Original Research Article

Randomized controlled study of effectiveness and timings of bupivacaine at port site in managing pain after laparoscopic cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy now a day is considered a day care procedure, but postoperative pain, requiring injectable analgesics is one of the hurdles in performing it as day care. Aim was to assess the effectiveness of port site instillation of bupivacaine in reduction of post-operative pain after laparoscopic cholecystectomy.

Methods: The study was conducted from November 2013 to November 2015 on 120 patients undergoing elective laparoscopic cholecystectomy at SGRDIMSAR, Sri Amritsar. The study was a randomized controlled in which patients were randomly allocated into 3 groups of 40 patients each. In group 1, pre-incisional local infiltration of the port sites with bupivacaine was done throughout all the layers of the abdominal wall. In group 2, local infiltration of the port sites with bupivacaine was done after the completion of surgical procedure and before the closure of skin. In Group 3 no local infiltration was done. The study was evaluated using Visual analog scale for a period of 24 hours post operatively.

Results: Instillation of bupivacaine at the port sites in laparoscopic cholecystectomy irrespective of the timing of instillation is an effective method of achieving pain control in the post-operative period as long as 24 hours after surgery.

Conclusions: Instillation of bupivacaine at the port sites in laparoscopic cholecystectomy is simple, safe, and without adverse effects and local anesthetics should be considered for instillation in all patients at the beginning and at the end of laparoscopic procedures.

Keywords: Bupivacaine, Laparoscopic cholecystectomy, Postop pain, Port site

INTRODUCTION

Laparoscopy is an excellent means to minimize the trauma and agony of the patient following surgery, however there still remains some challenge to minimize the post-operative pain in the patients. The pain reaches a maximum level within 6 hrs of the procedure and then gradually decreases over a couple of days, but varies considerably between patients.^{1,2}

The etiology of pain is complex, including damage to abdominal wall structures, the induction of visceral

trauma and inflammation, and peritoneal irritation because of CO₂ entrapment beneath the hemidiaphragms, neuropraxia of the phrenic nerve caused by distention of the diaphragm during gas insufflations, and/or acid milieu created by the dissolution of CO₂. Postoperative pain can be partially or completely relieved by one of these methods (a) Systemic analgesics and adjuvant drugs, (b) Regional analgesia with local anesthetics, (c) Regional analgesia with epidural or intrathecal opioids, (d) Regional analgesia with combined local anesthetics and opioids, (e) Electrical analgesia achieved with transcutaneous electrical stimulation or

electroacupuncture. Local anesthetic instillation at the end of laparoscopy prevents postoperative pain and dramatically decreases the need for morphine. This technique improves patient comfort, shortens the stay in the postoperative care unit and decrease nursing care in the ward.³

When administrated before surgery, infiltration of local anesthetics can decrease anesthetics and analgesic requirement during surgery as well as reduce the need for opioid containing analgesic postoperatively.⁴

Our controlled study aimed at assessing the effect of preincisional vs preclosure port site instillation of bupivacaine in reduction of post-operative pain after laparoscopic cholecystectomy.

This study aimed to provide impetus for further research and help in performance of laparoscopic cholecystectomy as a day care procedure. Aim of the study was to assess the effect of port site instillation of bupivacaine in reduction of post-operative pain after laparoscopic cholecystectomy. Objectives of the study was to study the effect of bupivacaine will be measured in terms of: Severity of post-operative pain and the amount of analgesic usage post operatively, to study the cost effectiveness of using bupivacaine against the conventional use of opioid drugs and to study the pain outcome amongst pre-incisional vs pre-closure vs control groups.

METHODS

The present study was conducted from November 2013 to November 2015 on a group of 120 patients diagnosed to have symptomatic cholelithiasis and who underwent elective laparoscopic cholecystectomy under General Anaesthesia at the department of surgery at Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Sri Amritsar. The diagnosis of cholelithiasis was made on the basis of clinical examination and ultrasonography.

The study was a randomized controlled in which patients were randomly allocated into 3 groups of 40 patients (group 1, 2 and 3) each.

The whole procedure and risks involved were fully explained to the patient and well informed and written consent in vernacular language was taken.

In group 1, pre-incisional local infiltration of the port sites with 20 ml of 0.5% bupivacaine was done throughout all the layers of the abdominal wall (till peritoneum).

In Group 2, local infiltration of the port sites with 20 ml of 0.5% bupivacaine was done after the completion of surgical procedure, and just before the closure of skin.

