Safety of chronic obstructive pulmonary disease patients undergoing carbon dioxide insufflation in extended endoscopic procedures

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ABSTRACT

Introduction: Carbon dioxide (CO2) insufflation for endoscopies has been shown to be more comfortable and safe, but only in patients without underlying chronic obstructive pulmonary disease (COPD). The aim of this study was to show that using CO2 is safe in COPD patients. Methods: Patients were retrospectively identified who underwent extended endoscopic procedures during the time period of January 2012 to December 2017. Patients were included if they also had COPD. A matched control group without COPD was created during the same timeframe. All the patients were sedated with continuous monitoring of their CO2 levels by end-tidal CO2 (EtCO2). Results: One hundred and ten patients had COPD and underwent an extended endoscopic procedure. These patients had a higher severity of their comorbidities (American Society of Anesthesiologists class 3 or 4) (93.6% [95% confidence interval [CI], 87.4%–96.9%] vs. 60.3% [95% CI, 51.1%–69.0%]; P < 0.01) and an increase of co-existing obstructive sleep apnea (33.6% vs. 6.3%, P < 0.01). There was no difference in baseline EtCO2, but the peak EtCO2 and postprocedure EtCO2 were both significantly higher in the COPD group. The only postprocedural complication found was an inability to be extubated immediately following the procedure with subsequent need to hospitalize the patient, which occurred in three patients (2.8%; 95% CI, 0.9%–7.9%) in the COPD group and one (0.9%; 95% CI, 0.2%–4.9%) in the non-COPD group (P = 0.37). Conclusion: The present study, which was the only study looking at CO2 insufflation specifically in COPD patients, provides evidence that CO2 insufflation is safe in COPD despite a slight increase in EtCO2.

KEY WORDS: Anesthesia, carbon dioxide, chronic obstructive pulmonary disease, endoscopy, humans

INTRODUCTION

Carbon dioxide (CO2) insufflation is used laparoscopic surgery and only recently has been adopted in endoscopic procedures performed by gastroenterologists. There have been many studies showing that using CO2 in these procedures significantly reduces peri-procedural pain, but with concerns for CO2 retention. Many studies have shown CO2 insufflation is safe in healthy sedated patients, associated with only minimal rises in either transcutaneous CO2 or end-tidal CO2 (EtCO2) measurements. All these studies excluded patients with underlying pulmonary disease. We sought to show the...
safety of CO₂ insufflation in chronic obstructive pulmonary disease (COPD) patients.

METHODS

We conducted a retrospective cohort study at a single tertiary referral center, comparing the EtCO₂ and postprocedural outcomes for COPD versus non-COPD patients for all extended endoscopic procedures performed between January 2012 and December 2017. The term “extended endoscopic procedure” was defined as an upper or lower enteroscopy using either a single or double balloon technique. COPD was defined as nonreversible airflow obstruction on a pulmonary function test. The institutional review board approved the study protocol 18-002171.

In the time period listed, we identified all patients (≥18 years of age) diagnosed with COPD who underwent an extended endoscopic procedure with CO₂ insufflation. Patients were excluded from this group if they did not have a pulmonary function test within 1 year of the procedure. A control group was defined by a matched group of non-COPD patients who underwent an extended endoscopic procedure during the same timeframe.

All patients were monitored by either an anesthesiologist or certified registered nurse anesthetist. Patients received sedation by propofol, midazolam, fentanyl, or any combination. In order to obtain the duration of procedure, the insertion and withdrawal times were recorded. EtCO₂ measurements were used to estimate the CO₂ levels. Continuous monitoring was possible as most patients were intubated and when not intubated a capnograph was attached to a nasal cannula. The EtCO₂ readings were recorded every 5 min throughout the procedures. For this study, only EtCO₂ readings from the start, peak EtCO₂ achieved, and end of the procedure were used.

The primary endpoint for the present study was that the procedure was safe with no more complications, including hospitalizations, inability to be extubated, and mortality. Secondary endpoints were EtCO₂ levels going to be higher throughout the study.

Statistical analyses were performed using JMP version 14.0.0 (SAS Institute Inc., Cary, North Carolina, United States). Continuous data were analyzed using a nonparametric Wilcoxon rank sum test. Pearson’s Chi-square or Fisher’s exact test, depending on the size of analyzed variables, was used for categorical data. Complication rates were analyzed by exact binomial 95% confidence intervals. P < 0.05 was considered statistically significant.

