# Effect of carbon dioxide versus room air insufflation on post-colonoscopic pain: A prospective, randomized, controlled study

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## ABSTRACT

**Background/Aims:** Room air (RA) and carbon dioxide ($CO_2$) are widely used to insufflate the colon to examine the mucosa in colonoscopy. Pain, discomfort, and bloating can be seen during and after colonoscopy secondary to bowel distention. This study aimed to investigate the effect of $CO_2$ on post-procedure pain sensation (PPPS) in comparison with RA.

**Materials and Methods:** Patients were randomly assigned to the RA and $CO_2$ insufflation groups in a 1:1 ratio. The visual analog scale (VAS) was used to measure the pain before and after the colonoscopy. VAS score of 0 was accepted as the absence of pain and above 0 was accepted as the presence of pain. The primary outcome was to investigate the effect of $CO_2$ insufflation on PPPS. Secondary outcomes were to investigate the other contributing factors affecting PPPS and the effect of $CO_2$ on PPPS in patients with inflammatory bowel disease (IBD).

**Results:** A total of 204 patients were enrolled in the study. No significant difference in PPPS was seen between the 2 groups at any point in time after the colonoscopy. Furthermore, there was no significant difference in pain sensation between the $CO_2$ and RA groups in patients with IBD. When we investigated the other contributing factors to pain sensation, body-mass index (BMI) was found to be significant at 30 minutes and BMI and colonoscopy time were found to be significant at 6 hours afterwards.

**Conclusion:** We found no favorable effect of $CO_2$ insufflation on PPPS in colonoscopy, including in patients with IBD.

**Keywords:** Carbon dioxide, colonoscopy, inflammatory bowel disease, pain

## INTRODUCTION

Colonoscopy is a widely used diagnostic and therapeutic tool for the evaluation of the lower gastrointestinal system. Room air (RA) insufflation was the first tool that was used to inflate the bowel and to examine the mucosa efficiently. In time, to increase the efficiency and safety, additional methods were introduced, including carbon dioxide ($CO_2$) insufflation, water exchange, and water immersion (1). However, RA insufflation remains the most common method during colonoscopy (2).

Pain, discomfort, and bloating can occur during and after colonoscopy, secondary to bowel distention. Insufflation is the major reason for bowel distention after a colonoscopy. RA has slower re-absorption through the intestinal mucosa than $CO_2$ (3). Theoretically, with a faster resorption speed, abdominal pain, discomfort, and bloating are expected to be less with $CO_2$ use. Nevertheless, in some clinical studies, $CO_2$ was not found to be superior to RA in terms of post-procedure pain sensation (PPPS) or vice versa (3-8).

In this study, our aim was to investigate the effect of $CO_2$ insufflation on PPPS. Other outcomes were to investigate the contributing factors affecting PPPS and the effect of $CO_2$ on PPPS in patients with inflammatory bowel disease (IBD).

## MATERIALS AND METHODS

### Participants and Study Procedures

Patients presenting for colonoscopy for different indications, such as colorectal cancer surveillance, iron deficiency anemia, constipation, assessing disease activity in inflammatory bowel disease, and hematochezia, to our Institute of Gastroenterology from May 2015 to August 2016 were enrolled in the study; informed consent was

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obtained from all of them. Exclusion criteria included a history of colorectal surgery, chronic obstructive pulmonary disease, and refusal to sign the informed consent. All the procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the ethical committee for scientific research of our university (approval date: 08 May 2015, approval number: 09.2015.092).

Polyethylene glycol was used for the standard bowel preparation. Patients were randomly divided into RA and $CO_2$ insufflation groups in a 1:1 ratio. The endoscopists and patients were blinded to the insufflation method. All the endoscopies were performed by 2 expert gastroenterology specialists. colonoscopes (PENTAX Ec-380LKp, Tokyo, Japan) were used for colonoscopy. $CO_2$ was used with an endoscopic insufflator that connected to a $CO_2$ tube, and RA was used with standard endoscopic insufflation system. The blood pressure was measured before the procedure. The patients were monitored during the procedure for blood oxygen saturation, blood pressure, $CO_2$ level with capnography, and heart rate. Midazolam and/or propofol were administered to all the patients for anesthesia. Sedation level and medication dose were adjusted according to the endoscopist's discretion. Abdominal compression and position changes were used when necessary at the discretion of the endoscopist. Completion of the colonoscopy was noted by identification of the appendiceal orifice. Sociodemographic data, body-mass index (BMI), previous abdominal surgery, pre- and post-procedure waist circumference, total procedure time (from inserting into the cecum to removing the scope from the anus), ileal intubation, and the medications used during the procedure were recorded.