Bupivacaine instillation in both groups 1 and 2 was allocated according to the diameter of the trocar; 7 ml for 10 mm port and 3 mL for 5 mm port.

In Group 3 no local infiltration was done and it was treated as the control group. The study was evaluated using Visual analog scale for a period of 24 hours post operatively.

Anaesthetic properties of bupivacaine

(a) The onset of action with bupivacaine is rapid and anesthesia is long lasting. The duration of anesthesia is significantly longer with Bupivacaine than with any other commonly used local anesthetic.

(b) Bupivacaine is approximately 3-4 times more potent than lidocaine and 8 times more than procaine.

(c) The duration of action for local anaesthesia is 2 -3 times longer than that of mepivacaine or lidocaine and 20-25% longer than that of tetracaine. It's action last for upto 6 hours.

(d) Maximum safe dose: 3 mgkg⁻¹.

The visual analogue scale (VAS)

The visual analogue scale uses a straight line with extremities of pain intensity on either end. The line is typically 10 cm long with one end defined as "no pain" and the other end being "excruciating unbearable pain". The line can be either vertical or horizontal. The patients are asked to place a mark on the line to describe the amount of pain that they are currently experiencing. The distance between the end labeled "no pain" and the mark placed by the patient is measured and rounded to the nearest centimeter. To assist in describing the intensity of pain, words can be placed along the scale (e.g., mild, moderate, or severe).

RESULTS

Repeated measure ANOVA and post hoc tests showed that the overall difference in mean pain scores on VAS scales measured at different time intervals post operatively was significant between the group that did not receive bupivacaine (group 3) and those that received (group 1 & 2) with a p value of 0.00.

However there was no statistically significant difference in the mean pain score in between the pre incisional & pre closure Group (p =0.455)

Therefore, bupivacaine provided a substantial reduction of pain intensity up to 24 hours postoperatively and this was found to be statistically significant.

The timing of anaesthesia however was found to be statistically insignificant in terms of preclosure vs pre incisional instillation of the port sites.

The mean duration of hospitalization amongst all the three groups was 3.49 days & was 3.23 days for group 1, 3.68 for group 2 & 3.58 days for group 3. The mean range was 1-6 days.

There was no statistical difference in the mean duration of hospitalization amongst the three groups. (F= 1.748, P= 0.179).

Figure 1: VAS score in three groups at different time intervals.

Table 1: VAS score.

Time	Group 1 Mean±SD	Group 2 Mean±SD	Group 3 Mean±SD	Gp 1 vs 2 (p value)	Gp 1 vs 3 (p value)	Gp 2 vs 3 (p value)
Baseline (0 Hrs)	4.38±1.10	4.73±1.09	6.63±1.64	0.455	<0.001**	<0.001**
30 mins	5.05±1.03	4.58±0.74	7.38±1.055	0.072	<0.001**	<0.001**
4 hrs	4.65±0.97	4.58±0.87	6.30±0.85	0.927	<0.001**	<0.001**
8 hrs	4.60±0.95	4.33±1.40	5.78±0.76	0.489	<0.001**	<0.001**
16 hrs	3.60±1.23	3.35±0.92	4.90±1.29	0.603	<0.001**	<0.001**
24 hrs	2.95±0.95	2.95±1.01	4.30±1.11	1.00	<0.001**	<0.001**

**p<0.001; Highly significant.

Table 2: Duration of hospitalization.

Group	N	Range	Duration (HOURS) Mean±SD	ANOVA [#]	Comparison	P value [#]
Group 1	40	1-5	3.23±0.92	F = 1.748; P = 0.179; NS	Group 1 vs 2	0.181 ^{NS}
Group 2	40	2-6	3.68±1.07		Group 1 vs 3	0.352 ^{NS}
Group 3	40	1-6	3.58±1.35		Group 2 vs 3	0.917 ^{NS}

p > 0.05; Not significant; *p<0.05; Significant.

Table 3: Time of giving first analgesic.

Group	N	Range	TIME Mean±SD	ANOVA [#]	Comparison	P value [#]
Group 1	40	0-24	9.83±6.36	F = 18.431; P <0.001**	Group 1 vs 2	0.977 ^{NS}
Group 2	40	0-24	9.55±7.03		Group 1 vs 3	<0.001**
Group 3	40	0.5-18	2.66±4.15		Group 2 vs 3	<0.001**

p > 0.05; Not significant; **p<0.001; Highly Significant.

