Effect of pre-incisional and intraperitoneal bupivacaine on postoperative pain in laparoscopic cholecystectomy: a study from Karbala in Iraq

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ABSTRACT

INTRODUCTION: Laparoscopic cholecystectomy has increased dramatically over the past several years; its Postoperative pain is multifactorial in origin; therefore, multimodal therapy may be needed. The use of local anaesthetic has been suggested as good postoperative analgesia.

OBJECTIVE: To assess the effect of preincisional and intraperitoneal infiltration of bupivacaine on the post operative pain and analgesia requirement after Laparoscopic cholecystectomy.

METHODS: A total of 46 patients in need for laparoscopic cholecystectomy were allocated randomly in two groups, (bupivacaine group n=24) and (non bupivacaine group n=22). In bupivacaine group, a 20 ml of 0.25% bupivacaine was injected subcutaneously into the incisional sites and a 10 ml in the gallbladder bed. Whereas patients enrolled in the second group, non bupivacaine group, have not received such injections and kept only on the traditional pain killers.

RESULTS: The highest pain levels were experience during the 1st and 2nd postoperative hours and these levels were gradually diminished with time, The pain score was lower in bupivacaine group with a p-value < 0.05. Regarding rescue analgesia doses, the first dose had no statistically significant difference, while second dose was significant P=0.032 and its requirement is less in bupivacaine group.

CONCLUSION: The preincisional and intraperitoneal injection of bupivacaine is good analgesia in the immediate postoperative period and it reduce opioid and analgesia requirement in post operative period.

Key words: bupivacaine, postoperative pain, laparoscopic, cholecystectomy.

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INTRODUCTION

Laparoscopic approaches to surgery have increased dramatically over the past several years. Reasons for their popularity are improving postoperative pain and healing time as compared to open techniques which can result in earlier recovery and discharge from the hospital.[1] Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[2]

Uncontrolled postoperative pain may produce a range of detrimental acute and chronic effects. The attenuation of intra-operative pathophysiology that occurs during surgery through reduction of nociceptive input to the central nervous system (CNS) and optimization of preoperative analgesia may decrease complications and facilitate recovery during immediate postoperative period and after discharge from the hospital.[3]

Pain is a subjective feeling that is very difficult to be quantified on a single scale. Many scoring systems for pain are invented to achieve this goal, the three most popular are Numeric Rating Scale (NRS), Verbal Descriptor Scale (VDS) and Face Pain Scale (FPS). Visual Analog Scale (VAS) is another very simple one. NRS is used for adults with no cognitive impairment while FPS is used for cognitively impaired adults.[4,6] The Universal Pain Assessment (UPA) is a tool chart which contains NRS, VDS and FPS.[5] It is an intended tool to help patient care providers assess pain according to individual patient needs, explain and use 0-10 scale for patient self as-

sessment, Use the face or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.[5] (figure 1) So we can get the corresponding numerical rating which have simplicity, reproducibility, easy comprehensibility, and sensitivity to small changes in pain.[6]

Pain following laparoscopic cholecystectomy (LC) can be divided into three major groups: 1) Parietal pain caused by surgical incision; 2) Visceral pain originating from gallbladder bed and caused by visceral manipulation during the operation, and finally 3) Shoulder pain secondary to distension of diaphragm by neuropraxia of phrenic nerve.[7-8]

A multimodal approach to pain management involving the use of non-steroidal anti-inflammatory drugs, opioids, and local anaesthetic infiltration has been suggested as the optimal combination for laparoscopic surgery.[9]

Different local anaesthetic drugs have been used to reduce postoperative pain like peritoneal infiltration, instillation of ropivacaine or bupivacaine into the peritoneal cavity or subdiaphragmatic area, intraperitoneal spraying above the gall bladder and combined peritoneal peritrocal ropivacaine.[10-13] Intra-peritoneal ropivacaine nebulization was also used for pain relief after LC.[14] Most of the studies have used longer acting local anaesthetics like bupivacaine,[10,16] ropivacaine[8,15] or levobupivacaine[17] to provide pain relief.