### MAIN POINTS

- *There was no significant difference was found in pain between $CO_2$ and room air groups at 30 minutes, 6 hours, and 24 hours after the colonoscopy.*
- *There was no significant difference was found in pain between the $CO_2$ and room air groups in patients with Inflammatory Bowel Disease.*
- *When the factors investigated that contributing to the pain sensation, lower BMI was significant at 30 minutes and also BMI and longer colonoscopy time were found to be significant at 6 hours.*
- *We found no favorable effect of $CO_2$ insufflation on pain following colonoscopy, including in patients with IBD.*

### Pain Assessment

The visual analog scale (VAS) was used to measure the pain before and after the colonoscopy. VAS scores range from 0 to 10, with a higher score indicating more pain and a score of 0 indicating the absence of pain. VAS score of 0 was accepted as the absence of pain, and a score above 0 was accepted as the presence of pain. An endoscopy nurse explained the VAS scoring system to each patient before the procedure and verified that it was understood. The VAS scores were collected by an experienced nurse face-to-face at 30 minutes and via telephone at 6 and 24 hours after the procedure.

### Statistical Analysis

A sample size of 178 patients was calculated so that for an effect size of 0.25, the VAS at 30 minutes, 6 hours, and 24 hours in the $CO_2$ group was less than that in the RA group, which would be detected with a power of 85% and a 2-sided significance level of 0.05 using linear mixed models. Baseline characteristics of the groups, which were continuous and normally distributed, were presented with mean and standard deviations. Variables that were not normally distributed were presented with medians. Categorical variables were reported using frequencies and percentages. The Shapiro-Wilk's test was used to analyze the data distribution. The chi-squared test was used to test the difference between the RA and $CO_2$ groups. Multivariate logistic regression analysis was performed to investigate the contributing factors affecting PPPS. A p-value of less than 0.05 was considered to be statistically significant.

## RESULTS

A total of 204 patients were enrolled in the study. Their mean age was 50.70±14.61 years, and 95 (46.6%) of them were women. $CO_2$ was used for insufflation in 99 (48.5%) patients. Anesthetic medication with analgesic effect was used in 69.5% of the RA group and 70.7% of the $CO_2$ group (p=0.87). There were no baseline differences with regard to age, sex, BMI, change in waist circumference, duration of the colonoscopy, anesthetic dose, analgesic use, previous abdominal operations, and ileal intubation (Table 1). There was also no difference in blood oxygen saturation, $CO_2$ capnograph level, arterial pulse rate, arterial blood tension, and breath rate before and after the colonoscopy.

A total of 23 (21.9%) patients in the RA group and 27 (27.3%) patients in the $CO_2$ group had pain at 30 minutes after the colonoscopy (p=0.37); 10 (9.5%) patients in the RA group and 16 (16.2%) in the $CO_2$ group had pain at 6

hours after the colonoscopy (p=0.15); 8 (7.6%) patients in the RA group and 8 (8.1%) in the $CO_2$ group had pain at 24 hours after the colonoscopy (p=0.90). There was no significant difference between the 2 groups at 30 minutes, 6 hours, and 24 hours after the colonoscopy (Table 2). In a subgroup analysis of the patients who did not receive any analgesics, we found no significant difference at 30 minutes, 6 hours, and 24 hours after the procedure (p=0.60, p=0.36, and p=0.91, respectively) (Table 3).

**Table 1.** Demographic and clinical data of the 2 groups.

| | RA group (n=105) | $CO_2$ group (n=99) | p |
|---|---|---|---|
| Age, (years), mean±SD, (years) | 49.97±14.51 | 51.47±14.75 | 0.46 |
| Sex, n (%) | | | |
| · Women | 47 (44.8%) | 48 (48.5%) | 0.67 |
| · Men | 58 (55.2%) | 51 (51.5%) | |
| BMI, (kg/m$^2$) | 26.51±4.50 | 27.48±4.97 | 0.18 |
| Increase in waist circumference, (cm); median, (min–max) | 3.0 (−2–9) | 2.0 (−1–10) | 0.68 |
| Duration of colonoscopy, (minutes); median, (min–max) | 15 (7–22) | 15 (5–25) | 0.77 |
| Midazolam dose (mg); median (min–max) | 5 (0–5) | 4 (0–5) | 0.17 |
| Propofol dose (mg); median (min–max) | 0 (0–280) | 0 (0–170) | 0.97 |
| Analgesic use, n (%) | 73 (69.5%) | 70 (70.7%) | 0.87 |
| Abdominal operation, n (%) | 22 (21.0%) | 22 (22.2%) | 0.82 |
| Ileum intubation, n (%) | 40 (38.1%) | 27 (27.3%) | 0.10 |