Figure 2: Mean duration of hospitalization.

Figure 3: Total amount of average analgesic doses consumed.

The range for timing of giving first analgesic was between 0-24 hours in groups 1 & 2 and 0.5 – 18 Hours in group 3, i.e. some of the patients needed analgesia right after extubation although bupivacaine instillation had been done.

The mean timing for giving first shot of analgesic was comparable in the preincisional & Pre closure group i.e 9.83 & 9.55 hours respectively, however it was significantly lower in the control group i.e. 2.66 hours ($p < .001$).

Bupivacaine instillation at the port site, irrespective of the timing of anesthesia, significantly lowered the time needed for giving the first analgesic dosage.

Figure 4: Total amount of average analgesic doses consumed.

Table 4: Total analgesics given.

Group	N	Range	Number of analgesics, Mean±SD	ANOVA [#]	Comparison	P value [#]
Group 1	40	0-5	2.53 ± 1.198	F = 29.915; P < 0.001**	Group 1 vs 2	0.148 ^{NS}
Group 2	40	0-5	2.03 ± 1.271		Group 1 vs 3	<0.001**
Group 3	40	2-6	4.00 ± 1.086		Group 2 vs 3	<0.001**

$p > 0.05$; Not significant; ** $p < 0.001$; Highly Significant.

Table 5: Shoulder tip Pain.

Shoulder tip pain	Group 1	Group 2	Group 3
Present	3 (7.5%)	1 (2.5%)	4 (10%)
Absent	37 (92.5%)	39 (97.5%)	36 (90%)

$\chi^2 = 1.875$; $df = 2$; $p = 0.392$; Not Significant.

Figure 5: Incidence of shoulder tip pain.

The average amount of total analgesics used in the control group 3 was significantly higher compared to the other two groups 1 and 2. But there was no significant difference among group 1 & 2 in terms of total number of analgesic dosages ($p > 0.05$).

Postoperative shoulder tip pain was present in all three groups, 3 patients in the pre incisional group 1 in the pre closure group & 4 patients in the control group complained of shoulder tip pain postoperatively.

However chi square test yielded that the results were insignificant with a p value = 0.392.

Table 6: Postoperative nausea.

Nausea	Group 1	Group 2	Group 3
Present	0	0	4 (10%)
Absent	40 (100%)	40 (100%)	36 (90%)

$\chi^2 = 8.276$; $df = 2$; $p = 0.016$ Significant.

Post-operative nausea was seen in 4 patients in the control group, and none of the patients had nausea in the preincisional and preclosure group.

Hence bupivacaine instillation had a significant effect on postoperative nausea. ($p = 0.016$).

None of the patients experienced post-operative vomiting. In this study no side effects were observed with the use of bupivacaine.

Table 7: Incidence of post-operative vomiting.

Vomiting	Group 1	Group 2	Group 3
Present	0	0	0
Absent	40 (100%)	40 (100%)	40 (100%)

Figure 6: Incidence of postoperative nausea.

DISCUSSION

Laparoscopic cholecystectomy is now considered as the gold standard approach to symptomatic cholelithiasis.⁵ Although laparoscopic surgery, compared with open procedures, may be associated with diminished surgical trauma response and shortened convalescence, early postoperative pain after laparoscopic procedures is a frequent complaint. Peripheral use of local anesthetics for postoperative pain relief is, in this context, an attractive method, which in theory may improve early pain control and minimize the need for opioids.

Even within the same type of procedure, pain after laparoscopic surgery may vary in quality and localization and is reported in several trials to be incisional, intra-abdominal, or referred (shoulder tip).

The analgesic effect of minimizing the size of port incision has been evaluated in multiple randomized studies. Aitola et al randomized patients to N₂O or CO₂ insufflation to evaluate any difference in pain indices.⁶

VAS scores

We observed a significant reduction in overall pain scores in the study groups 1 and 2 for up to 24 hours, which is consistent with a previous randomized control trial by Alexander DJ et al in which post-operative pain scores were significantly lower in group receiving periportal peritoneal bupivacaine for pain relief after laparoscopic cholecystectomy, as compared to controls.⁷

Hasaniya et al studied the effect of preincisional bupivacaine instillation and concluded that the mean pain scores were lower as compared to controls at 4th and 24th hour postoperatively.⁸

