Carbon dioxide insufflation during screening unsedated colonoscopy: a randomised clinical trial

Miroslaw Szura, Radoslaw Pach, Andrzej Matyja and Jan Kulig

One of the methods used to reduce pain and discomfort during colonoscopy is insufflation of carbon dioxide instead of air. However, the actual benefit of carbon dioxide insufflation is not unequivocally proven. The aim of the study was to evaluate the advantages of carbon dioxide insufflation during screening colonoscopy. A total of 200 patients undergoing screening colonoscopy between 2010 and 2011 were included in the prospective, randomized study carried out in a surgical referral center. Screening unsedated colonoscopy with either air or carbon dioxide insufflation was performed; patients were randomly assigned to air or carbon dioxide group by means of computer-generated randomization lists. All examinations were performed in an ambulatory setting with standard videocolonoscopes. The main outcomes analyzed were (a) duration of the entire procedure, (b) cecal intubation time, and (c) pain severity immediately, 15, and 60 min after the procedure. Group I included 59 women and 41 men and group II included 51 women and 49 men. The duration of the procedure was circa 10 min in both groups. Pain score values immediately and 15 min after the procedure were similar in both groups ($P=0.624$ and 0.305, respectively). A lower pain score was observed only after 60 min in patients insufflated with carbon dioxide (1.28 vs. 1.54, $P=0.008$). No pain reduction was observed in women and in obese patients (BMI > 30). Carbon dioxide insufflation during unsedated screening colonoscopy does not decrease the duration of the procedure and appears to reduce pain intensity at 60 min after examination to an extent without clinical significance. The study was registered at ClinicalTrials.gov, number NCT01461564. *European Journal of Cancer Prevention* 24:37–43 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.

European Journal of Cancer Prevention 2015, **24**:37–43

Keywords: carbon dioxide, cecal intubation, colonoscopy, screening

First Department of General Surgery, Jagiellonian University, Cracow, Poland

Correspondence to Radoslaw Pach, MD, PhD, First Department of General, Oncological and Gastrointestinal Surgery, Medical College Jagiellonian University, Kopernika Street 40, 31-501 Cracow, Poland
Tel/fax: +48 124 248 007; e-mail: rpach@o2.pl

Received 10 December 2013 **Accepted** 15 April 2014

Introduction

Colonoscopy is currently considered the most effective procedure used for the detection of colon cancer, especially in the early stages. Screening colonoscopies are performed in symptom-free patients at risk of familial colon cancer. During colonoscopy, air commonly used to insufflate the bowel may be retained after the procedure, causing pain and discomfort to the patients. One of the methods used to reduce pain and discomfort is insufflation of carbon dioxide instead of air during colonoscopy because it is readily absorbed through the small intestine and eliminated by the lungs. This does not occur with air. The use of carbon dioxide as the insufflating gas was introduced in 1952 and it was initially recommended to prevent explosion during endoscopic polypectomy (Carter, 1952). In 1965, carbon dioxide-producing suppositories were evaluated positively for sigmoidoscopy (Hamilton and Walker, 1965). Since Rogers (1974) published results of a study evaluating the safety of carbon dioxide insufflation during endoscopy, a few authors have evaluated its use in various endoscopic procedures. Techniques used to minimize pain during and after colonoscopy are welcome, especially when they can also shorten recovery times, reduce the risk of intraoperative explosions from diathermy, and even assist with more rapid insertion of the colonoscope (Macrae, 2008).

In a recent systematic review and meta-analysis of randomized controlled trials comparing air and carbon dioxide during colonoscopy, the authors concluded that there were no significant differences between air and carbon dioxide in terms of safety, gas volume, and cecal intubation rate (Wu and Hu, 2012). However, the meta-analysis indicated fewer patients with abdominal pain in the carbon dioxide group at 1, 6, and 24 h after the procedure. Thus, the influence of carbon dioxide insufflation on pain seems to be significant, but not shortly after the procedure, when the intensity of pain is highest.

Another meta-analysis, by Wang *et al.* (2012), included 13 randomized trials comparing carbon dioxide insufflation with room air insufflation in adult patients undergoing colonoscopy. Only eight studies reported the mean visual analogue scale (VAS) score for postprocedural pain intensity. All studies showed that, from the end of the procedure to 1 h after the procedure, the carbon dioxide insufflation group showed lower pain (VAS scores) than the air insufflation group. However, only five of the 13 studies analyzed colonoscopy in unsedated patients and only four studies reported postprocedural pain intensity.