BMI: body-mass index; cm: centimeter; $CO_2$: carbon dioxide; kg: kilogram; max: maximum; m: meter; mg: milligram; min: minimum; SD: standard deviation; RA: room air
p<0.05 accepted as statistically significant

**Table 2.** Pain sensations after the colonoscopy between the $CO_2$ and RA groups.

| | | VAS=0 (n) | VAS>0 (n) | p |
|---|---|---|---|---|
| 30$^{th}$ minute | RA | 82 | 23 | 0.37 |
| | $CO_2$ | 72 | 27 | |
| 6$^{th}$ hour | RA | 95 | 10 | 0.15 |
| | $CO_2$ | 83 | 16 | |
| 24$^{th}$ hour | RA | 97 | 8 | 0.90 |
| | $CO_2$ | 91 | 8 | |

$CO_2$: carbon dioxide; VAS: visual analog scale; RA: room air
p<0.05 accepted as statistically significant

We had also included 40 patients with IBD in the study. Their mean age was 40.43±13.12 years, and 16 (40.0%) of them were women. There were 12 (30%) patients with Crohn's disease and 28 (70%) with ulcerative colitis. $CO_2$ was used in 16 (40.0%) of the colonoscopies of patients with IBD. There was no significant difference in pain sensation between the $CO_2$ and RA groups in patients with IBD (Figure 1).

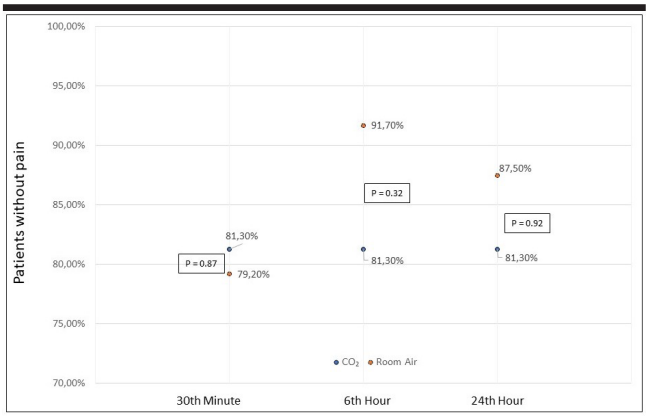


**Figure 1.** Effect of carbon dioxide and room air on pain after colonoscopy in patients with inflammatory bowel disease.

**Table 3.** Pain sensation after the colonoscopy between the $CO_2$ and RA groups in analgesic-free patients.

| | | VAS=0 (n) | VAS>0 (n) | p |
|---|---|---|---|---|
| 30 minutes | RA | 26 | 6 | 0.60 |
| | $CO_2$ | 22 | 7 | |
| 6 hours | RA | 29 | 3 | 0.36 |
| | $CO_2$ | 24 | 5 | |
| 24 hours | RA | 30 | 2 | 0.91 |
| | $CO_2$ | 27 | 2 | |

$CO_2$: carbon dioxide; VAS: visual analog scale; RA: room air
p<0.05 accepted as statistically significant

**Table 4.** Multivariate analysis of the factors affecting pain sensation after colonoscopy.

| | 30 minutes | | |
|---|---|---|---|
| | Coefficient | OR (95% CI) | p |
| BMI | -0.130 | 0.87 (0.79-0.96) | 0.01* |
| | 6 hour | | |
| | Coefficient | OR (95% CI) | p |
| BMI | -0.164 | 0.84 (0.72-0.98) | 0.03* |
| Duration of the colonoscopy | -0.204 | 0.81 (0.66-0.99) | 0.04* |

BMI: body-mass index; OR: odds ratio; CI: confidence interval
*p<0.05 accepted as statistically significant

We investigated the factors contributing to the pain sensation and found that lower BMI was significant at 30 minutes. BMI and longer colonoscopy time were found to be significant at 6 hours. There were no significant factors found at 24 hours (Table 4).

