.05–3.30) and an increased proportion of individuals with global relief (RR 1.75, 95% CI 1.48–2.07). In absolute terms, of 1,000 individuals treated with SPS, there would be 359 more responders (236 more to 516 more) and 357 more with global relief (228 more to 509 more). Use of SPS may increase the proportion of individuals who experience diarrhea compared with placebo (RR 8.76, 95% CI 4.99–15.39). One study reported serious adverse events but with only 3 events, results were very imprecise (RR 0.24, 95% CI 0.02–2.67). The rate of diarrhea leading to discontinuation of treatment was higher in the SPS group compared with placebo (RR 8.76, 95% CI 4.99–15.39).

Certainty in evidence of effects. The certainty of evidence was rated as moderate for the following outcomes: CSBM and SBM frequency, responder rate, global relief, and stool consistency (because of risk of bias). The certainty of evidence was very low for the outcomes of diarrhea and serious adverse events (because of risk of bias, indirectness, and imprecision) and low for quality of life (because of risk of bias and indirectness). The overall certainty of evidence for bisacodyl was moderate.

Discussion

Bisacodyl and SPS are converted in the gut into the same active metabolite, bis-(phydroxyphenyl)-pyridyl-2-methane (BHPM). Bisacodyl is converted into BHPM by small bowel and colonic mucosal deacetylase enzymes while SPS is converted into BHPM by colonic bacteria desulfate enzymes. BHPM acts directly on the colonic mucosa to stimulate colonic peristalsis and secretion. Similar to other stimulant laxatives (e.g., senna), use of antibiotics can potentially decrease the efficacy of SPS because they may affect colonic bacteria that produce the active metabolite of the drug (54).

Initial dosing in the available RCTs was 10 mg orally for bisacodyl and SPS, although dose reduction was permitted. At this dose, adverse effects were common (see below), and therefore in clinical practice, 5 mg orally is often used initially. Although not studied in RCTs, bisacodyl is also available as a rectal suppository (10 mg). The onset of action is typically 6–12 hours for the oral tablet while the suppository works within 30–60 minutes.

The most common adverse effects for bisacodyl and SPS were diarrhea and abdominal pain. For bisacodyl at the initial starting dose of 10 mg compared with placebo, diarrhea occurred in 53.4% vs 1.7%, respectively, while abdominal pain occurred in 24.7% vs 2.5%, respectively (51). Most adverse events occurred in the first week of treatment. For SPS at the initial starting dose of 10 mg compared with placebo, diarrhea was reported by 31.8% vs 4.5%, respectively, while for abdominal pain, it was reported by 5.6% vs 2.2%, respectively (52). Bisacodyl and SPS are contraindicated in individuals with ileus, intestinal obstruction, severe dehydration, or acute inflammatory conditions in the bowel.

Although effective, side effects are common, and the panel recommended the use of bisacodyl and SPS for a short term or rescue therapy. The long-term effectiveness of these agents has not been studied.

Recommendation 6: In adults with CIC, the panel suggests the use of senna over management without senna (conditional recommendation, low certainty of evidence).

Implementation considerations

- While the trials were conducted for 4 weeks, longer term use is probably appropriate, but data are needed to better understand tolerance and side effects.
- The dose evaluated in trials is higher than commonly used doses in practice. The panel suggests starting at a lower dose and increase if there is no response.
- Abdominal pain and cramping may occur with a higher dose of senna.

Senna

Summary of evidence. One placebo-controlled RCT examined the safety and efficacy of senna in the management of CIC (44). Participants were randomly assigned to 1 g of senna (n = 30) or placebo (n = 30) and treated for 28 days.

Benefits and harms. Participants treated with senna may have higher CSBMs per week (MD 7.60, 95% CI 5.90–9.30) and SBMs per week (MD 7.6, 95% CI 6.42–8.78) compared with the placebo group. The response rate might be higher in the senna-treated group compared with placebo (RR 5.25, 95% CI 2.05–13.47), 567 more per 1,000 in the senna group (from 140 to 1,000 more). The quality-of-life scores may be higher in the senna group compared with placebo (MD 7.80, 95% CI 1.40–14.20). Participants taking senna might have higher rates of diarrhea, 175 more per 1,000 (from 100 fewer to 1,000 more). No participants in the senna and placebo arms experienced a severe treatment-related adverse event.

Certainty in evidence of effects. The certainty of evidence was low for the outcomes of CSBMs per week, SBMs per week, and quality of life as the panel rated down because of concerns for indirectness and imprecision. The certainty of evidence for responder rate was moderate because of imprecision. The overall certainty of evidence for senna was low.

Discussion

Senna is a natural derivative of the senna plant. Sennosides A and B are sequentially metabolized by the gut microbiota to the active metabolites, rheinanthrone and rhein, which stimulate the production of prostaglandin E2 and secretion of chloride ions leading to attendant changes in colonic peristalsis and luminal water content (55,56). Over 90% of sennosides and their metabolites are excreted in the feces (56). Dosing in the single RCT published to date was 1 g by mouth daily for 4 weeks, which is higher than that typically used in clinical practice. It is notable that while no details were provided, 83% of participants randomized to senna reduced their daily dose during the trial (44). Most commercially available senna products contain 8–9 mg per tablet. Rigorous dose ranging data with senna are currently not available. In the clinical trial by Moshita et al. (44), no participants experienced a severe treatment-related adverse event. However, as Moshita et al. (44) did not provide rates for the mild treatment-related adverse events, the fact that 83% of participants