Premedication with peppermint oil capsules in colonoscopy : a double blind placebo-controlled randomized trial study

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Abstract

Background : **Colonic spasm is an important problem in colonoscopy for endoscopists to advance the colonoscope and visualize the mucosa.**

Study aims : **In the present study, we evaluated the efficacy of enteric-coated peppermint oil capsules (Colpermin®) as an orally administered antispasmodic premedication in colonoscopy.**

Patients and Methods : **Sixty-five adult patients undergoing colonoscopy were randomized to receive either Colpermin (n = 33) or placebo capsules (n = 32) as premedication, 4 hours before the procedure. An experienced endoscopist performed colonoscopy. Outcome measures included cecal intubation and total procedure time, spasm score, pain score, endoscopist satisfaction and patients' willingness to repeat colonoscopy.**

Results : **Duration of both total procedure time and cecal intubation time in patients in the Colpermin group were shorter than that in ones in the placebo group. Scores for colonic spasm and pain were significantly lower in the Colpermin group. The endoscopist satisfaction score was higher in the Colpermin group and patients in the Colpermin group were more willing to repeat colonoscopy in the future.**

Conclusions : **Premedication with Colpermin was beneficial in terms of the time required for cecal intubation and total procedure time, reducing colonic spasm, increasing endoscopist satisfaction and decreasing pain in patients during colonoscopy.** (Acta gastroenterol. belg., **2012**, 75, **349-353**).

Key words : peppermint oil, colonoscopy, premedication, colonic spasm.

Introduction

Colonoscopy is an important procedure for the diagnosis and treatment of colonic diseases (1). Meanwhile, it is a painful procedure for patients. In many endoscopic units, sedative and narcotic medications such as benzodiazepines and opioids are routinely used during colonoscopy to alleviate pain and anxiety (2). However, these medications have side effects and may affect cardiopulmonary function of patients (3-5). One of the most important problems for endoscopists to advance the colonoscope and visualize the mucosa is colonic spasm (6). This problem can lead to excessive air insufflation making more distention and discomfort for patients (1). Various antispasmodic drugs have been used as premedication to reduce spasm and facilitate colonoscope insertion. The use of anticholinergic drugs such as atropine, hyoscine butylebromide and hyoscyamine sulphate is accompanied with adverse effects (e.g. tachycardia, dry mouth, urinary retention, orthostatic hypotension, anaphylactic reactions and visual impairment) (7-9). Moreover, these drugs are contraindicated in patients with cardiac diseases, obstructive uropathy and narrow angle glaucoma (10). Glucagon is an alternative antispasmodic drug in such patients, but it is expensive and can cause delayed reactive hypoglycemia (7). For these reasons, a safer, easy to use, inexpensive and effective antispasmodic agent is required (10). Use of plant essential oils such as peppermint oil (PO) has recently been reported in several studies (10-16). Intraluminal administration of PO is a safe and useful antispasmodic agent for upper gastrointestinal endoscopy (11), double contrast barium meal and enema examinations (10,12,13), and colonoscopy (14-16). Colpermin® is an enteric coated PO which is useful in patients with irritable bowel syndrome (IBS) (17). Use of Colpermin does not have the limitations of intraluminal administration of PO such as changing the position of patients during colonoscopy. Preparation of PO solution is a complicated process, as well (16).

To our knowledge, few studies reported the effect of Colpermin in colonic spasm during colonoscopy. The aim of the present study was to evaluate the efficacy of Colpermin as an orally administered antispasmodic premedication in a randomized double blinded placebo controlled trial.

Methods

Patients

In a prospective double-blind placebo controlled clinical trial study, 65 adult patients were studied consecutively. Elective, diagnostic or screening colonoscopy was done by an experienced endoscopist at Alzahra University Hospital (Isfahan, Iran) in 2009.

Patients on whom total colonoscopy was not possible (due to obstruction by tumor or being high risk for perforation as in severe colitis or history of colectomy),

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pregnant and lactating women, and those with history of peppermint allergy were excluded from the study.

Written informed consent was taken from each patient. The trial was carried out in accordance with the declaration of Helsinki and approved by the research ethics committee of Isfahan University of Medical Sciences. The study was registered in the http://www.irct.ir under the clinical trial number IRCT201107056957N1.

Study design

PO capsule under the trademark Colpermin (Tillotts Pharma, Ziefen, Switzerland) was prescribed in the trial group. Each capsule consisted of 187 mg or 0.2 ml PO in a pH-dependent, enteric coated, hard gelatin capsules that resists disintegration and releases until it passes through the stomach and encounters an intestinal pH of 6.8 or higher (17).

The placebos (School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran) were prepared in capsules with similar appearance to Colpermin and filled with lactulose.

