Bisacodyl

Primary Literature

Kamm MA, Mueller-Lissner S, Wald A, Richter E, Swallow R, Gessner U. Oral bisacodyl is effective and well-tolerated in patients with chronic constipation. Clin Gastroenterol Hepatol. 2011 Jul;9(7):577-83. Epub 2011 Mar 25. <1>

Study objectives: This study's objective was to assess the efficacy and safety of bisacodyl for the treatment of chronic constipation, defined by Rome III criteria.

Methods:

Design: Randomized, placebo controlled.

Allocation: Allocation concealed

Blinding: Double-blinded

Follow-up period: 4 weeks

Setting: 27 centres across the United Kingdom

Participants: (n = 368). Qualified for study based on criteria defined by Rome III.

Intervention: Patients were randomly assigned, in a 2:1 ratio, to groups that were given 10 mg bisacodyl (n = 247) or placebo (n = 121), once daily, for 4 weeks

Outcomes: Number of complete spontaneous bowel movements (CSBMs) per week, number of complete spontaneous bowel movements for each single week, number of spontaneous bowel movement (SBMs), and constipation-associated symptoms

Patient follow-up: 295 out of 368 patients.

Main results: The mean number of complete spontaneous bowel movements per week during the treatment period increased significantly in the bisacodyl group compared to the placebo group. All secondary end points differed significantly between groups, demonstrating efficacy for bisacodyl. There was a statistically significant improvement in the overall Patient Assessment of Constipation quality of life (PAC-QOL) score and all subscales (satisfaction, physical discomfort, psychosocial discomfort, worries and concerns) in the bisacodyl-treated patients, compared with those that received placebo. Adverse events and discontinuation rate were higher in the bisacodyl group than placebo.

Conclusions: The author concluded that oral bisacodyl improves bowel function, constipation-related symptoms, and disease-related QOL. Hence, it is an effective treatment option for patients with chronic constipation.

Comments/critical appraisal: In terms of internal validity, there are some strengths and limitations of the study that must be noted. In terms of strengths, this study cleared outlined its outcomes, the criteria used for selecting patients and the setting. However, the sample

size could have been larger and a longer follow up period could have been used, especially considering the risk of tolerance developing after sustained use of bisacodyl.

When considering external validity, some of the strengths of the study were the strong inclusion criteria for the self-care population in question. Some limitations of the study include, almost double the drop out rate of patients in the bisacodyl group as compared to the placebo group. This study was performed mainly on an adult population, hence its results might not be extrapolated to fit other sections of the self care population.

In considering the suggested algorithm, this study does show that 10mg of bisacodyl is effective for treatment of chronic constipation. However, since chronic constipation is a long term problem, the efficacy of bisacodyl over a longer period of time remains in question due to potential tolerance issues with sustained therapy.

Kienzle-Horn S, Vix JM, Schuijt C, Peil H, Jordan CC, Kamm MA. Efficacy and safety of bisacodyl in the acute treatment of constipation: a double-blind, randomized, placebo-controlled study. Aliment Pharmacol Ther. 2006 May 15;23(10):1479-88 <2>

Study objectives: To determine the effectiveness and safety of oral bisacodyl on stool frequency and consistency in patients with chronic idiopathic constipation.

Methods:

Design: Randomized, placebo controlled

Allocation: Allocation concealed.

Blinding: Double-blinded

Follow-up period: 3 days

Setting: 8 primary care practices

Participants: 55 patients (age 19-89 years) with idiopathic constipation based on Rome II criteria

Intervention: 28 were randomized to receive bisacodyl, and 27 to receive placebo

Outcomes: Mean of the total number of stools per day during the three treatment days, mean stool consistency during the three treatment days.

Patient follow-up: 54 out of 55 patients.

Main results: The mean number of stools per day was significantly greater in the bisacodyl group compared with placebo. Mean stool consistency score improved during bisacodyl treatment, but remained about the same for placebo treatment. The investigator's global efficacy score was superior for the bisacodyl group compared with placebo. Both treatments were well tolerated. Serum electrolyte levels and incidence of adverse events were comparable between treatment groups.

Conclusions: The author concluded that bisacodyl is effective and safe in improving stool frequency and consistency in acute treatment of idiopathic constipation.

Comments/critical appraisal: When assessing the internal validity, there are some strengths and limitations of the study that must be noted. In terms of strengths, this study cleared outlined its outcomes, there was a low dropout rate and the setting was clearly established. Although the criteria used for selection was based on Rome II, authors admit that there where discrepancies in this selection process which could affect validity of the results. This study also used a very small samples size.

When considering external validity, there are some limitations, which have to be considered. There is no strong inclusion criterion for the self-care population in question. The treatment period of just 3 days looks at just an isolated episode of constipation does not shed light on issues related to long term use of bisacodyl which might be required for treatment of repeated episodes due to chronic constipation. This study was performed mainly on an adult population; hence its results might not be extrapolated to fit other sections of the population.

In considering the suggested algorithm, this study does show that bisacodyl is an effective treatment option for acute relief from an episode of constipation. However, with such a short treatment period of only 3 days and since chronic constipation is a long-term problem, the efficacy of bisacodyl over a longer period of time remains in question due to potential tolerance issues with sustained therapy.