The doses and the concentrations used were also variable. Seven studies have used bupivacaine with doses ranging from 70 to 140 mg; only one study had used ropivacaine 200 mg.[9] Narchi has found intraperitoneal local anaesthetic to be more effective in reducing pain up to 48 hours postoperatively in patients undergoing diagnostic laparoscopy.[18] Subsequent studies have failed to demonstrate the beneficial effect of intraperitoneal instillation of local anaesthetics in patients undergoing laparoscopic cholecystectomy;[19] However, there is a controversy about that. This study aimed to assess the effect of pre-incisional and intra-peritoneal bupivacaine on post operative pain and analgesia required after laparoscopic cholecystectomy.

METHODS

Setting of the study: A randomized controlled study was performed at Imam Al-Hussein Medical City in Karbala, Iraq from September 2015 to November 2015. The study was approved by the ethical committee at the hospital. All participants were asked to sign a written informed consent forms before participating in the study.

Inclusion criteria: All Patients who were above 20 years, diagnosed as gallbladder disease, in need for laparoscopic cholecystectomy under

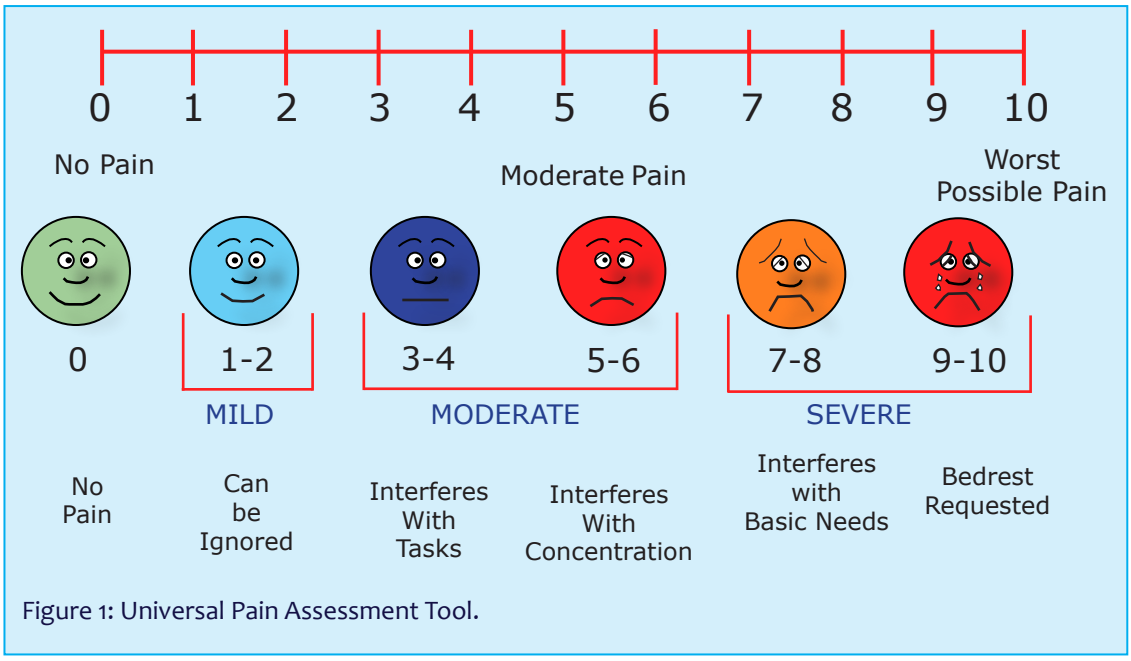

Figure 1: Universal Pain Assessment Tool.

general anaesthesia and had no exclusion criteria were enrolled in this study.

Exclusion criteria: We have excluded any patient who was obese (body mass index higher than 30 kg/ m2); had a history of opioid abuse, chronic pain, and previous laparotomy; his physical status fall in group III and IV according to the American Society of Anesthesiologists. Intra-operative decision to change to open cholecystectomy was also a reason for exclusion from this study.

Randomization: Patients were randomly allocated into two groups by simple randomization. We assigned a number for each patient sequentially according to his/her arrival to the theatre. Patients who coined with odd number were enrolled in group A, while those with even number were enrolled in group B. Assignment to each group was made by the theatre manager who was blinded to the type of drug used in each group. Group A had included patients who had received bupivacaine and group B had included patients who did not receive bupivacaine.