RESULTS

A total of 220 patients who underwent an extended endoscopic procedure were selected for this study with 110 of those patients having COPD. The baseline characteristics of both groups are displayed in Table 1. Both groups had similar age, sex, and race breakdowns. The COPD group had significantly more comorbidities (American Society of Anesthesiologists [ASA] Class 3 and 4) (93.6% [95% confidence interval [CI], 87.4%–96.9%] vs. 60.3% [95% CI, 51.1%–69.0%]; P < 0.01), along with more current smokers, more patients with co-existing obstructive sleep apnea, and supplemental oxygen use. In the COPD group, the mean FEV₁ was 59.45% ±15.93%. In the COPD group, 108 patients (98.18%) were on a short-acting beta-agonist, 34 patients (30.91%) were on a long-acting muscarinic agent, 37 patients (33.62%) were on a long-acting beta-agonist, and 43 patients (39.09%) were on inhaled corticosteroid.

The specifics of the procedure including type of procedure, length of procedure, endotracheal intubation rate, type of sedating medications, and amount of sedating medications were all similar in both groups [Table 2]. From the continuously monitored EtCO₂, there was no significant difference between the groups at the start of the procedure. In the COPD group, both the peak EtCO₂ (50 ± 12.9 vs. 46.6 ± 7.4; P = 0.01) and postprocedural EtCO₂ (43.2 ± 13.2 vs. 37.1 ± 12.4; P < 0.01) were higher [Table 2]. In both groups, there was a slight increase in EtCO₂ from baseline, but for the non-COPD group, it was in the normal range [Figure 1].

In this cohort in which the majority were intubated, there was no difference in total complications (P = 0.37) between the COPD (2.8%; 95% CI; 0.9%–7.85%) and non-COPD (0.9%; 95% CI; 0.1%–4.97%) groups [Table 3]. The only complication that occurred in both groups was an inability to extubate the patient immediately following the procedure, resulting in a short hospital stay (maximum length of stay was 3 days). This complication occurred in three patients (2.8%; 95% CI, 0.9%–7.9%) in the COPD group and one (0.9%; 95% CI, 0.2%–4.9%) in the non-COPD group (P = 0.37). The anesthesiologist was
concerned for an inability to protect the airway with potentially increased secretions for all patients who were not extubated immediately following the procedure in both groups. There was no difference in complication rate by severity of COPD (two patients had severe and one had moderate; \( P = 0.47 \)), length of procedure (1 of 100 min, 1 of 110 min, 1 of 135 min, and 1 of 185 min; \( P = 0.65 \)), ASA class (1 in Class 2 and 3 in Class 3; \( P = 0.93 \)), OSA (0 in OSA patients; \( P = 0.32 \)), oxygen use (0 in patients who used oxygen; \( P = 0.48 \)), and smoking status (one former smoker and three never smokers; \( P = 0.17 \)).

**DISCUSSION**

This study is the first to demonstrate the safety of CO₂ insufflation in COPD patients for extended endoscopies. Our results show that it is safe for COPD patients, despite severity, to undergo these procedures while intubated. This study does show that the patient’s EtCO₂ will rise, but without an increase rate of complications.

Concerns over the safety of CO₂ insufflation in the COPD population have been expressed. Several studies looked at the COPD population in specifically gastric endoscopic submucosal dissection.™15,16 In both of these studies, the total procedure time was about 60 min, which is approximately half of the total procedure time of the current study. Second, moderate sedation was used without any patients being intubated. Third, the severity of COPD in these studies was very mild with a FEV₁ above 70%. The patients in those studies had a minimal risk to develop complications from the procedure based on their severity level. Our study included all severity levels of COPD along with having these patients undergo procedures at least twice as long.

The maximum EtCO₂ reached was 79 mmHg in the COPD group and 73 mmHg in the non-COPD group. The elevated EtCO₂ is likely due to the CO₂ insufflation with some respiratory depression, which other studies have shown.™17-20 These maximum levels were not maintained long because the patient was mechanically ventilated. In addition, the postprocedure EtCO₂ was in the normal range for both groups. With COPD patients, this study shows their EtCO₂ level can increase to a dangerous level, but with close EtCO₂ monitoring and anesthesia support there are minimal complications.

This study has some limitations. First, this was a single-center retrospective analysis. Second, this study did not look at one type of procedure but any extended endoscopic procedure, so we can only generalize about extended procedures. The procedures included in the study were all significantly longer than

