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Oral bisacodyl is effective and safe for short term treatment of chronic constipation

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ABSTRACT A clinical decision report using

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;9(7):577-583. <https://doi.org/10.1016/j.cgh.2011.03.026>

to evaluate potential long term treatment with oral bisacodyl in a patient with a history of chronic constipation and recent non-surgical treatment of ischemic colitis.

Keywords: *bisacodyl, constipation*

Clinical-Social Context

Shirley Moore [pseudonym], a 76-year-old African American woman with a past medical history significant for well controlled hypertension, type II diabetes mellitus, and hypercholesterolemia, presented to the gastrointestinal clinic for follow up status post hospitalization and non-surgical treatment of ischemic colitis several weeks prior. She also had a well-established history of chronic idiopathic constipation, for which she was on a high fiber diet, probiotic and Miralax before her hospitalization with satisfactory control of her symptoms. Upon discharge from the hospital, she was prescribed Ultram for further treatment of her abdominal pain and oral Bisacodyl to take along with her prior constipation regimen. She stated that she initially tolerated Bisacodyl well, though as her abdominal pain lessened and she decreased the frequency of Ultram use, she began experiencing two loose stools daily. Her baseline stool frequency prior to admission was approximately three to four well-formed stools per week. She denied having any accidents but stated that she felt embarrassed and uncomfortable by her loose stools and worried about her bowel movements throughout the day. She denied any blood or mucus in her stools and felt well otherwise. Her vitals were within acceptable limits, and her physical exam was benign; specifically, it was negative for abdominal tenderness, distention, organomegaly, and peritoneal signs. She described her socioeconomic status as "middle class" with adequate transportation and access to healthcare, and she denied any difficulty affording her medications. She ate home cooked meals with an emphasis on incorporating vegetables and reported minimal alcohol use. She denied tobacco and illicit drug use. Ms. Moore inquired about the safety of using oral Bisacodyl and the possibility of adding it to her regimen for long term use if clinically appropriate, stating that the hospital did not give her clear instructions on discontinuing the medication.

Clinical Question

Is oral bisacodyl effective and safe for long term treatment of chronic idiopathic constipation in a medically stable patient?

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Research Article

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Description of Related Literature

PubMed was searched for articles published between 2005 and 2021 using the terms “Bisacodyl” and “constipation” and the clinical trials filter. This search yielded 17 articles, and their titles and abstracts were manually scanned to evaluate their relevance to the clinical question pursued in this manuscript. The search was then broadened by removing the clinical trials filter. This yielded a total of 118 articles, including reviews called “Long Term Treatment With Stimulant Laxatives – Clinical Evidence for Effectiveness and Safety?”¹ and “Comparison of Efficacy of Pharmacological Treatments for Chronic Idiopathic Constipation: a Systematic Review and Network Meta-analysis,”² which cited and arrived at the same conclusion regarding Bisacodyl as the article critically appraised by this paper. These reviews were not chosen for critical appraisal as they do not have experimental study designs with controls to analyze. Additionally, they compared the effectiveness and safety of multiple medications, which does not directly address the patient’s specific question about Bisacodyl. Moreover, in the meta-analysis by Nelson,² the majority of the patients in the included clinical trials were not given Bisacodyl. Lastly, UpToDate and Google Scholar were searched using the term “oral Bisacodyl” with no additional relevant citations.

There were two similar studies published in 2006 and 2007 to investigate the efficacy and safety of short-term use of stimulant laxatives in adult patients with established chronic constipation.^{3,4} These were randomized, placebo-controlled, double-blind studies that evaluated Bisacodyl and Sodium Picosulphate, respectively, and concluded that they are both effective and safe. However, the experimental population was relatively small for both studies (N=55 and N=57), and the laxative treatment duration for each patient was three days. This same group of authors also conducted an open label, four week, randomized, parallel group study (N=144) comparing safety and efficacy between Bisacodyl and Sodium Picosulphate, as they have the same active metabolite.⁵ This study confirmed safety and efficacy of both these medications for a longer treatment duration compared to the previous studies.

