RESEARCH ARTICLE

The Comparisons of Intra-Peritoneal Bupivacaine Instillation versus Trendelenburg Position and Valsalva Maneuver on the Laparoscopic Cholecystectomy-induced Abdominal and Shoulder Pain

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Background: Although laparoscopic cholecystectomy is associated with less post-operative pain compared to open cholecystectomy, diffuse shoulder and abdominal pain is one of the main postoperative complications in this technique. The aim of this study was to compare the abdominal and shoulder pain after laparoscopic cholecystectomy by applying intra-abdominal bupivacaine instillation versus the trendelenburg position and valsalva maneuver.

Methods: A double blind randomized clinical trial was conducted in the university hospital. 120 patients aged 25-55 years were scheduled for elective laparoscopic cholecystectomy and without any history of previous surgery, pregnancy or acute abdomen were enrolled. Patients were allocated into 4 groups (each 30 cases). Group 1 received just intra-peritoneal normal saline (NS). Group 2 patients who were placed in trendelenburg position plus valsalva maneuver and received intra-peritoneal NS. For group 3, intra-peritoneal bupivacaine instillation was done. Patients in group 4 received intra-peritoneal bupivacaine as well as were placed in trendelenburg position plus valsalva maneuver. Post-operative pain severity using visual analog scale, analgesic requirement and nausea and vomiting were recorded in all patients.

Results: Total mean pain score at 24 hours was 3.55±0.47 in group 1, 1.08 ±0.85 in group 2, 0.33 ±0.14 in group 3, and 0.20 ±0.59 in group 4 (P= 0.001). Mean total score of shoulder pain was 4.70 ±2.18 in group 1, 1.23 ±0.11 in group 2, 1.18 ±0.11 in group 3, and 0.70 ±0.12 in group 4 (P= 0.001).

Conclusion: Combined intra-peritoneal bupivacaine with trendelenburg positioning and valsalva maneuver was superior to either one alone in decreasing pain severity after laparoscopic cholecystectomy.

Keywords: laparoscopic cholecystectomy; pain; trendelenburg position; valsalva maneuver; intraabdominal bupivacaine

After introduction of laparoscopic cholecystectomy in the 1980s, this technique rapidly surpassed open cholecystectomy as the preferred method for gall bladder surgery. Advantages of this technique include less hemorrhage, more rapid recovery and better cosmetic outcome compared to open cholecystectomy and minilaparotomy [1]. This minimally invasive surgery, however, can be associated with some complications. One of these complications which usually patients complain of is pain in the shoulder as well as abdominal pain. Improper pain control after surgery can progress to more complications such as increased blood pressure, respiratory difficulty and even cardiovascular events. In fact, pain is noted as the major complaint patients report after laparoscopic cholecystectomy and is the main reason in prolonging hospitalization [2-3]. More dramatic is that it seems that this pain is undertreated [4]. In addition to postoperative pain, nausea and vomiting have been reported as major contributors in prolonging hospitalization and discomfort for patients after laparoscopic cholecystectomy [5]. Etiologies proposed for post-laparoscopy pain include stretching of the intra-abdominal cavity [6], inflammation of the peritoneum following increased intra-abdominal pressure [7], and irritation of the phrenic nerve induced by residual carbon dioxide in the peritoneal cavity which causes referred pain to C4-referred shoulder pain [8].

Intra-peritoneal instillation of local anesthetics has been reported to attenuate postoperative pain after laparoscopic surgery. In this regard, bupivacaine, levobupivacaine, and ropivacaine have been studied in previous clinical trials with promising results [3, 9-11]. These agents exert their effect

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by blocking nociceptive input in the peritoneum. Another method tested to decrease post-operative pain is positioning patient in an attempt to deflate intra-peritoneal gas. One of these positions is trendelenburg position (head down) accompanied by valsalva maneuver. It is thought that by expelling residual CO2 gas, the irritation caused by this gas will be less and subsequently patient will suffer less pain after surgery [8-12]. However, the results are not uniform and some negate beneficial effects of patient positioning in an effort to expel residual intra-peritoneal gas [13].