Patients and the endoscopist were blinded to the treatment modality. Patients were randomly allocated by opening a sealed envelope with a computer-generated code into groups to receive either Colpermin or placebo. Capsules were taken four hours before colonoscopy.

All patients received four liters of Poly Ethylene Glycol solution one day before colonoscopy as a bowel preparation. No medication was used before or during the procedure. A standard video colonoscope (165, Olympus Optical Co., Ltd., Tokyo, Japan) was used for all precipitants.

Baseline demographic data of all patients was obtained and any adverse effect of Colpermin administration (e.g. heartburn, perianal burning, allergic reactions, blurred vision, nausea and vomiting) was recorded before and after the colonoscopy.

Time required for intubation to the cecum and the total procedure time were recorded by the endoscopist. After the colonoscopy, patients were asked to rate their pain using a numerical rating scale (0 = no pain, 1 = mild, 2 = moderate, 3 = severe pain). Their willingness to repeat colonoscopy using the present method was also asked.

Quality of the bowel preparation [0 = excellent (more than 90% of mucosa seen, mostly liquid stool, minimal suction needed for adequate visualization), 1 = good (more than 90% of mucosa seen, mostly liquid stool, significant suction needed for adequate visualization), 2 = fair (more than 90% of mucosa seen, mixture of liquid and semisolid stool, could be suctioned and/or washed), 3 = inadequate/re-preparation required (less than 90% of mucosa seen, mixture of semisolid and stool, could not be suctioned or washed)], endoscopist satisfaction (0 = failure to complete the examination, 1 = difficult, 2 = fairly easy, 3 = easy), and colonic spasm score [0 = no movement encountered, 1 = minimal (just occasional spasm, no slow down), 2 = mild (a little waiting {< 5 sec.}, extra manipulation required), 3 = moderate (moderate waiting {5-10 sec.}, difficult to examine), 4 = marked (long waiting {> 10 sec.}, very difficult to examine)] were assessed by the endoscopist immediately after the procedure.

Statistics

All data were analyzed by SPSS version 15 (SPSS Corp, Chicago, IL, USA). Quantitative variables are presented as mean ± SD. Independent sample t-test was used to compare normally distributed continuous variables in different groups. Non-parametric data were analyzed with Mann-Whitney U test. Categorical outcome variables were analyzed with Chi-square or Fisher's exact tests where appropriate. A p value less than 0.05 was considered statistically significant.

Results

Sixty-six patients were enrolled into this study in the stage of randomization. Thirty-four patients received Colpermin and 32 patients received placebo. One patient in the Colpermin group was excluded because of having vomiting immediately after taking the drug. Therefore, we analyzed data from 65 adults (33 patients in the Colpermin group). Table 1 demonstrates baseline characteristics of participants.

There were no significant differences between two groups with regard to age, sex, educational level and quality of bowel preparation.

Two patients (1 in Colpermin group and 1 in placebo group) reported abdominal discomfort, 2 patients complained of nausea (1 in Colpermin group and 1 in placebo group) and one patient in the placebo group reported blurred vision. One patient in the Colpermin group complained of heartburn after taking the drug.

All outcome measures in patients are summarized in table 2. Duration of both total procedure time and cecal intubation time were significantly shorter in patients who received Colpermin (table 2). Scores for colonic spasm and pain were significantly lower in the Colpermin group (0.32 ± 0.68 vs. 2.12 ± 0.42 and 0.35 ± 0.60 vs. 1.84 ± 0.45, respectively, $P < 0.001$). The endoscopist satisfaction score was higher in the Colpermin group, too (2.71 ± 0.58 vs. 1.41 ± 0.56, $P < 0.001$). Quality of the bowel preparation did not differ significantly between the groups.

Discussion

In this study, we investigated the efficacy of enteric-coated PO capsules on reducing colonic spasm during colonoscopy. We showed PO capsules have beneficial effects on time required for cecal intubation and total procedure time, reducing colonic spasm, increasing

Table 1. — **Patients' demographic information at baseline**

	Colpermin group (n = 33)	Placebo Group (n = 32)	p-value
Age(years)			
Mean ± SD	42.5 ± 15	46 ± 17	0.4†
Range	18-72	17-81	
Sex (M:F)	15/18	13/19	0.8*
Education level			
Primary (%)	14(42)	17(53)	0.5‡
Secondary (%)	15(46)	14(44)	
Tertiary (%)	4(12)	1(3)	
No. of patients with previous colonoscopy (%)	3(9)	5(16)	0.4‡
Indication for colonoscopy			
Per rectal bleeding (%)	18(55)	17(53)	
Chronic diarrhea (%)	6(18)	3(10)	
Anemia & cancer screening (%)	7(21)	4(13)	
Polyp surveillance (%)	2(6)	1(3)	
Others (%)	0	7(21)	
Diagnosis			
Normal (%)	18(55)	16(50)	
Hemorrhoid (%)	7(21)	10(31)	
IBD (%)	3(9)	4(13)	
Polyp (%)	4(12)	2(6)	
Colon cancer (%)	1(3)	0	
Quality of bowel preparation			
Excellent (%)	9(27.3)	5(15.6)	0.5*
Good (%)	13(39.4)	16(50)	
Fair (%)	11(33.3)	11(34.4)	
Inadequate (%)	0	0	

SD : standard deviation ; † Independent samples t test,
* Chi-square test, ‡ Fisher's exact test.

endoscopist satisfaction and decreasing pain in patients during colonoscopy.

