

Senna

Primary Literature

Passmore AP, Wilson-Davies K, Stroker C and Scott ME. Chronic constipation in long stay elderly patients: a comparison of lactulose and a senna-fibre combination. *BMJ* (1993). 307(6907):769-71.

Study objectives: The authors wanted look at the use of a senna-fibre combination (54.2% ispaghula and 12.4% senna) and how its efficacy and cost effectiveness compared to lactulose in long stay elderly patients with chronic constipation.

Methods:

Design: Randomised, cross over study

Allocation: N/A

Blinding: Double blind

Follow-up period: Two 14 day periods, with 3-5 days before and between treatments

Setting: Hospital or nursing home

Participants: 77 long stay elderly patients (57 women; mean age 82.9 years) with a history of chronic constipation (fewer than three bowel movements per week) or a need for regular laxatives. Those patients with important bowel pathology, diabetes mellitus, severe renal impairment, anti-diarrheal therapy, and fecal incontinence were excluded.

Intervention: Lactulose (15mL BID) and a senna-fibre combination (10mL daily) with matching placebo. Doses could be decreased or increased according to response.

Outcomes: Stool frequency, stool consistency, and ease of evacuation; deviation from recommended dose; daily dose and cost per stool; adverse effects

Patient follow-up: Two 14 day periods, with 3-5 days before and between treatments

Main Results: The senna-fibre combination had a significantly higher mean daily bowel frequency and higher stool scores for consistency and ease of evacuation compared to lactulose, and the recommended dose was exceeded more with the lactulose group. The cost per stool was much less for the senna-fibre combination and there were no differences in adverse events between the two groups.

Conclusions: It was demonstrated that although both lactulose and the senna-fibre combination were effective and associated with minimal adverse events, the senna-fibre combination was more efficacious and more cost-effective.

Comments/critical appraisal: The main draw-back to this study, is that it does not compare senna alone to lactulose, instead it uses a senna-fibre combination. Fibre is an effective laxative, and it is thus impossible to attribute the results to senna alone. In addition, the study does not provide information about the patients in each group, to

demonstrate the similarities or differences as contributing factors. Along with that, the external validity of this study is questionable. The patients were quite elderly and in a hospital or nursing home setting. Without knowing other patient characteristics (ex. other medical conditions, medications, ethnicity), it is difficult to be able to generalize these results to the general population. The study also included some patients with only 'a need for regular laxatives'. Although they included patients with a history of chronic constipation, defined as fewer than three bowel movements per week, including those with a need for regular laxatives is very subjective, since that need is not defined. Overall, there were many drawbacks to this study, making it very difficult to use these study results when developing the chronic constipation algorithm.

Connolly P, Hughes IW and Ryan G. Comparison of 'Duphalac' and 'irritant' laxatives during and after treatment of chronic constipation: a preliminary study. *Curr. med. Res. Opin* (1975). 2,620.

Study objectives: To compare the effectiveness of lactulose (Duphalac) and irritant laxatives as a group (senna, anthraquinone derivatives or bisacodyl).

Methods:

Design: Comparative, randomised, crossover study

Allocation: N/A

Blinding: Not blinded

Follow-up period: 3 weeks

Setting: Multi-centre

Participants: 194 patients aged 4-90 years old identified by their doctor as having signs of constipation for over 3 months.

Intervention: Either lactulose (15mL BID) or a laxative of their choice was given in week 1. For 164 of the 194 participants, the laxative of their choice was an irritant laxative, either senna, anthraquinone derivative or bisacodyl at a dose normally prescribed by the doctor. Week 2 was a non-treatment week. In week 3, the patients received the alternative preparation. It was randomised so half of the patients would receive lactulose in the first week, and half would receive the laxative of their choice/irritant laxative.

Outcomes: Patients were asked to keep a daily record of stool consistency (none, hard, normal or loose) and whether or not they had any side effects.

Patient follow-up: 3 weeks

Main results: Lactulose was shown to be more efficacious compared to the group of irritant laxatives as by day 7, 58% of the patients receiving lactulose were passing normal stool and only 42% of those taking irritant laxatives were. When comparing the passing of stool, irrespective of its consistency, there were no significant differences between the two groups. In addition, 24% of patients who took lactulose in the first week were passing normal stools at the beginning of the third week (right after the one week of no treatment),

compared to 14.5% of patients taking irritant laxatives, demonstrating that the effects of lactulose are longer compared to irritant laxatives. There were no significant differences in side effects between the two groups.

Conclusions: Although difficult to draw conclusions from this preliminary trial, the study did demonstrate that lactulose is more effective in treating chronic constipation compared to irritant laxatives.

Comments/critical appraisal: It is very difficult to draw any conclusions specifically about senna from this study since a group of 'irritant' laxatives were compared to lactulose and the study did not define how many patients received which 'irritant' laxative. Although the study was randomised, it was not blinded, increasing the risk of bias. In addition, the study did not disclose patient characteristics (ie. average age in each group, medical conditions, medications etc), making it impossible to determine if any outlier could be contributing to the results and impossible to apply it to the general population.

