CO\textsubscript{2} insufflation for potentially difficult colonoscopies: Efficacy when used by less experienced colonoscopists

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Supported by The Japanese Foundation for Research and Promotion of Endoscopy (JFE)

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Received: July 27, 2009 Revised: September 1, 2009 Accepted: September 8, 2009 Published online: November 7, 2009

Abstract

**AIM:** To clarify the effectiveness of CO\textsubscript{2} insufflation in potentially difficult colonoscopy cases, particularly in relation to the experience level of colonoscopists.

**METHODS:** One hundred twenty potentially difficult cases were included in this study, which involved females with a low body mass index and patients with earlier abdominal and/or pelvic open surgery or previously diagnosed left-side colon diverticulosis. Patients receiving colonoscopy examinations without sedation using a pediatric variable-stiffness colonoscope were divided into two groups based on either CO\textsubscript{2} or standard air insufflation. Both insufflation procedures were also evaluated according to the experience level of the respective colonoscopists who were divided into an experienced colonoscopist (EC) group and a less experienced colonoscopist (LEC) group. Study measurements included a 100-mm visual analogue scale (VAS) for patient pain during and after colonoscopy examinations, in addition to insertion to the cecum and withdrawal times.

**RESULTS:** Examination times did not differ, however, VAS scores in the CO\textsubscript{2} group were significantly better than in the air group (P < 0.001, two-way ANOVA) from immediately after the procedure and up to 2 h later. There were no significant differences between either insufflation method in the EC group (P = 0.29), however, VAS scores for CO\textsubscript{2} insufflation were significantly better than air insufflation in the LEC group (P = 0.023) immediately after colonoscopies and up to 4 h afterwards.

**CONCLUSION:** CO\textsubscript{2} insufflation reduced patient pain after colonoscopy in potentially difficult cases when performed by LECs.

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Key words: CO\textsubscript{2} insufflation; Colonoscopy; Difficult colonoscopy; Experienced colonoscopist; Training

**INTRODUCTION**

Colonoscopy has a high profile because of its increasingly important role in successfully preventing, detecting and treating colorectal cancer\textsuperscript{1,2}, however, some patients experience considerable abdominal pain and discomfort when the procedure is performed using air insufflation. In particular, the so-called “difficult colonoscopy” cases\textsuperscript{3-4}, which involve female patients with a relatively...
low body mass index (BMI), patients with a history of abdominal and/or pelvic open surgery and male patients with diverticulosis, often require prolonged insertion to the cecum, thus this procedure can cause increased abdominal pain and discomfort for such patients.

Factors accounting for longer examination times and increased abdominal pain and discomfort can be derived from both a patient’s condition and the examining colonoscopist’s skill and experience[7–9]. Novice and even moderately skilled colonoscopists must improve their technical abilities by gaining experience in successfully handling difficult colonoscopies to become qualified experts, as a suitably high-level colonoscopy training environment has not been established as yet[10–11].

CO₂ insufflation has been reported to reduce patient abdominal pain and discomfort during and after colonoscopies[12–13]. Although the safety and efficacy of CO₂ insufflation during colonoscopies have been assessed in earlier studies, air insufflation is still the standard method due to a lack of suitable equipment and inadequate information as to when and on whom CO₂ insufflation should be used during colonoscopy examinations.

We decided to conduct a prospective randomized controlled trial to test the hypothesis that CO₂ insufflation reduces patient abdominal pain and discomfort during and after colonoscopy examinations in potentially difficult cases.

MATERIALS AND METHODS

Study protocol
Consecutive patients considered potentially difficult cases for colonoscopic intubation were included in this prospective randomized controlled trial which took place between September 2006 and October 2007. The aim of this study was to clarify the effectiveness of CO₂ insufflation during colonoscopy examinations, with the primary objectives of assessing both patient tolerance and the safety of CO₂ insufflation in these potentially difficult cases. A secondary objective was to clarify any differences between the two insufflation methods in relation to the experience level of the participating colonoscopists. This study was approved by the Ethics Committee at Okayama University Hospital.

Patients

Patients considered potentially difficult colonoscopy cases, based on published information and clinical experience, were selected, and included females with a relatively low BMI (BMI < 22), patients with a history of abdominal and/or pelvic open surgery, with the exception of low risk procedures for adhesions such as appendectomy or hernia repair, and male patients with previously diagnosed left-side diverticulosis[7–8].