Here, we decided to investigate trendelenburg positioning plus valsalva maneuver versus intra-peritoneal bupivacaine instillation in comparison to placebo regarding post-operative pain severity, analgesic requirement, and nausea during the first 24-hour period after elective laparoscopic cholecystectomy. By comparing these methods, we found intraperitoneal instillation together with trendelenburg position and Valsalva maneuver as a better method in decreasing post-operative pain after laparoscopic cholecystectomy.

Methods

Ethics

The study details were described for the patients prior to surgery. Written informed consent was obtained and they were reassured that the information will be kept confidential by the research team. This study was accepted by the Medical Ethics Committee of our medical university with the code of 91/S/130/643. The study protocol was in conformity with the ethical guidelines of the 1975 Declaration of Helsinki [15].

Setting and patients

This double blind randomized clinical trial included patients within the age range of 25-55 years with ASA (American Society of Anesthesiologists) class I or II who were candidate to undergo elective laparoscopic cholecystectomy at our university hospital. Exclusion criteria were previous history of surgery, pregnancy, choledocholithiasis and chronic biliary pain, emergency cholecystectomy, allergy to bupivacaine, prolongation of the surgery and need to perform open cholecystectomy, obesity (body mass index; BMI>35 kg/m2), smokers, and any hepatic, renal, hematologic, neurologic, or cardiovascular disorders. A total of 120 patients were entered into the study. The sample size was calculated based on previous data about the role of intra-peritoneal bupivacaine administration in decreasing post-operative pain and application of standard deviation (SD) of post-operative pain severity [14].

Randomization and intervention

The included patients were randomly (using random number table) divided into 4 groups (30 cases in each group). Group 1 (NS) received just intra-peritoneal normal saline (NS) as placebo. Group 2 were placed in trendelenburg position plus valsalva maneuver (head down at 30 degrees) and received intra-peritoneal NS. For group 3, intra-peritoneal bupivacaine instillation was done and without placing them at any position. Patients in group 4 received intra-peritoneal bupivacaine as well as were placed in trendelenburg position plus valsalva maneuver.

After pre-oxygenation for 5 minutes, fentanyl (2 micg/kg) and midazolam (0.03 mg/kg) were injected intravenously. Then induction was done by propofol (2 mg/kg) and atracurium (0.5 mg/kg). After achieving complete muscular relaxation, endotracheal intubation was done. During surgery, fentanyl (50 micg) and atracurium (10 mg) were injected every 30 minutes. Intraoperative monitoring included noninvasive blood pressure monitoring (NIBP), puls-oxymetry, EKG, and end-tidal CO2 (ETCO2). At the end of the surgery and prior to trocar removal, for patients of groups 3 and 4, bupivacaine was instilled by the surgeon through the trocars. Bupivacaine 0.25% (Bupivacaine hydrochloride 5mg/ml, Mylan, Delpharm Tours) was instilled at the base of gall bladder (20 mL) as well as at the subdiaphragmatic area (20 mL) during surgery. This was done by the attending surgeon. NS was instilled in the same way. In groups 2 and 4, the patient was placed in trendelenburg position (30 degrees) by the anesthesiologist and Valsalva maneuver (pressure of 30 cmH2O) applied thrice to allow egress of intra-peritoneal air from the abdominal cavity via the trocars. In group 4 where patients needed both positioning and intra-peritoneal bupivacaine instillation, first positioning was established and then bupivacaine was instilled. For all groups, 30 minutes before surgery termination, IV ondansetron (4 mg) was injected. Then, reversal of muscle relaxants was achieved using neostigmine (40 micg/kg) and atropine (20 micg/kg), and after assurance of adequate voluntary respiration, endotracheal extubation was performed.

Variables

Variables studied included post-operative pain severity, location of pain (shoulder, peri-umbilical, hypogastric, and generalized abdominal pain), nausea and vomiting, and dosage of analgesic administered in the 24-hour period after surgery. Pain severity was measured using a visual analog scale (VAS) designed as a 100-mm horizontal line (0=no pain at all and 10= worst pain imaginable). This scale was used to measure severity of pain at 1, 2, 4, 8, 12, and 24 hours after surgery. All post-operative follow-ups were made by the anesthesiology resident of this project who was blinded to the groups to which each patient had been assigned. The allocation of patients into the desired groups before starting the study was done by the administrative staff of the operation room and the authors were totally blinded to the groups. In case of nausea and vomiting, metoclopramide (10 mg IV) was injected. In case of considerable pain reported (i.e., VAS > 3) 3 mg morphine intramuscularly was injected. Besides, baseline characteristics were collected using a checklist.