Lastly, there was a multicenter, four week, double blinded, randomized, placebo-controlled trial of Sodium Picosulphate in patients with chronic constipation (N=367).⁶ This study design parallels that of the article chosen for this critical appraisal, with a focus on Sodium Picosulphate instead of Bisacodyl. Due to a combination of factors, including fewer biases resulting from the study design, larger population sample, longer duration of treatment, and overall clinical relevance to the patient in question, the remainder of this paper will discuss the article “Oral Bisacodyl Is Effective and Well-Tolerated in Patients With Chronic Constipation.”⁷

The Grade of Recommendation for the use of Bisacodyl for the management of temporary constipation is B, based on small, patient-oriented studies.⁸

Critical Appraisal

According to the SORT criteria, the quality of this publication is Level 1.⁸ This study was a multicenter, randomized, double-blind, placebo-controlled parallel group trial in which patients were recruited in 27 centers across the United Kingdom between September 2007 and June 2009. The recruited patients were required to be 18 years or older, suffering from chronic constipation as defined by the Rome III criteria, and willing to complete a daily electronic diary, use rescue medication, and provide written informed consent. Additionally, patients with acute conditions that either put them at risk for significant adverse events or were deemed to have confounding factors were excluded from the study.

According to the criteria presented, our patient, Ms. Moore, meets the requirements to participate, increasing the confidence in which data from this study could be applied to her case. Eligible patients underwent a 2-week baseline period without study treatment to allow data to be obtained for comparison prior to administering the study treatment. Those who met the constipation requirements (fewer than 3 complete spontaneous bowel movements per week on average with straining, incomplete evacuation, or hard stools occurring 25% of the time) were randomized into Bisacodyl and placebo treatment groups at a ratio of 2:1 using a computerized random-number generator. Each patient was given either two 5 mg Bisacodyl or matching placebo tablets and were permitted to take either 5 mg or 10 mg daily based on tolerability and symptom relief. Rescue medication, in the form of 10 mg



Bisacodyl rectal suppositories, was permitted in patients who did not achieve a bowel movement for >72 hours. No laxatives other than the study treatment, bulking agents, or prokinetic drugs were permitted. Follow up visits were conducted on day 16 and day 30 after beginning treatment.

The primary efficacy endpoint was the mean number of complete spontaneous bowel movements (CBSMs) per week over a 4-week period. Other measured outcomes included spontaneous bowel movements (SBM), improvement of quality of life (assessed using the Patient Assessment of Constipation questionnaire), and constipation related symptoms (assessed using a 5-point ordinal verbal rating scale). Safety endpoints included adverse events, vital signs, laboratory values, and overall assessment of tolerability by both the patient and the investigator.

Clinical significance and statistical adequacy were heavily considered in both the design of the study and the analysis of the results. The sample size for the study was chosen based on a statistical analysis concluding that an N=200 and N=100 were required for the Bisacodyl and placebo group, respectively, to detect a difference of 1 in the mean number of CSBMs per week with 90% power using a t test with a 0.05 two-sided significance level. The study met this goal with an N=247 for the Bisacodyl group and N=121 for the placebo group; a 20% drop out rate was anticipated. An analysis of covariance with treatment and center as fixed effects and baseline as covariate was performed between treatment groups regarding the number of CBSMs per week, number of SBMs per week, and evaluation of the change from baseline in constipation symptoms and PAC-QOL scores. Other tests utilized to assess significance of secondary end points included the Kaplan-Meier estimator, long-rank test, Wilcoxon rank test, and Fisher exact test. Any patient who took at least one dose of trial medication and provided any data for the primary efficacy endpoint was considered in the full set analysis, regardless of completion of the full 4-week trial, supporting an intention to treat analysis.

The patient population in each group was comparable in terms of gender, race, age, body mass index, duration of constipation, baseline number of CSBMs, and baseline number of SBMs. The mean age was 55, which is worth considering when applying this research to Ms. Moore, as geriatric patients often have more chronic conditions and complicated medication regimens compared to younger patients. Diet, fiber, and fluid intake were not assessed; however, patients were instructed not to make any significant lifestyle changes for the duration of the study. The number of patients who dropped out of the study were thoroughly reported. Incompletion of the study secondary to adverse events was higher in the Bisacodyl group, but all other reasons for dropping out were comparable between the groups.