Anti spasmodic effect of PO was shown in several in vitro studies. These studies revealed that PO relaxes smooth muscles of human and animal intestines by blocking calcium channels (18-21), resembling dihydropyridine calcium antagonists (7). Therefore, many trials have been designed to evaluate this effect on the treatment or endoscopic evaluation of common functional gastrointestinal disorders such as IBS and non-ulcer dyspepsia (10-16,22,23).

Studies on the treatment of IBS with PO showed controversial results (22,23). A meta-analysis in 1998 concluded that the role of PO had not yet been established beyond a reasonable doubt (24). Administration of PO was examined to reduce gastrointestinal spasm during upper endoscopy (11), double contrast barium meal examination (10), barium enema (12,13) and endoscopic retrograde cholangiopancreatography (25). These trials indicated that PO administration was useful and lessened side effects of systemic intravenous spasmolytics.

Few studies evaluated the efficacy of PO during colonoscopy. Recently, Asao *et al*. (16) reported the significant effect of PO in reducing colonic spasm during colonoscopy. They used a hand pump system for infusion of PO solution intraluminaly and saw a satisfactory spasmolytic effect in 88.5% of the treated patients and in 33.3% of those in the control group ($p < 0.0001$). They did not observe any adverse effect.

As mentioned before, preparation of the PO solution is a complicated process. Therefore, we used an orally administered PO which is available in most medical facilities. The relaxing effect of PO on the lower esophageal sphincter may result in gastroesophageal reflux. Therefore, it is popular to use enteric-coated formulations to facilitate its beneficial effect on lower gastrointestinal tract without affecting the upper gastrointestinal tract (26). Since peak release of Colpermin, is at about four hours after ingestion (27), in the present study we prescribed it four hours before the colonoscopy procedure.

In the current study, we found the stronger effect of Colpermin on reducing gastrointestinal spasm than placebo. Reduced colonic spasm can result in reducing pain and discomfort in patients. In addition, it helps endoscopists to insert and withdraw the colonoscope easier and improves inspection of the mucosal surface and increase endoscopists satisfaction. We could show all these findings in our study.

It should be noted that although in our study, cecal intubation and total procedure time were objectively measured and both of them were significantly shorter in the Colpermin group, our scales for evaluating colonic spasm, pain and endoscopist satisfaction were subjective.

In this study, two patients complained of abdominal discomfort and nausea and one patient who was excluded from the study had vomiting after the ingestion of the capsules. Only one patient reported mild heartburn

Table 2. — **Outcome measures after colonoscopy**

	Colpermin group (n = 33)	Placebo Group (n = 32)	p-value
Total procedure time (min) Mean ± SD	12.15 ± 1.78	15.90 ± 2.83	< 0.001†
Range	10-18	11-25	
Cecal intubation time (min) Mean ± SD Range	6.87 ± 1.63 5-12	10.58 ± 2.79 6-20	< 0.001†
Colonic spasm score No movement (%) Minimal (%) Mild (%) Moderate (%) Marked (%)	25(75.8) 6(18.2) 1(3) 1(3) 0	0 1(3.1) 26(81.3) 5(15.6) 0	< 0.001‡
Pain score No (%) Mild (%) Moderate (%) Sever (%)	23(69.7) 8(24.2) 2(6.1) 0	0 6(18.8) 25(78.1) 1(3.1)	< 0.001‡
Endoscopist satisfaction score Easy (%) Fairly easy (%) Difficult (%) Failure to complete (%)	25(75.8) 6(18.2) 2(6.1) 0	1(3.1) 11(34.4) 20(62.5) 0	< 0.001‡
Number of patients willing to repeat colonoscopy (%)	30(90)	6(19)	< 0.001*

SD : standard deviation ; † Independent samples t test,
‡ Fisher's exact test, * Chi-square test.

which might be due to dissolving of the capsules too early into the stomach.

Small sample size and short duration of patients' follow up were amongst the limitations of the present study. Further investigations are required to evaluate the efficacy and potential side effects of Colpermin in colonoscopy during a longer period.

Conclusion

According to the present study, administration of enteric-coated PO capsules is useful to reduce colonic spasm during colonoscopy.

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