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Effect of intraperitoneal CO_2 concentration on postoperative pain after laparoscopic cholecystectomy

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Purpose: This study set out to identify the association between the intraperitoneal CO_2 concentrations and postoperative pain by dividing the participants into a control group and 2 experimental groups receiving irrigation (1 L and 2 L), and directly measuring their intraperitoneal CO_2 concentrations with a CO_2 gas detector.
Methods: A total of 101 patients, American Society of Anesthesiologists physical status classification I and II patients aged 18–65 years were enrolled in the study. Group 1 did not receive irrigation with normal saline, while groups 2 and 3 were administered irrigation with 1 L and 2 L of normal saline, respectively, after laparoscopic cholecystectomy. Intraperitoneal CO_2 concentrations were measured with a CO_2 gas detector through the port, and postoperative pain was assessed on a visual analogue scale at 6, 12, and 24 hours after surgery.
Results: The intraperitoneal CO_2 concentrations were 1,016.0 ± 960.3 ppm in group 1, 524.5 ± 383.2 ppm in group 2, and 362.2 ± 293.6 ppm in group 3, showing significantly lower concentrations in groups 2 and 3. Postoperative pain was significantly lower in group 3 at 6 hours after surgery, and in groups 2 and 3 at 12 hours after the surgery. However, there was no significant difference between the 3 groups in postoperative pain 24 hours after the surgery.
Conclusion: This study found a causal relationship between the amount of normal saline used for irrigation and the intraperitoneal CO_2 concentrations in that irrigation with normal saline reduces pain on the day of the surgery.
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Key Words: Intraperitoneal carbon dioxide, Saline waters, Postoperative period pain, Carbon dioxide gas detector

INTRODUCTION

Lately, the popularity of laparoscopic cholecystectomy has been on the rise, owing mainly to the facts that laparoscopic surgeries leave minimal surgical scars, only require short hospital stays, and promote early recovery [1,2]. However, visceral pain, port-site pain, and referred shoulder pain are occasionally reported in laparoscopic cholecystectomy patients [3]. Among multiple reports of attempts to reduce these types of pain, we chose to focus on the suggestion that intraperitoneal CO_2 concentrations are associated with postoperative pain, and that washing with normal saline to reduce the CO_2 concentrations significantly lowers the pain. Accordingly, this study was designed to measure intraperitoneal CO_2 concentration and to examine its association with postoperative pain [4].

METHODS

This study was approved by the Institutional Review Board of Soonchunhyang University Cheonan Hospital (approval number: 2016-01-006), and all participants provided their informed consent. American Society of Anesthesiologists physical status

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classification I and II patients aged 20–65 years who were scheduled to undergo a planned laparoscopic cholecystectomy were enrolled in a prospective, randomized, double-blind study. The patients who were found to have a liver, kidney, or chronic obstructive disease in the preoperative visit, who did not provide their consent, or whose laparoscopic surgery was converted to open cholecystectomy, or was expanded because of severe inflammation were excluded.

Based on previous studies, the beta and alpha levels were calculated as 0.1 and 0.05, respectively (2-sided), with a sample size of 29 participants in each group. Due to a 30% withdrawal rate, 114 participants (i.e., 38 in each group) were enrolled [5].

Three patients in group 1, 1 patient in group 2, and 2 patients in group 3 were excluded for not providing their consent. Furthermore, 3, 3, and 1 patient(s) in groups 1, 2, and 3, respectively, were additionally excluded for acute cholecystitis or open conversion, yielding a total of 101 patients distributed as follows: 32 in group 1, 34 in group 2, and 35 in group 3.

All of the patients were premedicated with glycopyrrolate 0.2 mg intramuscular 30 minutes before induction with anesthesia. The anesthesia was induced along with lidocaine 1 mg/kg, propofol 1.5 mg/kg, and rocuronium 0.6 mg/kg intravenous, and was maintained with desflurane (6%–7% vol/vol). The intraoperative and postoperative pains were controlled with fentanyl 100 μg intravenous administered in 2 doses of 50 μg each.