The primary aim of this randomized clinical trial was to evaluate the results of using carbon dioxide insufflation during screening unsedated colonoscopy in terms of

 DOI: 10.1097/CEJ.0000000000000047

duration of procedure and postprocedural pain up to 1 h after examination.

Materials and methods

A total of 396 consecutive patients undergoing screening colonoscopies for the detection of early colon cancer between 2010 and 2011 were initially considered eligible for the study. In all, 188 patients were subsequently withdrawn because of inappropriate age for screening (97 patients), previous abdominal surgery (65 patients), and colonoscopy under general anesthesia (26 patients). The prospective, randomized study was carried out with 208 patients. After randomization, eight patients were excluded from further analyses because of incomplete colonoscopy resulting from poor preparation (one patient), neoplastic stenosis (three patients), and general anesthesia introduced during examination (four patients). The screening program was aimed at patients 50–65 years of age under surveillance of the Polish Ministry of Health and National Consultant in General Surgery; therefore, ethics committee approval was not compulsory. The research was performed in accordance with the ethical standards established in the 1964 Declaration of Helsinki and its later amendments. During the study, the rules of Good Clinical Practice were followed and therefore it was carried out in conformity with ethical and humane principles of research. Informed consent was obtained from every patient before their inclusion in the study. All patients were examined at our department during 2 consecutive years before the study. The flow diagram in Fig. 1 shows the passage of participants through the study. All examinations were performed using Olympus 165 videocolonoscopes (Olympus Corporation, Tokyo, Japan) by seven experienced endoscopists. The endoscopists were not blinded and all of them performed colonoscopies of high quality using the appropriate volume of gas (air or carbon dioxide) needed for examination. Each endoscopist who participated in the study had performed more than 2000 colonoscopies alone, and had a cecal intubation rate of more than 95% and a polyp detection rate of more than 20% in screening examinations.

The patients were assigned randomly to group I or group II with either air or carbon dioxide insufflation.

Fig. 1

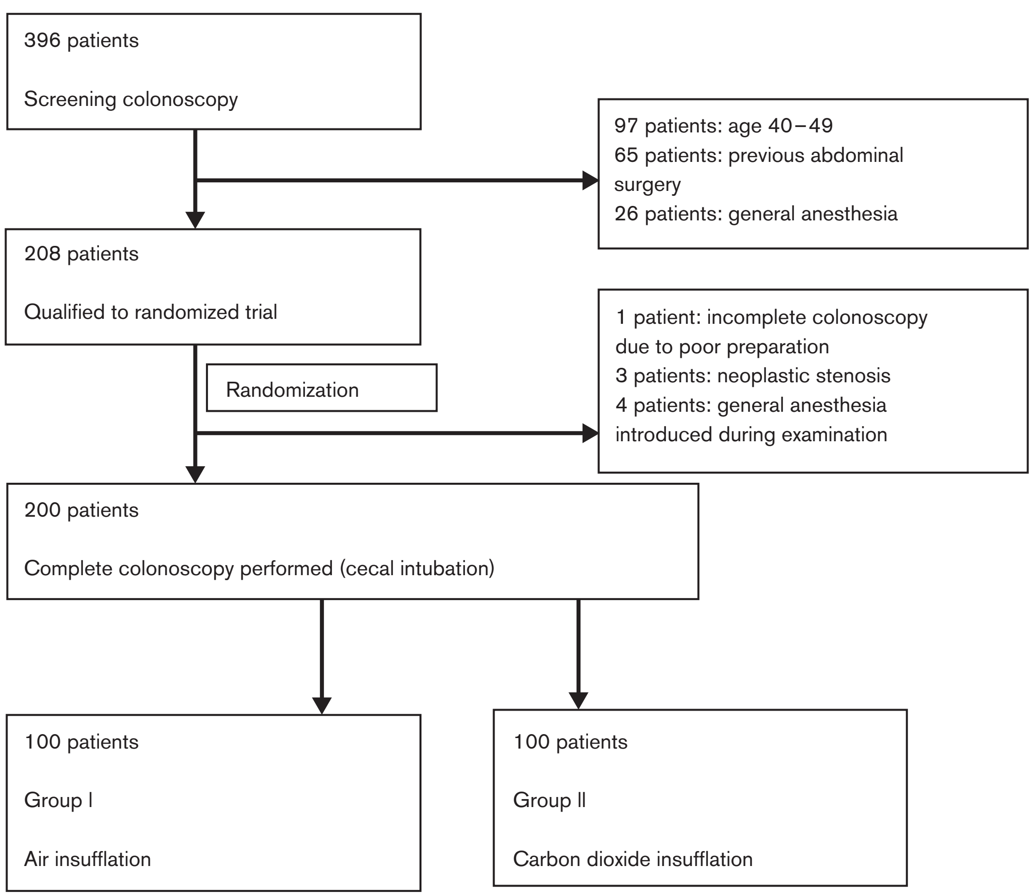

Diagram of patient selection.

