The use of senna with docusate for postoperative constipation after pelvic reconstructive surgery: a randomized, double-blind, placebo-controlled trial

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OBJECTIVE: The objective of the study was to compare time to first bowel movement (BM) after surgery in subjects randomized to placebo or senna with docusate.

STUDY DESIGN: Ninety-six subjects completed a baseline 7-day bowel diary before and after surgery. After pelvic reconstructive surgery, the subjects were randomized to either placebo (n = 45) or senna (8.6 mg) with docusate (50 mg) (n = 48). Time to first BM and postoperative use of magnesium citrate were compared.

RESULTS: There was a significant difference in the time to first BM in those receiving senna with docusate vs placebo (3.00 ± 1.50 vs 4.05 ± 1.50 days; $P < .002$). More subjects in the placebo group needed to use magnesium citrate to initiate a bowel movement (43.6% vs 7.0%; $P < .001$).

CONCLUSION: The use of senna with docusate decreases time to first BM in those undergoing pelvic reconstructive surgery compared with placebo. Subjects using senna with docusate are also significantly less likely to use magnesium citrate.

Key words: constipation, pelvic organ prolapse, senna with docusate

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Postoperative bowel function is a significant concern for women undergoing pelvic floor reconstructive surgery, as well as for their physicians. There are studies looking at treating constipation using fiber and wheat supplementation in pregnancy, general surgery, colorectal surgery, orthopedic surgery, and hospitalized patients.[1-4] Collectively, these studies show some benefit to using additional fiber and/or wheat to help relieve or prevent constipation.

Prior research has found a significant discordance between surgeon and patient impression of postoperative constipation, highlighting the need for better patient education.[5] Typically, the first bowel movement (BM) may not occur until at least the second postoperative day, and subsequent delays can predispose patients to impaction and discomfort.[6] The use of preoperative bowel preparations, lasting effects of anesthetic medications, narcotic pain medications, surgical manipulation, and general postoperative immobility predispose this patient population to constipation.

Senna has been shown to decrease gut transit time.[7] A study using a regimen of senna and docusate following different anorectal surgeries found that 80% of patients were able to have a BM on postoperative day 1 after only 2 tablets of senna with docusate. No patients in this study required an enema, and the only side effect reported was 1 case of diarrhea in a patient with "a history of loose stools in the past."[6]

There is no standardized medication regimen that has been tested for relief of constipation in the benign gynecology or urogynecology postoperative patients. The aim of this study was to compare the use of senna with docusate with placebo after pelvic reconstructive surgery to determine whether senna with docusate reduces time to first BM.

Materials and Methods

The institutional review board of Hartford Hospital approved this study. All subjects enrolled signed informed consent. All women, aged 18 years and older, undergoing pelvic reconstructive surgery requiring overnight admission, were eligible for enrollment. Patients with a history of ulcerative colitis, Crohn's disease, irritable bowel disease, and gastroparesis; those undergoing concurrent bowel resection anal sphincteroplasty or repair of rectovaginal fistula; and those with intraoperative bowel or rectal injury or extensive lysis of adhesions were excluded. Those who were dependent on bowel stimulants or laxatives were also excluded. Subjects were allowed to continue the use of fiber supplements if they had been on these before surgery. Any patients who were unable to provide informed consent or follow

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the instructions to complete study-related materials were also excluded.

After enrollment, subjects completed a 7-day bowel diary to provide a baseline assessment of bowel frequency, type of BM using the validated Bristol stool scale,[7] degree of strain and pain (measured on an 11-point visual analog scale from 0–10), and medications taken. The Bristol stool scale provides a reliable and valid measure of gut transit time based on the shape, consistency, and appearance of BMs. The subjects rate the type of BM on a scale from 1–7. Types 1 and 2 are consistent with reduced gut transit time; types 3 and 4 represent normal transit time; and types 5, 6, and 7 indicate increased gut transit time.[7]

After surgery, if there was no unintentional bowel or rectal injury or significant adhesions, the subject was randomized to either senna with docusate (SennaS; Purdue Pharmaceuticals, Stamford, CT) or matching placebo. The placebo pills were generated to match the senna with docusate pills by Pioneer Health compounding pharmacy (Vernon, CT).