All the laparoscopic cholecystectomies (LCs) were performed by the same team of experienced professionals. A pneumoperitoneum was created by insufflating CO_2 gas through a 10-mm trocar in the umbilicus, and was maintained at 12 mmHg throughout the surgery. Prior to the surgery, all patients were moved into a reverse Trendelenburg position with a left tilt (10°), and the LC was conducted using the standard 4-port technique. After complete hemostasis, a drain insertion was selectively performed only in cases with intraoperative bile leakage. The patients were then randomly divided into 3 groups (0, 1 L, 2 L) to be irrigated with normal saline in the space between the right diaphragm and the liver. The saline was suctioned immediately. After clipping 15 cm of the tip of an 18F nasogastric tube, the tube was inserted through the 2nd 5-mm trocar into the upper right subcostal incision, with its tip positioned at the end of the trocar. After deflating the CO_2 gas, the residual CO_2 gas in the abdominal cavity was carefully evaluated, mostly by manual compression through the umbilical trocar. The nasogastric tube placed in the upper right trocar was connected to a gas detector (SKT 1050, Testauction, China) to measure the intraperitoneal CO_2 concentration.

Postoperative pain was assessed on a visual analogue scale (VAS) at 6, 12, and 24 hours after the operation (i.e., within a time frame in which postoperative pain is clearly present), as patients show varying responses to intraoperatively administered fentanyl, and biases may be caused by unclear patient expressions in the recovery room. During this period, a rescue dose of Tridol 50 mg intravenous was additionally administered at the patient's request.

To eliminate evaluation biases, the anesthesiologist and another physician assessed the pain, and the rescue dose was evaluated based on the total dose used over 24 hours.

The demographic data were analyzed with a chi-square test, an analysis of variance, and a Kruskal-Wallis test, and the differences in the VAS scores of the 3 groups were analyzed with a *post hoc* Tukey HSD (honesty significant difference) test. The clinical significance was set to $P < 0.05$. All statistical analyses were performed with the SSPS ver. 14.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The participants' (n = 101) demographic characteristics, pneumoperitoneum duration, and intraperitoneal CO_2 concentration were assessed (Table 1). In addition, the postoperative pain was assessed on the VAS at 6, 12, and 24 hours after the operation, and the total rescue dose of Tridol was recorded (Table 2, Fig. 1).

The postoperative intraperitoneal CO_2 concentrations were significantly lower in groups 2 and 3 than in group 1 (Table 2, Fig. 1). To assess postoperative pain, shoulder pain and visceral pain were also assessed 6, 12, and 24 hours after the operation. The VAS score 6 hours postoperation did not significantly differ between groups 1 and 2, but was significantly lower in group 3. The VAS score 12 hours postoperation was significantly lower in groups 2 and 3 than in group 1. On the other hand, the three groups did not show significant differences on the VAS 24 hours after the operation (Table 2, Fig. 1).

DISCUSSION

Owing to several advantages including minimal scarring, early recovery, and early return to daily living, patients have come to widely prefer laparoscopic surgeries [1,2]. The pop-

Table 1. Demographic characteristics and intraoperative variables

Characteristic	Group 1 (n = 32)	Group 2 (n = 34)	Group 3 (n = 35)
Age (yr)	38.7 ± 8.3	43.3 ± 11.8	41.5 ± 12.1
Sex, female:male	21:11	21:13	21:14
Weight (kg)	67.3 ± 13.3	67.0 ± 13.6	65.5 ± 9.9
Duration of pneumo peritoneum (min)	25.4 ± 11.0	28.7 ± 9.9	30.7 ± 10.5

Values are presented as mean ± standard deviation.
Group 1, no irrigation group; group 2, 1-L irrigation group; group 3, 2-L irrigation group.