Computer-generated randomization lists were used for the purpose; the allocation ratio was 1 : 1. The patients were blinded in terms of the group to which they were allocated. The study groups were homogeneous in terms of sex, age, BMI, coronary disease, and diabetes (Tables 1 and 2). The randomization list was not available to patients to conceal the allocation sequence. The insufflation unit was covered during all colonoscopies; thus, the patients were unaware of the type of gas insufflated during examination. Endoscopists were not blinded to the type of gas used, but it did not affect their practice – they performed the procedure in the usual manner at our department, that is, minimizing the volume of gas insufflation during colonoscopy without decreasing the quality of mucosal visualization. Bowel preparation for colonoscopy was through oral ingestion of liquid propulsive agents, that is, 420 g of macrogolum in 4 l of water, taken in four doses every 6 h the day before the examination. On the day preceding and up to a few hours before the procedure, only clear liquids were consumed by the patients. Colonoscopy was performed in an outpatient setting without sedation, which was the standard approach during a screening program for early detection of colon cancer in Poland funded by the National Health Fund. All patients analyzed agreed to the examination without sedation. Patients with previous abdominal surgery, those younger than 50 years of age, and those who qualified initially for general anesthesia were excluded from the study. A total of 208 patients were randomized, but eight patients were excluded from further analyses (Fig. 1) because of poor preparation, neoplastic stenosis, or general anesthesia introduced during examination. Inclusion of patients with neoplastic stenosis (and subsequently shorter duration of procedure) or general anesthesia (lower pain intensity after the procedure) would lead to a possible bias in assessment of carbon dioxide values. Patient characteristics according to intention-to-treat analysis are summarized in Table 1. Table 2 presents data on the 200 patients included in further analyses.

Table 1 Patient characteristics in analyzed groups (intention-to-treat analysis)

Parameters	Group I (air) (N = 104)	Group II (CO_2) (N = 104)	P
Men	44	51	0.256[a]
Women	60	53	0.256[a]
Age	58 ± 4.6 (50–65)	57.2 ± 4.1 (50–65)	0.186[b]
Coronary disease	18	17	0.902[a]
Diabetes	4	6	0.517[a]
BMI	27.4 ± 3.5 (17.4–39)	27.7 ± 4.0 (21.6–40.8)	0.521[c]
Cecal intubation rate (%)	97	98.1	0.651[a]

[a] χ^2-test.
[b] Mann–Whitney *U*-test.
[c] Student's *t*-test.

Table 2 Patient characteristics in analyzed groups

Parameters	Group I (air) (N = 100)	Group II (CO_2) (N = 100)	P
Men	41	49	0.330[a]
Women	59	51	0.330[a]
Age	57.1 ± 3.9 (50–65)	57.2 ± 4.2 (50–65)	0.198[b]
Coronary disease	18	17	0.707[a]
Diabetes	4	6	0.516[a]
BMI	27.8 ± 4.1 (17.4–39)	27.5 ± 3.7 (21.6–40.8)	0.513[c]
Cecal intubation rate (%)	100	100	–

[a] χ^2-test.
[b] Mann–Whitney *U*-test.
[c] Student's *t*-test.

All patients had cecal intubation confirmed by a snapshot. Patients remained in the outpatient department for 1 h after the procedure; they passed gas and were discharged on the same day. Duration of the entire procedure, cecal intubation time, polyp detection rates, pulse rates before and immediately after the procedure, and subjective pain levels measured by a VAS in both groups were compared. Pain sensation was assessed by an independent assessor immediately after the procedure, and then 15 and 60 min later. The assessor was unaware of the insufflating gas used during the examination. Before examination, each patient was instructed on how to score pain using a linear analogue pain scale (VAS), ranging from 0 to 10 (0 – no pain at all, 10 – the worst pain imaginable). Cecal intubation time was defined as the time between insertion of the colonoscope and the time of successful cecal intubation. Duration of the procedure was defined as the time between insertion of the colonoscope and removal of the entire endoscope.

The primary outcome measure in the study was the duration of the endoscopic examination.

The secondary outcome measures in the study were as follows:

(1) pain severity after the procedure measured by a VAS immediately after, and 15 and 60 min after the examination,
(2) cecal intubation time,
(3) number of colonoscopies with any pathologies encountered (polyps, diverticulosis, inflammation),
(4) complication rate in both arms,
(5) comparison of outcome measures in patients of different sexes and BMIs.