Statistical analyses

The data gathered were entered into the SPSS software for Windows (ver. 20.0). Descriptive indices including frequency, percentage, interquartile range, mean, and SD were used to report the data. Comparisons of qualitative and continuous variables between the four studied groups were done using the Chi-square and ANOVA (analysis of variance) tests, respectively. Repeat measurement was applied to find the trend of change in variables over time.

Results

There were 78 females (65%) and 42 males (35%) with a mean age of 40.73±7.83. The number of women in groups 1, 2, 3, and 4 were respectively 20, 18, 20, and 20 (p value

0.6). Mean age was 41.09 (±7.85), 41.47 (±7.27), 39.80 (±8.40), and 40.57 (±7.74) years in groups 1, 2, 3, and 4, respectively (p-value 0.001). Overall mean post-operative pain was 1.63 (±1.37). This was 3.18 (±0.81) in group 1, 1.98 (±1.07) in group 2, 0.85 (±0.94) in group 3, and 0.49 (±0.09) in group 4 (p value 0.001). Overall mean pain at 1, 2, 4, 8, 12, and 24 hours after surgery was in order 1.38 (±1.19), 1.67 (±1.13), 1.71 (±1.15), 1.94 (±1.46), 1.77 (±1.60), 1.29 (±1.51). (p-value 0.002) The mean total pain in 4 studied groups at 1, 2, 4, 8, 12, and 24 hours after surgery was shown (Table 1). As observed, at all times mean pain score was lower in intervention groups than in placebo group. The mean scores of shoulder pain, peri-umbilical pain, hypogastric pain, and generalized abdominal pain are presented (Table 2).

As shown, this score was significantly lower in intervention groups compared to control group. (Table 3) depicts pain score at different locations recorded at 1, 2, 4, 8, 12, and 24 hours after surgery. Except for hypogastric pain, shoulder pain, peri-umbilical pain, and generalized abdominal pain showed a significant decrease over time.

The frequency of patients in each group who required analgesic at different times was recorded (Table 4). The lowest and highest frequency of analgesics use was seen in group 3, 4 and group 1 respectively. The frequency of patients in each group who reported nausea at different times was shown (Table 5). At 2 hours, nausea was more frequent in group 4, but then its frequency decreased significantly in this group until 24 hours after operation, when none of the patients reported nausea.

Table 1- The mean total pain score in all groups at 1, 2, 4, 8, 12, and 24 hours after laparoscopic cholecystectomy

	Total	Group 1	Group 2	Group 3	Group 4	P value
1 hour	1.38 ±1.19	2.78 ±0.64	1.88 ±0.79	0.33 ±0.11	0.53±0.10	0.001
2 hours	1.67 ±1.13	2.85 ±0.67	2.25 ±0.66	0.95 ±0.88	0.62±0.38	0.001
4 hours	1.71 ±1.15	2.53 ±1.05	2.50 ±0.68	1.28 ±0.83	0.52±0.44	0.001
8 hours	1.94 ±1.46	3.58 ±0.52	2.35 ±1.28	1.22 ±1.09	0.62±0.11	0.001
12 hours	1.77 ±1.60	3.83 ±0.39	1.85 ±1.33	0.98 ±0.99	0.43±0.15	0.001
24 hours	1.29 ±0.14	3.55 ±0.47	1.08 ±0.85	0.33 ±0.14	0.20±0.59	0.001

Group 1= normal saline, Group 2= trendelenburg position plus valsalva maneuver, Group 3= intra-peritoneal bupivacaine, Group 4= intra-peritoneal bupivacaine plus trendelenburg position plus valsalva maneuver

Table 2- The mean scores of shoulder pain, peri-umbilical pain, hypogastric pain, and generalized abdominal pain in all groups