The indications for colonoscopy examination were the standard clinical criteria: colorectal cancer screening, surveillance for polyps, a positive fecal occult blood test, abdominal symptoms or anemia. Exclusion factors included severe heart or lung disease, a prior colorectal resection, inflammatory bowel disease, severe hematochezia and repeat colonoscopy for therapeutic procedures including polypectomy.

Written informed consent was obtained from each patient and enrolled patients were randomly divided into two groups for colonoscopy examinations using either CO₂ or standard air insufflation. Group allocation for both patients and colonoscopists was performed by specially assigned nurses using standard randomization lists which contained consecutive patient numbers. Each number was linked to one of the two study groups for allocation purposes. These lists were not accessible by the participating colonoscopists.

Colonoscopy using CO₂ insufflation

Patients underwent bowel preparation with sodium picosulfate the day before their examinations and two liters of polyethylene glycol solution-containing lavage the morning of their colonoscopies. Scopolamine butylbromide (20 mg) was administered intramuscularly to suppress bowel movement, while patients with cardiac disease or benign prostatic hypertrophy received glucagon (1 IU) intramuscularly. Patients were not sedated, although midazolam (2-3 mg, iv) was administered based on the examining colonoscopist’s judgment or when requested by the patient due to abdominal pain or distension. Examinations were performed using a pediatric variable-stiffness colonoscope (PVSC) with a distal tip diameter of 11.3 mm (PCF-Q260AI, Olympus Co, Tokyo, Japan).

Procedures were randomly performed by eight colonoscopists who had earlier been divided into two groups according to their colonoscopy experience: four highly experienced colonoscopists (EC) group each of whom had been in colonoscopy practice for over 10 years (TU, JK, KT and SH), and four less experienced colonoscopists (LEC) group with 5-7 years of colonoscopy practice during which each had performed 900–1500 colonoscopies (MK, SI, KH and HF).

If an examining colonoscopist from the LEC group failed to pass through the sigmoid-descending colon junction within 15 min or a patient complained of severe pain, a colonoscopist from the EC group replaced the initial examiner before midazolam was administered and continued insertion to the cecum. When such a case involved a colonoscopist from the EC group as the initial examiner, a more experienced member of the EC group would continue the procedure. After reaching the cecum, the initial examiner proceeded with withdrawal of the colonoscope.

A “complete colonoscopy” was defined as successful insertion to the cecum bottom or terminal ileum. Insertion to the cecum and withdrawal time was recorded for every colonoscopy.

CO₂ insufflation and monitoring system

CO₂ was administered using a commercial CO₂ regulator (Gas Regulator, Crown, Model FR-IIS-P; Yutaka Engineering, Tokyo, Japan) connected to a CO₂ bottle.
The regulator delivered CO\(_2\) at the rate of 2 L/min. CO\(_2\) and air insufflations were used in a blind fashion both to patients and colonoscopists with full-day colonoscopy sessions randomly assigned CO\(_2\) or air insufflation to avoid unblinding caused by set-up changes between patients.

CO\(_2\) partial pressure was continuously measured using a transcutaneous CO\(_2\) monitoring system (TOSCA 500; Radiometer Basel AG, Switzerland). Processed transcutaneous CO\(_2\) readings (\(P_{tc\text{CO}_2}\)) correlate closely with directly obtained arterial blood gas results\(^{[16,17]}\). Sensors were attached to a patient’s ear lobe with a monitorspecific clip. A colonoscopy assistant recorded readings and an independent observer monitored gas readings to avoid potential serious side effects. CO\(_2\) insufflation was stopped immediately if \(P_{tc\text{CO}_2}\) registered > 60 mmHg during any colonoscopy examination.

**Pain and discomfort measurement**
A 100-mm visual analogue scale (VAS) consisting of a horizontal line 100 mm in length was used for measuring patient abdominal pain and discomfort (0 mm = painless, 100 mm = extremely painful)\(^{[18]}\). Patients recorded the pain level experienced upon reaching the cecum bottom, immediately following their examinations and 30 min, 1, 2, 4 and 6 h afterwards. The VAS score was the distance measured to the nearest millimeter from the left end of the line to the point of the patient’s mark.

