Effect of Wound Infiltration with Bupivacaine after Laparoscopic Cholecystectomy – A Randomized, Controlled Trial

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ABSTRACT

Background and Objective: Adequate post-operative pain management can improve surgical outcome. Patients undergoing surgery can be affected socially, psychologically, economically with undertreated pain. We aimed to evaluate the effect of 0.25% bupivacaine infiltration on postoperative pain, analgesic requirement, satisfaction level, hospital discharge and quality of life after laparoscopic cholecystectomy.

Methodology: Fifty eight patients undergoing laparoscopic cholecystectomy were enrolled and randomized in two groups – placebo and intervention. Patients were infiltrated with 10 ml 0.25% bupivacaine in intervention and 10 ml 0.9% normal saline in placebo group. Post-operative pain was managed with morphine using Patient Controlled Analgesia (PCA). Pain intensity was assessed on the matrix of visual analogue scale and verbal rating scale up to 12 post-operative hours. This study also assessed its effect on analgesic requirements, hospital stay, patient satisfaction level after 24hours, pain score on discharge, time taken to return to job and quality of life (on 15th and 30th post-operative day).

Results: It was revealed 0.25% bupivacaine can lower post-operative pain up to six post-operative hour of performing laparoscopic cholecystectomy. Total analgesic requirement was also reduced (p= 0.0003) with decreased side effect like vomiting (p= 0.0002). However, satisfaction and quality of life were not affected by bupivacaine infiltration in this study.

Conclusion: 0.25% Bupivacaine infiltration offered more effective management of postoperative analgesia with decreased analgesic requirement and less incident of vomiting. But it was not effective after long duration in terms of satisfaction level, hospital discharge, time to return to job or quality of life.

Keywords: Bupivacaine, Hospital Stay, Laparoscopic Cholecystectomy, Morphine, Opioid, Post-operative Pain, Pain, Patient Satisfaction, Patient Controlled Analgesia, Quality of Life, Surgical Outcome.

I. INTRODUCTION

Surgical interventions have achieved advancements, precision, and excellence in recent years. Newer metrics are being assessed for improvement of quality performance. Pain is one of these metrics which is related with post-operative outcome [1]. But still ‘pain free surgery’ is the word the world is still chasing. Effective relief of pain is utmost importance to anyone who is undergoing surgery. Some misbeliefs are considered that it will disappear with healing of wound. Instead, a consequence of evolving events is triggered at spinal, peripheral and cerebral level [2]. Thus, magnitude of post-operative pain is misjudged by health care providers. A standardized comparison by German Researchers showed that, the severity of pain following laparoscopic procedures was significantly higher in compared to thoracic and abdominal procedures. Even, patients received relatively low doses of opioids post-operatively or did not receive at all (72%) [3]. Poor management can contribute to medical conditions which may be life threatening [4], [5]. Pain management post-operatively is not only a humanitarian task which reduce patient’s sufferings, but also affects post-surgery mobility and mortality [6]. In addition, economic burden increased considerably directly as extra healthcare cost and indirectly as a result of absenteeism, decrease production and welfare payments in some countries [7]. To confront the challenge of undertreated post-operative pain, different treatment modalities and strategies are evolved and
implemented over years [8]. Wound infiltration is one of these techniques used with another analgesic regimen. Effect of peripherally applied local anesthetic, such as bupivacaine, may differ with the sites of application, such as intraperitoneal instillation, trocar and port site infiltration, and visceral infiltration [9].

This study aimed at evaluating if wound infiltration may have effect after laparoscopic cholecystectomy for management of post-operative pain, patient satisfaction with minimal hospital stays and early return to normal life and thus improve quality of life.

II. MATERIALS AND METHODS

This study was reviewed and approved by Institutional Review Board of Bangabandhu Sheikh Mujib Medical University. From December 2018 to May 2019, 58 patients undergoing laparoscopic cholecystectomy were enrolled, of which 29 patients received placebo and 29 patients received intervention. For 13 patient’s determination of the study end point was not possible and therefore they were excluded from the analysis. At the end of the research the evaluable patients were a total of 45 (Fig. 1).

