

## Addition of senna improves quality of colonoscopy preparation with magnesium citrate

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However, abdominal cramps were observed more often under the senna protocol (29.2%) compared to the magnesium citrate only protocol (9.9%,  $P < 0.0003$ ).

**CONCLUSION:** The addition of senna to the bowel preparation protocol with magnesium citrate significantly improves the cleansing outcome.

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**Key words:** Colonoscopy; Bowel preparation; Senna; Magnesium citrate; Polyp

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### Abstract

**AIM:** To prospectively investigate the effectiveness and patient's tolerance of two low-cost bowel cleansing preparation protocols based on magnesium citrate only or the combination of magnesium citrate and senna.

**METHODS:** A total of 342 patients who were referred for colonoscopy underwent a colon cleansing protocol with magnesium citrate alone ( $n = 160$ ) or magnesium citrate and senna granules ( $n = 182$ ). The colonoscopist rated the overall efficacy of colon cleansing using an established score on a 4-point scale. Patients were questioned before undergoing colonoscopy for side effects and symptoms during bowel preparation.

**RESULTS:** The percentage of procedures rescheduled because of insufficient colon cleansing was 7% in the magnesium citrate group and 4% in the magnesium citrate/senna group ( $P = 0.44$ ). Adequate visualization of the colonic mucosa was rated superior under the citramag/senna regimen ( $P = 0.004$ ). Both regimens were well tolerated, and did not significantly differ in the occurrence of nausea, bloating or headache.

### INTRODUCTION

Good bowel preparation is mandatory for optimal intraluminal visualization during colonoscopy. Inadequate bowel cleansing has a negative impact on completion rate<sup>[1]</sup> and polyp detection rate<sup>[1,2]</sup>. It also increases procedure time<sup>[1,3]</sup> and difficulty<sup>[1]</sup>, and it may affect the procedure safety profile<sup>[4]</sup>. All these factors negatively affect therapeutic efficiency and diagnostic accuracy and increase colonoscopy costs<sup>[5]</sup>.

Magnesium citrate is an osmotic saline agent that increases intraluminal volume resulting in a secondary increase of intestinal motility<sup>[6]</sup>. According to a prospective study of colonoscopy practice in 68 hospitals in the UK, magnesium salts are used as bowel cleansing agents in 36.8% of colonoscopies<sup>[7]</sup>. Magnesium citrate must be used cautiously in patients with impaired renal function.

Senna, an anthraquinone derivative, is a stimulant laxative stimulating intestinal motility<sup>[8]</sup>. Senna has been reported to be a useful adjunct to polyethylene glycol

(PEG) colonoscopy preparation regimens<sup>[9,10]</sup>. However, the role of senna as a potential adjunct of magnesium citrate for bowel preparation is yet to be explored.

In two prospective clinical audits, we compared the colon cleansing efficacy and patient tolerability of two colon preparation regimens for adults undergoing colonoscopy: (a) magnesium citrate; and (b) magnesium citrate combined with senna granules.

## MATERIALS AND METHODS

### Patients

A total of 345 consecutive adult out patients referred to the endoscopy unit of the John Radcliffe hospital for colonoscopy on routine clinical indications were prospectively invited to participate. Exclusion criteria were ileus or suspected bowel obstruction, significant gastroparesis or gastric outlet obstruction, toxic colitis or megacolon, pregnancy, or lactation. Patients included were referred mainly due to alarm symptoms such as altered bowel habit in patients > 45 years of age, blood per rectum, iron-deficiency anaemia, unintentional weight loss, and/or other symptoms suggestive of malignant disease. No patient refused to participate. Patients who could not be sedated for colonoscopy were excluded from further evaluation. All patients gave informed consent before participation.

From July to November 2006, we prospectively audited the performance of the large bowel cleansing with magnesium citrate (citramag-only group). The colon preparation protocol with magnesium citrate and senna (citramag/senna group) was audited from August 2007 to January 2008.