The subjects were provided with identical instructions on how to take the medications after surgery. The subjects started with 2 tablets at night on postoperative day 1 (either at home or in the hospital); followed by 2 tablets the following morning if no BM; followed by 3 tablets in the evening if no BM; and then, if no BM the following morning, 3 additional tablets. The subjects used 3 tablets twice per day until their first BM or took magnesium citrate if they did not have a BM on the fourth day after surgery.

Subjects were to use the minimum number of tablets of the medication to maintain soft regular BMs and start to cut back as they resumed their usual diet and activities. They were instructed to stop the medication if they had loose stools or diarrhea. If they had to use magnesium citrate on the fourth day after surgery and then became constipated, they could use either polyethylene glycol or milk of magnesia instead of the study medication.

Randomization was performed using computer-generated blocks by a neutral individual. Investigators, study nurse, and subjects were blinded to treatment allocation and were unblinded only if necessary for subject safety.

The study medication was dispensed to the subject on the postoperative floor prior to discharge by a neutral individual. The study medication was started on postoperative day 1. All subjects were given another diary to complete using the Bristol stool scale, pain, strain, and list of medications being taken. They recorded information on the diary until the first BM. If no BM occurred by the fourth postoperative day, subjects were instructed to use 5 ounces of magnesium citrate to initiate a BM. If they did not have a BM with the magnesium citrate, they were to call the office for further instructions to use an enema or come to the office for evaluation.

All subjects received a phone call within the first postoperative week about any pain, cramps, flatulence, or discomfort associated with the study medication. After the first BM, the subjects could follow the same regimen with the study medication, stop the study medication, or use a different medication to maintain regular BMs. All subjects were instructed to stop the study medication if they had loose stools or diarrhea.

Subjects were enrolled in a 1:1 ratio. We estimated that the patients taking senna with docusate would have a BM 2 days earlier than those receiving placebo, extrapolating from the study by Corman,[6] in which a majority of the patients receiving senna with docusate had a bowel movement on the first postoperative day after only 2 doses of the medication.

Because we did not know whether these patients had a preoperative bowel preparation, and preoperative bowel preparations can increase time of return of bowel movements after surgery, we estimated that 1 additional day would be necessary to initiate a BM in the senna with docusate group and those receiving placebo would not have a bowel movement until postoperative day 4 or beyond. Thus, a sample size of 49 subjects in each group (a total sample size of 98) was calculated to afford 90% power to detect a difference in mean time to BM of 2.0 days, assuming that the common SD was 3.0 days, using a 2-group Student t test with a 0.05 2-sided significance level.

This number of participants also would afford sufficient power to detect a statistically significant difference in the expected proportion of patients requiring magnesium citrate. We estimated a 5% dropout or exclusion rate of those who consented to participate. Therefore, we planned to enroll 104 patients, 52 subjects in each group, into the study.

The primary outcome, time to first BM in each group, was compared with a 2-group Student t test. Time to first BM was calculated as the difference between the date and time of the subject's surgery and the date and time of first BM after surgery, as listed on the postoperative bowel diaries.

The secondary outcome, use of magnesium citrate in each group, was compared using Fisher's exact test. Other comparisons were type of BM based on Bristol stool scale, frequency of bowel movements, straining at stool, and pain with bowel movements. A constipation score for subjects was calculated based on preoperative stool frequency, postoperative days to first BM, stool consistency, percentage of straining, and sensation of incomplete evacuation.

