The Effect of Placing 0.5% Bupivacaine-Soaked Gelfoam in the Gallbladder Bed on Pain after Laparoscopic Cholecystectomy

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ABSTRACT

Background: Patients undergoing laparoscopic cholecystectomy (LC) experiences post operative abdominal pain. This study aimed to determine the character of pain after LC and its relief with 0.5% bupivacaine-soaked gelfoam placed in the gallbladder bed.

Methods: A prospective randomized, double blinded placebo–controlled study was conducted on 200 patients with chronic cholecystitis, patients were divided into four groups of 50 patients :group A (2 mg/kg 0.5% bupivacaine-soaked gelfoam kept in gallbladder bed), group B (2 mg/kg 0.5% bupivacaine infiltrated at trocar sites), group C (1/2 of the required dose of 2 mg/kg 0.5% bupivacaine infiltrated into the gallbladder bed and at trocar sites, and group D (normal saline in the gallbladder bed and at trocar sites). Postoperatively, the character of pain was noted, and its relief was assessed with verbal rating scale (VRS) scoring.

Results: 77.50% of the patients had visceral, 60.50% had parietal, and 23.50% had shoulder pain postoperatively. The visceral pain was significantly less in group A patients than in the control patients (p < 0.01),the mean VRS score at 4, 8, 12 and 24 h in the group A patients also was less than in control group D. Trocar-site infiltration alone was not effective in relieving the parietal pain.

Conclusions: Visceral pain is prominent after laparoscopic cholecystectomy and can be effectively controlled by 0.5% bupivacaine-soaked gelfoam in the gallbladder bed alone.

Keywords: Laparoscopic cholecystectomy, Bupivacaine, Verbal rating scale (VRS)

INTRODUCTION:

Laparoscopic cholecystectomy (LC) is one of the most widely performed laparoscopic procedures [1], becoming the standard operation for symptomatic gallstone disease [2]. The recognized benefits of this technique compared with open cholecystectomy include less postoperative pain, earlier discharge from hospital, more rapid convalescence, and an earlier return to normal activities [3,4]. However, patients undergoing LC do experience postoperative pain, which is often maximal on the first postoperative day [5]. The pattern of pain after LC is complex, the peritoneal origin of the pain suggests that analgesia delivered locally to the peritoneal cavity may be of benefit postoperatively [4]. Intra-peritoneal instillation of local anesthetic around the operative site has been used as an analgesic technique on the premise that conduction from visceral sites is blocked and may reduce the extent of referred pain to the shoulder in the postoperative period [6]. Numerous clinical studies have investigated the use of regional local anesthetics for pain relief after LC [7] with conflicting results, some showing a beneficial effect [8,9], and others showing no effect [10-11].The aim of this study was to evaluate the character of postoperative pain after LC and to evaluate the effect of 0.5% bupivacaine – soaked gelfoam on post operative pain when it placed in the gallbladder bed after LC.

MATERIALS AND METHODS:

The study enrolled 200 patients with chronic cholecystitis admitted for elective

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LC in Rizgary teaching hospital and Hawler private hospital from August 2006 to April 2008. Routine pre-operative investigations were done and exclusion criteria included; patients with ASA 3 and 4, acute cholecystitis, choledocholithiasis, previous major upper abdominal surgeries, conversion to open cholecystectomy, or had history of allergy to local anesthetics, a history of severe systemic disease, and chronic pain diseases other than gallstone disease were excluded from the study. Consent was obtained, and patients were divided into four groups, each of 50 patients, using a prospective randomized, double blinded placebo–controlled study, as follows:

• Group A: Bupivacaine 0.5% (2 mg/kg) was instilled over the wet-stable, felt-like collagen haemostatic strips (Gelfoam), in the gallbladder bed, and an equal volume of normal saline was infiltrated at four port sites after the procedure.

• Group B: Bupivacaine 0.5% (2 mg/kg) was infiltrated at four port sites, and an equal volume of normal saline was instilled over Gelfoam kept in the gallbladder bed.

• Group C: Half of the bupivacaine 0.5% (2 mg/kg) was instilled over Gelfoam in gallbladder bed, and the other half was instilled at four port sites.

• Group D: Normal saline, equal to the volume of the test solution, was instilled over Gelfoam in the gallbladder bed and at four port sites.