### Bowel preparation regimens

All patients were asked to refrain from taking iron tablets 7 d prior to colonoscopy and any medications reducing gastrointestinal motility, e.g. loperamide, 4 d before colonoscopy, but continued all other medications. Two days before colonoscopy, all patients were instructed to eat a low-fiber diet such as white fish, chicken, white bread, eggs, cheese, or potato without skins. High-fiber kinds of food such as red meat, fruit, or vegetables, were to be avoided and patients were advised to consume plenty of fluids. On the day before colonoscopy patients, were instructed to have a low-fiber breakfast. Following that, patients were instructed not to eat any solid food until after colonoscopy and to consume plenty of clear fluids. On the day before colonoscopy at 5:00 pm, patients were instructed to dissolve one sachet of citramag in 200 mL of hot water, which was to be consumed half an hour later when cool. One sachet contains 11.6 g magnesium carbonate and 17.8 g anhydrous citric acid. At 7:00 pm, the patients were instructed to dissolve half of the second sachet of citramag in 100 mL of water and consume it once cooled. Patients were instructed to drink clear fluids (at least a cupful every 30 min) throughout the day and evening before colonoscopy. On the day of colonoscopy, at 6:00-7:00 am in the case of a morning appointment

or at 9:00-10:00 am in the case of an afternoon appointment, patients were instructed to consume the other half of a sachet of citramag as described above.

Patients in the citramag-only group underwent colonoscopy after bowel cleansing as described above (two sachets of citramag). Patients in the citramag/senna group were instructed to follow the above instructions but they were also asked to consume one sachet of senna in a cup of warm water and consume it at 2:00 pm on the day before colonoscopy (two sachets of citramag and one sachet of senna).

### Colonoscopy

In order to eliminate interobserver variability, all colonoscopies were performed by the same experienced endoscopist who was, however, not blinded as to the cleansing regimen used. The colonoscopist rated the overall cleansing of the bowel on a 4-point Likert scale as in previous studies<sup>[11-13]</sup>: 1 = "unacceptable" (large amounts of solid and semisolid fecal residue requiring additional cleansing resulting in rebooking); 2 = "poor" (enough feces or fluid to prevent a completely reliable examination); 3 = "satisfactory" (small amounts of feces or fluid not interfering with the exam); 4 = "good" (no more than small bits of adherent feces/fluid). For the primary efficacy variable, scores of 3 and 4 were considered "adequate" and scores of 1 or 2 were considered "inadequate".

### Symptom score

Prior to colonoscopy, patients were asked to describe their tolerance to the cleansing protocol. Symptoms of nausea, vomiting, bloating, abdominal pain/discomfort, and headache were documented. Patients were asked to rate their symptom severity on a 5-point Likert scale as in previous bowel cleansing studies<sup>[12-14]</sup>: 1 = "none"; 2 = "mild"; 3 = "moderate"; 4 = "severe"; and 5 = "extreme". Any adverse event reported during bowel cleansing and/or during the procedure and/or during stay in the recovery room after the procedure was also recorded.

### Statistics analysis

Data are shown as mean and standard deviation or as median and ranges, as appropriate. The  $\chi^2$  test was used for comparisons between categorical variables and the Student's *t* test was used for comparisons between quantitative variables. All tests were two-tailed and conducted at a 5% significance level.

## RESULTS

Overall, 345 patients underwent colonoscopy. Three patients in the citramag-only group could not be sedated for colonoscopy and were excluded from further evaluation. Data analysis was based on 160 patients who underwent colonoscopy after using the citramag bowel cleansing regimen and on 182 patients who performed bowel preparation for colonoscopy according to the combined citramag/senna regimen. Demographic and

**Table 1** Demographic and clinical data

	Citramag-only (n = 160)	Citramag/senna (n = 182)
Male/female	76/84	97/85
Age	60 ± 13	58 ± 14
History of bowel resection	6	9
Sedation		
Fentanyl iv (µg)	75 (0-200)	75 (0-200)
Midazolam iv (mg)	4 (0-10)	4 (0-10)
Polyp detection rate	37 (23.1%)	63 (34.6%) <sup>1</sup>
Colorectal cancer	17	16
Completion rate	86% (adjusted 92%)	92% (adjusted 97%) <sup>2</sup>

Data are presented as mean and standard deviation or *n* and percentage as appropriate. <sup>1</sup>*P* < 0.03, <sup>2</sup>*P* = 0.07.