Constipation scores were calculated as follows: days to first BM (2 points if >4 days, 0 points if 1–3 days); stool consistency (1 point if types 1 or 2 on Bristol stool scale, 0 points for types 3–7 on the Bristol stool scale); strain rating (0.5 points if for ≥ 5 on $\geq 25\%$ of the BMs; 0 points for ≤ 4 on 0–25% of the BMs; 0.5 point for rating of mild, moderate, or severe for sense of incomplete evacuation to the question: "Have you experienced the following symptom: incomplete bowel movement, like you did not finish?" with 0 point for rating of none).

The scoring system was developed by a study in cardiac patients using lactulose after surgery for treatment of constipation.[8] A score of 2 or more was consistent with constipation based on the Rome III criteria.[9] All analyses were conducted with SPSS 14.0 (SPSS, Inc, Chicago, IL) at the 0.05 significance level such that all comparisons yielding $P < .05$ were deemed statistically significant.

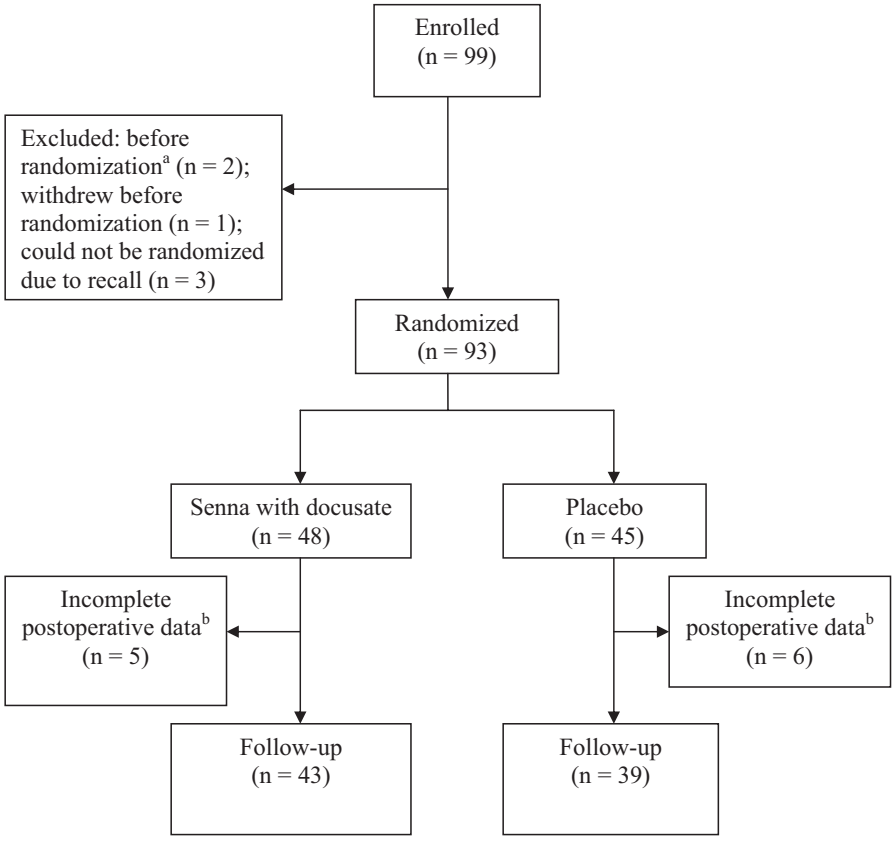
Results

A total of 82 subjects had complete data for analysis (Figure). There was a Food and Drug Administration (FDA) recall on senna with docusate before completion of the study because of 2 missing ingredients (lactose and tartaric acid) on the label of the medication, so enrollment was stopped early. In addition, analysis of results found that there was a significantly higher need for subjects in the placebo arm to use magnesium citrate, so for ethical reasons we elected not to resume enrollment once the medications were available. Three subjects were enrolled but not randomized because of the recall on the senna with docusate medications prior to surgery and were not included in this analysis. Two subjects were not randomized because of an intraoperative rectal injury that was recognized and repaired.

