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ORIGINAL RESEARCH

Ventilation strategies and postoperative pain in laparoscopic cholecystectomy: pulmonary recruitment maneuver versus extended hyperventilation: a prospective randomized study

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Abstract

Objectives: Acidic milieu created by carbon dioxide is associated with post laparoscopic surgical pain. Gas washing techniques were used to reduce such effects. This trial compared pulmonary recruitment maneuver (PRM) versus extended hyperventilation technique (EHV) regarding postoperative pain profile in laparoscopic cholecystectomy patients.
Methods: In a prospective, randomized controlled study, 90 patients, underwent laparoscopic cholecystectomy were divided into two equal groups; (PRM group) and (EHV group). Collected data included heart rate (HR), mean arterial blood pressure (MAP), visual analog score (VAS), the incidence of shoulder and sub-diaphragmatic pain, postoperative nausea, and vomiting (PONV).
Results: The overall incidence of shoulder and sub-diaphragmatic pain, late VAS score (at 12, 24 hours) were lower in the EHV group, while hemodynamics, early VAS scores, rescue analgesic consumption, and PONV were comparable in both groups.
Conclusion: Gas washing techniques improved safety and efficacy in improving pain profile following laparoscopic surgery. EHV provides less pain and more patients comfort than PRM, especially at delayed times.

Keywords

Laparoscopic surgery; Pain; VAS score; Hyperventilation; Recruitment maneuver

1. Introduction

Laparoscopic techniques have in growing expansion in surgical practice. Despite the advantages of using laparoscopy, post-surgical pain remains disturbing [1]. The etiology of pain after laparoscopic surgery is multifactorial [2]. In addition to the traumatized surgical site, one suggested cause of pain after laparoscopy is the peritoneal insufflation with CO_2 and phrenic nerve irritation in the peritoneal cavity [3–5]. The acid milieu and systemic absorption created by the dissolution of CO_2 gas cause peritoneal irritation and phrenic nerve damage. Shoulder and sub-diaphragmatic pain occur in about 12% to 60% of patients. The peak of pain intensity appears during the first few postoperative hours and usually declines in 2 or 3 days [2].

To date, administration of non-steroidal anti-inflammatory drugs (NSAIDs), narcotics, intra-peritoneal saline irrigation, intra-peritoneal use of local anesthetics, abdominal wall facial plane bocks, and neuro-axial analgesia were used to reduce pain after laparoscopic procedures. However, using these pain relief methods after laparoscopic procedures was associated with heterogeneous results and frequent side effects. Therefore, the optimum method for pain control after laparoscopic surgery remains controversial, and the use of multimodal and non-pharmacological techniques is an attractive area of research [2, 6–9].

Sub-diaphragmatic gas pockets were linked to visceral and shoulder tip pain after laparoscopy [10]. A pulmonary recruitment maneuver (PRM) was applied to promote exsufflation of intra-peritoneal carbon dioxide (CO_2) after laparoscopic surgery and was associated with improved postoperative analgesia [11]. Extended hyperventilation will rapidly wash CO_2, avoiding its accumulation in the peritoneal tissues. A short period of hyperventilation at the end of the surgery was associated with lower postoperative pain and morphine consumption [12].

In this trial, we assessed the efficacy of pulmonary recruitment maneuver versus extended hyperventilation regarding incidence and intensity of postoperative pain and gastrointestinal irritation symptoms in patients who underwent laparoscopic cholecystectomy.

