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# Carbon Dioxide Role in GI Endoscopy

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**ABSTRACT**

**Background:** Sufficient distension of the GI lumen is needed for safe advancement of endoscopes and for careful visualization of the mucosa. Carbon dioxide ($CO_2$) has been proposed as an alternative to room air for insufflation.

**Aim of the Study:** To assess the merits and demerits of the use $CO_2$ insufflation for endoscopy in terms of safety and efficacy.

**Methods:** Electronic and manual searches were combined to search RCTs (Randomized controlled trials). After methodological quality assessment and data extraction, the efficacy and safety of $CO_2$ insufflation were systematically assessed**.**

**Results:** Ten RCTs met the eligibility criteria and included in the present study; six of which on colonoscopy, two on endoscopic retrograde cholangiopancreatography (ERCP) and two on double-balloon enteroscopy (DBE). Postprocedural pain was assessed. Overall, pain was lower in the $CO_2$ insufflation group compared with the air group. Two RCTs found decreased flatus in the $CO_2$ group compared with the air group, and 3 RCTs showed there was decreased bowel distention on abdominal radiography in the $CO_2$ group compared with the air group. Moreover, $CO_2$ insufflation revealed no consistent advantages in the RCTs of DBE, yet it was still indicated safe as air insufflation in stomach/ oesophagus endoscopic submucosal dissection. $PCO_2$ level showed no significant variation during these procedures.

**Conclusion:** $CO_2$ insufflation is proven to be associated with decreased postprocedural pain, flatus, and bowel distention. $CO_2$ insufflation also appears to be safe in patients without severe underlying pulmonary disease.

**Keywords:** insufflation, Colonoscopy, Carbon dioxide, Transcutaneous partial $CO_2$ pressure, GI Endoscopy.

## INTRODUCTION

In the last decade, endoscopy has become an essential diagnostic and therapeutic instrument in daily clinical practice. As a consequence, the number of endoscopic examinations has increased continuously, in particular, as a result of constant efforts to improve patient's acceptance and compliance to participate in bowel cancer screening programs. However, some patients still have a fear of undergoing colonoscopy, as they associate it with considerable pain and discomfort [(1)].

The introduction of moderate or deep sedation has certainly been an essential step to increase its attractiveness and to reduce the anxiety and concerns of the patients [(2)].Recent evidence demonstrates that sedation can be safely administered in colonoscopy without increasing the risk of respiratory or abdominal complications [(3)].

Another technique that has emerged in the last few years is the use of carbon dioxide ($CO_2$) as an alternative insufflation gas [(4)]. Carbon dioxide ($CO_2$) is the most commonly used gas for creating a pneumoperitoneum during laparoscopic surgery due to its incombustibility, high diffusibility, and rapid rate of absorption and excretion. Insufflation with carbon dioxide ($CO_2$) instead of air has been shown to reduce pain and discomfort because $CO_2$ is rapidly absorbed from the intestinal lining [(5)].

For the past three decades, a series of investigations have examined the safety and efficacy of $CO_2$ insufflation during various GI endoscopic modalities. Based on previously published randomised and non-randomised trials, the most recent systematic review by Dellon *et al*. revealed that $CO_2$ insufflation is associated with decreased postprocedural pain, flatus and bowel distension, and appears to be safe in patients without severe underlying pulmonary disease [(6)].

Nevertheless, the use of air insufflation to distend the lumen has been suspected to be a cause of the



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nonspecific discomfort during and after an endoscopic procedure.

Concern has been expressed on the safety of $CO_2$ insufflation based on the possibility that the rapid absorption of $CO_2$ from the colon may temporarily increase the $CO_2$ concentration in blood. Several groups have reported the absence of adverse respiratory complications with the use of $CO_2$ insufflation in colonoscopy studies [7, 8]. In a matter of fact, only one research group has tried to speculate on the change in $CO_2$ levels during colonoscopy with $CO_2$ insufflation, ultimately reporting that they found no pathogenic increase in end-tidal $CO_2$ levels [7].

## MATERIALS AND METHODS

### Data Sources

We carried out a retrospective study for publications addressing $CO_2$ insufflation from January 1995 to November 2017 in the medical literature. Databases searched included Book Citation Index–Science (since 2005), Cumulative Index to Nursing and Allied Health, Conference Proceedings Citation Index–Science (since 1990), Embase, Google Scholar, PubMed/MEDLINE, Scopus, The Cochrane Library, and Web of Science.