Primary and secondary end points: The primary end point of this study is to assess subjectively the severity of pain post LC. Incidence and severity of the intensity of pain postoperatively were measured at rest using the universal pain assessment tool (UPA). According to this score, we quantified on a scale of 0 to 10 occurence and severity of pain at 1st, 2nd, 4th, 8th and 12th hours after the end of operation. Assessment of pain was measured at rest, avoiding moments of coughing or movement in order to preclude the effect of visceral and diaphragmatic irritation on quantinity of pain during such events. Incidence of nausea and vomiting were evaluated by a "yes" or "no" question at the same time, the patients were asked if they had nausea or vomiting. If the answer was positive, the frequency was recorded. All assessments were done by house officer doctors who were tought how to do this job properly. Those doctors were blinded to the study and group assignments.

Patients could request for rescue analgesia and anti-emetic at any time after the operation. 100 mg tramadol as a first rescue dose, 50 mg pethidine as a second rescue dose was administered intramuscularly if pain score exceeded 3. For controlling emesis, we used metoclopramide 10 mg intramacularly.

Procedure: Patients in both groups had received the same premedication and the same anaesthetic agents. We used midazolam 0.02 mg/kg as premedication. General anaesthesia was induced by 2 mcg/kg fentanyl, followed by ketamine 0.5 mg/kg. Thiopental 3-5 mg/kg and atracurium 0.6 mg/kg were used to facilitate tracheal intubation. Anaesthesia was maintained with 0.7 to 1% Halothane and fentanyl 50 mcg every 30 minutes. Muscle relaxation was achieved with intermittent atracurium. Ventilation (tidal volume 8-10 ml/kg) was adjusted to maintain end-tidal carbon dioxide between 34 and 40 mm Hg. During operation, Patients were placed in 15-20 degree reverse Trendelenburg's position with left-side down tilting position.

Pneumoperitoneum was created with a closed or opened 10 mm trucar technique and LC was performed using four ports. The first, 10 mm port, was inserted through the supraumbilical site; the next, 10 mm port, was inserted in the epigastrium just below the xiphisternum under direct vision; the third, 5mm port, was inserted about 2.5-3 cm below the right costal margin in the midclavicular line; and the fourth, 5-mm port, was inserted in right anterior axillary line at the level of umbilicus under direct vision. The gallbladder was retracted via the epigastric trocar port.

During laparoscopy, intra-abdominal pressure was limited to 10-12 mmHg. The CO_2 was carefully evacuated at the end of surgery by manual compression of the abdomen with open trocars.

Before incising skin of patients in group A (bupivacaine group), a 20 ml of 0.25% bupivacaine was injected subcutaneously, 5 ml for each site incised, into the periportal fascia, muscle and parietal peritoneum. After removal of the gallbladder, 10 ml of 0.25% bupivacaine was injected into its bed. Whereas patients in group B have not got such injections. For reversal of muscle relaxation, 40 mcg/kg neostigmine and 20 mcg/kg atropine were administered and patients were transferred to the post anaesthesia care unit (PACU) after tracheal extubation.

The statistical analysis: We used SPSS package, SPSS version 22. For statistical analysis of the demographic data and for comparison of the two groups Chi square, fisher's exact test and the student t-test analyses were used to test significance. P value < 0.05 was considered statistically significant.

Table: 1. patients' char¬acteristics (age, gender and ASA classification).

Variable		Group A Bupivacaine	Group B Non Bupivacaine	P-Value*
Age (Year)	Mean±SD	42.29±130.09	36.23±10	0.092
Gender	Male No. (%)	4 (16.7%)	6 (27.3%)	0.384
	Female No. (%)	20 (83.3%)	16 (72.7%)	
ASA Classification	ASA1 No. (%)	14 (58.3%)	14 (63.6%)	0.713
	ASA2 No. (%)	10 (41.7%)	8 (36.4%)	

*P value <0.05 is Significant.

Table 2: Operative data: Systolic Blood Pressure SBP, diastolic blood pressure DBP, Heart rate HR, oxygen saturated pressure SPO2, Surgery and Recovery Time.

