Docusate

Primary Literature

Mcrorie, J., Daggy, P., Morel, J., Diersing, P., Miner, P., & Robinson, M. (1998). Psyllium is superior to docusate sodium for treatment of chronic constipation. *Ailment Pharmacol Ther* , 491-497

Study Objectives: "To compare stool softening (stool water content) and laxative efficacy of psyllium hydrophilic mucilloid vs. docusate sodium in subjects with chronic idiopathic constipation"

Methods:

Design: Multi-site, parallel-design study of 170 subjects.

Allocation: Randomized, using intention to treat protocol.

Blinding: Double-blind

Follow-up period: 2 week placebo lead-in for baseline followed by 2 week treatment, with bowel movements checked ongoing throughout each day

Setting: Participants took interventions at home, sending their stools (frozen) and stool diary back to the investigators every 48-72h.

Participants: 20-74 year old patients with chronic idiopathic constipation (primarily females). The primary inclusion criterion was a BM frequency of less than 3/week during the baseline placebo lead-in. BMs were required to be considered "productive" to be included in the weekly BM count. A productive BM was determined based on the size (greater than) a 2cm diameter marble. Patients already on a laxative were not admitted.

Intervention: Psyllium 5.1g bid + docusate placebo vs. Docusate 100mg bid + psyllium placebo

Outcomes: BM frequency, stool weight, water content, consistency, straining/pain with BM and evacuation completeness.

Patient follow-up: 381 patients were enrolled in the study, with 187 being randomized for treatment (met criteria after placebo lead-in). 170 of these were considered "evaluable", although the reasoning was not specified. Patients were treated with intention to treat protocol and only had one patient drop out due to a serious adverse event, which was an unrelated motor vehicle accident.

Main Results: At week one, BM frequency increased from baseline in the psyllium group and decreased from baseline in the docusate group. Psyllium performed better for total stool weight, water weight and water content. By week two, psyllium showed an increased BM frequency (3.51 vs 2.87/week), stool water content (73.89 vs 71.58%), and directional improvement of all other subjective measures compared to docusate. Effects of psyllium were also seen beginning at 3 days, whereas effects of docusate were not seen until nearly the 2nd week. Overall, effects from docusate did not differ greatly from baseline.

Conclusions: Psyllium proved a more effective laxative both in increasing BMs/week and water content (softens stool, decreases straining) over docusate sodium for patients with idiopathic chronic constipation. The onset of psyllium was quicker than docusate. Docusate did not significantly change outcomes from baseline.

Comments: This RCT was well controlled, double-blinded, had no perceivable biases and had an adequate number of participants. The participants were handled with intention to treat protocol and all reasons for leaving the trial were documented. The dose of docusate was quite low (200mg/day) as compared to the max dose of 500mg/day. This may have underrepresented docusate. However, the typical OTC use of docusate is appropriately represented with this dose.

Goodman, J., Pang, J., & Bessman, A. (1976). Dioctyl Sodium Sulfosuccinate- An Ineffective Prophylactic Laxative. *J Chron Dis , 29*, 59-63.

Study Objectives: To assess the efficacy of dioctyl sodium sulfosuccinate (docusate sodium) as prophylactic treatment for chronic constipation in elderly patients.

Methods:

Design: Prospective study of 34 patients, not placebo-controlled.

Allocation: Randomized, using intention to treat protocol.

Blinding: No blinding was discussed

Follow-up period: 3 month-long study with daily assessments of BMs (bowel movements)

Setting: General medical ward.

Participants: 34 elderly patients (mean age 56) at risk or with history of chronic constipation. Spinal cord injuries, acute MIs, or those admitted due to diarrhea were excluded. Other disease states were similar in distribution between control and treatment group.

Intervention: Docusate sodium 100mg bid vs. no treatment (no placebo mentioned). If > 2 days without a bowel movement, patients were treated with an algorithm of laxatives to restore BMs.

Outcomes: Days between BM and quality of BM (scale as determined by nurses: watery, hard, soft etc.)

Patient follow-up: 34 patients were enrolled. They were followed over the course of 3 months and none were lost to follow-up. There were no major adverse events or events requiring removal from program.

Main Results: The mean number of stools per patient and frequency of stool per patient days were comparable in both groups. In addition, there were no significant stool quality differences between the groups.

Conclusions: Docusate at the dose given (100mg bid) is ineffective as prophylaxis for idiopathic chronic constipation.

Comments: This study was small, prospective, and un-blinded. There was no placebo control in place, although the population of patients being evaluated was not prone to the placebo effect since they were often confused, disoriented and on a large quantity of medication as it were. This was, clearly, a low-quality study, although the results should certainly not be discounted. Once again, a dose of 200mg/day of docusate was used, which leaves room for higher-dose studies. Unfortunately, there is a scarcity of good quality primary literature available for the efficacy of docusate sodium and most of the existing articles were unobtainable (even through the school's library).

Secondary Literature

American College of Gastroenterology Chronic Constipation Task Force. (2005). An Evidence-Based Approace to the Management of Chronic Constipation in North America. *American Journal of Gastroenterology* , S1-S22.

Study Objectives: To educate physicians about constipation's epidemiology, diagnostic approach and treatment.