Keywords, phrases, and MeSH terms searched included "carbon dioxide," "endoscopy" ," colonoscopy. A PubMed/MEDLINE search example is ("$CO_2$"[MeSH]) OR "GI Endoscopy" OR "Colonoscopy" OR "ERCP") and ("sophagogastroduodenoscopy"[MeSH])). Authors independently reviewed titles and abstracts and then downloaded relevant studies. References were reviewed for additional studies.

### Study Selection and Criteria

**Search results were screened by scanning abstracts for the following**

***Inclusion Criteria***

1- Articles in English and Arabic languages
2- Randomized controlled trials (RCTs that compared $CO_2$ insufflation with air insufflation in adult patients undergoing GI endoscopy, including EGD, flexible sigmoidoscopy, colonoscopy, ERCP and DBE
***3-*** Reports of intraoperative endoscopy

***Exclusion Criteria:***

1- Articles concerning laparoscopic surgery, other non-GI endoscopic surgery, pneumoperitoneum, bronchoscopy, thorascopy, hysteroscopy, cystoscopy
2- Articles addressing addressed nonhuman and basic science subjects

### Data Extraction

Two reviewers independently reviewed studies, abstracted data, and resolved disagreements by consensus. Studies were evaluated for quality. A review protocol was followed throughout.

### *Data analysis*

Provided the extensive range of all included studies, a systematic review was conducted based on endoscopy type. The primary outcomes (mean VAS score of pain, percentage of patients without pain, $PCO_2$ level, flatus, bowel gas and complications) were reviewed to assess the efficacy and safety of $CO_2$ insufflation.

Given as well the wide range and heterogeneity of studies, meta-analytic techniques could not be applied to the data in a valid fashion [9]. For example, in the identified publications, there were 4 different endoscopic modalities, different patient inclusion and exclusion criteria, different primary and secondary end points, and different methodologies for determining these end points. Therefore, descriptive statistics were used to summarize findings. The methodology for this systematic review conformed to accepted guidelines [9].

## RESULTS

Searches identified 541 publications in addition to another 13 publications that were found through manual research. After removal of duplicates, abstracts and titles 303 publications were assessed as identified from title and abstract, and 201 papers were excluded. 12 papers full text could not be retrieved and another 43 papers with the same cohort. There were also 37 papers excluded because they did not assess the safety and efficacy of $CO_2$ spot on or didn't include Placebo" Air". We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in reporting the results **[10]** Figure 1.