	Total	Group 1	Group 2	Group 3	Group 4	P value
Shoulder pain	1.95 ±0.09	4.70 ±2.18	1.23 ±0.11	1.18 ±0.11	0.70 ±0.12	0.001
Peri-umbilical pain	1.40 ±0.07	2.80 ±1.94	1.98 ±0.14	0.70 ±0.10	0.10 ±0.03	0.001
Hypogastric pain	1.06 ±0.06	2.00 ±1.13	1.88 ±0.16	0.30 ±0.05	0.07 ±0.03	0.001
Generalized abdominal pain	2.09 ±0.06	3.23 ±1.91	2.83 ±0.09	1.21 ±0.11	1.08 ±0.08	0.001

Group 1= normal saline, Group 2= trendelenburg position plus valsalva maneuver, Group 3= intra-peritoneal bupivacaine, Group 4= intra-peritoneal bupivacaine plus Trendelenburg position plus valsalva maneuver

Table 3- The mean of pain score at different locations recorded at 1, 2, 4, 8, 12, and 24 hours after laparoscopic cholecystectomy

	1 hour	2 hours	4 hours	8 hours	12 hours	24 hours	P -value
Shoulder pain	2.14 ±0.28	2.40 ±0.27	2.33 ±0.20	2.17 ±0.16	1.80 ±0.16	0.89 ±0.12	0.001
Peri-umbilical pain	0.58 ±0.09	0.84 ±0.10	1.26 ±0.19	1.55 ±1.92	1.90 ±0.19	1.88 ±0.22	0.001
Hypogastric pain	0.95 ±0.12	1.13 ±0.12	1.13 ±0.12	1.08 ±0.17	1.15 ±0.18	0.93 ±0.13	0.7
Generalized abdominal pain	1.84 ±0.13	2.29 ±0.11	2.11 ±0.12	2.59 ±0.18	2.23 ±0.19	1.46 ±0.17	0.001

Table 4- The frequency of patients who required analgesic in each group at 1, 2, 4, 8, 12, and 24 hours after laparoscopic cholecystectomy in all groups

	Total	Group 1	Group 2	Group 3	Group 4	P value
1 hour	0	0	0	0	0	-
2 hours	39 (32.5%)	9 (30%)	18 (60%)	8 (26.7%)	4 (13.3%)	0.001
4 hours	35 (29.2%)	21 (70%)	9 (30%)	5 (16.7%)	0	0.001

Table 4- The frequency of patients who required analgesic in each group at 1, 2, 4, 8, 12, and 24 hours after laparoscopic cholecystectomy in all groups (Continued)

8 hours	5 (4.2%)	0	3 (10%)	2 (6.7%)	0	0.1
12 hours	37 (30.8%)	27 (90%)	3 (10%)	3 (10%)	4 (13.3%)	0.001
24 hours	9 (7.5%)	6 (20%)	3 (10%)	0	0	0.008

Group 1= normal saline, Group 2= trendelenburg position plus valsalva maneuver, Group 3= intra-peritoneal bupivacaine, Group 4= intra-peritoneal bupivacaine plus trendelenburg position plus valsalva maneuver

Table 5- The frequency of nausea in each group at 1, 2, 4, 8, 12, and 24 hours after laparoscopic cholecystectomy in all groups

	Total	Group 1	Group 2	Group 3	Group 4	P value
1 hour	2 (1.7%)	0	0	0	2 (6.7%)	0.1
2 hours	45 (37.5%)	9 (30%)	6 (20%)	14 (46.7%)	16 (53.3%)	0.03
4 hours	31 (25.8%)	21 (70%)	6 (20%)	4 (13.3%)	0	0.001
8 hours	3 (2.5%)	0	3 (10%)	0	0	0.02
12 hours	3 (2.5%)	3 (10%)	0	0	0	0.02
24 hours	0	0	0	0	0	-

Group 1= normal saline, Group 2= trendelenburg position plus valsalva maneuver, Group 3= intra-peritoneal bupivacaine, Group 4= intra-peritoneal bupivacaine plus trendelenburg position plus valsalva maneuver