The groups were similar with respect to age, body mass index (BMI), vaginal parity, race, menopausal status, history of prior prolapse surgery, median preoperative stage of prolapse, types of surgeries performed for prolapse and incontinence, and median days in the hospital (Table 1). There was no significant difference between the 2 groups for the day that the study medications were started. Only 1 subject did not receive the medication at all because of an early postoperative ileus that developed into a partial small bowel obstruction requiring surgical exploration. She was randomized and kept for intention-to-treat analysis; however, she did not receive any study medications.

The subjects receiving senna with docusate had a statistically significant decrease in time to first BM compared with placebo, mean 3.0 ± 1.5 days vs 4.0 ± 1.5 days, respectively ($P = .002$). In addition, there was a significant increase in the use of magnesium citrate in the group using placebo compared with the senna with docusate group, 43.6% vs 7.0%, respectively ($P < .001$). Time to first BM was not significantly different (3.52 vs 3.44; $P = .800$) in those undergoing abdominal vs vaginal reconstructive surgery, respectively.

FIGURE
Enrollment and follow-up of subjects



[a]These 2 subjects were excluded due to an inadvertent rectal injury noted during surgery and so they were not randomized, as this was an exclusion criterion for randomization; [b]These subjects provided the day of first BM after surgery and if they had to use magnesium citrate but did not provide information on the type of BM or degree of strain or pain associated with the BM.

BM, bowel movement.

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The range of constipation scores was from 0–4.5. Constipation scores were significantly higher in those receiving placebo compared with senna with docusate (1.34 vs 0.68; $P = .011$). The mean strain and pain scores for postoperative bowel movements were not significantly different between groups (Table 2). The distribution of types of BMs before surgery, most commonly type 4, consistent with normal transit time, was not significantly different between the 2 groups. After surgery, the types of BMs varied widely between the 2 groups, with the most common types of BMs in the senna with docusate group being type 1 and in the placebo arm type 3.

Side effects with either the placebo or senna with docusate were mild. In the senna with docusate group, 15.4% (6/39) experienced cramping or bloating that was not bothersome. In the placebo group, 4.6% (2/43) experienced bloating. This difference was not statistically significant. In the placebo group, 7% (3/43) stated they had cramps and discomfort related to using magnesium citrate.

One subject in the senna with docusate group experienced persistent loose stools, despite stopping the study medication, and was observed in the hospital overnight. Evaluation was negative for *Clostridium difficile* infection or bowel obstruction; she had normal electrolytes and was discharged after receiving intravenous fluids. One subject in the senna with docusate treatment group developed a partial small bowel obstruction

TABLE 1
Demographics of subjects[a]

Demographic	Senna with docusate (n = 43)	Placebo (n = 39)
Age, mean (SD)	59.5 (12.6)	56.2 (10.0)
BMI, mean (SD)	27.3 (5.2)	27.0 (5.2)
Vaginal parity	2 (range, 0–4)	3 (range, 0–7)
Race, n (%)		
White	35 (81.4)	32 (82.1)
Black	1 (2.3)	2 (5.1)
Asian/Pacific Islander	2 (4.7)	0 (0)
Not reported	5 (11.6)	5 (12.8)
Stage prolapsed, median (range)	2 (2–4)	2 (2–4)
Menopause, n (%)		
Yes	30 (69.8)	19 (48.7)
No	8 (18.6)	15 (38.5)
Unknown/not recorded	5 (11.6)	5 (12.8)
Prior prolapse surgery, n (%)		
Yes	10 (23.3)	13 (33.3)
No	28 (65.1)	21 (53.8)
Unknown/not recorded	5 (11.6)	5 (12.8)
Surgery type, n (%)[b]		
Vaginal	24 (55.8)	19 (48.7)
Abdominal	4 (9.3)	6 (15.4)
Laparoscopic/robotic	15 (34.9)	15 (38.5)
Days in hospital, median (range)	2 (1–25)	2 (1–7)

[a] No significant difference in any parameter between treatment groups; [b] Surgeries were for prolapse and incontinence.