Clinical Practice Guidelines/recommendations

Pare P et al. Recommendation on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. *Can J Gastroenterol* (2007). Suppl B:3B-22B.

Study Objectives: A group of 10 gastroenterologists was formed to develop guidelines for the management of primary chronic constipation or constipation associated with irritable bowel syndrome. The goal was to optimize the approach in clinical care based on the available evidence using recommendations and treatment algorithms. These guidelines focus on epidemiology; quality of life and threshold for treatment; definitions and diagnostic criteria; lifestyle changes; bulking agents and stool softeners, osmotic agents, prokinetics, stimulant laxatives, suppositories, enemas and other drugs; biofeedback and behavioural approaches; surgery; and probiotics.

Scope: These guidelines are based off randomised-control trials where available. The consensus group followed the process outlines by the Canadian Association of Gastroenterology. With regards to senna, these recommendations are not based off any large, good-quality trials, as they do not exist. One trial used compared a senna-fibre combination to lactulose, and this study is summarized above. In addition, another trial compared irritant laxatives (including senna) to lactulose and that trial is also summarized above. Another trial compared senna to sodium picosulphate which is not available in Canada. Therefore, the authors used a combination of the available evidence and their expertise to come up with recommendations.

Methods: A need for recommendations on chronic constipation was identified by physician surveys. A consensus group of 10 gastroenterologists was formed that had expertise in diverse areas in gastroenterology. These members then performed a literature review to determine clinical relevant topics, and each topic was assigned to one group member to research and create recommendations. When available, an evidence-based approach was used using MEDLINE, PubMed or EMBASE searches, or a Cochrane review. In the cases of insufficient evidence, expert opinions were used. The consensus group then voted on the recommendations and the statements were defined. The recommendations were graded was voted on, according to the quality of available data. A grade of A is a meta-analysis of

RCTs for interventions or RCTs for interventions with consistency, direct or strong indirect evidence and no important flaws. A grade E indicates expert opinion. A treatment algorithm was then created.

Main Results: For senna, the guidelines indicate that there is some evidence to support its short-term use and no evidence supporting long-term use.

Conclusions: Senna is a commonly-used laxative for chronic constipation, despite the lack of large, good quality studies. There is some evidence for the short-term use of senna so it is recommended only as a rescue medication for intermittent or occasional use at any stage of treatment.

Commentary/critical appraisal: The authors were very clear in explaining how they came up with the topics, researched the topics, and came up with recommendations. They did a very thorough review of the available literature, and when needed, combined that with expert opinion. These recommendations were voted on, helping to increase accuracy and decrease the potential for bias.

One issue that the authors did raise in these guidelines was the lack of strong, large trials involving senna. There are no available trials comparing senna to placebo, and very few comparing it to another agent. However, when compared to another agent, senna was either mixed with a bulk laxative, grouped with other 'irritant' laxatives, or compared to an agent not available in Canada.

Other Literature Types

Liu LWC. Chronic constipation: Current treatment options. *Can J Gastroenterol* (2011). 25:22B-28B.

Source description: Review article focusing on evidence for various treatment options available in Canada for primary chronic constipation.

Summary: For the management of chronic constipation, there are no clinical controlled trials to support the use of senna. There are long-term safety concerns with the use of stimulant laxatives, although there is no well-documented evidence to support these concerns. Overall, senna and other stimulants should only be recommended for occasional use as a 'recue' therapy while using prokinetic or osmotic laxatives.

Comments/critical appraisal: The authors did a thorough literature review and their recommendations accurately reflect the lack of evidence available for the use of senna in chronic constipation. Due to the availability of other effective laxatives for the use in chronic constipation, it is reasonable to leave senna for occasional use only. This article indicates that senna can be used for occasional use as 'rescue' therapy while using either prokinetic or osmotic laxatives, which coincides with other recommendations that are available.

Bowels-Jordan J. Constipation. Patient Self-Care (2002). First Edition. 21:222-236.

Source description: Patient Self-Care is a textbook resource that is published by the Canadian Pharmacists Association. The first edition of the textbook was published in 2002.

The information provided is based on evidence where available, and a large variety of references are provided. In the absence of clinical evidence, expert opinion from practicing pharmacists with specific expertise is provided.

Summary: Despite its popular use, senna is a third-line agent and should only be used for short-term relief of chronic constipation, after all other agents have failed. It is thought that long-term use of stimulant laxatives can damage the enteric nervous system and smooth muscles of the colon, despite the lack of supporting studies.

Comments/critical appraisal: This chapter reflects the lack of evidence available for the use of senna in chronic constipation. After performing a thorough literature review, it is appropriate to leave senna as a third-line agent used short-term since the studies are small and poorly designed. Although there is no evidence to indicate that there are long-term safety concerns with the use of senna or other stimulants, there is a theoretical concern. It is appropriate to recommend senna for short-term use especially because there are other options for laxatives that are not associated with any long-term safety concerns. This chapter can be generalized to the general population and included sections on special populations as well.