Another member of the medical staff, who did not know how the procedures were performed, interviewed the patients 30 min after completion of their colonoscopies. A questionnaire was then given to the patients to take home to complete as instructed at intervals of 1, 2, 4 and 6 h and the completed forms were then mailed to the hospital the following day. The completed questionnaires were subsequently mailed to our medical office. No follow-up phone calls were made as 98% of all questionnaires were promptly returned.

**Statistical analysis**
A preliminary pilot study was conducted to estimate the SD in pain measurements. With an assumed SD of 19 mm, the study sample size was calculated at 110 patients in order to have an 80% power with two-sided \(\alpha\) levels of 0.05 to detect any differences in VAS scores between the two insufflation groups (\(\geq 10\) mm was considered clinically important).

The outcomes for our secondary objective to clarify any differences between the two insufflation methods in relation to the experience level of participating colonoscopists were analyzed on an intention-to-treat basis, given the fact that a number of the initial examining colonoscopists were replaced during the insertion phase of the procedure. Statistical comparisons were made using chi-square and Fisher’s exact tests. ANOVA was used for repeated measures statistical analysis of pain. Some variables were not distributed normally, thus the Wilcoxon rank sum test was applied for supplementary analysis to compare groups at each measurement point. Statistical analyses were performed using Prism version 5.0 (GraphPad Software, San Diego, CA, USA) and JMP version 6.3 (SAS Institute, Cary, NC, USA). A \(P\) value < 0.05 was considered significant.

**RESULTS**

**Baseline characteristics**
A total of 130 patients were asked to participate and 120 consenting patients were randomized into two groups prior to their colonoscopy examinations (Figure 1). Three poor bowel preparation patients were not included and one (0.85%, 1/117) incomplete intubation patient in the air insufflation group with a history of abdominal and pelvic open surgery, whose examination was performed by an EC, was not submitted for consideration. Completed questionnaires were received from 98% of the 116 remaining patients, thus a final total of 114 patients (68% female/32% male) were analyzed in this study. Exactly half or 57 patients were examined using CO\(_2\) insufflation and the other 57 patients were examined with air insufflation. There were no significant differences in baseline patient characteristics including eligibility criteria for potentially difficult cases between the two groups (Table 1).

**Outcome measures comparing CO\(_2\) and air insufflation groups**
There were no significant differences in procedure times including intubation, withdrawal and total time between the two groups (Table 2). Midazolam was administered to two patients (4%) in each group. There were no instances of \(P_{tc\text{CO}_2}\) > 60 mmHg in the CO\(_2\) insufflation patients or any procedure-related complications in either group.

Figure 2 shows the mean VAS scores during and after colonoscopy examinations. VAS scores in the CO\(_2\) insufflation group were significantly better than those in the air insufflation group \((P < 0.001,\) ANOVA for repeated measures). The overall mean difference was 5.3 mm (95% CI: 3.5-7.1, \(P < 0.001\)). Comparison by nonparametric analysis at each measurement point produced results favoring CO\(_2\) insufflation immediately following the examinations and up to 2 h afterwards. The maximum mean difference of 9.2 mm (95% CI: 0.4-18.0, \(P = 0.0049\)) was recorded 30 min after the examinations.
Table 1  Patient characteristics (n = 114)  n (%) Median age, yr (IQR) CO₂ group (n = 57) Air group (n = 57) P value
Females 65 (59-73) 62 (47-71) 0.107
Eligibility criteria for difficult cases
Females with relatively low BMI (< 22) 36 (63) 35 (61) 0.133
Previous abdominal and/or pelvic open surgery 47 (72) 37 (65) 0.546
Males with previously diagnosed left-side diverticulosis 6 (11) 2 (4) 0.271
One or more previous colonoscopies 16 (28) 15 (26) 1.00

Some patients had more than one difficult case factor. IQR: Interquartile range; BMI: Body mass index.

