Impact of low-pressure pneumoperitoneum and local anesthetic combination on postoperative pain in patients undergoing laparoscopic cholecystectomy

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ABSTRACT

Objectives: Despite the advantages of laparoscopic cholecystectomy (LC), postoperative pain remains a major complaint for many patients. In this study, in patients undergoing LC, the application of LC via incisional bupivacaine and low inflation pressure, alone or combined, and a comparison of the effects on postoperative pain has been purposed.

Methods: Patients were randomly assigned into the following 4 groups: the standard pressure (SP) group (n = 30); patients with an intraabdominal insufflation pressure of 12 mmHg, where bupivacaine application was not performed at the trocar locations. The SP+local anesthetic (LA) (SP+LA) group (n = 30); patients with an intraabdominal insufflation pressure of 12 mmHg, where bupivacaine application was performed at the trocar locations. The low pressure (LP) group (n = 30); patients with an intraabdominal insufflation pressure of 8 mmHg, where bupivacaine application was not performed at the trocar locations. The (LP+LA) group (n = 30); patients with an intraabdominal insufflation pressure of 8 mmHg, where bupivacaine application was performed at the trocar locations. Postoperative pain was evaluated using the visual analogous scale (VAS).

Results: When the relationships between the VAS scores, gender, age, and American Society of Anesthesiologists classification were evaluated, no significant relationships between the groups were observed ($p > 0.05$). A significant relationship between the groups was detected with regards to the VAS scores, 1st analgesic application, 2nd analgesic application, and patients' satisfaction ($p < 0.05$).

Conclusions: The combination of low insufflation pressure with intrafacial preincisional local anesthetic infiltration in post-LC pain palliation is thought to be more effective and applicable.

Keywords: Laparoscopic cholecystectomy, local anesthetic, low pressure

Laparoscopic cholecystectomy (LC) has been the gold standard method of treatment since the 1990s for symptomatic gallbladder stones [1]. Studies in the literature comparing it with open surgery have revealed that LC leads to a decrease in postoperative pain, analgesic consumption, and hospital stay.

Despite the advantages of laparoscopic surgery, postoperative pain is a significant complaint factor for many patients. Pain reaches its peak value within several hours postoperatively and disappears within an average of 48-72 h. Postoperative pain may lead to tachycardia, an increase in the cardiac load, nausea, vomiting, and deceleration of the bowel passage. This situation is strongly related with a long hospital stay

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and morbidities, such as pulmonary complications, which is especially important in centers where this operation is executed on a daily basis [2].

In most cases, postoperative pain after LC is encountered on the abdominal wall at the incision site, with the systemic and local affect at abdominal region that pneumoperitoneum leads and at liver on the bed where gall bladder is located.

Based on carbon dioxide insufflation, an increase in intraabdominal pressure leads to a change of function in many organs in the body, which then also leads to postoperative pain. The degree of intraabdominal pressure is directly related to these changes. LC can be performed through pneumoperitoneum that was formed via low pressure, but the obtained operational area will be more limited than the area obtained via high pressure. There are studies in the literature indicating that, with low-pressure pneumoperitoneum, it is possible to reduce postoperative pain [3, 4].

Local anesthetic infiltration at the trocar site is effective postoperatively within the first 24-48 h of pain palliation and a decrease in pain occurs after 24 h. It has be seen that the application is simple, secure, and low-cost, but when its effectiveness is researched, there are many studies that indicate results with opposite opinions [5, 6].

The pain visual analogous scale (VAS) is a valid tool for measuring pain at one point in time. After LC, regarding pain palliation, studies regarding the use of various local anesthetics (tenoxicam [7], non-steroidal anti-inflammatory medications [8], tramadol [9], morphine [10], beta blockers [11], and fentanyl [12]) do exist in the literature, but they do not offer much hope.

Within this study, in patients undergoing LC, the application of LC via incisional bupivacaine and low inflation pressure, alone or combined, and a comparison of the effects on postoperative pain has been purposed.

METHODS

Before beginning this study, approval was granted by the Research Ethical Committee of Guven Hospital, Ankara, Turkey. Included in this randomized, placebo-controlled study were 120 patients above the age of 18, who gave written and oral approval, and were due to have elective LC. LC were performed for symptomatic gallbladder stones. Exclusion criteria for the study included the following: patients with defined psychiatric diseases stories, alcohol addiction, or pregnant women; patients who use psychotropic and opioid medications, defined chronic pain not related to gall bladder stones, use steroids, are sensitive to local anesthetics, or have had operations because of acute cholecystitis, due to the risk of bleeding or surgery-related risks after drainage. Patients were categorized according to the American Society of Anesthesiologists (ASA) classification I or II, and operated on between June 2016 and June 2017.