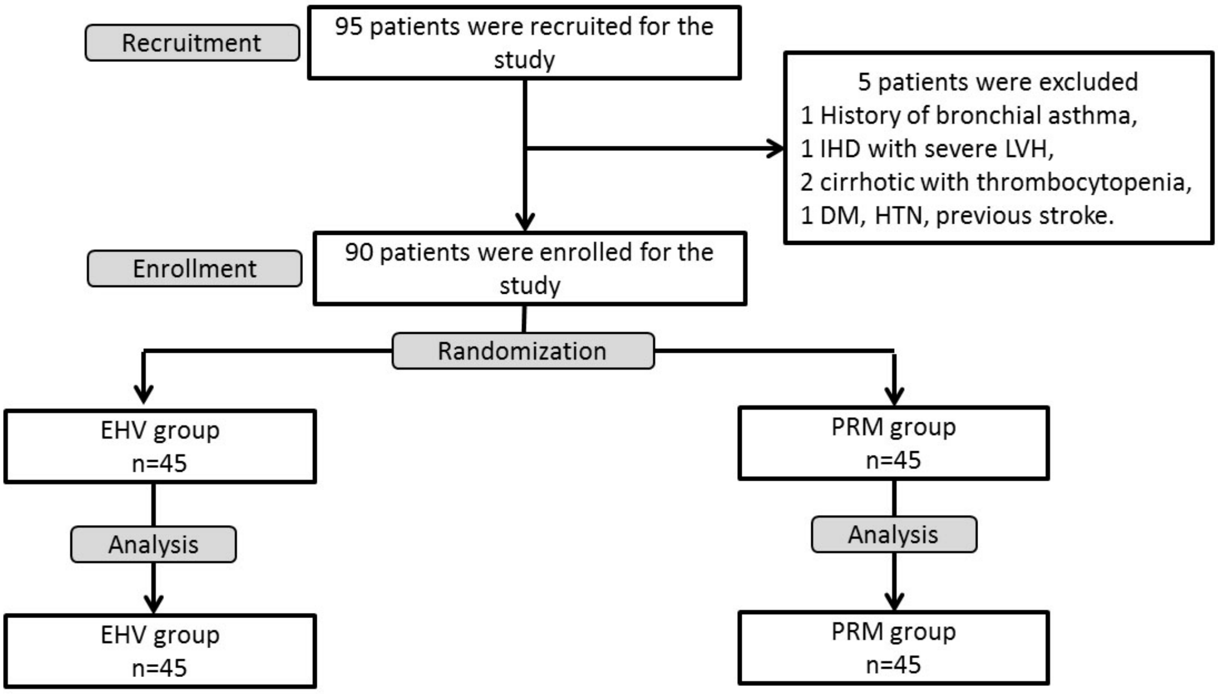

FIGURE 1. Consort flow diagram for the study.

2. Methods

The Institutional Research Board approved this study, Mansoura Faculty of Medicine (IRB # R.20.08.970.R1.R2.R3, 20 September 2020), and informed consent was obtained from all subjects participating in the trial. Before patient enrolment, the trial was registered in the Pan African clinical trial registry (PACTR-202009470667596, date of registration: 30 September 2020). Ninety patients were enrolled in this study which adheres to the applicable CONSORT guidelines (Fig. 1). Included patients were adults of both sex ASA I or II, age 18–65, scheduled for laparoscopic cholecystectomy in Mansoura Gastrointestinal surgery center. Exclusion criteria were patient refusal, pulmonary disease as COPD, asthma, lung bullae, cyst, psychological problems, or complicated procedure. Random number generator with closed envelope technique randomized patients into two groups based on used technique: pulmonary recruitment group (PRM group, n = 45), extended hyperventilation group (EHV group, n = 45).

All patients were subjected to routine preoperative assessment for anesthesia fitness. Upon arrival to the operating room and after connection to basic monitors (ECG, NIBP, SpO_2), anesthesia was induced using propofol 1–2 mg/kg, fentanyl 1 μ/kg, atracurium 0.5 mg/kg. A proper-sized endotracheal tube was inserted and fixed in place after confirmation of correct positioning by chest auscultation. Patients were ventilated using (GE Datex Ohmeda Aisys ventilator, USA) using the volume-controlled mode, with initial setting tidal volume (TV) 6 mL/kg of ideal body weight, respiratory rate (RR) of 14 per minute, positive end-expiratory pressure (PEEP) 5 cm H_2O, and FiO_2 0.4. Anesthesia was maintained using isoflurane 1.2% in a 40% oxygen air-gas mixture, and a top-up dose of atracurium was given on clinical demand. In the EHV group, Subsequent ventilatory management targeted an $EtCO_2$ of 30 $\pm$ 2 mmHg. Targeted $EtCO_2$ was achieved by increasing RR two breaths per minute to a maximum of 18 breaths per minute, and then TV can be increased by 1 mL/kg of ideal body weight (with maximum level 10 mL/kg) every 2 minutes till the target $EtCO_2$ obtained. So, the patients were kept hyperventilated during the whole procedure in the EHV group, while in the PRM group, end-tidal carbon dioxide ($EtCO_2$) is kept around (35 $\pm$ 2 mmHg) with the initial setting of ventilation. After completion of the surgery, patients were kept in the supine position; the surgeon did gentle pressure to exsufflate the abdomen in all patients of both groups. Later, in the PRM group: PRM was done with vital capacity (35 cm H_2O) for 10 seconds, repeated six times within 2 minutes. In both groups, trocars were removed, and it is a site infiltrated by 10 mL lidocaine 2% to relieve pain from this site at the end of surgery. Awake extubation was performed after giving neostigmine 0.05 mg/kg + atropine 0.02 mg/kg and fulfillment of extubation criteria. Postoperative paracetamol 1 g/6 H was administered intravenously on a regular basis. Rescue analgesia used (IV pethidine 0.5 mg/kg) when VAS $>$ 4. Intraoperative hemodynamic and ventilation data were documented every 15 minutes (HR, MAP, SpO_2, and $EtCO_2$) by the researcher anesthesiologist. Postoperative pain (shoulder and sub-diaphragmatic pain) was recorded 1, 6, 12, 24 hours postoperatively. VAS score was recorded immediate postoperative and at 1, 2, 4, 6, 12, 24 hours after recovery. Time to first analgesic request and numbers of rescue analgesia requirements in the first postoperative day was documented. Also, gastrointestinal irritation symptoms (nausea, vomiting) were recorded at consecutive times. All postoperative data were recorded by a trained nurse, who was blinded to intervention techniques.

