# The Effect of Preoperative Versus Postoperative Intra-Incisional Bupivacaine-Lidocaine Mixture Infiltration on Early Postoperative Pain after Laparoscopic Cholecystectomy

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## ABSTRACT

**Objective:** To compare the postoperative pain relief quality of intra-incisional local infiltration of lidocaine-bupivacaine mixture, pre- or post-laparoscopic cholecystectomy.

**Methods:** Our prospective and randomized investigation included 110 adult patients, of both genders, middle aged, classed I-II by the American society of anesthesiologists and scheduled for elective laparoscopic cholecystectomy after written informed consent and local ethics committee approval had been obtained at Prince Ali Bin Hussein Hospital, Karak-Jordan, during the period of January 2012 to July 2013. After induction of intravenous general anesthesia, patients were divided into two groups in a random manner. Group I received local infiltration prior to incision of 15ml of bupivacaine 0.25% mixed with 5ml of lidocaine 1%, subcutaneously, 14ml in the 10mm trocar site incisions and 6ml at the 5mm trocar site. Group II received the same volume; dose and division of local anesthesia incisional injection after the trocar sites were sutured. Postoperative pain quality was evaluated during the first six postoperative hours using the visual analogue scale, and the data was analyzed for significance.

**Results:** Mean postoperative pain score was significantly less in group II than in group I, especially at six hours where it was 3.1 and 1.1 in groups I and II, respectively ($p<0.05$). Postoperative morphine demand was 78.8% and 41.4% in groups I and II, respectively ($p<0.05$).

**Conclusions:** Intraincisional local infiltration after incision suturing is more effective than before incisions making, in managing postoperative pain after laparoscopic cholecystectomy.

**Key words:** Analgesia, Bupivacaine-lidocaine, Incisional, Morphine, Preemptive local infiltration.

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## Introduction

Less invasive surgical techniques occupy an important part in recent surgical practice. The introduction of laparoscopic procedures to general surgery has modified the perspective to the postoperative progression of patients.

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Laparoscopic cholecystectomy is the most frequent laparoscopic surgical technique done in most countries as an outpatient technique since the last 10 years at least.[1] Although the most important advantages of laparoscopic surgical techniques are less hospital stay, fast return to usual work activity and minimal discomfort, patients commonly complain of post-operative pain mainly by respiratory movements, coughing and movements during the first postoperative hours, which may prolong hospital admission, increase postoperative morbidity and delay patients discharge, all in all increasing the hospital costs.[2] In general, patients don't have severe pain after laparoscopic surgery. Traditional pain relief drugs in laparoscopic surgery have adverse effects. Narcotics for example induce nausea, vomiting and constipation. Post-operative pain after laparoscopic cholecystectomy can be moderate to severe with the need for non-steroidal anti-inflammatory drugs or opiates management, which may control the pain effectively.[3] Postoperative pain management is not a philanthropic issue; it has a crucial physiological role in postoperative outcome. Although opiates can manage early post-operative pain after laparoscopic cholecystectomy, their adverse effects including nausea and vomiting may delay hospital discharge. The different available post-operative pain management protocols can reduce the opiates administration in such cases.[4]

Post-operative pain management is one of the most important issues, which a surgeon seriously accounts for. More than 70% of subjects in the surgical wards after different types of non-laparoscopic surgery have severe pain and 75% of patients having acute or chronic pain still complain of pain later.[5] Diverse techniques for early postoperative pain management are needed to attain optimum control.[6] Patients are discharged home on the first postoperative day. It is a safe procedure and suitable as an outpatient intervention in properly selected subjects. Pain relief and patient comfort during the early postoperative time are important. Pain on the day of surgery is often reported as a diffuse abdominal, right upper quadrant and right shoulder. Reduction in postoperative pain after local anesthetic infiltration into the surgical incision was noticed in patients undergoing herniorrhaphy.[7] Although some maneuvers were performed using intra-incisional local anesthesia infiltration, the outcome regarding pain severity decrease and analgesic rescue were confusing.[8] Local anesthetic agents are increasingly administered for pain management. Application of local anesthetic drugs can be used at skin incisions or intra-peritoneal administration after laparoscopic cholecystectomy.In laparotomy with large incisions, this application is not suitable because a high dosage is required which may cause complications. This method has the benefit of having no opiate side effects which may lengthen postoperative hospital stay. Although bupivacaine as local anesthetic agent is administered during such technique, the timing and the route of infiltration of such local anesthetic are different between practitioners.