**Table 2** Quality of colon cleansing as evaluated by the endoscopist *n* (%)

	Citramag-only (n = 160)	Citramag/senna (n = 182)
Good	20 (12.5)	41 (22.5)
Satisfactory	88 (55.0)	107 (58.8)
Poor	41 (25.6)	26 (14.3)
Unacceptable	11 (6.9)	8 (4.4)

clinical data of the patients are given in Table 1. The two groups did not differ regarding age, gender, previous history of colorectal surgery, caecal intubation rate, and sedation required (Table 1).

### Patients following the citramag-only bowel cleansing regimen

In six of 160 patients (3.8%) using the citramag only cleansing protocol, bowel preparation was so poor with solid fecal residues that the procedure was abandoned in the rectosigmoid, and we did not attempt further insertion. In five other patients the cecum was reached but the view was unacceptable due to fecal residues, especially on the right side. Therefore, a repeat colonoscopy was indicated in these patients as well. Totally, 11/160 (6.9%) of the patients had to be rebooked for colonoscopy or virtual colonoscopy because of insufficient bowel cleansing after the citramag regimen.

Complete colonoscopy with visualization of the cecum was reached in 137/160 colonoscopies (86%). Adjustment for tumor strictures (4), cancellation of the procedure due to poor bowel preparation (6) or severity of colitis (1) raised the completion rate to 92% (137/149).

### Patients following the citramag and senna bowel cleansing regimen

Five out of 182 patients (2.7%) were not examined further than the rectosigmoid because of insufficient bowel cleansing after taking the senna protocol, and three had to be rebooked because of insufficient views despite intubation of the cecum. Thus, eight of 182 patients (4.4%) had unacceptable bowel cleansing under the senna/citramag regimen.

The unadjusted completion rate for cecal intubation

was 92%. Adjustment for tumor strictures<sup>[4]</sup> and exclusion of procedures abandoned in the rectosigmoid due to poor bowel preparation<sup>[5]</sup> resulted in a completion rate of 97%.

Table 2 shows the quality of colon cleansing results for the two regimens used in the current study as assessed by the endoscopist. The combined citramag/senna regimen proved superior in bowel cleansing as it achieved “adequate” colon visualization (quality of colon cleansing rated as “good” or “satisfactory” in 148/182 (81.3%) compared to 108/160 (67.5%) colonoscopies using the citramag protocol (*P* = 0.004; Table 3). The colonic polyp detection rate was higher in the citramag/senna group compared to the citramag-only group (*P* < 0.03; Table 1).

### Side effects and tolerability

Both protocols were well tolerated. None of the side effects observed were categorized as extreme, and five patients reported severe side effects during bowel preparation. The two bowel cleansing regimens did not significantly differ in the occurrence and intensity of nausea, vomiting, bloating or headache (Table 3). Abdominal cramps occurred more often in the citramag/senna group (*P* < 0.003; Table 3). Two patients reported “severe” abdominal pain/cramps both of whom had a stricturing tumor in the rectosigmoid.

## DISCUSSION

According to our findings, the overall cleansing results were superior using the combination of senna compared to the citramag-only regimen. Although we did not perform a segmental evaluation of colon cleansing, the general impression was that particularly the right colon was better visualized in the citramag/senna group, while in the citramag-only group the cecum and ascending colon were often still covered in sticky solid fecal layers. Having reviewed the relevant bibliography and to the best of our knowledge, the current study is the first to evaluate the efficiency of senna as an adjunct to magnesium citrate for large bowel preparation prior to colonoscopy.