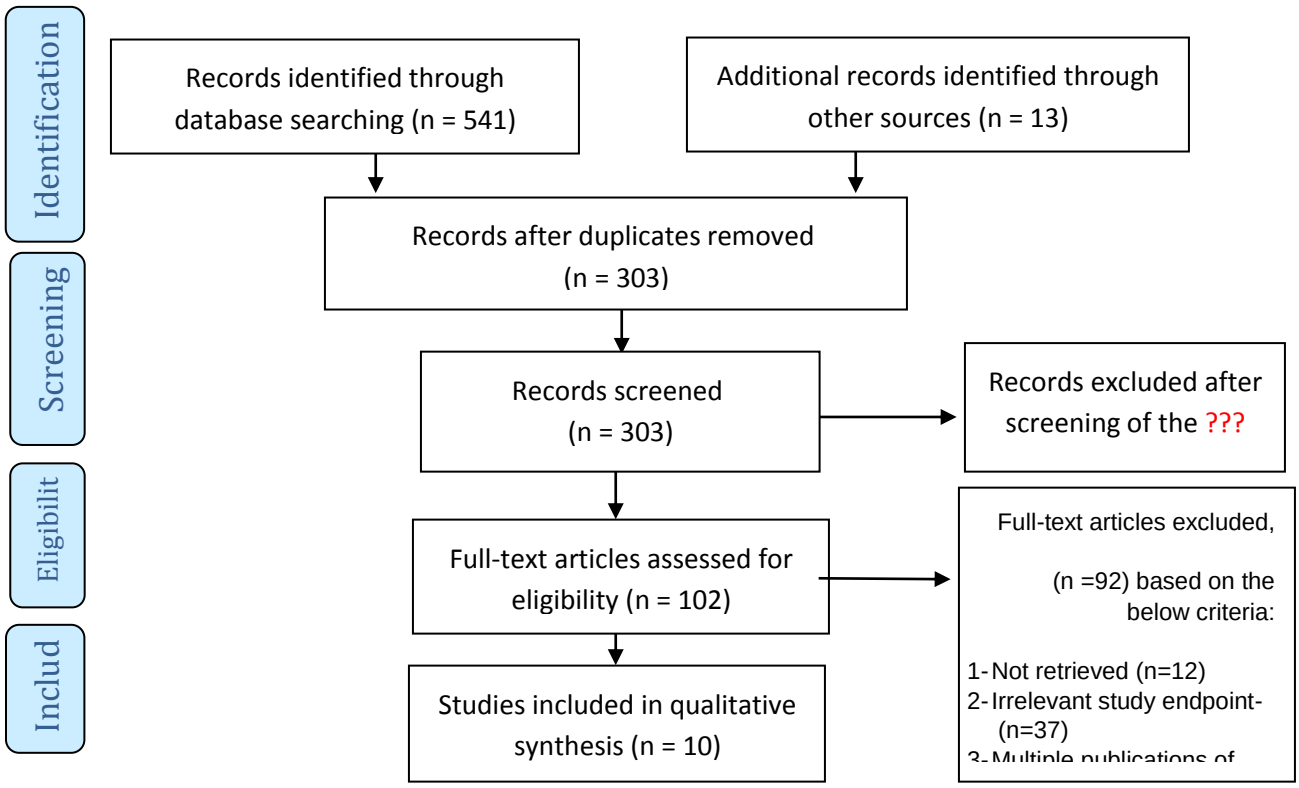


**Figure 1:** PRISMA flow diagram showing the selection criteria of the assessed studies[10].

**TABLE 1.** baseline characteristics of the included RCTs

| Procedure | Authors | Year of publication | Country | Sample size ($CO_2$/air) | Placebo Type | Blinding | No of centers | $CO_2$ delivery system |
|---|---|---|---|---|---|---|---|---|
| **1. Colonoscopy** | ***Sumanac et al.*** [11] | 2002 | Canada | 29/51 | Air | Double | 1 | Olympus ECR |
| | ***Bretthauer et al.*** [7] | 2002 | Norway | 121/119 | Air | Double | 1 | Olympus ECR |
| | ***Bretthauer et al.*** [11] | 2003 | Norway | 126/123 | Air | Double | 1 | Olympus ECR |
| | ***Church and Delaney*** [8] | 2003 | USA | 23/124 | Air | Single | 1 | cylinder to specialized water bottle |
| | ***Bretthauer et al.*** [5] | 2005 | Norway | 52/51 | Air | Double | 1 | Olympus ECR |
| | ***Yamano et al.*** [12] | 2010 | Japan | 66/54 | Air | Double | 1 | Olympus ECR-TOSCA 500 system |
| **2. ERCP** | ***Bretthauer et al.*** [13] | 2007 | Norway | 39/52 | Air | Double | 2 | Olympus ECR-TCM 30 , Radiometer inc. |
| | ***Dellon et al.*** [14] | 2010 | Japan | 36/38 | Air | Double | 2 | Olympus ECR-TOSCA 500 system |
| **3. DBE** | ***Domagk et al.*** [15] | 2007 | Norway | 48/52 | Air | Double | 3 | E-Z-EM Inc CO2-EFFICIENT |
| | ***Hirai et al.*** [16] | 2011 | Japan | 20/20 | Air | Double | 4 | Gas regular, Crown,Blood gas study |

## STUDY OUTCOME

### EFFECT OF $CO_2$ INSUFFLATION on

### 1. Abdominal pain (procedural and postprocedural)

All showed decreased pain in the $CO_2$ insufflation group in comparison with the air insufflation group. Pain was assessed in a variety of ways, including visual analog and 5-point and 10-point Likert scales, and at a variety of time points, including before the procedure, during the procedure, and 10 minutes, 1 hour, 6 hours, and 24 hours after the procedure, which made summary statistics impossible.