Randomization was done by online software “Sealed envelope” into framework of “block of four”. These blocks were again divided into two comparable groups. So, in each block 2 patients were in intervention and 2 placebo group.

Tab Bromazepam 3 mg at night before the day of operation was prescribed. Same protocol was followed in all patients for induction, maintenance and recovery from general anesthesia. At the end of laparoscopic cholecystectomy, all 4 ports were subcutaneously infiltrated with 10 ml 0.9% normal saline in Placebo group and 10 ml 0.25% bupivacaine in intervention group. A 10 mm disposable syringe with 29 G needle was used for this purpose.

Patients were managed with inj. Morphine (1 mg/ml) through patient controlled analgesia for pain. Loading dose 3 mg and PCA dose 1 mg was given. Lockout interval was 30 minutes. Maximum dose of Morphine was 4 mg in 4 hours.

Outcome variables such as pain intensity with VAS and VRS, systolic and diastolic blood pressure, respiratory rate sedation score, total analgesic requirement and side effects were recorded up to 12 post-operative hours.

Patient’s satisfaction level was assessed with “Revised American Pain Society Patient Outcome Questionnaire (APS-POQ-R)” after 24th post-operative hour. Pain intensity with VAS on discharge day was evaluated and the duration of post-operative hospital stay was counted before discharge.

Quality of life was assessed with ‘The Gastrointestinal Quality of Life Index’ on 15th and 30th postoperative day along with time taken to return to job or normal daily activities on telephone interview.

Data analysis was done using Microsoft Office Excel 2013 on Windows 10. Pain intensity, systolic and diastolic blood pressure, sedation score, analgesic requirement, time duration for hospital stay, satisfaction level and quality of life was investigated using Independent Students T test, where variance of gender and incidence rate of side effects were analyzed with Chi-squared Test. Correlation between pain intensity and duration of hospital discharge was investigated with Pearsons correlation test. Mean ± standard deviation was used for descriptive analysis.

III. RESULTS

No statistically significant difference was found in any demographic factors compared (age, sex, systolic and diastolic blood pressure, respiratory rate, and preoperative gastrointestinal quality of life index score) (Table I).

![Number of Patients, n=58](image)

Patients aged more than 18 years, able to follow the instructions on usage of VAS scale and PCA machine, no history of psychiatric illness, allergy or hypersensitivity to anesthetic drugs and not on any analgesic therapy were included in this study.

Prior enrolment into the study all patients were informed about aims, method, anticipated benefits, and potential hazards of this study. All the patients were instructed on the usage of VAS scale and PCA machine for post-operative pain management. Pre-operative quality of life with “The Gastrointestinal Quality of Life Index” was evaluated on same sitting.

| Variables          | Placebo* n=23 | Intervention* n=22 | P value |
|--------------------|---------------|--------------------|---------|
| Age (years)        | 39.17±16.21   | 38.82±13.72        | 0.47    |
| Male               | 5             | 9                  | 0.08    |
| Female             | 17            | 13                 |         |
| Systolic Blood pressure | 109.94±4.61  | 108.25±3.29        | 0.24    |
| Diastolic blood pressure | 69.45±2.83  | 68.33±3.06         | 0.26    |
| Respiratory rate   | 15.37±0.31    | 15.26±0.24         | 0.24    |
| Pre-operative GQOL | 124.23±8.38   | 125.43±10.46       | 0.33    |

*Placebo arm received wound infiltration with 10ml 0.9% normal saline.
*Intervention arm received wound infiltration with 10ml 0.25% Bupivacaine.
P value was reached from independent student’s t-test and chi-squared test. P<0.05 is statistically significant.
A. Post-operative Pain and Analgesic Requirements

Pain intensity in VAS and VRS and analgesic requirement gradually reduced in both placebo and intervention group with increasing time. Placebo group reported more pain score and analgesic requirement than other group at all time periods. The difference of pain scores and analgesic consumption was statistically significant for up to 6 hours. Pain score was almost same in both groups at 8, 10 and 12 postoperative hour (Fig. 2, 3). Total analgesic requirement was also statistically significant up to 12 post-operative hours (Table II).