The rationale for using an osmotic agent such as magnesium citrate, together with a stimulant laxative such as senna for colonoscopy preparation, is that increased fluid bowel content produced by the osmotic agent may be more readily evacuated upon bowel stimulation by the stimulant agent<sup>[15]</sup>. Previous studies have shown that the combination of PEG with stimulant bisacodyl allows for less volume of PEG to be used for colonic cleansing<sup>[14,16]</sup>. Furthermore, the adjunctive use of senna with PEG has been shown to improve the quality of bowel preparation<sup>[9]</sup> and to reduce the amount of PEG required for colonic cleansing<sup>[10]</sup>. Similarly, we could demonstrate that the combination of senna with magnesium citrate was associated with improved quality in bowel preparation as assessed by a single experienced endoscopist. Although no cost-effectiveness analysis was undertaken, considering the relatively low price of senna<sup>[13]</sup> and that bowel preparation has been reported

**Table 3** Proportions of patients with side effects reported under bowel cleansing using citramag only or the combination of senna and citramag

Side effect	Treatment group	None (%)	Mild (%)	Moderate (%)	Severe (%)	Extreme (%)	P-value <sup>1</sup>
Nausea	Citramag	83.5	7.9	7.9	0.7	0	NS
	Citramag/senna	76.5	10.3	12.6	0.6	0	
Vomiting	Citramag	94.8	2.6	2.6	0	0	NS
	Citramag/senna	92.6	3.4	4	0	0	
Bloating	Citramag	88.1	5.3	6.6	0	0	NS
	Citramag/senna	81.7	7.4	10.3	0.6	0	
Abdominal pain	Citramag	90.1	6	3.9	0	0	P < 0.0003
	Citramag/senna	70.8	16	12	1.2	0	
Headache	Citramag	95.4	3.9	0.7	0	0	NS
	Citramag/senna	93.7	3.4	2.9	0	0	

<sup>1</sup>P-value (significant at the 0.05 level) was obtained using a  $\chi^2$ -test to compare the frequency of side effects in treatment groups.

to have an impact on colonoscopy costs<sup>[5]</sup>, our results suggest that it may be a useful adjunct to magnesium citrate for outpatient colonoscopy preparation.

Bowel preparation was well tolerated in both the magnesium citrate-only and the magnesium citrate/senna group with no self-reported “extreme” symptoms during preparation in any one group. The prevalence of gastrointestinal symptoms did not differ between the two groups with the exception of an about three times increased frequency of abdominal pain noted in the magnesium citrate/senna group which, however, did not seem to affect compliance. No serious adverse events were recorded in either preparation group. Nevertheless it must be noted that no monitoring of laboratory values and electrolytes was performed, which is a limitation of the current study.

Although the majority of patients enrolled had alarm symptoms suggestive of colonic neoplasia (which may explain the relatively high polyp detection rate in both patient groups), our aim was not specifically to explore the potential role of the addition of senna to magnesium citrate in polyp detection. However, more colonic polyps were found in the group receiving bowel preparation with the addition of senna to magnesium citrate, which is in accordance with previous studies showing that the detection of polyps is dependent on bowel cleansing quality<sup>[1,2]</sup>.

There are certain limitations to the evaluation of the present audits. Although it was conducted in a prospective manner, no placebo was used and the endoscopist was not blinded to the patient group that was colonoscoped. Second, the scales used for the assessment of bowel cleansing and patient symptom severity were not previously validated. Third, no segmental assessment of bowel cleansing quality was performed, and finally, no monitoring of electrolyte levels was performed. As all consecutive patients underwent the same bowel preparation protocol during the audit periods, we can consider the allocation of the bowel cleansing regimen a block randomization.

In conclusion, the addition of senna to bowel preparation protocol with magnesium citrate significantly improves the cleansing outcome. It produces no major side effects but abdominal pains occur more often.

Senna might be a useful adjunct to magnesium citrate for colonoscopy preparation.

## COMMENTS

### Background

Adequate colon preparation is essential for the quality of colonoscopy. The completion and polyp detection rate as well as the complication risk and the duration of the colonoscopy are strongly affected by poor bowel cleansing.

### Innovations and breakthroughs

As far as we know, this is the first study to evaluate the efficacy of senna as an adjunct to magnesium citrate for large bowel preparation prior to colonoscopy. Our findings demonstrate that the addition of senna to the bowel cleansing protocol with magnesium citrate significantly improves the cleansing outcome, but also increases the occurrence of side effects such as (mild) abdominal pains and discomfort.

### Applications

Our study results suggest that senna can be used as a helpful adjunct to a cleansing protocol based on magnesium citrate and will increase the efficacy of the bowel preparation before colonoscopy.