Scope: Studies observed were North American patients suffering from chronic constipation and centered on establishing efficacy/safety of treatment options. North American epidemiological studies were also included. Studies needed to be RCTs, placebo controlled (if applicable), evaluating CC (chronic constipation) relief symptoms and published in English.

Methods: Standard criteria for systematic reviews included "comprehensive literature searching, use of pre-specified study selection criteria and use of a standardized and transparent process to extract and analyze data from studies". PUBMED and MEDLINE searches were searched from 1966-2003 for search terms: "constipation," "laxatives, stimulant," "laxatives, os- motic," "laxatives, irritant," "laxatives, bulk," "fecal softeners," "sorbitol," "lactulose," "milk of magnesia," "mag- nesium sulphate," "bisacodyl," "calcium polycarbophil," "polyethylene glycol," "danthron," "cascara," "ispaghula, "bran," "celandin," "docusate," "poloxalkol," "mineral oil," "glycerine," "psyllium," "methylcellulose," "senna," and "tegaserod". Only treatments available in the US were included. Recommendations were graded as A, B or C based on descending level of evidence. 81 studies were reviewed, only 4 of these directly related to docusate.

Main results: In respect to docusate, the review's main result was that it has proven ineffective in comparison to psyllium, as effective as placebo and (in an isolated, small trial) superior to placebo in respect to stool frequency.

Conclusion: The author's conclusion was that there is insufficient data to make a recommendation regarding docusate. The available evidence, however, leads the author to believe that docusate has no effect on symptoms of CC (chronic constipation).

Comments: The review made an excellent conclusion based on the evidence available. The limitations to each RCT reviewed were documented and considered in the conclusion. The review found only 4 available RCTs comparing docusate to placebo or intervention. The authors of this appraisal have confirmed this finding.

Hurdon, V., Viola, R., & Schroder, C. (2000). How Useful is Docusate in Patients at Risk for Constipation? A Systematic Review of the Evidence in the Chronically Ill. *Journal of Pain and Symptom Management* , 130-136.

Study Objectives: To clarify the utility of docusate in populations with advanced disease

Scope: Prospective, randomized controlled trials of docusate in the chronically ill. Patients were required to have risk factors for or preexisting constipation. Sample sizes ranged from 15-74 and were generally low quality studies (score ranged from 0.46-0.52). Outcomes were generally frequency and quality of BMs. Patients ranged in age but were generally the elderly population. Duration of therapy ranged from 20-26 days. Doses ranged more severely from 60-480mg/day.

Methods: The authors searched Medline 1966-1997, CINAHL 1982-1997, Current Contents 1996-1997, Cochrane Library, Index Medicus 1940-1966 and some palliative journals, articles and texts. Only English or French studies were considered. Articles were required to have a full report or abstract. Retrospective, Case series, case reports and studies looking at docusate combo products were excluded. The terms "docusate", "constipation", "dioctyl" and "doxidan" were used, with "drug therapy" and "prevention and control" as floating subheadings. Only 4 studies were found that matched the criteria given.

Main results: Due to the poor quality of mixed-characteristic studies, the review concluded that the evidence available would not be useful to make a review-based conclusion on the results.

Conclusion: The author's conclusion was that the current use of docusate in chronically ill patients for the prevention and treatment of constipation is founded on inadequate evidence.

Comments: The author was correct in abstaining from making a result-based conclusion on the evidence reviewed. There is currently insufficient evidence to make a claim for chronically ill patients using docusate for chronic constipation. The reviewer's were not blinded, although this would not have made the evidence any more useful. One incidence of selection bias occurred in the fact that the author did not search European databases such as EMBASE and, thus, has excluded that evidence from the review. Their conclusion was sound, however.

Ramkumar, D., & Rao, S. (2005). Efficacy and Safety of Traditional Medical Therapies for Chronic Constipation: Systematic Review. *Americn Journal of Gastroenterology* , 936-971.

Study Objectives: To conduct a systematic review of the efficacy/safety of traditional chronic constipation medication treatments and to make evidence-based recommendations.

Scope: Randomized trials conducted on adults with chronic constipation. The mean age ranged from 37-82. Duration ranged from 2-4 weeks. All trials were single or double blinded. All compared docusate oral (100-240mg bid) to placebo or another intervention.

Methods: English literature was searched (MEDLINE and PUBMED) for chronic constipation drug trials between 1966-2003. Studies were required to be randomized with full manuscripts published. All studies were assigned a quality score before their results were used to aid in a conclusion. "Docusate", "dioctyl", "constipation" and "fecal softeners" were searched and exploded terms were reviewed and included in search where appropriate. All abstracts were screened. Four studies were found.

Main results: Docusate 100mg bid was proven inferior to psyllium in normal doses for BM frequency and quality. One small study suggests docusate calcium may be more effective than docusate sodium. All benefits over placebo were modest to none.

Conclusion: Level III Evidence, Grade C to recommend docusate for chronic constipation treatment. (Poor quality of evidence and inadequate abundance/quality of evidence to make a recommendation).

Comments: This review was performed meticulously and accounted for quality of studies, differences in populations and provided standardized recommendations for each drug investigated. They did not, however, consider EMBASE and the European literature. The conclusion was sound.