The patients were randomly assigned into 4 groups using the closed envelope method as follows: The standard pressure (SP) group (n = 30); patients with an intraabdominal insufflation pressure of 12 mmHg, where bupivacaine (Marcaine®) application was not performed at the trocar locations. The SP+local anesthetic (LA) (SP+LA) group (n = 30); patients with an intraabdominal insufflation pressure of 12 mmHg, where bupivacaine application was performed at the trocar locations. The low pressure (LP) group (n = 30); patients with an intraabdominal insufflation pressure of 8 mmHg, where bupivacaine application was not performed at the trocar locations. The (LP+LA) group (n = 30); patients with an intraabdominal insufflation pressure of 8 mmHg, where bupivacaine application was performed at the trocar locations. In a preoperative meeting with the patients, detailed information regarding the VAS was provided and the patients were instructed with regards to how to evaluate themselves postoperatively, as follows: 0 indicates no pain and 10 represents the highest level of pain. The postoperative pain levels were inquired about and collected by responsible nurses, who were not provided with any information regarding the intraoperative local anesthetic applications and insufflation pressure. With regard to the nurses collecting the VAS pain scores, both questioning and analgesic requirement application training was provided. In cases where a VAS pain score of ≥4 was attained, intravenous (iv) dexketoprofen (Arveles® 50 mg) was administered. In cases requiring an analgesic, iv dexketoprofen was administered.. None of the patients received a preemptive analgesic application. Anesthetic induction

was executed through Fentanyl (Talinad®) (1-2 mg/Kg/min iv infusion) and Propofol (Propofol®) (2mg/kg, iv). Every patient received tracheal intubation. Sustainability of the anesthetics was provided via Sevoflurane 1%-1.5% at intervals with Fentanyl, oxygen/air. The end tidal CO_2 pressure was sustained at 35-45 mmHg via mechanical ventilation. Metoclopramide (Metpamide®) iv 10 mg was administered to all of the patients, either during the operation or after, in order to prevent nausea and vomiting before they woke up.

All of the LC applications were executed by surgeons who had performed at least 200 LC operations. In order to avoid pneumoperitoneum, and avoid a vasovagal reaction, an initial slow current (3 L/min) was administered followed by a fast current (15 L/min) afterwards in the LP group, whereas in the SP group, the value was fixed. After which, the patients were placed into the reverse-Trendelenburg position. All of the LCs were performed with 4 trocars. At both the 10-mm infraumbilical and 10-mm subxiphoid incision locations and again at the 5-mm frontal axis, and 5-mm midclavicular incision locations, the incision was performed on the left-side of the abdomen. After which, the cystic artery and cystic ductus were clipped with non-absorbable clips and the gall bladder was separated from the liver bed, and placed inside of an endobag, which was then taken out through the subxiphoid at the 10-mm trocar incision and removed via the abdomen. At the infraumbilical and subxiphoid incision locations, the fascia was closed with number 0 non-absorbable

sutures. The skin was closed subcutaneously with 3-0 absorbable suture material. Bupivacaine of 0.5% (50 mg) (each 10 mL, containing bupivacaine hydrochloride 52.8 mg equivalent to anhydrous bupivacaine hydrochloride 50 mg) was then diluted with 10 mL of physiological saline solution until a solution of 20 mL was reached. Next, 6 cc infraumbilical, 6 cc subxiphoid, if 4 cc to lateral incision trocar locations just before the incision was injected intrafascially. At 8 h postoperatively, all of the patients were offered something to eat and drink.

Zero-hour was considered to be when the patients were returned to their rooms for recovery. From this point onward, the requirement for analgesics within the first 24 h (0 min, 30 min, 1 h, 2 h, 6 h, 12 h, and 24 h) and the pain scores were recorded. Patients with VAS pain scores of ≥ 4 were administered iv dexketoprofen (50 mg).

Statistical Analysis

Significant differences in the various categorical variables, such as gender, ASA, patient satisfaction, etc., were analyzed via chi square analysis, whereas significant differences in the quantitative variables, such as age, operation duration, and VAS values were analyzed via 1-way analysis of variance (ANOVA) analysis. As a result of the 1-way ANOVA analysis, in cases where differences were observed within the groups, the Tukey test was used in order to identify which group represented that distinction. Analysis was applied using the Statistical Package for the Social Sciences 20.0 software at a 95% significance level.