The baseline number of CSBMs per week was 1.1 ± 0.1 in both groups. The adjusted mean number of CBSMs per week increased to 5.2 ± 0.3 in the Bisacodyl group and to 1.9 ± 0.3 in the placebo group. The adjusted mean difference of 3.3 ± 0.4 between the treatment groups had statistical significance with a $P < .0001$. There was also a statistically significant increase in mean SBMs per week, CBSMs per day, quality of life, and Bristol Stool Scale scores, along with a decrease in time to first SBM following the first dose of study medication, straining symptoms, and sense of anorectal obstruction. Adverse events were similar in both groups with the exception of abdominal pain and diarrhea, which were significantly higher in the Bisacodyl group. However, these adverse effects were highest in the first week and decreased the second through fourth weeks, likely as a result of dose reduction to 5mg in patients who did not tolerate 10mg of Bisacodyl daily.

The increase in the primary efficacy endpoint greatly exceeded the 10-15% improvement generally considered to be clinically significant for therapeutic gain. This study did not define any specific criteria to consider the treatment efficacious, however, the number needed to treat (NNT) can be calculated from the global assessment of efficacy reported by patients. 79.5% of patients in the Bisacodyl group reported satisfactory treatment, whereas only 49.6% of the patients in the placebo group reported satisfaction, resulting in a NNT of 3.34. Similarly, the number needed to harm (NNH) can be calculated by the percentages of patients that reported adverse events (72% in the Bisacodyl group and 37% in the placebo group). This results in a NNH of 2.86, however, it is worth noting that many of these adverse effects were not severe and were preferred by patients compared to their constipation symptoms.

Clinical Application

At the time of Ms. Moore's follow up visit with us, she had been taking oral Bisacodyl for three weeks following discharge from the hospital. We informed her that Bisacodyl is shown to be relatively safe in short term use up to four weeks, but there is uncertainty in chronic use. Other factors considered in the clinical decision making in Ms.

Moore's case included her age, which was 21 years older than the mean age of the study, her co-morbid conditions and their possible effects on her constipation (i.e. diabetes mellitus), and the other medications she was taking. For instance, she was discharged from the hospital with Ultram for short term control of her abdominal pain, which may have contributed to increased constipation and the need to add Bisacodyl to her regimen acutely. This is further supported by the loose stools experienced upon decreasing her Ultram usage. Additionally, Ms. Moore was treated with antibiotics for her recent episode of ischemic colitis, which could be an alternative explanation for her loose stools given that antibiotic exposure is a common cause of *Clostridium difficile* infections. However, this is less likely considering the timing of antibiotic exposure compared with the timing of loose stools, frequency and quality of her bowel movements, lack of other symptoms, and benign physical exam. Lastly, her preferences and social factors were considered.

Given Ms. Moore's satisfaction with her bowel regimen prior to her hospitalization and discomfort with her recent loose stools, compounded with the uncertainty of safety and efficacy of Bisacodyl chronically, we suggested that she discontinue Bisacodyl and Ultram. We discussed that Bisacodyl could have a role for short term treatment of acute on chronic constipation with the goal of improving discomfort and reducing risk of future hospitalization. Ms. Moore agreed to this plan and stated that she felt comfortable in her ability to return to the clinic for worsening symptoms affecting her quality of life and purchase oral Bisacodyl over the counter to use as a rescue medication.

New Knowledge Related to Clinical Decision Science

Bowel dysfunction can be an embarrassing topic for patients to discuss, and both constipation and loose stools as a result of treatment side effects can significantly impair daily living. This case also highlights the dynamic nature of clinical decision making—the Bisacodyl was appropriate when opioid medication was needed, but the patient needed guidance for ongoing management as she recovered from an acute episode. For this patient, the plan to continue her current treatment regimen and self-administer Bisacodyl for acute on chronic constipation episodes gave the patient a sense of control of the matter and decreased the need for additional appointments if her standard regimen was not sufficient. Additionally, the patient was only offered Bisacodyl in addition to her existing constipation regimen. Exploring different medications could have been an alternative as well.

Conflict Of Interest Statement

The author declares no conflicts of interest.

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