Original Article

Improvement of Quality of Nonanesthetic Colonoscopy by Preoperative Administration of Pinaverium Bromide

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Abstract

Background: Nonanesthetic colonoscopy is popular in clinical practice in China. However, intestinal spasms often result in a prolonged examination time, increased operating difficulties, decreased polyp detection rate, and failure to complete the procedure clinically. Therefore, exploring alternative approaches that can reduce the pain in patients during colonoscopy is of utmost importance, and finding the optimal preoperative administration to improve the quality of nonanesthetic colonoscopy is also necessary. This study aimed to investigate the effects of the prophylactic administration of pinaverium bromide before colonoscopy and the effects of pinaverium bromide alone at different time points or combined with scopolamine butylbromide.

Methods: A randomized controlled trial was performed on a cohort of 1000 patients who underwent colonoscopy in outpatient clinic of Wuhan Union Hospital. The patients were randomly assigned to the following groups: Group A, given oral pinaverium bromide (100 mg, three times a day) one day before examination combined with intramuscular injection of scopolamine butylbromide (20 mg) 10 min before colonoscopy; Group B_0, given pinaverium bromide alone on the day of colonoscopy (100 mg, three times a day); Group B_1, given pinaverium bromide alone (100 mg, three times a day) one day before colonoscopy; Group B_2, given pinaverium bromide alone (100 mg, three times a day) two days before colonoscopy; and Group C, given scopolamine butylbromide alone (20 mg) before colonoscopy. The successful rate of colonoscopy, procedure time, degree of abdominal pain, and polyp detection rate were recorded and compared among all groups.

Results: The successful rate of colonoscopy in Group B_1 (82.0%) and Group B_2 (83.0%) was significantly higher than that in Group B_0 (62.0%, all $P < 0.01$). The time to reach the ileocecal region in Group B_1 and Group B_2 were lower than those in Group B_0 (all $P < 0.05$). However, no significant differences were observed in polyp detection rate between Group B_1 (24.0%) or Group B_2 (26.0%), and Group B_0 (22.4%, all $P > 0.05$). Furthermore, there were no significant differences in the various parameters examined between Group B_1 and Group B_2 ($P > 0.05$). The successful rate of colonoscopy in Group A (92.0%) was significantly higher than that in Group B_1 (82.0%) and Group C (80.0%; both $P < 0.05$). Moreover, the time for the colonoscope to reach the ileocecal region in Group A were markedly shorter as compared to those in Group B_1 and Group C ($P < 0.05$). The polyp detection rate in Group A was 32.0%, significantly higher than that in Group B_1 (24.0%, $P < 0.05$) and Group C (24.2%, $P < 0.05$).

Conclusion: Administration of pinaverium bromide alone one day before examination was beneficial to relieve symptoms of abdominal pain during nonanesthetic colonoscopy. In addition, therapeutic effects were improved when pinaverium bromide administration was combined with intramuscular injection of scopolamine butylbromide. Therefore, the combined use of pinaverium bromide with scopolamine butylbromide might have great application value to improve the quality of nonanesthetic colonoscopy in the preoperative preparation.

Key words: Abdominal Pain; Pinaverium Bromide; Routine Colonoscopy

Introduction

Currently, improving the detection rate of colorectal polyps is imperative for the prevention of the high incidence of colorectal cancer.[1] Colonoscopy is the most direct and effective procedure for diagnosing a variety of colorectal diseases. Nonanesthetic colonoscopy is popular in clinical

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practice in China. However, the intestinal spasms often result in a prolonged examination time, increased operating difficulties, decreased polyp detection rate, and failure to complete the procedure clinically. Previous studies have shown that colonoscopic examination could not be completed in 2.4% patients because of pain associated with the procedure.[2] In addition, re-examination was refused in 20.7% of patients due to a high fear factor. Therefore, exploring alternative approaches that can reduce the pain in patients during colonoscopy is of utmost importance, and finding the optimal preoperative administration to improve the quality of nonanesthetic colonoscopy is also necessary. In this randomized controlled trial, we investigated the effects of the prophylactic administration of pinaverium bromide before colonoscopy and the effects of pinaverium bromide alone at different time points or combined with scopolamine butylbromide on the successful rate of colonoscopy, procedure time, abdominal pain, and polyp detection rate, in order to provide insights in the application of pinaverium bromide during nonanesthetic colonoscopy in China.