Variable (Mean ± SD)	Group A Bupivacaine	Group B Without Bupivacaine	P-Value*
Preoperative SBP	137.96±13.23†	141.55±9.20	0.296
Preoperative DPB	86.83±8.59	84.95±10.05	0.498
Preoperative HR	9.88±12.62‡	93.32±9.71	0.309
Preoperative SPO2	8.75±0.53**	98.45±0.73	0.124
Surgery Time	32.75±13.80	37.27±14.36	0.282
Recovery SBP	140.75±1.87	139.68±15.18	0.791
Recovery DBP	86.46 ±8.02	87.27± 13.31	0.801
Recovery HR	94.88 ±12.36	98.32± 15.78	0.413
Recovery SPO2	97.46 ±.050	98.68± 0.89	0.077
Recovery Time	9.46±4.38	11.09±6.73	0.331

*P value <0.05 is Significant
† mm mercury
‡ Beat /minute
** Percent
†† Minute

RESULTS

A total of 48 patients were assessed in this study, 24 patients in each group. Two patients in (group B) have developed ventricular ectopic beat during surgery and they received more opioid, lidocaine 100 mg as antiarrhythmic agents and changed halothane to sevoflorane so we excluded them from statistical analysis. There were no significant differences between the groups with respect to patient's characteristics and ASA classification. The bupivacaine (group A) and non bupivacaine (group B) did not differ significantly in mean age (42.29±13 vs. 36.23±10 years), Female patients comprised (83.3%) of the bupivacaine group (A) and (72.7%) of the non bupivacaine group (B), indicating no statistical significance in this regard (P = 0.384) **Table1.**

Group A and group B were similar regarding surgery time, recovery time, preoperative and recovery systolic, diastolic blood pressure, heart rate and SPO2. P value was > 0.05 (**Table 2**). Mean values for the universal pain assessment scale (UPAS) during rest in 1st, 2nd, 4th, 8th and 12th hours following operation are presented in (**Table 3**). The highest pain levels were experience during the 1st and 2nd postoperative hours and these levels were gradually diminished with time, it was lower in bupivacaine group (A), p-value < 0.005. No significant difference was found between the two groups during 4th, 8th and 12th hours (**Figure 2**). Regarding rescue analgesia doses, the first dose had no statistically significant difference between group A and B. Two patient in group A and eight patient in group B required second dose which was significant P=0.032 (**Table 3**).

Vomiting occurred with five patients in the bupivacaine group (A) and two in the non bupivacaine group (B) (**table 3**), who were then treated with 10 mg metoclopramide.

Table 3: Postoperative pain score assessment, rescue analgesia, nausea and vomiting analysis.

Timing		Group A	Group B	P-value*
st hour		4.58± 1.283	6.45±1.565	0.001
2nd hour		2.75±0.53	3.82±1.50	0.002
4th hour		1.92±0.881	2.00±0.756	0.733
8th hour		1.04±0.751	1.27 ±0.456	0.219
12th hour		0.50±0.511	0.36±0.492	0.362
First rescue analgesia dose	YES	17 (70.8%)	20 (90.9%)	0.139
	NO	7 (29.2%)	2 (9.1%)	
Second rescue analgesia Dose	YES	2 (8.3%)	8 (36.4%)	0.032
	NO	22 (91.7%)	14 (63.6%)	
Post Operative Nausea	YES	8 (33.3%)	8 (36.4%)	0.95
	NO	16 (66.7%)	14 (63.6%)	
Post Operative vomiting	YES	5 (20.8%)	2 (9.1%)	0.268
	NO	19 (79.2%)	20 (90.9%)	