2.1 Sample size statistical analysis and data collection

The incidence of shoulder pain after laparoscopic cholecystectomy reached 66% of cases in previous studies [12, 13]. The sample size was calculated using G*Power for Windows (ver. 3.0.10). Assuming a 30% reduction of the incidence of shoulder pain after applying the CO_2 washing technique, a total sample size of 77 patients for both groups was found enough to achieve a study power of 90% with an alpha error of 0.05. We added 13 cases to reach a total sample size of 90 patients for drop-out cases. Perioperative data will be tabulated and analyzed using IBM SPSS software version 22. Continuous data will be presented as mean SD or median IQR according to the normality of distribution. Nominal and categorical data will be presented as numbers and percentages. Independent sample T-test, Mann-Whitney test, or chi-square test was utilized to detect statistical differences between the studied groups.

3. Results

In this prospective study, 95 patients were recruited for the study, 5 cases were excluded, while 90 patients were equally distributed between groups and completed the study protocol, Fig. 1. As shown in Table 1, no statistically significant differences were detected between the two study groups regarding patient demographics, basal hemodynamic measurements, or duration of surgery.

TABLE 1. Perioperative characteristics in the two studied groups.

	EHV group	PRM group	P
	n = 45	n = 45	
Age (years)	46 ± 13	43 ± 12	0.26
Weight (Kg)	87 ± 9	91 ± 13	0.1
Height (cm)	165 ± 6	164 ± 6	0.24
Basal HR (bpm)	81 ± 15	84 ± 14	0.25
Basal MAP (mmHg)	93 ± 7	94 ± 8	0.88
Duration of surgery (minutes)	48 ± 13	46 ± 15	0.65

bpm, beat per minute; HR, heart rate; MAP, mean arterial blood pressure.
Data are presented as mean ± SD. P-value is considered significant if less than 0.05.

Similarly, intraoperative hemodynamics (heart rate and mean arterial pressure) did not show any statistical significance between the study groups. The timeline measurements of the hemodynamic data are illustrated in Fig. 2. Intraoperative $EtCO_2$ was achieved according to the targeted level of each group.

Fig. 3 shows a box plot comparison of the VAS in the study groups at 1, 2, 4, 6, 12, 24 hours after surgery completion. VAS scores were comparable in both study groups at 1, 2, 4, 6 hours after surgery (P 0.37, 0.18, 0.39, 0.36 respectively); however, at 12 hours and 24 hours, VAS was statistically lower in the EHV group than in the PRM group (P 0.049, 0.02, respectively). The overall incidence of postoperative shoulder pain is presented in Fig. 4, showing a statistically significant drop in both and EHV groups compared to the PRM group.

Time to first analgesic request and the number of rescue analgesic requirements, the incidence of PONV were comparable in both PRM group and EHV group, Table 2.

TABLE 2. Postoperative analgesia demand and PONV in the studied group. Data are presented as n (%), median (interquartile range).

	EHV group	PRM group	P
Time to analgesic request (hour)	24 (22)	24 (12)	0.09
No. of analgesic requirements	1 (1)	1 (1)	0.9
PONV n (%)	16 (36%)	10 (22%)	*0.12*

PONV, postoperative nausea and vomiting.
P-value is considered significant if less than 0.05.