Methods

Subjects

This randomized controlled trial was performed on a total of 1000 patients, who visited the outpatient clinic of Wuhan Union Hospital from August 2015 to June 2016 for a routine colonoscopy, and patients were randomly assigned in a controlled fashion into five groups (n = 200 in each group): Group A, given oral pinaverium bromide (100 mg, three times a day) one day before examination combined with intramuscular injection of scopolamine butylbromide (20 mg) 10 min before colonoscopy; Group B_0, given pinaverium bromide alone on the day of colonoscopy (100 mg, three times a day); Group B_1, given pinaverium bromide alone (100 mg, three times a day) one day before colonoscopy; Group B_2, given pinaverium bubromide alone (100 mg, three times a day) two days before colonoscopy; and Group C, intramuscularly given scopolamine butylbromide alone (20 mg) before colonoscopy. Pinaverium bromide alone at different time points or combined with other medication were randomly assigned according to the random number table. The individuals in each group were randomly assigned to different treatment groups. Patients with the following conditions were excluded from this study: Colon surgery, an incomplete intestinal obstruction or evidence of previous severe intestinal stenosis, severe cardiopulmonary disease, pregnancy, and administration of antispasmodic or anticholinergic medications within one month before the procedure. Colonoscopy was performed by an experienced gastroenterologist who was also responsible for evaluating the examination duration, the degree of abdominal pain, and polyp detection, which were recorded by the assistants. This study was approved by the Ethics Committee of Wuhan Union Hospital, and all patients provided written informed consent.

Drugs and equipment

The drugs and equipment in this study were as follows: pinaverium bromide, 50 mg/tablet (Abbott, USA); polyethylene glycol electrolyte powder composed of 64 g polyethylene glycol 4000, 5.7 g anhydrous sodium sulfate, 1.68 g sodium bicarbonate, 1.46 g sodium chloride, and 0.75 g potassium chloride; 30 ml simethicone emulsion (1 ml emulsion containing 40 mg simethicone); scopolamine butylbromide, 20 mg/ampoule and an Olympus CF-Q260AI colonoscope (Japan).

Bowel preparation

Administration of polyethylene glycol electrolyte

Only clear liquid food was allowed one day before the procedure, and fasting began at 8 p.m. Two packets of polyethylene glycol electrolyte were dissolved in 2000 ml warm water and consumed within 2 h. At 4 am on the day of the procedure, another two packets of polyethylene glycol electrolyte were dissolved in 2000 ml warm water and consumed within 2 h. At 6 a.m. on the day of the procedure, 30 ml simethicone was taken orally.

Administration of pinaverium bromide

Patients in Group B_0 were orally administered with 100 mg pinaverium bromide (50 mg/tablet) 2 h before the examination; those in Group B_1 were given 100 mg pinaverium bromide (three times a day) with meals one day before examination and another 100 mg was given 2 h before the examination, and those in Group B_2 were given 100 mg pinaverium bromide (three times a day) with meals two days before examination and another 100 mg was given 2 h before examination.

Administration of scopolamine butylbromide

Scopolamine butylbromide 20 mg dissolved in 1 ml of 0.9% saline was intramuscularly injected 10 min before examination.

Outcome measures

Abdominal pain scores

The degree of abdominal pain experienced by the individuals during colonoscopy was recorded by the physicians and assistants and scored as follows: Grade I, no abdominal pain with successful examination; Grade II, slight abdominal pain with successful examination; Grade III, moderate but tolerable abdominal pain with successful examination; and Grade IV, severe abdominal pain with un-completed procedure and unsuccessful examination.

Time to reach the ileocecal region

The time for the colonoscope to reach the ileocecal region was defined as <5 min, 5–10 min, and >10 min.

Polyp detection

The number and sizes of polyps detected in different sections of the intestine were recorded, and biopsy samples were collected and sent for histopathological examination. The percentage of polyps detected in each group was calculated (number of patients detected with polyps/total number of

patients × 100%), and the differences in detection rates between groups were statistically analyzed.

Statistical analysis

The data were statistically analyzed using SPSS statistical software version 20.0 (SPSS Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation (SD) for quantitative variables or as percentages for qualitative variables. Data comparison was performed using the Chi-square test. A $P < 0.05$ was considered statistically significant.

Results

Group A included 108 males and 92 females with mean age of 47.5 ± 5.6 years; Group B_0 consisted of 105 males and 95 females with mean age of 46.4 ± 6.3 years; Group B_1 included 94 males and 106 females with mean age of 49.7 ± 4.8 years; Group B_2 included 103 males and 97 females with mean age of 47.1 ± 7.5 years; and Group C included 94 males and 106 females with mean age of 45.3 ± 5.2 years. Among these five groups, no significant differences were observed in gender, age, body mass index, reasons for colonoscopy, and severity of the disease [Table 1].