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**Table 1: Baseline patient characteristics**

|                   | COPD group (\( n=110 \), \( n (%) \)) | Non-COPD group (\( n=110 \), \( n (%) \)) | \( P \) |
|-------------------|--------------------------------------|------------------------------------------|--------|
| Gender, female    | 68 (61.8)                            | 71 (64.6)                                | 0.28   |
| Age (year)        | 69.1±9.9                             | 57.8±10.1                                | 0.44   |
| BMI               | 30.07±9.27                           | 28.17±6.8                                | 0.0218 |
| Race              |                                      |                                          |        |
| Black             | 11 (10)                              | 11 (10)                                  | 0.3011 |
| Native Hawaiian   | 1 (0.9)                              | 0                                        |        |
| White             | 98 (89.1)                            | 97 (88.2)                                |        |
| Not disclosed     | 0                                    | 2 (1.8)                                  |        |
| ASA class         |                                      |                                          |        |
| Class 1           | 0                                    | 3 (2.7)                                  | <0.0001|
| Class 2           | 7 (6.4)                              | 42 (38.2)                                |        |
| Class 3           | 87 (79.1)                            | 60 (54.5)                                |        |
| Class 4           | 16 (14.5)                            | 5 (4.5)                                  |        |
| Smoking status    |                                      |                                          |        |
| Current           | 30 (27.3)                            | 12 (10.9)                                | <0.0001|
| Former            | 67 (60.9)                            | 36 (32.7)                                |        |
| Never             | 13 (11.8)                            | 62 (56.4)                                |        |
| OSA               | 37 (33.6)                            | 7 (6.3)                                  | <0.0001|
| Treated           | 21 (19.1)                            | 5 (83.3)                                 | 0.8847 |
| Supplemental oxygen | 22 (20)                           | 2 (1.8)                                  | <0.0001|

**Table 2: Parameters of enteroscopy in chronic obstructive pulmonary disease and nonchronic obstructive pulmonary disease groups**

|                   | COPD group (\( n=110 \)) | Non-COPD group (\( n=110 \)) | \( P \) |
|-------------------|---------------------------|-------------------------------|--------|
| Intubated for procedure | 106 (96.4)            | 109 (99.1)                    | 0.1747 |
| Mediations        |                           |                               |        |
| Propofol used     | 106 (96.4)                | 108 (98.2)                    | 0.4077 |
| Amount of propofol (mg) | 221±223                 | 232±198                       | 0.1891 |
| Fentanyl used     | 65 (59.1)                 | 69 (62.7)                     | 0.5805 |
| Amount of fentanyl (mcg) | 121±53                   | 117±60                        | 0.2585 |
| Midazolam used    | 0                         | 3 (2.7)                       | 0.0812 |
| Amount of midazolam (mg) | 0                      | 1.3±0.6                      | 1      |
| Length of procedure (min) | 143.5±58.6             | 140.2±55.4                    | 0.2340 |
| Initial EtCO₂ (mmHg) | 30.4±10.6               | 29.6±9.6                      | 0.5941 |
| Peak EtCO₂ (mmHg)  | 50.2±12.9                | 46.6±7.4                      | 0.0120 |
| Peak time into procedure (min) | 84.9±52.4             | 78.6±45.1                     | 0.0224 |
| Post EtCO₂ (mmHg)  | 43.2±13.2                | 37.1±12.4                     | 0.0004 |

**Table 3: Outcome data for both chronic obstructive pulmonary disease and nonchronic obstructive pulmonary disease groups**

|                   | COPD group (\( n=110 \), \( n (%) \)) | Non-COPD group (\( n=110 \), \( n (%) \)) | \( 95\% \ CI \) | \( 95\% \ CI \) | \( P \) |
|-------------------|--------------------------------------|------------------------------------------|-------------|-------------|--------|
| Total complications | 3 (2.8)                              | 1 (0.9)                                  | 0.9%-7.85% | 0.1%-4.97% | 0.3669 |
| Hospitalization   | 3 (2.8)                              | 1 (0.9)                                  |             |             | 0.3669 |
| Prolonged PACU stay | 0                                   | 0                                        |             |             | 0.3669 |
| Not extubated     | 3 (2.8)                              | 1 (0.9)                                  |             |             | 0.3669 |
| Death             | 0                                    | 0                                        |             |             |        |

COPD: Chronic obstructive pulmonary disease, 95% CI: 95% confidence interval, PACU: Postanesthesia care unit, CI: Confidence interval.
esophagastroduodenoscopies and colonoscopies, which the length of time under sedation increases the risk for COPD patients to retain CO₂. Third, the sedation medication or intubation was not standardized and at the discretion of the anesthesiologist. Furthermore, there was no accounting of actual minute ventilation at the time of measurements which would have varied by anesthesiologist. This variation could have occurred because of experience with COPD patients and recognizing that this group of patients needs to be ventilated more aggressively.

CONCLUSION

This study suggests that CO₂ insufflation is safe for patients with COPD undergoing extended endoscopies. In these COPD patients, the majority were intubated for the procedure for easier ventilation, but there remains a risk for a dangerous increase in CO₂, so EtCO₂ should be monitored closely.

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Conflicts of interest
There are no conflict of interest.

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