No other perioperative complications related to the study procedure to be reported.

4. Discussion

This study investigated the effect of two CO_2 washing techniques on pain after laparoscopic cholecystectomy. Ninety patients were randomly allocated into two groups; EHV group, which adopted hyperventilation to wash out CO_2 preventing its accumulation in visceral tissues, thus cutting the cycle of peritoneal acidosis and irritation incriminated in post-laparoscopy pain [14, 15], While in the PRM group, patients exposed to 6 cycles of lung recruitment at the end of surgery to promote gas expulsion out of the abdomen [11, 16, 17]. Our results show that pain scores (VAS) were comparable in the two groups in the first 6 hours after surgery, yet, the analgesia profile was better in the EHV group than in the PRM group at 12, 24 hours after surgery regarding shoulder tip pain and overall pain scores. Rescue analgesia and gastrointestinal irritation symptoms were comparable in both groups.

Nowadays, laparoscopic techniques take the upper hand in surgical practice, not only in elective procedures but also in emergency situations. Acute cholecystitis, acute appendicitis, acute diverticulitis, perforated peptic ulcer, ectopic pregnancy, and ovarian torsion can be done with laparoscopy by the trained surgeon for better cosmesis, less pain, enhanced recovery, and less hospital stay [18]. Despite these advantages, post laparoscopic pain remains disturbing [1]. The optimum method for pain control after laparoscopic surgery remains controversial, and the use of multimodal and non-pharmacological techniques is an attractive area of research.

Pain after laparoscopic cholecystectomy has three main components; somatic pain, visceral pain, and shoulder pain. Visceral pain is related to peritoneal irritation by gas pockets in the abdomen after surgery, acidic media produced as a reaction to the carbonic acid formation from the insufflated CO_2 gas [19, 20]. Visceral pain and shoulder pain after laparoscopic surgery can pose significant discomfort and continue for few postoperative days [2, 21]. The leading mechanism of shoulder pain after laparoscopic surgery is

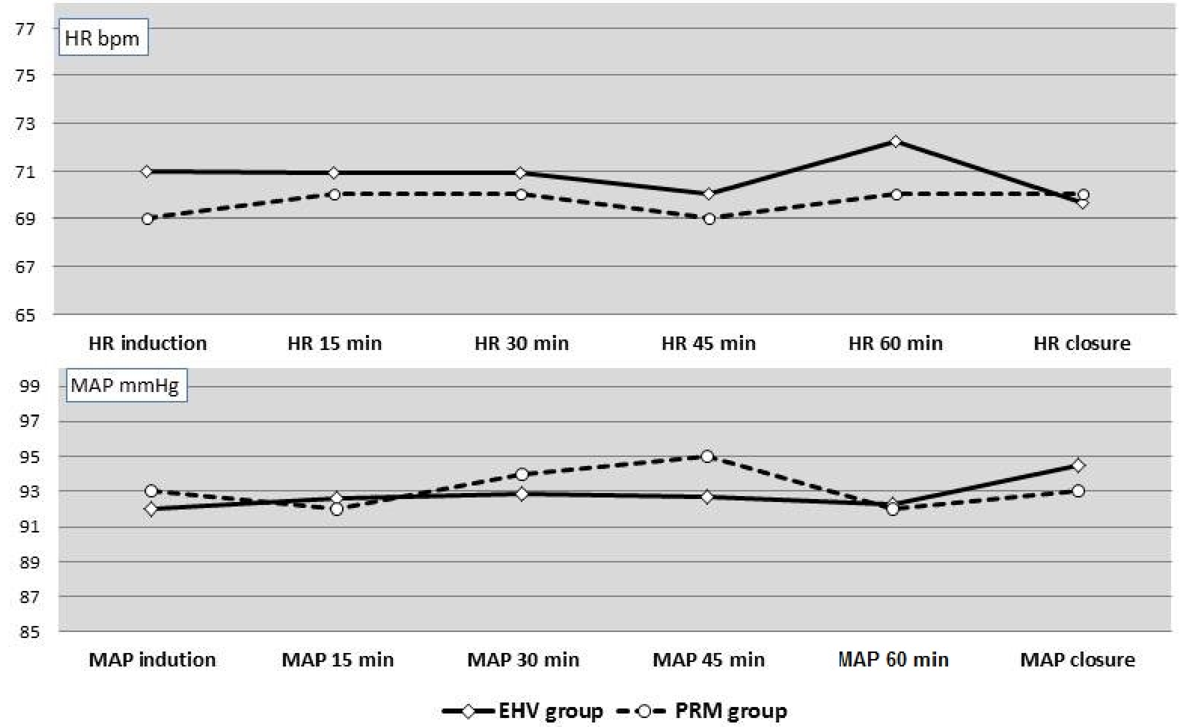

FIGURE 2. Intraoperative hemodynamics data (HR, MAP) of the included patients.