![Fig. 2. Comparison of pain score (VAS) up to 12 post-operative hours between placebo and intervention arm.](image)

![Fig. 3. Comparison of pain score (VRS) up to 12 post-operative hours between placebo and intervention arm.](image)

**TABLE II: COMPARISON OF TOTAL MORPHINE CONSUMPTION (MG/ML) BETWEEN PLACEBO AND INTERVENTION GROUP**

| Total morphine consumption (mg/ml) | Placebo | Intervention | P value |
|-----------------------------------|---------|--------------|---------|
| Mean ± SD                         | Mean ± SD |             |         |
| Placebo                          | 8.63 ± 1.48 | 7.27 ± 0.98 | 0.0003  |
| Intervention                      | n=23     | n=22         |         |

\^Placebo arm received wound infiltration with 10ml 0.9% normal saline.
\^Intervention arm received wound infiltration with 10ml 0.25% Bupivacaine.
P value was reached from independent student’s t-test.
P<0.05 is statistically significant.

B. Side Effects

Six side effects – nausea, vomiting, decreased O₂ saturation (<92%), burning sensation in chest, sweating and cough were recorded during the study. Only incidence rate of vomiting in placebo and intervention was statistically significant (P=0.0002).

Other side effects were observed in both placebo and intervention group, but difference between them were not statistically significant (Fig. 4).

![Fig. 4. Side effects observed up to 12 post-operative hours.](image)

C. Satisfaction Level, Hospital Stay, Pain Score during Discharge and Time Taken to Return to Job and Normal Activities

Satisfaction level (124.18 ± 6.33 vs. 125.18 ± 7.17, P=0.13), Hospital Stay (3.65 ± 0.88 vs. 3.32 ± 1.09, P=0.13), Pain Score during Discharge and Time Taken to Return to Job or Normal Activities (38.74 ± 7.54 and 36.36 ± 11.24, P=0.2) were not statistically significant.

D. Quality of Life

Quality of Life assessed pre-operatively and at 30th post-operative day was almost similar, but at 15th post-operative day this score was different. None of them was statistically significant (Fig. 5).

![Fig. 5. Comparison of preoperative, 15th postoperative and 30th postoperative quality of life between placebo and intervention arm.](image)
IV. DISCUSSION

Gradual reduction of pain score, assessed with VAS and VRS was experienced by patients of both arm for 12 postoperative hours after laparoscopic cholecystectomy. Pain intensity was highest and statistically significant after 2 hours post-operatively in both groups. The reason of this increased pain score may be the movement from recovery room to postoperative room. Pain scores reduced with time in each assessment. But after six hours of performing procedure, pain scores were not statistically significant. Different variation of pain scores at each assessment time was observed. Several patient or technical factors may have affected pain score in this study. Patients who suffered from chronic pain may had reported pain which was unrelated to surgical procedure. Patients who had previous history of surgery and narcotic consumption may had an increased tolerance to analgesic and reported more pain. In some patient’s epigastric and umbilical ports had to make widened to facilitated removal of gallbladder. This widening may had resulted in increased pain score. After six hours, pain score between placebo and intervention were almost close. Administration of Morphine with Patient Controlled Analgesia Machine in both groups might be the reason of adequate pain control according to their need.

Optimal post-operative pain control with minimal side effects is expected after surgery. In this study, six side effects were observed at post-operative ward. It can be said that these side effects are result of opioid infusion with PCA or anesthetic protocol. Nausea is the most common side effect experienced by patients. Vomiting was present in both groups and difference was statistically significant. Increased morphine requirement for pain control may be the cause of increased incidence in placebo group. Decreased intensity of post-operative pain has benefits over reduced analgesic requirements. Total morphine consumption was significantly lower in intervention (7.27 mg/ml) compared with placebo group (8.63 mg/ml). Difference of morphine consumption was decreasing with time in both groups. This was significantly different at first six hours. But at last, six hours this difference was not significant. So, with decreasing pain score morphine consumption also decreased significantly at first six hours.

In this study, duration of post-operative hospital stay was almost similar between both groups. Relationship between pain score at discharge and hospital stay was not found. But it was also observed that pain score was not used as one of the discharge criteria.