Examination was considered successful when patients experienced Grades I and II abdominal pain. The successful rate in Groups A, B_0, B_1, B_2, and C was 92.0% (184/200), 62.0% (124/200), 82.0% (164/200), 83.0% (166/200), and 80.0% (160/200), respectively. In Groups A, B_1, and B_2, the colonoscopy was not terminated early due to intolerable abdominal pain in all cases.

The successful rate in Groups B_1 and B_2 was significantly higher than that in Group B_0 ($\chi^2 = 19.840$, $P < 0.001$and $\chi^2 = 22.120$, $P < 0.001$). No significant difference in successful rate was observed between Groups B_1 and B_2 ($\chi^2 = 0.070$, $P = 0.448$). The time for the colonoscope to reach the ileocecal region in Groups B_1 and B_2 was significantly shorter than that in Group B_0 ($\chi^2 = 19.410$, $P < 0.001$ and $\chi^2 = 25.080$, $P < 0.001$); however, no significant difference was found between Groups B_1 and B_2 ($\chi^2 = 0.69$, $P = 0.236$). Furthermore, there were no significant differences in polyp detection rate among Groups B_1 (24.0%), B_2 (26.0%), and B_0 (22.4%) (B_1 vs. B_2: $\chi^2 = 0.220$, $P = 0.057$; B_1 vs. B_0: $\chi^2 = 1.060$, $P = 0.152$; B_2 vs. B_0: $\chi^2 = 0.320$, $P = 0.314$).

It was found that the successful rate in Group A was significantly higher than that in Group B_1 and Group C ($\chi^2 = 8.842$, $P = 0.002$ and $\chi^2 = 11.960$, $P < 0.001$). In addition, the time for the colonoscope to reach the ileocecal region was significantly shorter in Group A than that in Group B_1 and Group C ($\chi^2 = 21.240$, $P = 0.030$ and $\chi^2 = 24.750$, $P = 0.028$). Furthermore, the polyp detection rate was markedly higher in Group A (32.0%) than that in Group B_1 (24.0%; $\chi^2 = 3.170$, $P = 0.027$) and Group C (24.2%; $\chi^2 = 4.470$, $P = 0.044$). No adverse reactions occurred, except for the presence of dry mouth in two patients, each from Group A and Group C. The information of colonoscopy in these five groups is shown in Table 2.

Discussion

Effective bowel preparation and strictly followed endoscopic procedures are vital to the success of colorectal cancer examination.[2] Nonanesthetic colonoscopy involves intermittent air insufflation and constant rotation of the endoscope, which, due to the anatomical characteristics

Table 1: Baseline clinical characteristics among five groups in this study

Characteristics	Group A	Group B_0	Group B_1	Group B_2	Group C	Statistical values	*P*
Male/female, *n*	108/92	105/95	94/106	103/97	94/106	3.336*	0.503
Age (years), mean ± SD	47.5 ± 5.6	46.4 ± 6.3	49.7 ± 4.8	47.1 ± 7.5	45.3 ± 5.2	0.076†	0.990
BMI (kg/m^2), mean ± SD	21.1 ± 3.2	19.8 ± 4.2	22.6 ± 3.1	20.9 ± 4.7	20.1 ± 5.4	0.067†	0.992

*χ^2 value; †*F* value. BMI: Body mass index; SD: Standard deviation.

Table 2: Comparison of parameters among five groups in this study

Parameters	Group A (*n* = 200)	Group B_0 (*n* = 200)	Group B_1 (*n* = 200)	Group B_2 (*n* = 200)	Group C (*n* = 200)
Completion rate, *n* (%)	200 (100.0)	194 (97.0)	200 (100.0)	200 (100.0)	198 (99.0)
Successful rate, *n* (%)	184 (92.0)	124 (62.0)	164 (82.0)	166 (83.0)	160 (80.0)
Degree of abdominal pain, *n*					
I	76	16	68	72	66
II	108	108	96	94	94
III	16	70	36	34	38
IV	0	6	0	0	2
Time to reach the ileocecal region, *n*					
<5 min	66	12	34	36	32
5–10 min	94	108	110	114	106
>10 min	40	74	56*,†	50*	60†
Polyp detection rate (%)	32.0	22.4	24.0†,‡	26.0	24.2†

*$P<0.05$, versus Group B_0; †$P<0.05$, versus Group A; ‡$P>0.05$, versus Group B_0.

of the intestine, can easily stretch and pull the intestines to form loops. The stretch might induce intestinal spasms, especially when patients are under stress, which might lead to abdominal pain and other discomforts. In the most severe cases, patients might not be able to tolerate the pain and the examination needs to be terminated early. Therefore, gastroenterologists are constantly exploring alternative, effective, and safe approaches to reduce the discomfort and pain in patients during colonoscopic examination. In the past, intramuscular injections of anisodamine or diazepam were given before colonoscopy, but general anesthesia is more commonly used in recent years. Although these methods can partially reduce intestinal cramps and alleviate abdominal pain, they are also often accompanied with various adverse reactions such as dry mouth, dysuria, drowsiness, palpitations, and dizziness. In addition to the adverse effects of short-acting anesthetics on the respiratory and cardiovascular systems, the need for anesthesiologists and additional personnel during colonoscopy significantly increases the cost of surgery. Furthermore, if operation-induced intestinal looping occurs when the patient is under general anesthesia, the risk of intestinal injury increases whereas the overall safety factor decreases.