All data were prospectively collected and entered into Access 2010 software and then transferred to StatSoft Inc. (Tulsa, Oklahoma, USA) STATISTICA (data analysis software system), version 10. The distribution of variables was assessed using the Kolmogorov–Smirnov test. Data were expressed either as mean and SD or as median and range. Differences between continuous variables were assessed by Student's *t*-test or the Mann–Whitney *U*-test, as appropriate. Categorical variables were analyzed using the χ^2-test or Fisher's exact test. Correlations were assessed by the Spearman coefficient. A *P*-value of 0.05 or less was considered to indicate statistical significance. The differences in the duration of the entire procedure as well as cecal intubation time between the two groups analyzed were estimated at 1 min and the difference in pain measured by the VAS scale was estimated at 0.5 point. Sample Power release 2.0 (SPSS Inc., Chicago, Illinois, USA) was used to calculate the population required to achieve test power of 90% for the two main end-points. The sample size needed for each arm was established as 86 patients (two-sided test, $\alpha = 0.05$, estimated SD 2.0). The actual recruitment in the study was higher than required (100 patients in both arms). The study was registered at ClinicalTrials.gov, identifier: NCT01461564.

Results

The study cohort included 200 patients (100 randomized to carbon dioxide insufflation – group II). Group I included 59 women and 41 men, mean age 58 years and mean BMI 27.8. Group II included 51 women and 49 men, mean age 57.2 years and mean BMI 27.5. The analysis was carried out by the original assigned groups, but not 'intention-to-treat', as patients without cecal intubation were excluded from the study. The mean duration of the procedure was 10.6 min in the first group and 10.9 min in the second group ($P = 0.492$). The average gas volume used for colonoscopy in both groups was 8 l, which is comparable with data in the literature (Bretthauer *et al.*, 2003). The mean cecal intubation time was 3.5 min in both groups ($P = 0.599$). The average pulse rate measured before the examination was 79.1/min in group I and slightly higher (82.5/min) in group II ($P = 0.031$). The average pulse rate immediately after the examination was 73.2/min in group I and 73.4/min in group II ($P = 0.834$). The value of the pain score immediately after colonoscopy was 2.44 in the group 1 versus 2.40 in patients insufflated with carbon dioxide ($P = 0.624$). The value of the pain score measured 15 min after the procedure was similar in both groups ($P = 0.305$). The value of the pain score measured 60 min after the procedure was 1.54 in group I and 1.28 in group II ($P = 0.008$). The number of colonoscopies with polyp detection did not differ significantly between the two groups analyzed (23 vs. 30, respectively, $P = 0.262$). No complications were observed, which is consistent with reports in the literature (serious complication rate after colonoscopy 0.05%) (Sewitch *et al.*, 2012). The results are summarized in Table 3.

All analyzed patients were subsequently divided into three groups with different BMI values (normal, overweight, obese). Then, the outcomes were analyzed in groups with different BMIs (Table 4). Sixty minutes after colonoscopy, the value of the pain score was significantly lower only in overweight patients insufflated with carbon dioxide (1.26 vs. 1.62, respectively, $P = 0.049$). Other parameters analyzed were comparable in all BMI groups independent of the gas type used during endoscopy.

Moreover, the measured outcomes were compared in men and women separately (Table 5). The value of the pain score was lower only in men insufflated with carbon dioxide and only 1 h after colonoscopy (1.14 vs. 1.63, respectively, $P = 0.006$). Neither in men nor in women were other significant differences observed.

The last step in our study was to assess whether there was a correlation between the duration of the procedure and the VAS scale immediately, and 15 and 60 min, after colonoscopy. No significant correlation was observed in all 200 analyzed patients and in groups with different gases used for insufflation (Table 6).

Discussion

Colonoscopy is widely considered the most sensitive and specific of all the available diagnostic tools for early identification of colorectal cancer (Yasumasa *et al.*, 2006). Air insufflation during colonoscopy is considered the

Table 3 Comparison of measured outcomes in the two analyzed groups (air vs. carbon dioxide insufflation)