Table 2  Use of antispasmodic drugs & median procedure times for CO₂ & air insufflation groups

|                          | CO₂ group (n = 57) | Air group (n = 57) | P value |
|--------------------------|--------------------|--------------------|---------|
| Patients receiving antispasmodic drug (%) | 54 (95) | 56 (98) | 0.616 |
| Median total procedure time, min (IQR) | 22.5 (17.9-29.6) | 22.3 (16.3-43.9) | 0.734 |
| Insertion to cecum | 10.3 (6.5-16.6) | 9.6 (5.8-16.2) | 0.601 |
| Withdrawal | 11.9 (10.1-13.6) | 12.0 (9.8-14.2) | 0.986 |

Table 3  Median procedure times for colonoscopist groups

|                          | EC group (n = 53) | LEC group (n = 61) | P value |
|--------------------------|-------------------|--------------------|---------|
| Median total procedure time, min (IQR) | 19.5 (15.3-25.8) | 23.8 (19.2-34.5) | 0.005 |
| Insertion to cecum | 7.7 (5.1-13.2) | 12.5 (7.0-18.9) | 0.036 |
| Withdrawal | 10.9 (10.0-13.0) | 12.5 (10.2-15.1) | 0.003 |
| Examiner replaced during intubation | 1 | 5 | 0.213 |

EC: Experienced colonoscopist; LEC: Less experienced colonoscopist.

Subgroup analysis
Based on the subgroup analysis relative to experience level of the participating colonoscopists, we evaluated 53 patients (46%) in the EC group and 61 patients (54%) in the LEC group. There were no significant differences in eligibility criteria for potentially difficult cases between the two groups, however, the EC group achieved insertion to the cecum significantly faster, while withdrawal and total procedure times were also significantly shorter than those in the LEC group (Table 3). The number of replacements by another colonoscopist was larger in the LEC group (5) than in the EC group (1), however, there was no significant difference between the two groups.

Figure 3 shows the mean VAS scores for 27 CO₂ insufflation patients and 26 air insufflation patients during and following colonoscopy examinations performed by the EC group. There were no significant differences in the mean VAS scores between the two patient groups

DISCUSSION
The increase in patient abdominal pain and discomfort
often encountered in difficult colonoscopy examination cases is a concern that needs to be satisfactorily resolved by colonoscopists. In this study, we successfully demonstrated the clinical effectiveness of CO₂ insufflation in potentially difficult colonoscopy examination cases. We also clarified the efficacy of CO₂ insufflation for LECs compared to highly ECs.

CO₂ with its characteristic rapid rate of absorption into surrounding tissue has been reported to be more suitable than atmospheric air in various clinical settings[12-15]. In fact, several randomized trials have shown that CO₂ insufflation reduced post-colonoscopy abdominal pain and discomfort compared to conventional air insufflation in ambulatory settings. Brettbauer et al[16] demonstrated that CO₂ insufflation was not only effective, but also safe during colonoscopies in patients receiving conscious sedation. Saito et al[17] introduced the use of CO₂ insufflation during lengthier colorectal endoscopic submucosal dissections in patients receiving conscious sedation. Their results demonstrated the effectiveness and safety of CO₂ insufflation as well as a resultant reduction in total dosage of midazolam. CO₂ insufflation has also been applied in endoscopic retrograde cholangiopancreatography (ERCP)[18] and endoscopic dilatation therapy using a double balloon endoscope[19]. There have been few detailed investigative reports on the use of CO₂ insufflation during difficult colonoscopy cases. In addition, the effect of the relative experience of colonoscopists using CO₂ insufflation has not been previously analyzed.

This study validated our theory that CO₂ insufflation is more effective than air insufflation in potentially difficult colonoscopy cases with the comparative difference for the two procedures being particularly discernable between LECs and ECs. Colonoscopy is a technically demanding procedure requiring considerable instruction and on-the-job experience for optimal performance. A suitable training program and sufficient opportunities to improve practical skills in a clinical setting are essential for beginners as well as colonoscopists with a moderate degree of experience[20,21,22].

Difficult colonoscopy examinations performed by LECs require additional time as do ERCP and therapeutic endoscopic procedures, and can cause patient abdominal pain and discomfort both during the procedure and afterwards. The results of our study demonstrated a difference not only in intubation times, but also in withdrawal and overall examination times according to the experience of the participating colonoscopists. Avoiding prolonged insufflation especially during insertion, however, might have led to similar results in the LEC group concerning the clinical effectiveness of CO₂ in reducing patient pain and discomfort.