The aim of our investigation was to compare the effect of intra-incisional local anesthetic infiltration (bupivacaine-lidocaine mixture) between pre-incision making period and post-incision suturing period for the control of early post-operative pain relief after laparoscopic cholecystectomy.

## Methods

This prospective, study enrolled 110 adult patients, of both sexes, aged 31-44 years, classed I-II by the American society of anesthesiologists and assigned for elective laparoscopic cholecystectomy at Prince Ali Bin Hussein Hospital, Karak-Jordan, during the period between January 2012 and July 2013, after obtaining written informed consent from all participants and approval from our local ethical committee of Royal Jordanian Medical Services.

All patients were subjected to general anesthesia and induced by intravenous route using fentanyl 2mcg/kg, propofol 2.5mg/kg and atracurium 0.5mg/kg, after which a suitable endotracheal tube (through which a mixture of oxygen 2L/min with 1MAC of isoflurane was delivered) and an oral gastric tube was inserted.

Patients were ruled out from the study if laparoscopic cholecystectomy was switched to open technique. Subjects were divided in a random fashion into two groups. Group I (n=52) received intra-incisional local anesthetic infiltration of 15ml of bupivacaine 0.25% mixed with 5ml of lidocaine 1% (a total volume of 20ml solution), subcutaneously, divided in 14ml peri-the 10mm trocar sites at the two intra-proposed incisions (7ml for each 10mm port) and 6ml peri-the 5mm trocar sites at the two intra-proposed incisions (3ml for each 5mm port), before incisions were made. Group II (n=58) received the same volume, dose and division of bupivacaine 0.25%-lidocaine 1% mixture, subcutaneously and intra-incisionally after incisions had been sutured at the end of the surgical intervention. Patients were monitored for heart rate, oxygen saturation, non-invasive blood pressure and end-tidal $CO_2$. Regarding surgical technique, standard laparoscopic cholecystectomy using the 4-port trocar sites procedure was achieved by one team of surgeons. All patients received postoperative diclofenac sodium 75mg intramuscularly at the end of surgery with oral diclofenac sodium 50mg twice daily during the postoperative 24 hours. Morphine was given on demand 1-2mg intravenously in the recovery room and 5mg intramuscularly in the surgical ward.

All patients were assessed during the first postoperative 24 hours for abdominal pain frequency and intensity using the visual analogue scale (VAS, 0-10cm). VAS was recorded at 15 min (in the recovery room), two hours, six hours,10 hours and 24 hours (in the surgical ward) postoperatively. The number of patients demanding postoperative morphine was reported in both groups.

Parametric data was compared using variance (ANOVA). Student's t test was used to assess continuous variables. A probability value (p) less than 0.05 was considered statistically significant.

## Results

There were no significant differences between the two groups in terms of number, age, sex, weight, ASA classification and duration of surgery (p>0.05). Most of the studied subjects were females (87, 79, 1%, p<0.05), 48.3% in group I (42) and 51.7% in group II (45), p>0.05. Mean duration of surgery was not significantly different between the two groups as it was 52.5 minutes in group I and 50.7 minutes in group II (p>0.05) (Table I).