Parameters	Group I (air) ($N = 100$)	Group II (CO_2) ($N = 100$)	P
Duration of the procedure (min)	10.6 ± 2.9	10.9 ± 2.8	0.492[a]
Cecal intubation time (min)	3.5 ± 1.7	3.5 ± 1.6	0.599[a]
Number of endoscopies with polyp detection	23	30	0.262[b]
Number of polypectomies	23	30	0.262[b]
Number of endoscopies with adenoma detection	19	22	0.599[b]
Number of endoscopies with cancer detection	0	0	–
Number of endoscopies with diverticulosis detection	25	25	1.0[b]
Number of endoscopies with other pathologies encountered (inflammation)	30	38	0.232[b]
Pulse rate before colonoscopy	79.1 ± 10.9	82.5 ± 11.3	0.031[c]
Pulse rate immediately after colonoscopy	73.2 ± 7.6	73.4 ± 8.6	0.834[c]
Pain score (VAS) immediately after the procedure	2.44 ± 1.2	2.40 ± 1.3	0.624[a]
Pain score (VAS) 15 min after the procedure	2.26 ± 1.6	2.03 ± 1.5	0.305[a]
Pain score (VAS) 60 min after the procedure	1.54 ± 1.2	1.28 ± 1.2	0.008[a]
Complications	None	None	–

VAS, visual analogue scale.
[a]Mann–Whitney *U*-test.
[b]χ^2-test.
[c]Student's *t*-test.

Table 4 Comparison of measured outcomes in the three groups of patients with different BMIs

Parameters	Group I (air)	Group II (CO_2)	*P*
Normal BMI (< 25) (*n* = 54)			
Number of patients	29	25	–
Duration of the procedure (min)	11.1 ± 3.3	10.5 ± 2.4	0.527[a]
Cecal intubation time (min)	3.7 ± 1.8	3.4 ± 1.4	0.615[a]
Number of endoscopies with polyp detection	7	6	0.991[b]
Pulse rate before colonoscopy	80.7 ± 11.8	83.3 ± 11.8	0.423[c]
Pulse rate immediately after the procedure	72.2 ± 6.8	75.2 ± 8.7	0.167[c]
Pain score (VAS) immediately after the procedure	2.3 ± 1.2	2.5 ± 1.2	0.585[a]
Pain score (VAS) 15 min after the procedure	2.2 ± 1.6	2.3 ± 1.5	0.802[a]
Pain score (VAS) 60 min after the procedure	1.45 ± 1.3	1.36 ± 1.3	0.546[a]
Overweight (BMI 25–30) (*n* = 95)			
Number of patients	37	58	–
Duration of the procedure (min)	10.1 ± 2.8	10.9 ± 2.9	0.089[a]
Cecal intubation time (min)	3.0 ± 1.6	3.5 ± 1.6	0.103[a]
Number of endoscopies with polyp detection	7	6	0.236[b]
Pulse rate before colonoscopy	76.3 ± 11.3	82.5 ± 10.6	0.008[c]
Pulse rate immediately after the procedure	72.9 ± 9.0	72.2 ± 8.9	0.834[c]
Pain score (VAS) immediately after the procedure	2.43 ± 1.4	2.36 ± 1.3	0.521[a]
Pain score (VAS) 15 min after the procedure	2.19 ± 1.5	1.90 ± 1.5	0.366[a]
Pain score (VAS) 60 min after the procedure	1.62 ± 1.2	1.26 ± 1.2	0.049[a]
Obesity (BMI > 30) (*n* = 51)			
Number of patients	34	17	–
Duration of the procedure (min)	10.8 ± 2.5	11.2 ± 2.8	0.719[a]
Cecal intubation time (min)	3.7 ± 1.8	3.7 ± 1.5	0.905[a]
Number of endoscopies with polyp detection	9	8	0.142[b]
Pulse rate before colonoscopy	80.7 ± 9.1	81.2 ± 13.2	0.875[c]
Pulse rate immediately after the procedure	74.2 ± 6.6	74.7 ± 6.7	0.789[c]
Pain score (VAS) immediately after the procedure	2.53 ± 1.2	2.41 ± 1.2	0.742[a]
Pain score (VAS) 15 min after the procedure	2.38 ± 1.6	2.00 ± 1.6	0.454[a]
Pain score (VAS) 60 min after the procedure	1.53 ± 1.1	1.24 ± 1.2	0.142[a]

VAS, visual analogue scale.
[a]Mann–Whitney *U*-test.
[b]χ^2-test.
[c]Student's *t*-test.