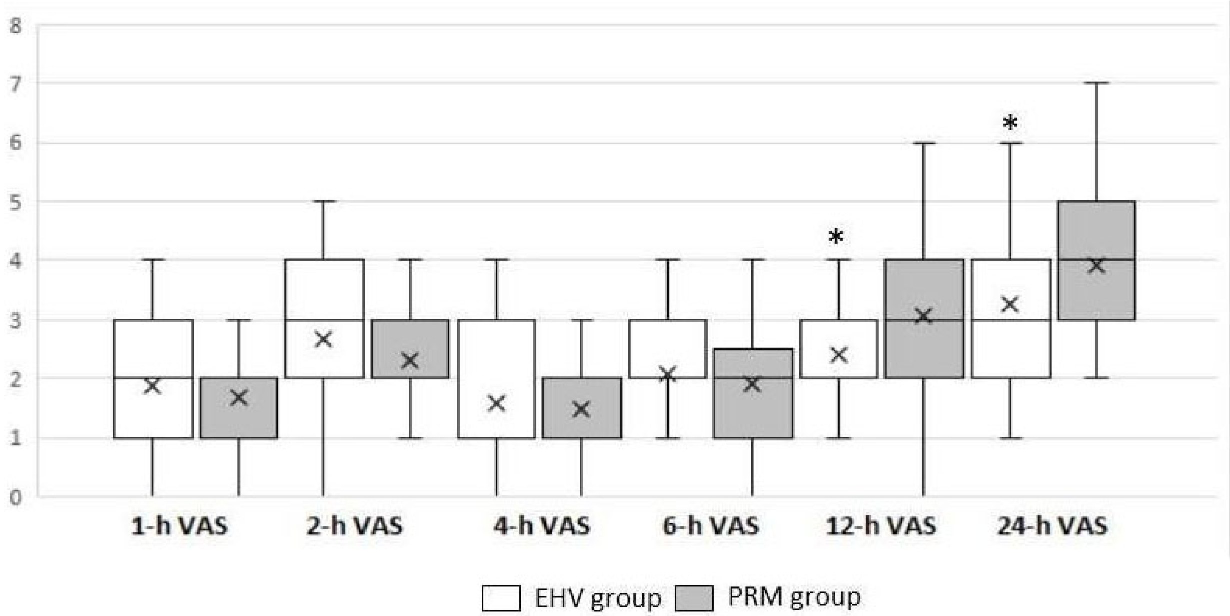

FIGURE 3. Box and Whiskers chart presentation for the postoperative VAS score of the included patients. The horizontal line within the box indicates the median value, the boxes represent the 25th to 75th percentile, and the whiskers outside the box indicate the entire VAS range. The x mark represents the mean value. *P*-value is significant if less than 0.05. * indicates statistical significant difference between the two study groups.

the irritation of the phrenic nerve and the diaphragm by intra-peritoneal insufflation of CO_2 [10, 16, 19, 22].

Strategies applied to reduce pain after laparoscopic cholecystectomy involved multimodal analgesia, regional blocks, and intra-peritoneal instillation of local anesthetics. Also, to avoid shoulder pain, low pressure, complete evacuation of the abdomen, and gasless surgeries were postulated to avoid peritoneal irritation by CO_2 [23–25].