For both the 1-hour and 6-hour postprocedure times, the $CO_2$ group had a higher proportion of pain-free patients (63%-93% at 1 hour, 64%-91% at 6 hours) compared with the air group (17%-64% at 1 hour, 28%-69% at 6 hours). At the 24-hour time point, the proportions were more comparable (64%-95% in the $CO_2$ group, 38%-82% in the air group). Results were consistent across the colonoscopy, flexible sigmoidoscopy, ERCP, and DBE modalities

**Bowel-gas distention**

Two studies of colonoscopy used a 5-point Likert scale to characterize the amount of residual gas in the small and large intestine at 1 hour after the procedure[7,9]. These studies found significant less gas in both sites in the $CO_2$ group compared with the air group. The other study of ERCP used a 4-point grading scale to assess bowel distention 5 minutes after the procedure.4 In the $CO_2$ group, 29% had a normal appearance and 13% had severe distention; in the air group, 7% had a normal appearance and 29% had severe distention [11].

### 2. Flatus

Two studies of colonoscopy (Table 2) assessed the quantity of flatus passed after the procedure, at 1, 6, and 24 hours when using a 5-point scale (none, a little, moderate, a lot, extreme) [7,9]. In the first study, there was less flatus reported in the $CO_2$ group at all time points[7]. For example, 1 hour after the procedure, 92% of the $CO_2$ group reported passing no gas compared with 46% of the air group. At 6 hours, these proportions were 83% and 4%, respectively, and, at 24 hours, they were 60% and 12%. In the second study, less flatus was reported in the $CO_2$ group at the 1-hour and 6-hour time points but not at the 24-hour assessment[9].

### 3. Other outcomes

The use of $CO_2$ during colonoscopy also allowed for successful performance of barium enema in the case of incomplete colonoscopy[2] and $CO_2$ insufflation for CT colonoscopy is also tolerated after incomplete conventional colonoscopy[29]. During DBE, deeper insertion depths14 and higher procedure completion rates15 were noted with $CO_2$ insufflation compared with air.

**Table (2):** show the manifestation

| Procedure | Authors | Year of publication | Sample size | | Pain | Bowel Gas | Flatus | % of patients without pain | | | | | | Complications |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 1 hour | | 6 hours | | 24 hours | | |
| | | | $CO_2$ | Air | | | | $CO_2$ | Air | $CO_2$ | Air | $CO_2$ | Air | |
| **1. Colonoscopy** | ***Sumanac et al.*** [11] | 2002 | 51 | 49 | D | D | D | 93 | 55 | 91 | 69 | 85 | 82 | No adverse respiratory complications reported |
| | ***Bretthauer et al.*** [7] | 2002 | 119 | 121 | D | NA | NA | 90 | 55 | 90 | 60 | 90 | 80 | No adverse respiratory complications reported |
| | ***Bretthauer et al.*** [11] | 2003 | 126 | 123 | NA | NA | NA | NA | NA | NA | NA | NA | NA | Same amount of gas insufflated in each group |
| | ***Church and Delaney*** [8] | 2003 | 124 | 123 | D | D | NA | NA | NA | NA | NA | NA | NA | No adverse respiratory complications reported |
| | ***Bretthauer et al.*** [5] | 2005 | 52 | 51 | D | NA | NA | 63 | 17 | 70 | 40 | 70 | 52 | ET $CO_2$ values were slight higher in $CO_2$ group |
| | ***Yamano et al.*** [12] | 2010 | 66 | 54 | D | NA | NA | 87 | 68 | 87 | 84 | 93 | 98 | A slight increase in both groups without clinical significance |
| **2. ERCP** | ***Bretthauer et al.*** [13] | 2007 | 58 | 58 | D | NA | D | 66 | 24 | 64 | 28 | 64 | 38 | No difference in transdermal $PCO_2$ levels between groups |
| | ***Dellon et al.*** [14] | 2010 | 36 | 38 | D | D | D | NA | NA | NA | NA | NA | NA | Slight higher in air group |
| **3. DBE** | ***Domagk et al.*** [15] | 2007 | 48 | 52 | D | NA | NA | NA | NA | NA | NA | NA | NA | No adverse respiratory complications reported |
| | ***Hirai et al.*** [16] | 2011 | 20 | 20 | D | D | NA | NA | NA | NA | NA | NA | NA | Post-DBE higher without significance |

## DISCUSSION

In the out study, we dedicated all efforts to investigate and evaluate the competitive advantage of $CO_2$ vs Air for insufflation in GI endoscopy and conclude on the overall safety and efficacy of the gas.