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TABLE 2
Comparison of results between groups

Variable	Senna with docusate	Placebo	*P* value
Time to first BM, d (mean [SD])	3.0 (1.5)	4.0 (1.5)	.002[a]
Use of magnesium citrate, % (n)	7.0 (3)	43.6 (17)	< .001[a]
Constipation score,[b] mean (SD)	0.68 (0.75)	1.34 (1.23)	.011[a]
Strain scores before surgery,[c] mean (SD)	2.01 (1.75)	1.67 (1.33)	.33
Strain scores after surgery, mean (SD)	2.29 (2.23)	2.06 (2.39)	.70
Pain scores before surgery,[c] mean (SD)	0.85 (1.15)	0.48 (0.78)	.11
Pain scores after surgery,[c] mean (SD)	2.52 (2.38)	2.36 (2.95)	.795

BM, bowel movement.

[a] Values are significantly different at $P < .05$; [b] Constipation score was calculated as follows: days to first BM (2 points if >4 days, 0 point if 1-3 days); stool consistency (1 point if types 1 or 2 on Bristol stool scale, 0 point for types 3-7 on the Bristol scale); strain rating (0.5 point if for ≥5 on ≥25% of the BMs, 0 point for ≤4 on 0-25% of the BMs, 0.5 point for rating of mild, moderate, or severe for sense of incomplete evacuation to question: "Have you experienced the following symptom: incomplete bowel movement, like you did not finish?" with 0 point for rating of none"); [c] The strain and pain scores were rated by the subjects on a visual analog scale from 0 to 10.

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after surgery and randomization but prior to taking any of the study medications.

These were the only 2 subjects that were unblinded before completion of the study. There were no other admissions or office visits related to the use of the study medication. Those who did not have a BM using the study medication were able to initiate a BM using magnesium citrate.

Comment

The use of senna with docusate was associated with a decrease in time to first BM undergoing pelvic reconstructive surgery compared with placebo. There was a significantly reduced need to use magnesium citrate to initiate BM in those using senna with docusate compared with placebo. Route of pelvic reconstructive surgery did not have an impact on time to first BM, which is likely related to random assignment of subjects to either senna with docusate or placebo. There were mild side effects associated with use of senna with docusate after pelvic reconstructive surgery.

The strengths of our study are its randomized, double-blind, placebo-controlled design. We were able to maintain blinding throughout the study to minimize bias in analysis. We were able to obtain postoperative data from almost all subjects and maintained intent-to-treat analysis for the duration of the study. Despite having to stop enrollment early, there nonetheless was a significant difference in time to first BM between the groups.

The FDA recall was due to 2 ingredients, tartaric acid and lactose, that were not listed on the label. These 2 ingredients are part of many other food substances and so did not affect the safety of the medication. We did not find any allergic reactions among the subjects taking the senna with docusate. The recall affected all medications with either senna or docusate; however, all medications are available now after appropriate correction was made on the ingredient label.

A limitation of our study was that subjects were restricted to 4 days after sur-

gery before taking magnesium citrate, which may have made the time difference between the 2 study groups less dramatic. However, for ethical reasons, we could not allow subjects to go beyond 4 days before using an additional intervention to initiate a BM. Despite finding a difference of 1 day, we believe that this is clinically significant for subjects who are very concerned about having a BM as soon as possible after surgery. In addition, senna with docusate significantly reduced the need to use magnesium citrate, which is a stronger laxative and can be unpleasant for patients.

It is interesting to note that the most common types of BMs among the subjects was type 4, which is consistent with a normal transit time. Studies looking at women with prolapse suggest increased risk for constipation with prolapse;[10,11] however, based on our baseline diaries, there is minimal straining and normal gut transit time in women with prolapse.

The symptoms of constipation in women with prolapse may be related to symptoms of stool trapping and difficulty with evacuation, with large prolapse rather than reduced frequency of BMs and straining related to BM. A reduced gut transit time (type 1 or 2 on the Bristol stool scale) was seen after surgery in both groups, likely due to delay in return to bowel movements for 3 or 4 days in the senna with docusate or placebo group, respectively. The placebo group was more likely to use magnesium citrate to initiate a BM, which may explain why this group experienced type 3 BMs more often after surgery than the senna with docusate arm.