According to previous studies, PRM proved efficacy in reducing post laparoscopy pain compared to non-interventional groups [11, 17, 26, 27]. Procedures applied for lung recruitment under anesthesia markedly varied regarding the applied pressure, its frequency, and the duration used for the procedure. In normal weight patients; it has been shown that, a single

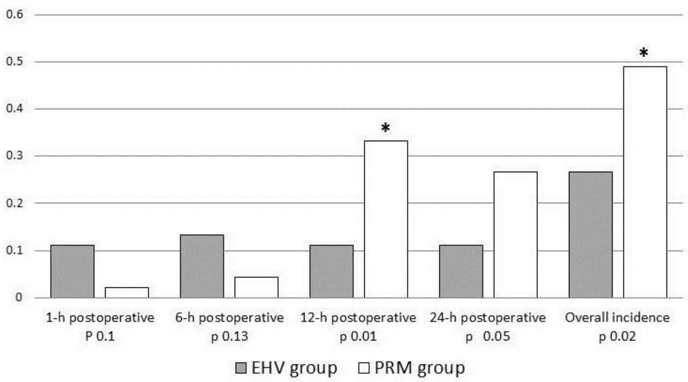

FIGURE 4. Postoperative shoulder and subdiaphragmatic pain of the included patients. Data are presented as percentages. *P*-value is significant if less than 0.05. * indicates statistical significant difference between the two study groups.

insufflation of 40 cm H_2O for 8 seconds was sufficient to open atelectatic areas after induction of anesthesia, while obese patients may need a more forceful technique. In laparoscopic gynecologic surgery [17, 26], simple PRM succeeded significantly in decreasing shoulder pain incidence. The authors postulated that the technique decreased peritoneal acidosis by facilitating the wash of CO_2 from the abdomen. Also, the effect of PRM on post-laparoscopic shoulder pain and upper abdominal pain was augmented by intra-peritoneal infusion of normal saline [28].

According to our results, VAS was significantly lower at 12, 24 hours postoperatively in the EHV group. Also, shoulder pain was significantly lower at 12 hours, and overall incidence during the first postoperative 24 hours in the EHV group. Better pain profile in the EHV group in these delayed times can be explained by the concept that EHV will avoid the peritoneal irritation initiated by CO_2 storage accumulation in the abdominal organs and subsequent inflammatory process. During pneumoperitoneum, abdominal organs will serve as a storage site for excess CO_2, which will be excreted or buffered, even after gas insufflation out of the pneumoperitoneum [10, 14]. Because the lungs are the main way for CO_2 elimination, lowering $EtCO_2$ by extended hyperventilation is assumed to decrease the tissue CO_2 concentration, thus, reducing acidic milieu, visceral pain, and improving overall pain profile subdiaphragmatic, and shoulder pain in postoperative duration. Chung *et al.* [10] found that lower intra-peritoneal CO_2 concentration was associated with lower pain scores after being measured through an intra-peritoneal catheter attached to a gas detector. This is also reinforced when carbonic anhydrase inhibitor, acetazolamide, reduced the referred pain after laparoscopic surgery due to its ability to inhibit H+ ion production from CO_2 and water [29].

In our study, time to first analgesic request and numbers of rescue analgesia requirements were comparable in both the PRM and EHV groups. Also, rescue analgesia profiles were comparable in the investigated period (first postoperative 24 hours); a better pain profile in the EHV group's delayed times will logically reduce rescue analgesic consumption in consecutive days and improve patients' recovery experience toward surgery and anesthesia practice. Gastrointestinal irritation symptoms were comparable in both groups; no unanticipated complications could be detected regarding both techniques.

Our study had some limitations; the anesthesiologist collecting intraoperative data was not blinded to intervention techniques. We did not have a detector for intra-peritoneal CO_2 concentration. The measurement of intra-peritoneal CO_2 concentration and inflammatory mediators would add to the strength of the study. The limited-time for postoperative monitoring, only for 24 hours, may have concealed some clinical differences between the studied techniques. Larger scale studies with measurement of peritoneal gas concentration, inflammatory mediators, and longer patient follow-up periods are recommended.

5. Conclusions

While PRM proved efficacy in controlling post laparoscopy pain as a gas washing technique in previous trials, EHV showed better pain reduction results in patients who underwent laparoscopic cholecystectomy without detectable complications. Further large-scale studies are encouraged to explore the exact mechanism of pain modulation by lung recruitment maneuvers, tissue levels, and splanchnic organ CO_2 levels would be of great value.

AUTHOR CONTRIBUTIONS

MAA: the author prepared the study design, participate in data collection, writing the manuscript and submission. AKA: the author participates in data collection, reviewing the manuscript, and did statistical analysis.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Institutional Research Board approved this study, Mansoura Faculty of Medicine (IRB # R.20.08.970.R1.R2.R3, 20 September 2020), and informed consent was obtained from all subjects participating in the trial. Before patient enrolment, the trial was registered in the Pan African clinical trial registry (PACTR-202009470667596, date of registration: 30 September 2020).

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

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