Table 5 Comparison of measured outcomes in men and women

Parameters	Group I (air)	Group II (CO_2)	*P*
Men (*n* = 90)			
Number of patients	41	49	–
Duration of the procedure (min)	10.5 ± 2.9	10.6 ± 2.5	0.557[a]
Cecal intubation time (min)	3.3 ± 1.7	3.4 ± 1.5	0.584[a]
Number of endoscopies with polyp detection	10	18	0.208[b]
Pulse rate before colonoscopy	77.2 ± 10.5	83.1 ± 11.9	0.015[c]
Pulse rate immediately after the procedure	74.3 ± 8.0	73.2 ± 9.0	0.549[c]
Pain score (VAS) immediately after the procedure	2.39 ± 1.1	2.45 ± 1.4	0.774[a]
Pain score (VAS) 15 min after the procedure	2.27 ± 1.5	1.96 ± 1.5	0.329[a]
Pain score (VAS) 60 min after the procedure	1.63 ± 1.3	1.14 ± 1.1	0.006[a]
Women (*n* = 110)			
Number of patients	59	51	–
Duration of the procedure (min)	10.7 ± 2.8	11.1 ± 3.0	0.625[a]
Cecal intubation time (min)	3.6 ± 1.8	3.7 ± 1.6	0.776[a]
Number of endoscopies with polyp detection	13	12	0.852[b]
Pulse rate before colonoscopy	80.4 ± 11.0	81.9 ± 10.7	0.475[c]
Pulse rate immediately after the procedure	72.4 ± 7.3	73.6 ± 8.2	0.413[c]
Pain score (VAS) immediately after the procedure	2.47 ± 1.3	2.35 ± 1.2	0.647[a]
Pain score (VAS) 15 min after the procedure	2.25 ± 1.6	2.10 ± 1.6	0.647[a]
Pain score (VAS) 60 min after the procedure	1.47 ± 1.1	1.41 ± 1.2	0.311[a]

VAS, visual analogue scale.
[a]Mann–Whitney *U*-test.
[b]χ^2-test.
[c]Student's *t*-test.

standard component of colonoscopic examinations worldwide. Prolonged bowel distension caused by intraluminal air insufflation may result in postcolonoscopic abdominal pain, bloating, or even perforation. Many methods have been reported to minimize patient discomfort during colonoscopy: use of pediatric colonoscope, variable stiffness colonoscope, inhalation of nitrous oxide, hypnosis, music, audio distraction, and allowing the patients to participate in administration of sedatives (Leung, 2008). A few studies have reported reduced abdominal pain after colonoscopy with carbon dioxide insufflation instead of air (Gellett *et al.*, 1999; Bretthauer *et al.*, 2002; Wong *et al.*, 2008;

Table 6 Correlation between duration of the procedure and the visual analogue scale in patients insufflated with air versus carbon dioxide (Spearman's test)

Parameter 1	Parameter 2	Spearman's *R*	*P*
Air (*N* = 100)			
Duration of the procedure	Pain score (VAS) immediately after the procedure	−0.11	0.277
	Pain score (VAS) 15 min after the procedure	−0.05	0.592
	Pain score (VAS) 60 min after the procedure	−0.12	0.248
Carbon dioxide (*N* = 100)			
Duration of the procedure	Pain score (VAS) immediately after the procedure	−0.01	0.961
	Pain score (VAS) 15 min after the procedure	0.03	0.749
	Pain score (VAS) 60 min after the procedure	0.08	0.437
All (*N* = 200)			
Duration of the procedure	Pain score (VAS) immediately after the procedure	−0.06	0.394
	Pain score (VAS) 15 min after the procedure	−0.01	0.835
	Pain score (VAS) 60 min after the procedure	−0.03	0.653

VAS, visual analogue scale.

Yamano *et al.*, 2010). These studies included mainly unsedated patients. At least two studies reported reduced pain after colonoscopy with carbon dioxide insufflation in deeply sedated patients during the entire procedure (Bretthauer *et al.*, 2005; Riss *et al.*, 2009). The hypothetical benefits of carbon dioxide usage have been considered a result of rapid shrinkage of the distended intestinal loops as carbon dioxide is water soluble and easily absorbable from the intestinal lining (Yasumasa *et al.*, 2006).