All laparoscopic cholecystectomies were performed according to the standard four – ports technique and under a standard general anesthesia. After complete hemostasis of the gallbladder bed, gelfoam strips were inserted through the epigastric port over the gallbladder bed and 0.5% bupivacaine solution or normal saline(according to the group) was instilled over the gelfoam with the help of veress needle inserted through a small skin puncture just lateral to the midclavicular port, (Figure 1). The port-site infiltration was accomplished using 0.5% bupivacaine or normal saline (according to the group) before its closure, with three-fifths of it infiltrated at the umbilical and epi-

ports and the remaining two-fifths at the midaxillary and midclavicular ports.
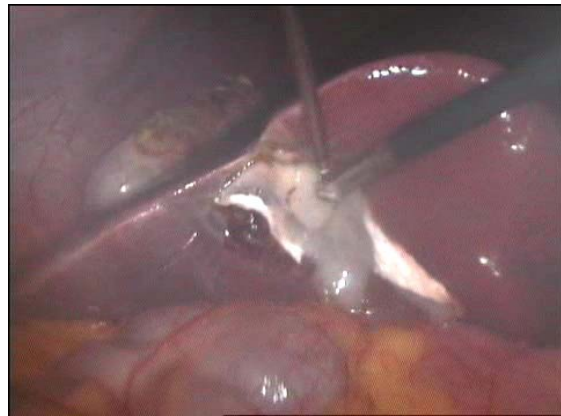
Figure(1): Gelfoam in the gall bladder bed and bupivacaine instilled in the gelfoam through Verres neddle.

Carbon dioxide was evacuated through the ports by applying gentle pressure all over the abdomen. No intra-peritoneal tube drain was used in any of the procedures. Rescue analgesia (intramuscular tramadol 100 mg), rescue antiemetic (intramuscular metoclopramide 10 mg) was administered if the VRS was high (patient complaining from moderate, severe or intractable pain), or patient had complained of vomiting. Because of the great variation in the educational level of our patients, assessing the pain with a horizontal 100-mm visual analog pain scale was not applied.

Thus postoperatively, pain was assessed by verbal rating scale (VRS), (0=absent, 1=mild, 2=moderate, 3=severe and 4 = intractable pain) 4, 8, 12 and 24 h after surgery. Before surgery the patients were instructed to use a verbal rating scale (VRS), to register the following three pain components retrospectively as described below: Intra-abdominal pain: (visceral pain component) was defined as pain inside the abdomen, which may be deep, dull, and more difficult to localize. Incisional pain: (somatic pain component) was defined as a superficial pain, wound pain, or pain located in the abdominal wall, a pain that one can `touch'. Shoulder pain: (presumably referred visceral pain) was defined as a sensation of pain in the shoulder. All patients were discharged home on the first postoperative day and were reviewed in the private clinic after seven days, where they were questioned again about pain and any postoperative complications. Statistical analysis was done using the statistical package for social science (SPSS) version (15.0). The mean postoperative VRS scores for the various groups were compared at different times with control subjects using analysis of variance (ANOVA). The VRS score was expressed as mean ± standard deviation. The statistical analysis for descriptive data was performed using the chi-squire test with Yates correction. Significance was considered at the 0.05 level, with the 0.01 level considered highly significant.

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RESULTS:

The 200 studied patients; 163(81.5%) women and 37(18.5%) men varied in age from 16 to 69 years. The four groups relatively did not differ in mean age, body weight, or ASA status; there was no significant difference in the duration of surgery among the four groups ($p > 0.05$), (Table 1). The overall incidences of visceral, parietal, and shoulder pain in our study were 77.50%, 60.50%, and 23 %, respectively. The overall incidence of visceral pain in group A was significantly less than control group (D) ($p > 0.05$), while there was no significant difference in the incidence of parietal pain between the studied groups, and there was as a highly significant difference in the incidence of shoulder pain between group A and control group (D) ($p < 0.01$) as shown in Figure 2. The VRS score decreased after surgery for all the patients. The VRS score for visceral pain in group A was significantly less than D at 4 h, 8 h, 12 h, and 24 h, while the difference between the two groups was not significant when the scores of parietal pain was compared, and there was a highly significant

Table(1): Patients characteristic.