Conflicting results have been reported by Ke et al stating that the popular practice of infiltrating bupivacaine at time of incision closure does not offer any benefit in the control of pain after laparoscopy.⁹ A Cochrane review was published in 2014 in the wiley online library,

reviewing a total of 26 papers on grounds of wound infiltration with local anaesthetics for laparoscopic cholecystectomies.¹⁰ In the review, the authors have concluded that serious adverse events were rare in studies evaluating local anaesthetic wound infiltration (very low quality evidence). There is very low quality evidence that infiltration reduces pain in low anaesthetic risk people undergoing elective laparoscopic cholecystectomy. However, the clinical importance of this reduction in pain is likely to be small. Studies carried out by Ashraf M et al, Jhonson et al, Ke et al, Saff et al, Ure et al, Deans et al and Maier et al compared bupivacaine with saline; procedures included were diagnostic and operative gynecological laparoscopy, cholecystectomy, and hernia repair.¹²⁻¹⁷ The local anesthetic was infiltrated subcutaneously, subfascially, or preperitoneally or into all layers of the abdominal wall, including the cutaneous tissues, muscle, and parietal peritoneum.¹¹⁻¹⁷ The concentrations used were between 0.125% and 0.5%, in volumes between 5 and 60 mL with a mean dose of 76 +/-48 mg. Infiltration of port sites was performed preoperatively in two.^{13,14} Overall, only 2 of the 7 trials were positive for at least one of the evaluated pain measures.¹² Only the study by Johnson et al showed significant degree of pain control with local anesthetics.¹²

In all the seven trials no effect on supplemental analgesic consumption was observed. No obvious relationship was apparent between application site, dose of the local anesthetic, and degree of obtained pain relief.

Timing of anaesthesia

Table 8: Timings of anaesthesia and its result in different studies.

Study	Timing of anaesthesia	Results
Our Study	Preclosure vs Pre incisional	Pre incisional = Pre closure
Lee et al ¹⁸	Pre incisional vs pre closure	Y (pre incisional > pre closure)
Sarac et al ¹⁷	Pre incisional vs preclosure	Y (pre incisional > pre closure)
Uzunkoy et al ¹⁹	Pre incisional vs pre closure	Pre incisional = Pre closure

In our study the timing of local infiltration was found to be insignificant, i.e similar pain scores were obtained with both preincisional and preclosure infiltration of bupivacaine. This is in accordance with Uzunkoy et al but in contrast to the study by Sarac et al Lee et al.^{17,18}

Timing of giving first rescue analgesia

The timing of giving first analgesic dosage in our study group was significantly less as compared to the control group, this is consistent with the studies carried out by Maharajan et al.²⁰

Total analgesic requirement

We did find an appreciable difference in total postoperative analgesic requirement between the control and bupivacaine group and this was consistent with the findings that of Bisgaard et al in a randomized control study.²¹

Duration of hospitalization

In our study we found that instillation of bupivacaine at port sites did not have much effect on the post-operative stay in contrast to studies by Yu-Yin Liu et al and Paulson J et al who found significantly shorter hospital stay than the control group.^{22,23}

The longer duration of hospitalization in our study can be attributed to other factors related to the surgery, i.e. all patients are inserted abdominal drains as a standard protocol & in our wards removal of the drain is done at the 2nd to 3rd day post operatively. However, individually some patients were discharged on the same day in both the study groups.

Shoulder tip pain

Postoperative shoulder tip pain was observed equally in all the three groups. There was no overall statistically significant difference in the occurrence of shoulder tip pain.

Pavlidis et al obtained similar results with an unchanged incidence of shoulder tip pain.²⁴

Side effects/toxicity

In our study we did not observe any side effects of bupivacaine which is consistent with the studies of T. Callesen et al and Narchi et al who also in their study found no signs of local anesthetic toxicity.^{25,26}

Post-operative nausea vomiting (PONV)

We observed that none of our study group cases complained of post-operative nausea in comparison to 4 controls.

None of the patients in our study experienced post-operative vomiting.

CONCLUSION

To conclude, instillation of bupivacaine at the port sites in laparoscopic cholecystectomy irrespective of the timing of instillation is an effective method of achieving pain control in the post-operative period as long as 24 hours after surgery. This technique is simple, safe, and without adverse effects and local anesthetics should be considered for instillation in all patients at the beginning and at the end of laparoscopic procedures. It is likely to

be cost effective, because it decreases post-operative usage of NSAIDS or opioids, and helps in better resource utilization in the ward for treatment of postoperative pain and helps the surgeon to provide a more comprehensive and comfortable post-operative stay.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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