Table 1. Demographic characteristics of the patients, time of first dose of analgesic, and operation duration details.

		**Groups**	
		\multicolumn{2}{c	}{**SP**}	\multicolumn{2}{c	}{**SP+LA**}	\multicolumn{2}{c	}{**LP**}	\multicolumn{2}{c	}{**LP+LA**}	*p*
		n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Gender	Male	18	32.10%	11	19.60%	12	21.40%	15	26.80%	0.260
	Female	12	18.80%	19	29.70%	18	28.10%	15	23.40%	
ASA	I	9	22.50%	6	15.00%	12	30.00%	13	32.50%	0.212
	II	21	26.30%	24	30.00%	18	22.50%	17	21.30%	
Age		47.1±11.6	50.7±2.2	51.3±12.1	52.2±14.7	0.437
First analgesic time		5.1±12.7	91.4±117.5	44.2±72.9	193±208,9	**0.000**
Surgery time		32.3±9.6	30.4±9.5	42.8±10.8	40.4±11.3	**0.000**

ASA = American Society of Anesthesiologists classification, LA = local anesthetic, LP = low pressure, SP = standard pressure
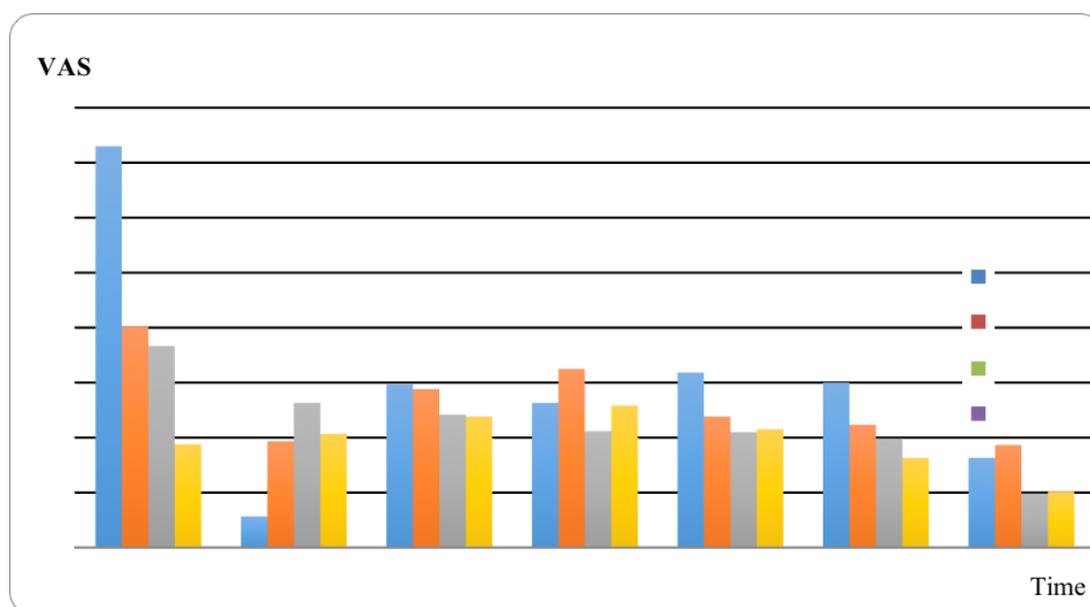
Figure 1. Pain scores according to hours. VAS = visual analogous scale

RESULTS

The demographic characteristics of the patients, average time of the 1st dose of analgesic, and operation duration details, as well as distinctions among the groups can be seen in Table 1.

When the relationship between the VAS scores and gender was evaluated, it was observed that there was no significant relationship between the groups and gender ($p > 0.05$). When the relationship between the ASA and VAS scores was evaluated, no significant relationship was detected ($p > 0.05$). When we evaluated whether the distinction was significant between the VAS scores and gender averages, and the differences between these averages, among the groups regarding age, it was determined that there was no significant distinction ($p > 0.05$).

When we examined the groups with regards to the average time of the 1st dose of analgesic and whether the distinctions between those averages were significant or not, a significant difference among the groups was observed ($p < 0.05$). That average time in the LP+LA group was detected as significantly higher than that of the average values in the other groups ($p < 0.001$). Additionally, in the SP+LA group, the average time of the 1st dose of analgesic was found to be only slightly higher than that of the standard group average ($p < 0.001$). The other groups were identified as having no significant distinction.