Pinaverium bromide is a highly selective L-type calcium channel blocker that regulates visceral hypersensitivity and abnormal intestinal movement by inhibiting calcium influx.[3-6] Pinaverium bromide not only promotes regular bowel movement and reduces colonic transit time but also partially relieves abdominal pain by lowering the pain threshold in patients through modulating visceral hypersensitivity. Pinaverium bromide has been used to alleviate the symptoms of irritable bowel syndrome and pains related to colon cramps.[7] Its inhibitory effect on intestinal smooth muscle contraction primarily reduces ineffective and transient spastic contractions but does not affect the spontaneous contraction of the intestine.[8] During colonoscopy, air is intermittently insufflated to dilate the intestine, which in turn causes pain in the patients. A previous study has shown that pinaverium bromide could inhibit the activities of reagents that induced colon contractility;[3] however, it could also alleviate pain by reducing sigmoid pressure.[9] Pinaverium bromide has no anticholinergic activity and has a very low systemic absorption rate, with only 10% of the oral dose going into blood circulation. Of the 10% present in the circulation, 95–98% is bound to plasma proteins and is excreted through the intestinal tract after being metabolized in the liver. Therefore, pinaverium bromide acts mainly on the gastrointestinal tract with high selectivity and has no adverse cardiovascular effects.[10]

It has previously been reported that pinaverium bromide was a simple and effective reagent in preventing abdominal pain caused by intestinal cramps during colonoscopy.[11] In the current study, we demonstrated that abdominal pain and discomfort were significantly reduced when patients were given pinaverium bromide 1–2 days before colonoscopy. In addition, significant sense of intestinal relaxation, ease of endoscope maneuver, and a shortened procedure time were observed during colonoscopy. However, the study also found that pinaverium bromide taken two days before examination had no additional beneficial effect over pinaverium bromide taken one day before colonoscopy. This indicated that the administration of pinaverium bromide alone one day before procedure was as effective as pinaverium bromide administered two days before colonoscopy. Pinaverium bromide could alleviate the symptoms of abdominal pain in routine colonoscopy.

Scopolamine butylbromide is a synthetic, peripheral cholinergic receptor blocker that ameliorates the hyperreactivity of cholinergic receptors in the preganglionic sympathetic neurons and reduces the overcontraction of visceral smooth muscles.[11-13] In contrast, an M-cholinergic receptor blocker, anisodamine, can inhibit peripheral cholinergic activities but its therapeutic dose has no significant inhibitory effect on excessive smooth muscle spasm. Meanwhile, the highly water-soluble and nearly lipid-insoluble properties of scopolamine butylbromide prevent it from passing through the blood-brain barrier.[14] It has no antagonistic effect on central M-cholinergic receptors and has very weak activities in the central nervous system, and therefore rarely causes dry mouth or other clinical adverse reactions. A study has shown that scopolamine butylbromide is safe and effective for endoscopic examination and treatment of the gastrointestinal system.[15] The current study revealed that the combined use of pinaverium bromide and scopolamine butylbromide achieved significantly better results than pinaverium bromide or scopolamine butylbromide used alone.

This study had certain limitations that should be taken into consideration. This was only a single-blind trial. In addition, the sample size was a little small.

In summary, the study demonstrated that pinaverium bromide alone taken one day before colonoscopy can effectively alleviate abdominal pain, facilitate the completion of routine colonoscopy, and reduce the examination time. Preoperative administration of pinaverium bromide has improved the quality of nonanesthetic colonoscopy. Moreover, the combined use of pinaverium bromide one day before the colonoscopy and intramuscular injection of scopolamine butylbromide shortly before colonoscopy demonstrated even better therapeutic effects, with significantly enhanced polyp detection rate. In conclusion, the combination of pinaverium bromide and scopolamine butylbromide treatment is inexpensive and safe, does not show significant adverse effects and significantly improves patient compliance. Therefore, the combination of pinaverium bromide and scopolamine butylbromide might be a promising and novel approach in the preoperative administration to improve the quality of nonanesthetic colonoscopy.

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Conflicts of interest

There are no conflicts of interest.

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