Systematic Reviews and Meta-analyses

Ford AC, Suares NC. Effect of laxatives and pharmacological therapies in chronic idiopathic constipation: systematic review and meta-analysis. Gut. 2011 Feb;60(2):209-18. <3>

Study objectives: examining the effect of laxatives and pharmacological therapies in chronic idiopathic constipation

Scope: Placebo-controlled trials of laxatives or pharmacological therapies in adult patients were selected. Minimum duration of therapy was 1 week. Trials had to report either a dichotomous assessment of overall response to therapy at last point of follow-up in the trial, or mean number of stools per week during therapy.

Methods: MEDLINE, EMBASE, and the Cochrane central register of controlled trials were searched (up to September 2010). Twenty-one eligible RCTs were identified. Seven of these trial pertained to laxatives (n=1411 patients).

Main results: In all 7 laxative trials, laxatives were superior to placebo in terms of a reduction in risk of failure with therapy (RR=0.52; 95% CI 0.46 to 0.60). Total number of adverse effects associated with laxatives was not significantly more than with placebo, with the exception of one trial.

Conclusions: This systematic review and meta-analysis concluded that lalaxatives, prucalopride, lubiprostone and linaclotide are all superior to placebo for the treatment of CIC

Comments/critical appraisal (including assessment of internal and external validity): In acknowledging the internal validity of this systematic review, some limitations need to be stated. There was only borderline heterogeneity when data from laxative studies were pooled. This limits the power of presenting results from numerous studies that were designed with similar methods and with common outcomes. In terms of strengths of the review, the search strategy, eligibility criteria, and data extraction processes was described in detail.

When considering external validity, there are major criticisms that can be made. Like many systematic review and meta-analysis, there are major concerns about the quality and reporting of the trials included. There were fewer trials reporting efficacy of the stimulant laxatives- sodium picosulfate and bisacodyl (which are converted to the same active metabolite), lubiprostone and linaclotide. Out of all 21 RCT's studied only 2 were from a primary care setting and only 1 out of the 7 laxative RCT's were based on results from a primary care setting. There is no strong inclusion criterion for the self-care population in question.

The applicability of this study to the algorithm is limited due to the poor study design from both an internal and external validity perspective. The limited data from this review does conclude that laxatives (bisacodyl) are effective for treatment of chronic constipation, however its applicability in a primary care setting does not appear to be fully justified.

Clinical Practice Guidelines

Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. Canadian Journal of Gastroenterology. 2007 Apr;21 Suppl B:3B-22B. <4>

Study objectives: A consensus group of 10 gastroenterologists was formed to develop treatment recommendations for chronic constipation.

Scope: The final consensus group was assembled and the recommendations were created following the exact process outlined by the Canadian Association of Gastroenterology for the following areas: 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; other drugs; biofeedback and behavioural approaches; surgery; and probiotics. A treatment algorithm was developed by the group for chronic constipation and constipation associated with irritable bowel syndrome. Where possible, an evidence-based approach and expert opinions were used to develop the statements in areas with insufficient evidence.

Methods: Clinically relevant topics or issues pertaining to chronic constipation and IBS-constipation treatments were identified through a literature review by members of the consensus group. Supporting evidence was primarily retrieved through a MED-LINE, PubMed or EMBASE search, or Cochrane review on each topic. Articles were restricted to English-language full publications of research in adults between 1966 and April 2006. A series of statements were voted on using a five-point Likert scale. Recommendations were accepted only if 80% of participants voted for 'accept completely' or 'accept with some

reservations'. The group created a treatment algorithm for chronic constipation and IBS-constipation based on the recommendations that achieved a voting consensus.

Main results: The authors concluded that stimulant laxatives (bisacodyl) have some evidence to support their use in short term situations but not enough evidence to support their long term use in patients with chronic constipation.

Conclusions: Bisacodyl has efficacy for short term use in chronic constipation but no established efficacy for long term use.

Comments/critical appraisal: From an internal validity stand-point a strength was the fact that the authors included a good search strategy that explained how they chose to discuss the selected studies, thus giving this systematic review and guideline recommendations more credibility and less bias.

In considering the external validity, there are some limitations to be noted. In terms of laxative use for chronic constipation the clinical data supporting their use were derived from small, older and poorly designed studies. These studies were often done in specific subsets of patient populations and had ill-defined end points.

In considering the application to the algorithm, these guidelines provide a general overview of current approach to therapy of various pharmacological agents used for chronic constipation. Although there are some limitations to extrapolating the results from these findings, the author's expert opinion provides tertiary level of evidence that acknowledges evidence based management approaches.

Other Literature Types

Canadian Pharmacists Association . (2002). Patient Self-Care: Helping patients make therapeutic choices. Ottawa: CPhA. <5>

Source description: This is a textbook resource complied by the Canadian Pharmacists Association. It has individual chapters and topics contributed by various experts and practicing pharmacists. It is well referenced and the recommendations in the book are based mainly on sound clinical evidence and if required expert clinical opinions.

Summary: describe the author's recommendations for the therapeutic agent. The author states there are only a few trials comparing the effectiveness of different types of laxatives and based on current data there is insufficient evidence to distinguish treatment approaches among laxatives. In terms of bisacodyl use, the author does not feel it is a first line therapy for chronic constipation. It is however states to be the first line of therapy in opioid users.

Comments/critical appraisal (including assessment of internal and external validity): In terms of assessing internal and external validity there are only a few points to consider. Firstly, majority of the data used to assess use of laxatives is from nursing homes and hospitals hence limiting its applicability to the self care population in question. In addition, most of the data was derived from small older studies that are lacking in quality.