Table 2. Pain scores with VAS, resque dose, and CO_2 concentration

Variable	Group 1	Group 2	Group 3	P-value[a]	*Post hoc*[b]
VAS 1 (6 hr)	5.9 ± 1.6	5.6 ± 1.4	4.4 ± 1.4	<0.001	G1 = G2 < G3
VAS 2 (12 hr)	4.4 ± 1.3	3.6 ± 1.2	3.4 ± 1.0	0.001	G1 < G2 = G3
VAS 3 (24 hr)	3.3 ± 1.1	2.6 ± 1.2	2.3 ± 1.2	0.001	G1 = G2 = G3
Tridol sum (resque dose)	150.0 ± 71.8	136.8 ± 77.1	161.42 ± 84.7	0.428	
Intra-abdominal CO_2 concentration (ppm)	1,016.0 ± 960.3	524.5 ± 383.2	362.2 ± 293.6	<0.001	G1 < G2 = G3

Values are presented as mean ± standard deviation.
Group 1, no irrigation group; group 2, 1-L irrigation group; group 3, 2-L irrigation group. VAS, tridol sum, and CO_2 concentration.
$P > 0.05$, not significant difference among the groups.
[a]By one way analysis of variance. [b]By adjusted by Turkey HSD (honestly significant difference).

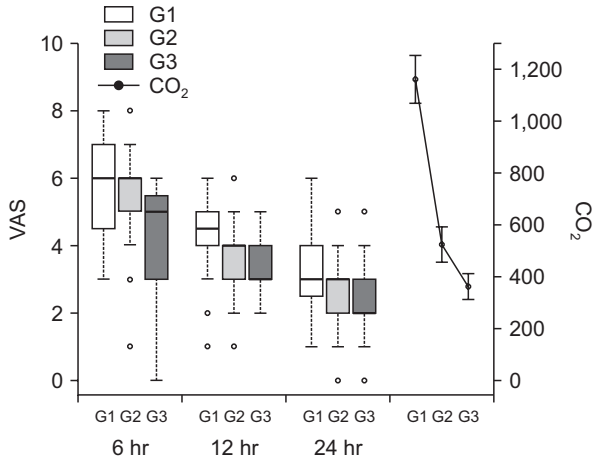

Fig. 1. VAS for postoperative pain at 6, 12, and 24 hours after laparoscpic cholecystectomy. And difference of intra-abdominal CO_2 concentration among 3 groups. G1, no irrigation group; G2, 1-L irrigation group; G3, 2-L irrigation group.

ularity of laparoscopic cholecystectomy among patients and surgeons has also increased for the same reasons. Nevertheless, the surgery has frequently been associated with postoperative pain, including referred pain in the shoulder and parietal pain at the trocar site. Several attempts and extensive research have been conducted to reduce these problems.

It has been reported that a reduction in the pressure of insufflated CO_2 gas leads to a lower intensity or incidence of postoperative pain and less demand for analgesics [6]. Low pressure has also been reported to be associated with low hemodynamic variation and to have benefits to patients with heart disease [7].

Postoperative shoulder pain occurs in about 30%–45% of laparoscopic patients [8,9] and irrigation with normal saline has been shown to reduce the incidence of postoperative shoulder tip pain at 8, 16, and 24 hours after the surgery by 35%, 15%, and 10%, respectively [5]. One study reported that the infiltration of local anesthetics in the postoperative trocar site was not effective in reducing parietal pain [10]. Meanwhile, another study reported that the preoperative administration of carbonic anhydrase inhibitors such as acetazolamide was effective in reducing postoperative pain, and suspected that postoperative pain is caused by the production of carbonic acid and acidification of the abdominal cavity from CO_2 insufflation [5].

Furthermore, some studies have suggested that residual intraperitoneal CO_2 may be the cause of postoperative pain, and have attempted to wash the intraperitoneal cavity with normal saline [11-13]. Normal saline irrigation is a simple, cheap, and effective way to reduce postoperative pain.