Generally speaking, room air, being the broadly used gas for GI luminal distension, possesses the advantages of universal availability and low cost. However, room air is poorly absorbed by the GI tract and is largely evacuated through belching or passage

of flatus [17]. Notwithstanding this practice, older studies indicated that 50% of patients reported pain after completion of colonoscopy, with 12% of patients describing the pain as severe, even at 24 hours after the procedure [18].

$CO_2$ insufflation has been extensively evaluated during colonoscopy. A recent meta-analysis performed on 21 randomized control trials, including a total of 3607 participants, compared $CO_2$ with air insufflation during colonoscopy [19]. $CO_2$ insufflation was associated with significantly less pain during the procedure (9 studies, odds ratio [OR] 0.5; 95% CI, 0.3-0.84), at 1 hour postprocedure (7 studies, OR 0.24; 95% CI, 0.07-0.85), at 6 hours postprocedure (9 studies, OR 0.25; 95% CI, 0.11-0.55), and at 24 hours postprocedure (8 studies, OR 0.42; 95% CI, 0.23-0.77) [19].

The overall results of the current systematic review are prominent considering the heterogeneity of the studies included and the inability to use formal meta-analytic techniques.

To start with, across all endoscopy types studied in a randomized trend to date (colonoscopy, ERCP and DBE) and despite the different methods of pain quantification, there was commonly less postprocedural pain for at least 6 hours in the $CO_2$ insufflation group compared with the air group. The data at the 24-hour time point were conflicting, with some studies that showed a persistent benefit in the $CO_2$ group and others that showed no difference among the groups by this time point. In addition, in the few studies that examined flatus or bowel distention, there was less flatus and less distention in the $CO_2$ group compared with the air group.

Moreover, the consistency across these findings could also be clarified, since a single group of investigators; Bretthauer *et al.* [5,7,11,13] originated or participated in 4 of the 10 RCTs included in our analysis. Although additional confirmation from other centers would be helpful, the fact that the results are consistent across trial designs and endoscopic modalities speaks to their validity.

For colonoscopy, the $CO_2$ group showed lower pain VAS scores from procedure end to 3 h post procedure compared with the air group. $CO_2$ insufflation increases the proportion of patient without pain at 1 and 6 h post procedure. However, these differences disappeared at 24 h post procedure[13].

Despite the fact that ERCP and DBE examinations are prolonged and complex, included RCTs regarding ERCP and DBE supported the superiority of $CO_2$. ERCP could not result in apparent reduction in pain intensity though. In this review, only two RCTs reported $CO_2$ insufflation in EGD and it just evaluated the safety without measuring pain relief[20].

Furthermore, another randomized controlled study [21] has compared room air and $CO_2$ as insufflation agents during flexible sigmoidoscopy and during combined upper and lower GI endoscopy. $CO_2$ use was associated with improved pain scores at 1 and 6 hours after completion of sigmoidoscopy.

Nevertheless, the advantages of $CO_2$ insufflation during ERCP, DBE, EGD and flexible sigmoidoscopy are still uncertain and more RCTs are needed to assess this issue and to answer concerns about the safety of $CO_2$ insufflation, mostly in patients with pulmonary disease. For those without underlying pulmonary disease, however, the current literature is clear: $CO_2$ insufflation for endoscopic procedures is safe. Because it is possible that patients with respiratory disorders, sleep apnea, or morbid obesity, or with known $CO_2$ retention may be at risk for ventilatory compromise with $CO_2$ insufflation, it would be prudent to continue to use room-air insufflation in these potentially at-risk populations until the question is further studied. An additional benefit of using $CO_2$ for insufflation is that this gas reduces the risk of colonic gas explosion during colonoscopies with electrocautery compared with air insufflation [22].

Last not least, it was not possible to review the cost-effectiveness in this review due to lack of related data. As far as our knowledge goes, the clear majority of endoscopy facilities around the world still use air insufflations for endoscopic procedures.

Since also the majority of endoscopists are not aware of the possibility that room air can be replaced by $CO_2$ for gut distension during endoscopy [22], another reason would be the lack of $CO_2$ insufflators adequately tailored for GI endoscopy. Moreover, Cost-effectiveness is another important factor for patients and medical agencies.

## CONCLUSION

Consistent RCT-based body of evidence shows that $CO_2$ insufflation is commonly associated with decreased postprocedural pain, flatus, and bowel distention. $CO_2$ insufflation also appears to be safe in patients without severe underlying pulmonary disease.

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