Lee et al[23] recommended that trainees perform over 150 examinations in a colonoscopy training program to be technically competent for diagnostic colonoscopy. Our results revealed significant differences in examination times and patient abdominal pain and discomfort after colonoscopy between the EC and LEC groups. The four colonoscopists in the LEC group had each performed a minimum of 900 colonoscopies, thus the question arises as to whether a minimum of 150 cases referred to in the report by Lee above, is sufficient for conducting examinations in potentially difficult colonoscopy cases.

A recent study in Ontario, Canada analyzed factors associated with incomplete colonoscopies based on the following settings: an academic hospital, a community hospital and private medical offices. The incomplete colonoscopy rate was highest in private offices with an odds ratio increase of more than three-fold[24], thus introducing CO₂ insufflation may be particularly useful in reducing patient complaints in non-hospital environments. We refrained from using novice colonoscopists in this study because of the formidable nature of potentially difficult colonoscopy cases. Such novices should only conduct difficult colonoscopies after gaining the necessary experience performing routine colonoscopy examinations.

A number of techniques and devices have reportedly been effective in reducing patient abdominal pain and discomfort during difficult colonoscopies, improving the rate of successful insertion to the cecum, shortening insertion time to the cecum and reducing the dosage of sedatives[25] including the use of a pediatric colonoscope[26], variable stiffness colonoscope[27], gastroscope[28], double balloon endoscope[29] and hood attached to the top of the colonoscope[30]. A PVSC featuring both variable stiffness on demand and a thin diameter was used in our trial. Previously, this instrument was shown not to be superior to adult or standard pediatric colonoscopes[29-32]. However, there have been reports that use of the PVSC made it possible to complete colonoscopies that would have been much more difficult or impossible to perform using an adult colonoscope, including patients who had undergone hysterectomies[31] and patients with diverticular disease and severe stenosis[32].

There was only one case (0.85%) of incomplete insertion to the cecum in our study and just four (3.5%) patients required sedation. Complete screening colonoscopy without sedation or with on-demand sedation in
academic medical centers has been reported to be in the 88%-99% range\textsuperscript{33-36}, with the optimum intubation rate obtained using a PVSC. In this study, the PVSC more than likely contributed to the impressive successful intubation rates and reduction in pain during insertion to the cecum achieved in both groups, as well as the favorable intubation times for each group. In several studies performed by ECs at academic medical centers, insertion to the cecum times varied between 7-13 min for colonoscopies performed without sedation or with on-demand sedation\textsuperscript{33-36}. Our median intubation times of 7.7 and 12.5 min for ECs and LECs, respectively, were in line with these earlier reports.

In conclusion, we clearly demonstrated the clinical effectiveness of CO\textsubscript{2} insufflation in potentially difficult colonoscopy examination cases performed without sedation. We also successfully clarified the efficacy of CO\textsubscript{2} insufflation for LECs.

**COMMENTS**

**Background**
Colonoscopy is the preferred method for preventing, detecting and treating colorectal cancer, however, prolonged cecal intubation can cause increased patient abdominal pain and discomfort especially in difficult cases, such as female patients with a relatively low body mass index, patients with a history of abdominal and/or pelvic open surgery and male patients with diverticulosis. CO\textsubscript{2} with its rapid rate of absorption has been reported to be more suitable than atmospheric air as an insufflation agent in various clinical settings, although air insufflation is still the standard method due to a lack of suitable equipment and inadequate information as to when and on whom CO\textsubscript{2} insufflation should be used during colonoscopy examinations.

**Research frontiers**
This prospective randomized controlled study was conducted to clarify the effectiveness of CO\textsubscript{2} insufflation in potentially difficult cases, particularly in relation to colonoscopist experience level.

**Innovations and breakthroughs**
The clinical effectiveness of CO\textsubscript{2} insufflation was clearly demonstrated in potentially difficult colonoscopy examination cases performed without sedation. The procedure that was followed also clarified the efficacy of CO\textsubscript{2} insufflation for less experienced colonoscopists (LEC) particularly in comparison to more experienced colonoscopists.

**Applications**
The use of CO\textsubscript{2} insufflation can be incorporated into existing and future colonoscopy training programs in order to further improve the technical skills of colonoscopists.

**Peer review**
The authors successfully demonstrated that CO\textsubscript{2} insufflation with its rapid rate of CO\textsubscript{2} absorption and improved efficacy reduced patient pain in potentially difficult cases particularly when colonoscopy examinations were performed by LECs.

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