**Table I:** Patients demographics (mean+/-SD, range, no.)

| | G I | G II | P |
|---|---|---|---|
| n= | 52 | 58 | >0.05 |
| ASA(no) | | | |
| I | 41 | 46 | >0.05 |
| II | 11 | 12 | >0.05 |
| Weight(kg)(range) | 55-70 | 60-75 | >0.05 |
| Age(yr)(range) | 30-44 | 31-42 | >0.05 |
| Sex (no) | | | |
| M | 10 | 13 | >0.05 |
| F | 42 | 45 | >0.05 |

The mean postoperative pain severity score was 3.4 at 15 minutes in group I while it was 1.7 in group II (p<0.05). At two hours, the mean postoperative pain intensity score was 3.7 in group I and 1.5 in group II (p<0.05).The difference between the two groups regarding mean postoperative pain severity score was significant as it was 3.1 in group I and 1.1 in group II, both at six hours postoperatively (p<0.05). At 10 hours, postoperatively, the mean postoperative pain intensity score was 2.5 in group I and 1.0 in group II (p<0.05). This significance continues until 24 hours postoperatively, where the mean postoperative pain severity score was 1.9 in group I and 0.7 in group II (p<0.05). Postoperative abdominal pain was significantly reduced in group II than in group I. This discrepancy continued from 15 minutes postoperatively for the first 24 hour (Table II). The mean pain score in group I increased from 15 minutes postoperatively until six hours postoperatively then began to decrease until 24 hours postoperatively. In group II, mean postoperative pain score decreased from 15 minutes postoperatively until 24 hours postoperatively. In group I, the mean pain score increased to more than 3 while in group II, the mean pain score did not exceed 2. The difference between the mean postoperative pain scores in both groups was in the following order: 2.0 at six hours, 1.5 at 10 hours, 2.2 at two hours and 1.7 at 15 minutes.

Postoperative morphine demand during the first postoperative 24 hours was 78.8% (41) in group I and was 41.4% (24) in group II ($p<0.05$) (Table II). In the recovery room, 10 and 18 patients in groups I and II needed 2mg morphine while 31 and 6 patients in groups I and II needed 5mg morphine. Mean morphine demand was 4.3 and 2.8 mg in groups I and II.

**Table II:** Postoperative pain quality (mean+/-SD, percentage)

| | G I | G II | P |
|---|---|---|---|
| VAS (mean,+/-SD) at | | | |
| 15 min | 3.4+/-0.6 | 1.7+/-0.7 | <0.05 |
| 2 h | 3.7+/-0.7 | 1.5+/-0.9 | <0.05 |
| 6 h | 3.1+/-0.5 | 1.1+/-1.0 | <0.05 |
| 10 h | 2.5+/-0.4 | 1.0+/-0.6 | <0.05 |
| 24 h | 1.9+/-0.5 | 0.7+/-0.3 | <0.05 |
| Morphine demand (%, no) | 78.8%(41) | 41.4%(24) | <0.05 |
| Mean morphine consumption (mg) | 4.3 | 2.8 | <0.05 |

## Discussion

Laparoscopic cholecystectomy is the treatment of choice for symptomatic cholelithiasis. Laparoscopic cholecystectomy is a frequent outpatient surgical procedure. The postoperative pain accompanied with this less invasive surgical intervention is commonly less severe, lasting less time than that after an open traditional cholecystectomy. Postoperative pain of this situation is an important issue mainly in the early postoperative period, causing lengthening of postoperative hospital stay. This type of postoperative pain attains a peak during the first hours and a decrease in time.[9] Pain post-laparoscopic cholecystectomy has a multifactorial origin. It originates from the incision area (somatic pain), from the gall bladder site (visceral pain) and due to pneumoperitoneum. Source of pain following laparoscopic techniques has controversy. Placement of trocars via the abdominal wall is the primary one, although intraperitoneal dissection and $CO_2$ insufflations (with distension of abdominal wall and lengthened elevation of diaphragm) cause the most of pain. Surgeons are aware of the effect of opiates in postoperative analgesia but their adverse effects diverse. Most severe adverse effects are confusion, respiratory depression, vomiting and weakness, and minor ones include constipation, itching and mouth dryness, which reduce patient's satisfaction, and at the same time causes the wrong idea that having pain is better than having postoperative opiate complications. Any technique with the ability to achieve pain relief without adverse effects will be more wise to be used. Early pain is a complex process including various pain parts due to various pain mechanisms as surgical trauma of abdominal wall, intra-abdominal wall due to gall bladder removal and abdominal distension.