*P value <0.05 is Significant

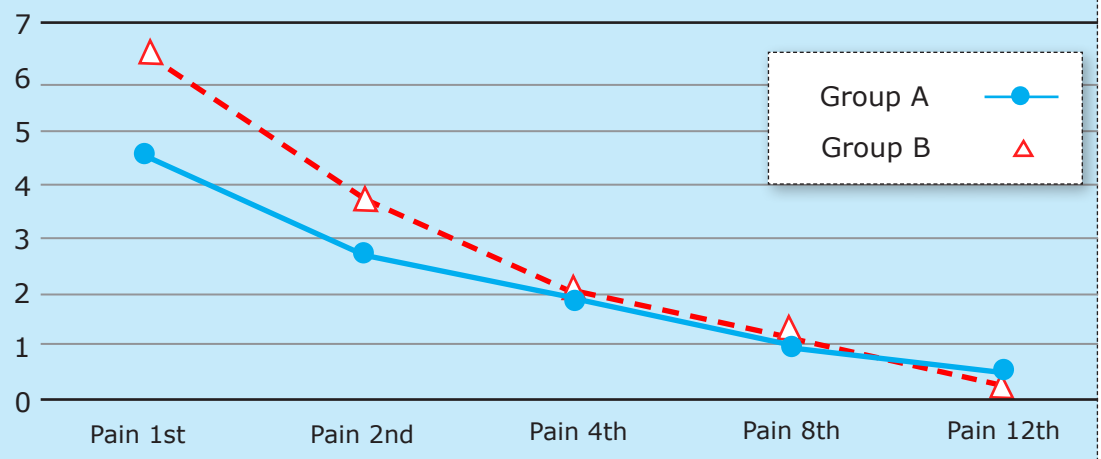

Figure 2. Trend of pain score in group A and Group B postoperativly.

DISCUSSION

Postoperative pain in LC is multifactorial in origin, and therefore, multimodal therapy may be needed to optimize pain relief.[8,10,11] In our study, we tried to control somatic pain by preincisional injection of bupivacaine, and to control visceral pain and part of shoulder pain by injecting bupivacaine into the gall bladder bed.

The mean pain score using universal pain assessment tool was lower in group A during the 1st and 2nd postoperative hours than in group B, p-value was < 0.005. Thereafter, no statistical difference was seen in the mean pain score between the two groups.

Patients in group B needed more 1st rescue analgesia, intramuscular tramadol 100 mg, than those in group A (90.9 % versus 70.8 %) but without statistical significance (p value = 0.139). However, the need for the 2nd rescue analgesia as intramuscular pethidine 50 mg, was much higher in group B than in group A, 36 % versus 8 % , with statistical significance (p value = 0.032); this result is similar to that of Bisgaard finding.[9]

In a review article by Jaime Ortiz et al, in-

filtration of ropivacaine or saline into the port incisions and intraperitoneally at several sites[22] has significantly reduced incisional pain during the first 3 hours post operatively but did not have any benefit on visceral or shoulder pain. Nausea was significantly less in the ropivacaine group when compared to the placebo group,[22] but in our study there was no significant difference with regard to nausea.

In a review article by Bisgaard et al[9] on LC, seven studies have showed that incisional local anesthetics provided superior analgesia and significantly decreased the amount of opioid used in the post-operative period, the results which is similar to our finding.

Coughlin et al has showed a significant improvement in postoperative pain at 4 hours and 24 hours when local anaesthetic agent was injected preemptively compared to placebo.[20] This result is consistent to ours with regards only to the first two hours but not thereafter. Our results were much closer to Yari et al who demonstrated that injecting a 20 ml of 0.25% bupivacaine at the beginning and the end of the LC can reduce visceral and shoulder pains during the first four postoperative hours.[21] The sustainable effect of the local anaesthetics used by Coughlin[20] and Yari[21] more than 2 hours can be explained by using them for larger volume of bupivacaine than we did in our study.

We did not report any significant complications in patients who were injected with bupivacaine in comparison to those who were not. Many other studies [11,18,20,21,22] have reached to the same conclusion proving that using bupivacaine in safe as well.

CONCLUSIONS

The pre-incisional and intra-peritoneal injection of bupivacaine is an easy, cheap, safe, and non-invasive method which provides good analgesia in the immediate postoperative period after laparoscopic surgery. However, further studies are needed on larger populations with larger volumes and concentrations of bupivacaine and also combination of bupivacaine and other analgesic drugs, to gain the maximum benefits of preincisional and intraperitoneal analgesic in post-operative pain treatment.

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Abbreviation list: Central Nervous System (**CNS**), Laparoscopic Cholecystectomy **(LC)**, Numeric Rating Scale **(NRS)**, Verbal Descriptor Scale **(VDS)**, Face Pain Scale **(FPS)**, Visual Analogue Scale **(VAS)**, Post Anaesthesia Care Unit **(PACU)**, Universal Pain Assessment Tool **(UPAT)**, Systolic Blood Pressure **(SBP)**, Diasystolic Blood Pressure **(DBP)**, Heart Rate **(HR)**, Saturated Partial Pressure of Oxygen **(SPO_2)**, and American Society of Anaesthesiologists **(ASA)**.

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