According to the group results, when the operation durations were analyzed, a significant distinction was also detected. In the LP group, the average operation was observed to be significantly longer than that in the SP group ($p < 0.05$). Different times of the analysis results, in cases of coughing and at rest, in order to identify whether or not there was a significant difference between the group VAS scores, are shown in Table 2 ($p < 0.05$). At 0 min, the rest and coughing VAS scores were identified as significantly high in the SP group ($p < 0.001$). At 30 min, the VAS scores in the SP group were detected as significantly low ($p < 0.001$). When the LP+LA group average was compared with that of the standard treatment group, it was observed to be significantly low at 12 and 24 h ($p < 0.05$). Moreover, in the SP group, the pain scores at 12 and 24 h were significantly higher than those in the SP+LA group. A graphical representation of the pain scores according to the hour can be seen in Figure 1.

According to the relationship between the group and patient satisfaction; in the SP group, 40% of the patients had negative opinions and feedback, 43.3% were averagely satisfied, and 16.7% were satisfied; in the SP+LA group, 20% had negative feedback, 60% were averagely satisfied, and 20% were satisfied; in the LP group, 16.7% had negative feedback, 50% were averagely satisfied, and 33.3% were satisfied, and in the LP+LA group, 10% had negative feedback, 26.7% were averagely satisfied, and 63.3% were satisfied. It

Table 2. VAS scores in cases of coughing and at rest.

Time		SP	SP+LA	LP	LP+LA	*p*
0 min	Rest	6.73±1.89	3.67±1.3	3.37±1.38	1.5±1.36	**0.000**
	Coughing	7.87±1.91	4.37±1.81	3.97±1.69	2.27±1.2	**0.000**
30 min	Rest	0.53±1.72	1.93±1.64	2.47±2.03	1.83±1.29	**0.000**
	Coughing	0.6±1.96	1.93±1.74	2.8±2.4	2.3±1.26	**0.000**
1 h	Rest	2.63±1.16	2.63±1.63	2.17±1.64	2.13±1.14	0.323
	Coughing	3.3±1.64	3.13±1.74	2.67±2.09	2.63±1.16	0.323
2 h	Rest	2.5±1.2	2.97±1.94	1.9±1.4	2.37±1.07	**0.044**
	Coughing	2.77±1.57	3.53±2.34	2.33±1.52	2.8±1.19	0.059
6 h	Rest	2.73±2.02	2.2±2.06	1.8±1	1.87±1.57	0.141
	Coughing	3.63±2.44	2.57±2.56	2.4±1.19	2.43±1.92	0.076
12 h	Rest	2.77±2.56	1.9±1.37	1.77±1.1	1.37±1.35	**0.015**
	Coughing	3.23±2.84	2.57±1.55	2.2±1.1	1.9±1.42	**0.038**
24 h	Rest	1.4±1.07	1.73±0.83	1.07±0.87	0.73±0.78	**0.000**
	Coughing	1.87±1.25	2±1.05	0.9±0.84	1.3±0.88	**0.000**

LA = local anesthetic, LP = low pressure, SP = standard pressure, VAS = visual analogous scale

was also detected that there is significant relationship between the group and patient satisfaction (*p* = 0.001) (Table 3).

Within the groups, when the requirement for a 2nd dose of analgesic was reviewed, it was found that 76.7% of the SP group, 23.3% of the SP+LA group, 13.3% of the LP group, and 3.3% of the LP+LA group received the 2nd dose. Hence, a significant relationship between the groups and the 2nd dose of analgesic was observed (*p* = 0.001) (Table 3).

DISCUSSION

In 1993, the first published study of laparoscopic surgery with regards to pain palliation and local anesthetics was conducted [13], and many more such studies have been conducted since then. The most important component of postoperative pain is incision-sourced pain, as incisional pain is much stronger, especially within the first 48 h when compared to visceral pain [14]. In many studies, with regards to the effectiveness of a local anesthetic injection at the trocar entry locations in pain palliation, it has been indicated that an intrafacial injection was very effective for pain control [15, 16]. Within the literature, there are many publications regarding the prevention of post-LC pain in subcutaneous or intraperitoneal infiltration, using such local anesthetics as bupivacaine, ropivacaine, and levobupivacaine [17]. Bupivacaine is a local analgesic with a half-life of 2.7 to 3.5 h, which controls pain for an average of 6 h [18]. In small incisions, bupivacaine's security margins are quite broad. At the upper limit of 2.5 mg

Table 3. Requirement for a 2nd dose of analgesic and patient satisfaction results.