Discussion

Post-operative pain is one of the common complications that should be controlled by anesthesiologists and if not controlled properly will lead to respiratory complications, prolonged hospitalizations, and other morbidities. Finding effective and safe methods that substitute systemic medications such as opioids has always been of interest for anesthesiologists. Our findings indicate that total pain score was significantly lower in intervention groups at 1, 2, 4, 8, 12, and 24 hours postoperatively compared to placebo group. However, the pain score was similar between groups 2, 3, and 4 who were placed in trendelenburg position plus valsalva maneuver, intra-peritoneal bupivacaine instillation and in combined intra-peritoneal bupivacaine and trendelenburg position plus valsalva maneuver, respectively. In intervention groups, we observed a downward change in pain score, but after 8 hours placebo group presented an increase in pain score. The most severe pain in placebo group was in the shoulder area. However, shoulder pain was the least severe pain recorded in group which received both trendelenburg position plus valsalva maneuver and intra-peritoneal bupivacaine. When observing data, it is obvious that patients in group 4 who received both trendelenburg position plus valsalva maneuver and intra-peritoneal bupivacaine had better outcomes regarding pain, nausea, and analgesic requirement. These outcomes are superior when compared to either trendelenburg position plus valsalva maneuver or intra-peritoneal bupivacaine instillation. The role of residual carbon dioxide is well documented in the literature as a contributor to abdominal pain after laparoscopy. So studies have been carried out with the objective of introducing methods which will help expel this gas from abdomen at the end of surgery [18].With these techniques, abdominal and shoulder pain may be reduced. Here we observed a favorable outcome in group 2 that were placed in trendelenburg position plus valsalva maneuver when compared to placebo group. A method called pulmonary recruitment maneuver (PRM) has been studied previously with significant effects in reducing post-operative pain [16-17]. This technique works by pulmonary inflation with positive pressure of (about 30-40 cm H2O) to remove CO2 gas from abdominal cavity. Sharami et al. [17] studied pulmonary recruitment maneuver (exerted as manual ventilation of lung with a positive pressure of 40 cmH2O) on shoulder pain after gynecologic laparoscopy operation in a double blind trial. They reported that shoulder pain severity was significantly lower at 12, 24, and 48 hours after surgery in the intervention group compared to the control group. This is somehow similar to what we observed in our study.

After 8 hours, group 2 reported less severe pain when compared to placebo group considering the discrepancy in patient population between ours and the mentioned study which included gynecologic laparoscopy cases. Compatible with our results, the control group required higher dosages of analgesic [17]. Tsai et al. [16] also investigated the efficacy of PRM and compared it with intra-peritoneal NS infusion in decreasing abdominal and shoulder pain in a randomized trial on patients who underwent laparoscopic gynecologic operations [16]. According to their findings, at 24 hours about 66%of patients complained of shoulder pain in PRM group. But in NS group, this was significantly lower (40.7%). They concluded that NS infusion was superior to PRM referring to the role of NS in increasing intra-peritoneal pressure and providing a physiologic buffer medium helping in dissolving residual CO2 [16].

Intra-peritoneal analgesic instillation has also been studied in previous studies with promising effects in alleviating pain and nausea after laparoscopic cholecystectomy. Golubović et al. [19] compared intra-peritoneal bupivacaine with intra-peritoneal combination of bupivacaine and tramadol on 90 patients who underwent laparoscopic cholecystectomy. They reported that the pain score was lower in combination group compared to bupivacaine alone and in both groups pain was less severe when compared to the control group (with saline). There is controversy about the effect of intra-peritoneal instillation of bupivacaine in reducing pain after laparoscopic cholecystectomy. Some authors have reported

that this technique was superior to placebo [3, 20-21], while others reported it to be similar to placebo [6, 21]. Joris et al. [6] reported that instillation of 80 mL of intra-peritoneal bupivacaine 0.125% under the right hemidiaphragm did not significantly influence pain score compared to the group which received the same volume of saline. Jiranantarat et al. [21] reported a similar outcome by intra-peritoneal instillation of 0.5% bupivacaine into the hepatodiaphragmatic space when compared to same volume saline infusion with no advantage for postoperative analgesic requirement after laparoscopic cholecystectomy. Szem et al. [22] though reported a significant reduction in post-operative pain in patients who received intraperitoneal bupivacaine (0.1%, 100 ml) under the right hemidiaphragm over Glisson's capsule, concluded that this method yielded minimal benefit to patients and its effect was transient. We detected less severe pain in those who received intra-peritoneal bupivacaine compared to NS, but more severe pain than group 4 who received both interventions.

In conclusion, we found that combined intra-peritoneal bupivacaine with trendelenburg positioning plus valsalva maneuver was superior to either one alone in decreasing pain severity after laparoscopic cholecystectomy.

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