Character	Group A	Group B	Group C	Group D	P value
N	50	50	50	50	NS
Male/Female	9/41	11/39	7/43	10/40	NS
Age (yr)	45.96 ± 15.05	48.86 ± 15.47	49.09 ± 14.91	49.45 ±15.3	NS
Weight (kg)	74 ± 10	71 ± 8	72 ± 11	69 ± 9	NS
ASA I (M / F)	6/36	10/35	7/40	8/35	NS
ASA II (M / F)	3/5	1/4	0/3	2/5	NS
Duration of anesthesia (min)	40 ± 8	39 ± 9	42 ± 6	40 ± 7	NS
Duration of surgery (min)	32 ± 9	34 ± 10	37 ± 5	34 ± 8	NS

Data are expressed as number of patients or mean ± SD, NS= not significant

difference when the scores of shoulder pain was compared. There was no significant difference in pain scores for visceral, parietal and shoulder pain between groups B and C when each was compared to group D, (Table 2). No side effects could be attributed to the use of bupivacaine or to the application technique.
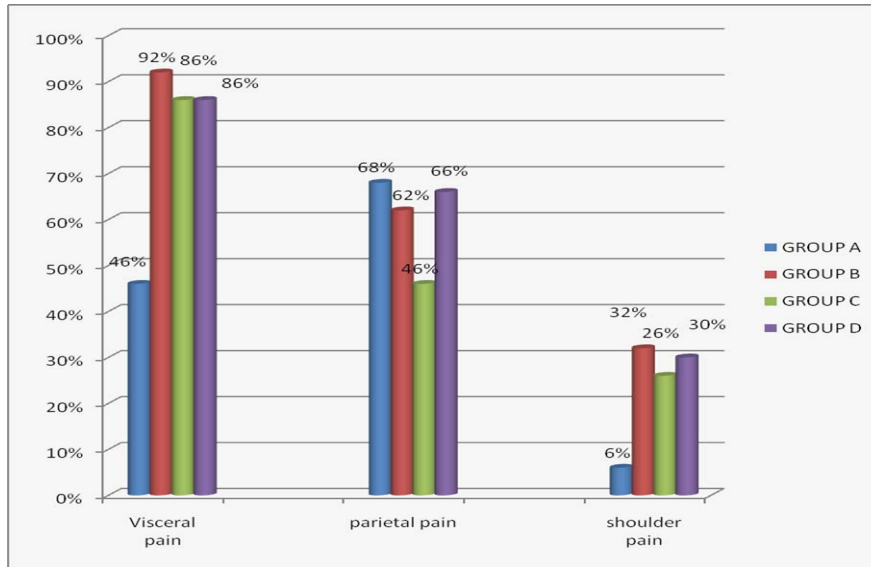

Figure (2): Visceral, parietal and shoulder pain in the studied groups

Table(2): Character of visceral, parietal, and shoulder pain comparatively evaluated between the studied groups (A, B, and C) and the control group D.

Timing	(A) n (%	(B) n (%)	(C) n (%)	(D) n (%)	P Value between (A)&(D)	P Value between (B) &D)	P Value between (C)& (D)
Visceral Pain							
4 h	23 (46%)	46 (92%)	30 (60%)	43 (86%)	< 0.05	> 0.05	> 0.05
8 h	17 (34%)	46 (92%)	43 (86%)	40 (80%)	< 0.01	> 0.05	> 0.05
12 h	12 (24%)	38 (76%)	35 (70%)	40 (80%)	< 0.01	> 0.05	> 0.05
24 h	3 (6%)	33 (66%)	30 (60%)	40 (80%)	< 0.01	> 0.05	> 0.05
Parietal Pain							
4 h	40 (80%)	37 (74%)	23 (46%)	33 (66%)	> 0.05	> 0.05	> 0.05
8 h	40 (80%)	23 (46%)	23 (46%)	33 (66%)	> 0.05	> 0.05	> 0.05
12 h	45 (90%)	16 (32%)	23 (46%)	32 (64%)	> 0.05	> 0.05	> 0.05
24 h	47 (94%)	13 (26%)	23 (46%)	30 (60%)	> 0.05	> 0.05	> 0.05
Shoulder pain							
4 h	0 (0%)	8 (16%)	10 (20%)	10 (20%)	< 0.01	> 0.05	> 0.05
8 h	0 (0%)	12 (24%)	10 (20%)	10 (20%)	< 0.01	> 0.05	> 0.05
12 h	0 (0%)	12 (24%)	12 (24%)	12 (24%)	< 0.01	> 0.05	> 0.05
24 h	3 (6%)	16 (32%)	16 (32%)	16 (32%)	< 0.01	> 0.05	> 0.05

P value (< 0.01) highly significant, (< 0.05) significant, (> 0.05) not significant

DISCUSSION:

Early postoperative pain remains the most prevalent complain after LC [2]. Abdominal pain following LC can occur for a number of reasons; stretching of the parietal peritoneum from the insufflations of gas intraperitoneally [12], release of inflammatory mediators of pain and irritation produced by blood [13]. The reason for the marked variation of pain between individuals remains unclear but could be due to multiple factors, including patient demographics, nature of underlying disease, anesthetic technique, surgical factors (duration of surgery, degree of invasiveness of the procedure), and post-operative care [14, 15]. In this study there were no significant differences among the treating groups in terms of patients demographic characters, nature of the disease (chronic cholecystitis), type of the surgery (all underwent LC), and anesthetic drug administered. Therefore the differences between the treating groups in the rate at which post operative pain relief was achieved, can be attributed to the drug (2 mg/kg of 0.5%Bupivacaine), used in the study. Pain after LC involves three different components with different intensity, time course, and pathophysiological mechanisms. These pain components are deep intra-abdominal pain (visceral pain component), incisional pain (parietal pain component), and shoulder pain (presumably referred visceral pain) [16]. In our study the overall incidence of visceral pain was 77.5% which was the main pain experienced by our patients, this may be attributable to greater surgical handling of the dissection area and diaphragmatic irritation by dissolved CO_2, while parietal pain was 60.5% and was less intense probably because of the small incisions and limited damage to the abdominal wall [17], similar results were obtained by Joris et al [18]. Whereas visceral and parietal pain tends to decrease in 24h, shoulder pain may become more prominent later [19]. In our study we have observed a significant reduction of pain after gallbladder bed instillation with 0.5% bupivacaine alone, 46% of our patients reported visceral pain 4 h after surgery and this incidence came down to 6% after 24 h. This effect is indirectly reflected by progressive reduction in both the VRS score and the visceral pain in this group of patients, although the majority (94%) continued to experience parietal pain. This suggests that progressive reduction of the VRS score in this group of patients was primarily attributable to the effective control of visceral pain. It seems that parietal pain was mild and did not contribute substantially to the VRS score. The VRS score in the group that had parietal infiltration alone group B (62%) did not differ from that in the control subjects group D (66%), suggesting that trocar-site infiltration does not provide pain relief after LC. This is similar to the experience of Adams et al [20]. In our study, gelfoam soaked with 0.5% bupivacaine in the gallbladder bed was also effective in controlling shoulder pain, only 3 (6%) patients in the group that received intra-peritoneal bupivacaine alone (group A) experienced shoulder pain, while 12 (24%) patients in the group that received half of the estimated volume of intra-peritoneal bupivacaine (group C), and 16 (32%) patients in each of the groups in which no intra-peritoneal bupivacaine were used (groups B & D), had shoulder pain. Similar results were observed by other authors [21-23]. With combined gallbladder bed and port-site infiltration, it was expected that these patients would respond at least in much the same way as or better than those in whom bupivacaine was instilled only in the gallbladder bed. However, contrary to our expectations, this did not happen. This probably because the amount of bupivacaine was insufficient to control visceral pain, as, only half of its estimated volume was administered in the gallbladder bed. The inefficacy of intraperitoneal bupivacaine in minimizing pain after LC reported by some authors was attributed to the lower concentration of bupivacaine, in addition to the site and method of its administration [15,24]. The optimal dose and

concentration of bupivacaine (2 mg/kg) could be one of the reasons that our results were among those series that reported benefits in term of pain reduction. Some authors injected bupivacaine under the right dome of the diaphragm directly [18,25,26] or by using a low pressure spraying device [27]. In their opinion, the local anesthetic tended to get deposited away from the gallbladder bed because of intraperitoneal flux, hence, it was ineffective in relieving postoperative pain. We soaked the gelfoam with 0.5% bupivacaine and kept it in the gallbladder bed. This ensured that the drug remained in contact with the wound for a longer time. This appears to be the second reason for its efficacy in our study. The peak serum level of intraperitoneal bupivacaine is reached 20 to 30 min after its application and lasts for 2 to 24 h after surgery [6,28] and even 48h after surgery[29,30]. We could not measure the plasma concentration of bupivacaine, but several reports have shown that the range of mean plasma concentration (0.92–1.14 µg/ml) after the intraperitoneal administration of plain bupivacaine (100–150 mg) is well below the toxic concentration of 3 µg/ml [15, 29, 31]. In our study we did not observe any side effects attributable to the local anesthetic. We conclude that visceral pain is the more prominent type of pain after LC, and 0.5% bupivacaine (2 mg/kg)-soaked gelfoam in the gallbladder bed alone is effective in controlling both visceral and shoulder pain after LC, while parietal pain, although present in about two thirds of patients, is usually mild and injecting LA into port sites is not clinically effective.

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