There are data to support the use of fiber supplementation, intensive nursing interventions, and patient education for preventing or alleviating constipation.[2,4,12,13] A high-fiber diet can reduce symptoms of constipation experienced by women with pelvic organ prolapse (POP), but this was not in the setting of surgery to correct POP.[14]

Constipation can be associated with many different factors, including reduced fiber intake; use of narcotics; and medications, such as anticholinergics, calcium channel blockers, iron, and calcium. By randomly assigning subjects, these factors were not significantly different between the study groups, reducing the chance for bias. We used the Rome III criteria[9] to calculate a constipation score[8] to compare the groups in a more objective manner. The scores did show a difference between those receiving placebo vs senna with docusate, strengthening our findings in favor of using senna with docusate to reduce constipation after pelvic reconstructive surgery.

There are few studies looking at postoperative bowel function. The use of fiber supplementation is beneficial in various patient populations,[12-14] but our clinical experience is that after pelvic reconstructive surgery, laxatives are often needed to initiate BMs because of narcotic use and dietary changes. These medications are safe and effective to use in the short term. Constipation and obstipation after surgery can be unpleasant and increase patient phone calls, office visits, and possibly hospitalization. Finding a safe, reliable, and effective bowel regimen after surgery is important. Our study supports the use of senna with docusate to reduce time to first BM and decrease need for magnesium citrate after pelvic reconstructive surgery. ■

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REFERENCES

1. Jewell DR, Young G. Interventions for treating constipation in pregnancy. Cochrane Database Syst Rev 2000;2:CD001142.
2. Kochen MM, Wegscheider K, Abholz HH. Prophylaxis of constipation by wheat bran: a randomized study in hospitalized patients. Digestion 1985;31:220-4.
3. Schmelzer M. Effectiveness of wheat bran in preventing constipation of hospitalized orthopaedic surgery patients. Orthop Nurs 1990; 9:55-9.
4. Kacmaz Z, Kasici M. Effectiveness of bran supplement in older orthopaedic patients with constipation. J Clin Nurs 2007;16:928-36.
5. Franneby U, Gunnarsson U, Wollert S, Sandblom G. Discordance between the patient's and surgeon's perception of complications following hernia surgery. Hernia 2005;9:145-9.
6. Corman ML. Management of postoperative constipation in anorectal surgery. Dis Colon Rectum 1979;22:149-51.
7. Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scand J Gastroenterol 1997;32:920-4.
8. van der Schaaf M, Vermeulen H, Storm-Versloot MN, Goossens A, Simons R, Eijsman L. Effectiveness of lactulose syrup after cardiac surgery. Appl Nurs Res 2004;17:48-54.
9. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. Gut 1999;45(suppl II):II43-7.
10. Arya LA, Novi JM, Shaunik A, Morgan MA, Bradley CS. Pelvic organ prolapse, constipation and dietary fiber intake in women: a case control study. Am J Obstet Gynecol 2005;192: 1687-91.
11. Jelovsek JE, Barber MD, Paraiso MFR, Walters MD. Functional bowel and anorectal disorders in patients with pelvic organ prolapse and incontinence. Am J Obstet Gynecol 2005;193:2105-11.
12. Griffenberg L, Morris M, Atkinson N, Levenback C. The effect of dietary fiber on bowel function following radical hysterectomy: a randomized trial. Gynecol Oncol 1997;66:417-24.
13. Voderholzer WA, Schatke W, Muhldorfer BE, Klauser AG, Birkner B, Muller-Lissner SA. Clinical response of dietary fiber treatment of chronic constipation. Am J Gastroenterol 1997;92:95-8.
14. Shariati A, Maceda JS, Hale DS. High fiber diet for treatment of constipation in women with pelvic floor disorders. Obstet Gynecol 2008; 111:908-13.