### Terminology

Magnesium citrate acts as an osmotic laxative which is often used for bowel preparation; senna is a stimulative agent increasing peristaltic movement.

### Peer review

This interesting study evaluates how the addition of senna alters the cleansing outcome and the occurrence of side effects under a bowel preparation protocol based on magnesium citrate. The results suggest that senna might be a helpful adjunct to standard bowel preparation protocols.

## REFERENCES

- 1 **Froehlich F**, Wietlisbach V, Gonvers JJ, Burnand B, Vader JP. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc* 2005; **61**: 378-384
- 2 **Harewood GC**, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc* 2003; **58**: 76-79
- 3 **Bernstein C**, Thorn M, Monsees K, Spell R, O'Connor JB. A prospective study of factors that determine cecal intubation time at colonoscopy. *Gastrointest Endosc* 2005; **61**: 72-75
- 4 **Joseminders DF**, Spillenaar Bilgen EJ, van Sorge AA, Wahab PJ, de Vries RA. Colonic explosion during endoscopic polypectomy: avoidable complication or bad luck? *Endoscopy* 2006; **38**: 943-944
- 5 **Rex DK**, Imperiale TF, Latinovich DR, Bratcher LL. Impact of bowel preparation on efficiency and cost of colonoscopy. *Am J Gastroenterol* 2002; **97**: 1696-1700
- 6 **Binder HJ**. Pharmacology of laxatives. *Annu Rev Pharmacol*

- Toxicol* 1977; **17**: 355-367
- 7 **Bowles CJ**, Leicester R, Romaya C, Swarbrick E, Williams CB, Epstein O. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? *Gut* 2004; **53**: 277-283
  - 8 **Hardcastle JD**, Wilkins JL. The action of sennosides and related compounds on human colon and rectum. *Gut* 1970; **11**: 1038-1042
  - 9 **Ziegenhagen DJ**, Zehnter E, Tacke W, Kruis W. Addition of senna improves colonoscopy preparation with lavage: a prospective randomized trial. *Gastrointest Endosc* 1991; **37**: 547-549
  - 10 **Iida Y**, Miura S, Asada Y, Fukuoka K, Toya D, Tanaka N, Fujisawa M. Bowel preparation for the total colonoscopy by 2,000 ml of balanced lavage solution (Golytely) and sennoside. *Gastroenterol Jpn* 1992; **27**: 728-733
  - 11 **Regev A**, Fraser G, Delpre G, Leiser A, Neeman A, Maoz E, Anikin V, Niv Y. Comparison of two bowel preparations for colonoscopy: sodium picosulphate with magnesium citrate versus sulphate-free polyethylene glycol lavage solution. *Am J Gastroenterol* 1998; **93**: 1478-1482
  - 12 **DiPalma JA**, Wolff BG, Meagher A, Cleveland M. Comparison of reduced volume versus four liters sulfate-free electrolyte lavage solutions for colonoscopy colon cleansing. *Am J Gastroenterol* 2003; **98**: 2187-2191
  - 13 **Radaelli F**, Meucci G, Imperiali G, Spinzi G, Strocchi E, Terruzzi V, Minoli G. High-dose senna compared with conventional PEG-ES lavage as bowel preparation for elective colonoscopy: a prospective, randomized, investigator-blinded trial. *Am J Gastroenterol* 2005; **100**: 2674-2680
  - 14 **Adams WJ**, Meagher AP, Lubowski DZ, King DW. Bisacodyl reduces the volume of polyethylene glycol solution required for bowel preparation. *Dis Colon Rectum* 1994; **37**: 229-233; discussion 233-234
  - 15 **Barnes MR**. How to get a clean colon--with less effort. *Radiology* 1968; **91**: 948-949
  - 16 **Sharma VK**, Chockalingham SK, Ugheoke EA, Kapur A, Ling PH, Vasudeva R, Howden CW. Prospective, randomized, controlled comparison of the use of polyethylene glycol electrolyte lavage solution in four-liter versus two-liter volumes and pretreatment with either magnesium citrate or bisacodyl for colonoscopy preparation. *Gastrointest Endosc* 1998; **47**: 167-171

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