## DISCUSSION

In our study, we did not find any significant differences in PPPS when comparing RA and $CO_2$ insufflation. We found that lower BMI and longer colonoscopy time affected the PPPS after colonoscopy.

There are multiple studies that have investigated the effect of $CO_2$ on PPPS. These studies are heterogeneous in terms of study design, patient population, and outcomes. In our study, we did not find any difference in PPPS between $CO_2$ and RA insufflation during colonoscopy. Several studies have reported lower pain scores in patients who underwent $CO_2$ insufflations (6-10). However, several studies have shown no advantage with $CO_2$ insufflation in PPPS (3-5). In a previous study of patients with advanced colonic polypectomy, PPPS was lower in patients who underwent $CO_2$ insufflation at 1 hour but there was no difference at 3, 6, and 24 hours between the RA and $CO_2$ groups (8). Large polypectomy increased the pain sensation more than diagnostic colonoscopies. In our study, we did not have any complicated polypectomies. A previous randomized controlled study conducted in the pediatric population found no difference in PPPS between the $CO_2$ and RA groups at 1 hour, similar to our study (3). Another study also found no significant difference in PPPS between the $CO_2$ and RA groups when they assessed pain sensation using an internet questionnaire after hospital discharge (4). In another study, a significant difference was found in PPPS between the $CO_2$ and RA groups at 1, 3, and 6 hours but no difference was found at 6, 12, and 24 hours. This study had a smaller patient population than our study, and also midazolam was used in all the colonoscopy procedures for sedation. The 6- and 24-hour results were similar to those in our study, but the 1-hour results were different (7). In another randomized controlled study with a similar sample size, no difference was found in PPPS between the $CO_2$ and RA groups at 1, 3, 6, and 24 hours, similar to our study (5). Moreover, $CO_2$ was found to be favorable in decreasing PPPS. Pain was assessed using the VAS scale with mean scores, not dichotomy, and the assessment was made immediately after the procedure and at discharge rather than studying outcomes 24 hours after the procedure (6). These previous studies do not reach a common conclusion about the effect of $CO_2$ insufflation on PPPS in colonoscopy. Different anesthetic medications, variable pain assessment methods, study population, statistical methods, and patient-dependent measurements of pain may explain this heterogeneity. We investigated the pain dichotomously according to the VAS score, and we did not find a significant favorable effect of $CO_2$ insufflation on PPPS.

There were 40 patients with IBD in our study population. We did not find any difference in PPPS between the $CO_2$and RA groups in these patients either. In a previous study conducted with 64 patients, PPPS was lower in the $CO_2$ group than in the RA group at 1 and 3 hours but no difference was found at 6, 12, and 24 hours. In this study, midazolam was used for sedation and we used propofol with or without midazolam for the same. Anesthetic medications and population size may explain the inconsistency in results between the 2 studies.

We found that lower BMI at 30 minutes and longer colonoscopy time at 6 hours were associated with increased PPPS. The volume of the insufflated gas increased with longer time; therefore, PPPS increased with longer colonoscopy time periods. In previous studies, similar with our results, lower BMI was found to be related to decreased pain sensation (11, 12). However, longer colonoscopy time was found to be related to greater PPPS in another study (13).

There were several limitations to this study. Midazolam has an analgesic effect, and its use for sedation could affect pain perception post colonoscopy in some patients. We also did not record the large polyp excisions and organic mucosal diseases, such as ulcer, lipoma, and angiodysplasia, or evaluate their relationship with PPPS. These perhaps could play a role in PPPS and could count as limitations.

In conclusion, we found no favorable effect of $CO_2$ insufflation on PPPS in colonoscopy, including in patients with IBD.

***Ethics Committee Approval:*** The study was approved by the Marmara University local ethics committee (Approval Date: 08 May 2015, Approval Number: 09.2015.092).

***Informed Consent:*** Written informed consent was obtained from the patients who participated in this study.

***Peer-review:*** Externally peer-reviewed.

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Analysis and/or Interpretation – E.A., H.T.K.; Literature Search – F.G., H.T.K.; Writing – F.G., H.T.K., S.C.; Critical Reviews – F.G., H.T.K., S.C., E.A., F.E., Y.Y., Y.O.A.

***Conflict of Interest:*** The authors have no conflict of interest to declare.

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