It still remains to be evaluated whether carbon dioxide insufflation decreases pain and increases patient compliance with colorectal cancer screening. In a screening setting, the main objective for the colonoscopist is the completion of high-quality total colonoscopy with high sensitivity of disease detection and a low complication rate (Macrae, 2008). Our study addresses the issue of the hypothetical advantages of carbon dioxide use for patients undergoing screening colonoscopies for the detection of early colon cancer. A total of 200 patients were included in this trial and assigned randomly to either carbon dioxide or air insufflation. The groups were comparable in terms of age, sex, BMI, polyp detection rate, and cecal intubation rate. No complications were observed in the patients analyzed. All colonoscopies reported in our study were performed without sedation, as are the majority of such procedures in Poland where only very difficult examinations require sedation. However, most of the screening patients in the USA undergo sedation for their examinations. Colonoscopists engaged in screening procedures in other cultural settings may consider the results of our trial useful as the difference between groups should be similar, although the pain intensity in sedated patients would be presumably lower after sedation. The feasibility of high-quality examinations even in unsedated patients may encourage endoscopists to perform more colonoscopies without anesthesia as, in our opinion, the additional cost of sedation seems not to be reasonably justified in cancer screening procedures. In contrast to some previous reports, duration of colonoscopy, pain level (coded as VAS score) immediately and 15 min after colonoscopy, and pulse rate immediately after the procedure were comparable in both groups analyzed. Only the pain score assessed 60 min after endoscopy was lower in patients insufflated with carbon dioxide. Nevertheless, this result has no clinical significance as the difference in the pain score between groups was only 0.26 (1.28 in carbon dioxide group vs. 1.54 in controls). The difference in the pain score 1 h after colonoscopy was significant only in men and in overweight patients, but not in women and patients with normal weight or obesity. As a conclusion of our study, we presume that the use of carbon dioxide during colonoscopy seems to be not obviously superior to air insufflation in terms of the duration of the procedure and abdominal pain shortly after examination. The lack of difference in the duration of colonoscopy was independent of sex and BMI level as we carried out analyses separately for men and women, on the one hand, and patients with normal BMI and overweight and obese patient on the other. On the whole, implementation of carbon dioxide insufflation during screening unsedated endoscopy can be unnecessarily expensive because of the need for special equipment such as a pressure-gated valve applicable to some makes of colonoscopes, without unequivocal advantages. Similarly, Macrae (2008) emphasizes that a tailored sedation management plan is more important for the best patient outcomes than the gas type used for insufflation. More benefits of carbon dioxide insufflation should be expected in colonoscopies performed by endoscopists in their early career stage or by endoscopists experienced with anesthetized patients who start examinations in unsedated individuals. These endoscopists should focus on reducing patient discomfort and minimizing the gas volume used for insufflation to achieve low pain intensity after colonoscopy. In addition, for a longer procedure time than in our study (>11 min), the advantages of carbon dioxide insufflation may be significant, especially in terms of reduction of pain intensity.

In accordance with Church and Delaney (2003) and Riss *et al.* (2009), no benefit from the use of carbon dioxide in relation to the cecal intubation time was observed. A high complete cecal intubation rate (more than 95% in both groups) in our study may have resulted from the fact that all endoscopists in our department were well experienced and had performed at least 2000 colonoscopies before the study began. In contrast, Yamano *et al.* (2010) reported a significantly faster cecal intubation time and a trend toward a shorter examination time in 66 patients undergoing colonoscopy with carbon dioxide insufflation. The high rate of cecal intubation in our study is consistent with data published by Kaminski *et al.* (2010), who reported a median cecal intubation rate of 95% (interquartile range 92–98%) for most experienced endoscopists with at least 20% adenoma detection rate.

An above-mentioned meta-analysis by Wang *et al.* (2012) included 13 randomized trials that compared carbon dioxide insufflation with room air insufflation in adult patients undergoing colonoscopy. Only two studies (both from Japan) reported pain intensity immediately after, and 30 min and 1 h after, examination. In both studies, the duration of the entire procedure was longer than that in our study, namely 22.5 and 38.7 min versus 11 min in our study. Longer examinations were probably performed by less experienced endoscopists. It may be presumed that after longer examinations performed by less experienced endoscopists, carbon dioxide insufflation decreases postprocedural pain. When examinations are performed by experienced colonoscopists and the duration of the procedure is shorter, carbon dioxide seems to have no impact on pain intensity immediately after and 30 min after colonoscopy.

One limitation of our study is that endoscopists were not blinded to the gas type used for insufflation. However, patients were not informed as to which group they were allocated to and endoscopists attempted to minimize insufflation for all examined individuals. On balance, we believe that the results may be comparable with double-blind studies and should be taken into consideration when the optimal colorectal screening procedures are discussed. The lack of a difference in the pain score in patients with normal BMI and obese patient observed in our study may result from the fact that the majority of patients analyzed were overweight (n=95) and the number of patients in other BMI groups was too small to reach statistical significance. The lack of difference in the pain score for air versus carbon dioxide insufflation even 1 h after colonoscopy may be a result of distinct pain perception by women, and suggests that not all patients benefit from carbon dioxide insufflation.