The association of somatovisceral local anesthetic protocols decreases incisional pain after laparoscopic cholecystectomy. Local anesthetic drugs cause antinociception by acting on the nerve membrane. They reversibly reduce the rate of depolarization and repolarization of excitable membranes (nociceptors).[10] There are various local anesthetic agents administration routes, such as local parietal anesthesia, for potent controlling of postoperative pain.[11] The use of local long lasting anesthetic decreases postoperative pain. Bupivacaine is one of the most available effective local anesthetics in Jordan. Patients can have additional advantage from an intra-incisional local tissue infiltration of anesthetic. Bupivacaine has a half life of 2.5 to 3.5 hours and has been shown to attain pain relief for a mean of six hours. The limit of safety of bupivacaine need for anesthesia is large. At the upper margin of 2.5mg/kg, 100 mg of bupivacaine may be administered safely in a patient with a lean body mass of 40 kg.

Regarding timing of local anesthetic administration during surgery, there are questions to be answered. Some have demonstrated no significant difference between the time of discharge and postoperative pain[12] while others showed that the timing of local anesthetic administration is important.[13] In our investigation, we assessed intraincisional infiltration of combination between bupivacaine and lidocaine, before incision making and after incision suturing.

We showed that intraincisional infiltration of bupivacaine mixed with lidocaine after incision suturing is a more potent route than before incision making route in managing

postoperative abdominal pain after laparoscopic cholecystectomy. Our conclusions were in accordance with those of Sarac *et al.*[14] who compared incisional infiltration before surgery and incisional infiltration of local anesthetic at the end of surgery. They showed more significant decrease in postoperative abdominal pain after intraincisional local infiltration of the anesthetic agent at the end of surgery. In their work, the mean pain intensity was 5.9 and 5.1 in the preoperative and postoperative groups, respectively. In the preoperative group, 50% of patients and 28% of patients in the postoperative group, needed analgesics ($P<0.05$).[14] Seyyed *et al*. showed that 65% of patients responded effectively to local anesthetic infiltration for laparoscopic cholecystectomy without any requirement for non steroidal anti-inflammatory agents or opiates. In the same group study, only 5% needed opiates and 35% needed NSAIDs. The administration of local anesthetic infiltration at the end of surgery delayed the time of the first administration of opiates and NSAIDs.[15] In their control group which did not receive local anesthetic infiltration, 85% of patients needed opiates and 15% of patients needed NSAIDs. Local anesthetic agents used adequately may reduce the requirements for opiates in some situations and abolishes their need in others, which is one of the main techniques for reducing adverse effects of opiates. Others who used pre-incision local infiltration of levobupivacaine, demonstrated the significant decrease of pain and analgesic needs post-laparoscopic cholecystectomy.[16] Due to pain relief actions of local anesthetic drugs, some hormonal modifications were useful as reduced plasma level of cortisol may decrease the duration of inflammatory process. Although minimal invasive surgery has reduced pain, it is not painless. We expected the action of bupivacaine-lidocaine mixture to stop after six to eight hours, there was no increase in pain severity at 24 hours postoperatively. The main action of bupivacaine was amelioration of pain peak during the first six hours after surgical intervention. If laparoscopic cholecystectomy is to be performed as an outpatient surgery, early postoperative pain must be managed well.

This kind of local anesthesia infiltration may decrease nursing and hospital costs, has less adverse effects and has no sedative action leading to early recovery. Our study has limitations. Namely, it has small sample, it is confined only to laparoscopic cholecystectomy and to patients of good medical conditions with adequate body mass index.

## Conclusion

Intraincisional infiltration of bupivacaine mixed with lidocaine is more effective when infiltrated after incisions were sutured than when infiltrated before incisions were made in managing postoperative pain after laparoscopic cholecystectomy, regarding pain perception and postoperative morphine demand.

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