As described here, a number of previous studies have conjectured that normal saline irrigation reduces postoperative pain by diluting intraperitoneal CO_2 concentrations (the suspected cause of pain). However, none of them have actually measured the intraperitoneal CO_2 concentrations. Hence, we designed this study to examine whether intraperitoneal CO_2 concentrations decrease according to the amount of normal saline used for irrigation by directly measuring residual CO_2 concentrations in the intra-abdominal cavity with a CO_2 gas detector, and to examine whether a reduced CO_2 concentration is associated with lower postoperative pain. To this end, we measured the intraperitoneal CO_2 concentrations after laparoscopic cholecystectomy and assessed postoperative pain on the VAS 6, 12, and 24 hours after surgery to identify the association between residual intraperitoneal CO_2 concentrations and postoperative pain. Postoperative laparoscopic cholecystectomy pain has 2 major components including abdominal pain (right upper quadrant pain, trocar site pain) and shoulder pain [14]. Although we initially intended to assess shoulder pain (referred pain) only, we expanded the scope to the overall postoperative pain, including shoulder pain, right quadrant pain, and trocar site pain in consideration of the incidence of referred pain in previous studies and of previous reports suggesting that patients would have difficulty in distinguishing between postoperative referred pain and overall pain.

In a previous study, a volume of 30 mL/kg was effective in diluting the carbonic acid, while irrigation with a small amount of about 500 mL was not. Therefore, we set the irriga-

tion amount to 2 L and 1 L in the 2 experimental groups, respectively, and provided no irrigation to the control group [15].

Intraperitoneal CO_2 concentration tended to decline according to irrigation amount. While groups 2 and 3 differed statistically from group 1, there was no significant difference between groups 2 and 3. A rescue dose of Tridol 1 (50 mg) was administered to patients who complained of pain after surgery, and the total rescue dose over a 24-hour period did not differ significantly between the 3 groups.

Postoperative pain at 6 hours did not differ significantly between groups 1 and 2, but did differ significantly from that of group 3. This was in line with a previous report that suggested that irrigation with an amount of 30 mL/kg or greater contributed to lowering pain. Groups 2 and 3 showed no significant difference in their residual intraperitoneal CO_2 concentration, although the mean concentrations of the 2 groups showed numerical differences, at 524.33 and 362.17 respectively.

Groups 2 and 3 experienced significantly lower postoperative pain 12 hours after the surgery. This finding that the normal saline irrigation groups showed significant reductions in postoperative pain in the first 12 hours after surgery, a period during which postoperative pain is most often present, is meaningful. At 24 hours after the surgery, the level of pain in the three groups did not differ significantly, which is believed to owe to the fact that the VAS decreased for all 3 groups over time as the patients began to recover from the laparoscopic surgery.

This study had a few limitations. First, we did not check the rescue doses administered in the intervals between the first demand and 6, 12, and 24 hours after the surgery, and relied on the total rescue dose only. This may be problematic since, although the total dose did not differ significantly, the rescue doses used within the first 6 hours and the first 12 hours—i.e., the period during which patients experience the most severe pain—may have induced a bias in the VAS scores. In addition, due to the difficulty in distinguishing referred pain in the shoulder from incisional and parietal pain, we assessed the overall postoperative pain. This prevented a detailed detection of the changes in the referred pain. In future studies, time-specific rescue doses should be evaluated, and the pain assessments should be extended to 2 days after the surgery in order to consider long-lasting pain. Further, a detailed evaluation of the types of pain may allow for a more accurate examination of the associations between the parameters.

Despite these limitations, this study makes a valuable contribution in that it measured intraperitoneal CO_2 concentrations and verified that irrigation with normal saline reduces the intraperitoneal CO_2 concentrations, which is subsequently associated with a reduction in postoperative acute pain.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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