Carbon dioxide insufflation during screening unsedated colonoscopy does not decrease the duration of the procedure and that of cecal intubation, and does not reduce pain immediately and 15 min after the examination, in comparison with patients insufflated with air. Slightly lower pain intensity is observed only 60 min after the procedure, but the difference is not clinically significant. The actual impact of carbon dioxide insufflation on postendoscopic pain and duration of the procedure has not been unequivocally shown in screening unsedated colonoscopy so far and should be fully elucidated in further randomized trials. The trials should compare procedures performed by less experienced endoscopists or colonoscopists experienced only in examinations performed in sedated patients. Other possibilities for reducing pain during unsedated colonoscopies are also being investigated (transcutaneous electrical nerve stimulation, warm water consumption, three-dimensional MRI) – their effectiveness may exceed the potential benefits of carbon dioxide insufflation.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

Bretthauer M, Hoff G, Thiis-Evensen E, Grotmol T, Holmsen ST, Moritz V, Skovlund E (2002). Carbon dioxide insufflation reduces discomfort due to flexible sigmoidoscopy in colorectal cancer screening. *Scand J Gastroenterol* **37**:1103–1107.

Bretthauer M, Hoff G, Thiis-Evensen E, Huppertz-Hauss G, Skovlund E (2003). How much gas do we insufflate during colonoscopy? Air and carbon dioxide volumes insufflated during colonoscopy. *Gastrointest Endosc* **58**:203–206.

Bretthauer M, Lynge AB, Thiis-Evensen E, Hoff G, Fausa O, Aabakken L (2005). Carbon dioxide insufflation in colonoscopy: safe and effective in sedated patients. *Endoscopy* **37**:706–709.

Carter HG (1952). Explosion in the colon during electrodesiccation of polyps. *Am J Surg* **84**:514–517.

Church J, Delaney C (2003). Randomized, controlled trial of carbon dioxide insufflation during colonoscopy. *Dis Colon Rectum* **46**:322–326.

Gellett LR, Farrow R, Bloor C, Farmer KD, Maskell GF (1999). Pain after small bowel meal and pneumocolon: a randomized controlled trial of carbon dioxide versus air insufflation. *Clin Radiol* **54**:381–383.

Hamilton W, Walker WH (1965). Carbon dioxide-producing suppositories as preparation for sigmoidoscopy. *J Natl Med Assoc* **57**:496–497.

Kaminski MF, Regula J, Kraszewska E, Polkowski M, Wojciechowska U, Didkowska J, *et al.* (2010). Quality indicators for colonoscopy and the risk of interval cancer. *N Engl J Med* **362**:1795–1803.

Leung FW (2008). Methods of reducing discomfort during colonoscopy. *Dig Dis Sci* **53**:1462–1467.

Macrae F (2008). Pain and colonoscopy and CO_2. *ANZ J Surg* **78**:836.

Riss S, Akan B, Mikola B, Rieder E, Karner-Hanusch J, Dirlea D, *et al.* (2009). CO_2 insufflation during colonoscopy decreases post-interventional pain in deeply sedated patients: a randomized controlled trial. *Wien Klin Wochenschr* **121**:464–468.

Rogers BH (1974). The safety of carbon dioxide insufflation during colonoscopic electrosurgical polypectomy. *Gastrointest Endosc* **20**:115–117.

Sewitch MJ, Jiang M, Joseph L, Barkun AN, Bitton A (2012). Rate of serious complications of colonoscopy in Quebec. *Can J Gastroenterol* **26**:611–613.

Wang WL, Wu ZH, Sun Q, Wei JF, Chen XF, Zhou DK, *et al.* (2012). Meta-analysis: the use of carbon dioxide insufflation vs. room air insufflation for gastrointestinal endoscopy. *Aliment Pharmacol Ther* **35**:1145–1154.

Wong JC, Yau KK, Cheung HY, Wong DC, Chung CC, Li MK (2008). Towards painless colonoscopy: a randomized controlled trial on carbon dioxide-insufflating colonoscopy. *ANZ J Surg* **78**:871–874.

Wu J, Hu B (2012). The role of carbon dioxide insufflation in colonoscopy: a systematic review and meta-analysis. *Endoscopy* **44**:128–136.

Yamano HO, Yoshikawa K, Kimura T, Yamamoto E, Harada E, Kudou T, *et al.* (2010). Carbon dioxide insufflation for colonoscopy: evaluation of gas volume, abdominal pain, examination time and transcutaneous partial CO_2 pressure. *J Gastroenterol* **45**:1235–1240.

Yasumasa K, Nakajima K, Endo S, Ito T, Matsuda H, Nishida T (2006). Carbon dioxide insufflation attenuates parietal blood flow obstruction in distended colon: potential advantages of carbon dioxide insufflated colonoscopy. *Surg Endosc* **20**:587–594.