		SP		SP+LA		LP		LP+LA		
		n	%	n	%	n	%	n	%	
Patient satisfaction	Poor	12	40.00%	6	20.00%	5	16.70%	3	10.00%	**0.001**
	Mild	13	43.30%	18	60.00%	15	50.00%	8	26.70%	
	Good	5	16.70%	6	20.00%	10	33.30%	19	63.30%	
2nd dose analgesic	No	7	23.30%	23	76.70%	26	86.70%	29	96.70%	**0.001**
	Yes	23	76.70%	7	23.30%	4	13.30%	1	3.30%	

LA = local anesthetic, LP = low pressure, SP = standard pressure

of bupivacaine per kg of body weight, 100 mg of the drug can be used safely in a patient with a lean body mass of 40 kg (total body weight, 70 kg). In our study, we used bupivacaine as an intrafacial local anesthetic agent. Despite the fact that there are studies in the literature indicating the fact that the usage of local anesthetics postoperatively is effective in pain palliation [19], it is thought that local anesthetics decrease postoperative pain via the prevention of transmission of nociceptive stimulus in the central nervous system when applied immediately before the incision [20, 21]. In the LA group, we administered a bupivacaine intrafacial injection immediately before making an incision like a study by Cantore *et al.* [22] and others [23, 24]. Pain scores after LC in the SP group were significantly high, despite the fact that an intrafacial bupivacaine injection was administered (in both the SP and SP+LA groups) when compared to those in the LP group, and this effect was obvious, especially at 2 and 24 h. This means that in the SP group, the sole application of local anesthetic did not provide sufficient analgesic when compared to the LP group.

According to Ingelmo *et al.* [25], after laparoscopic surgery, pain is primarily connected to the parietal peritoneal distention generated by carbon dioxide or damage that is caused by electrocauterization. Carbon dioxide, due to its fast diffusion characteristics, is used frequently to generate pneumoperitoneum [26]. Carbon dioxide insufflation and an increase in intraabdominal pressure leads to changes in organ physiology and hence, postoperative pain occurs. The degree of intraabdominal pressure is strongly and directly related to these changes. Thus, within the LC procedure, intraabdominal insufflation pressure is directly related to postoperative pain. Studies in which it has been foreseen that low pressure pneumoperitoneum leads to less postoperative pain do exist in the literature [3, 4]. In our study, when the pain scores of the LP group were compared to those of the SP and SP+LA groups, postoperative pain was observed at 2 and 24 h at significantly low levels. However, concerning patient satisfaction and the requirement for a 2nd dose of analgesic, no significant distinctions were detected. LC can be successfully applied via low-pressure carbon dioxide; however, the obtained operational area will be more limited than the area obtained via high pressure. However,

pneumoperitoneum that is generated by low pressure has been indicated to form a satisfying surgery zone for the surgeon in many studies [27]. Since we did not question to the surgeons about their satisfaction postoperatively, we could not identify whether or not low pressure LC provides the patient with a sufficient surgery zone. In LP+LA group, early postoperative (0 min) pain scores were significantly low when compared to the other groups. At 30 min, in the SP group, where no treatment was applied, the fact that the pain scores were significantly low is that we think to the most of this group at 0 min, since their pain scores were high analgesic application has been done. In the LP+LA group, immediately before the patients were discharged from the hospital (24 h), the VAS scores were detected as significantly low. While having a rest and while coughing, the pain scores were observed as significantly low, and this was also obvious at 0 min, 12 h and 24 h during rest. Within the LP+LA group, the fact that the requirement for a 2nd dose of analgesic was extremely low, the patient satisfaction rate was rather high when compared to the other groups, and the time of the 1st dose of analgesic was significantly late when compared to other groups leads us to believe that this application is more effective with regards to pain palliation. In addition, the operation duration was also quite a bit longer than in the other groups.

The Limitation of the Study

We did not question to the surgeons about their satisfaction postoperatively, we could not identify whether or not low pressure LC provides the patient with a sufficient surgery zone.

CONCLUSION

In cases of symptomatic cholelithiasis, LC can be used effectively and safely in selected patients with severe pulmonary and cardiac co-morbidities in centers with intraabdominal low-head and local anesthetic infiltration and advanced laparoscopy experience.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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