Satisfaction depends on past experience and future expectations of patient [10]. With significant lowering of pain intensity, satisfaction was insignificant in this study. Patients do not need to have ‘no pain’ to be ‘very satisfied’. Mild pain averaging less than 40 on a 0-100 mm visual rating scale is acceptable [11]. Based on this it can be said that after 4 hours of performing surgical procedure patient experienced ‘mild pain’ in intervention group. In placebo group this time was after 6 hours of surgery. Moreover, patients had analgesic on the basis of their need. Patient’s satisfaction with management of postoperative pain depended on these factors. Patients’ expectation, intensity of pain, response of nurses, and titration of analgesic and professional attitude might influence patient’s satisfaction level.

Graphical representation shows improvement of total score gradually from pre-operative, 15th post-operative day, 30th post-operative day. This improvement might be the symptom relieving effect from performing surgical procedure, rather than decreased post-operative pain from wound infiltration.

V. TRIAL REGISTRATION

This clinical trial was registered in Clinicaltrials.Gov with the trial ID number NCT03958513.

VI. CONCLUSION

This study demonstrates potential ability of bupivacaine infiltration to decrease pain score, analgesic requirement, and side effects. Routine practice of this intervention can be used for better surgical outcome.

REFERENCES

[1] Kehlet H. Future perspectives and research initiatives in fast-track surgery. Langenbecks Arch Surg. 2006 Sep 1; 391(5): 495-8.
[2] Eisenach JC. Transition of acute post-operative pain to persistent pain and development of chronic postsurgical pain services. Anesthesiology: The J Am Society of Anesthesiologists. 2009; 111:461-3.
[3] Gerbershagen HJ, Aduckathil S, van Wijk AJ, Peelen LM, Kalkman CJ, Meissner W. Pain Intensity on the first day after surgery a prospective cohort study comparing 179 surgical procedures. Anesthesiology Society of Anesthesiologists. Anesthesiology. 2013 Apr 1; 118(4): 934-44.
[4] Thomas MA. Pain management—the challenge. Ochsner J. 2003 Mar 20;5(2):15-21.
[5] Wells N, Pasero C, McCaffery M. Chapter 17. Improving the quality of care through pain assessment and management. In: Hughes RG, editor. Available from: https://www.ncbi.nlm.nih.gov/books/NBK2658/. Patient safety and quality: an evidence-based handbook for nurses. Rockville, (MD): Agency for Healthcare Research and Quality (US); 2008 Apr.
[6] Misiolik H, Zajęczkowska R, Daszkiewicz A, Woreń J, Dobrogowski J, Wodziczek J, Owczuk R. Postoperative pain management—2018 consensus statement of the Section of Regional Anaesthesia and Pain Therapy of the Polish Society of Anaesthesiology and Intensive Therapy, the Polish Society of Regional Anaesthesia and Pain Therapy, the Polish Association for the Study of Pain and the National Consultant in Anaesthesiology and Intensive Therapy. Anesthesiol Intensive Ther. 2018 Jan 1;50(3).
[7] Meissner W, Coluzzi F, Fletcher D, Huynen F, Morlion B, Neugebauer E, Montes AM, Pergolizzi J. Improving the management of post-operative acute pain: priorities for change. Curr Med Res Opin. 2015 Nov 2; 31(11): 2131-43.
[8] Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Beckler S, Brennan T, Carter T, Cassidy CL, Chittenden EH, Degenhardt E, Griffith S, Manworren R, McCarberg B, Montgomery R, Murphy J, Perkal MF, Suresh S, Sluka K, Strassels S, Thrilby R, Viscusi E, Walco GA, Warner L, Weissman SJ, Wu CL. Management of Postoperative Pain: a clinical practice guideline from the American Pain Society, the American Society of Anaesthesiology and Pain Therapy, the American Society of Regional Anaesthesia and Pain Medicine, and the American Society of anaesthesiologists’ committee on regional anaesthesia, executive committee, and administrative council. J Pain. 2016 Feb 1; 17(2): 131-57.
[9] Moiniche S, Jorgensen H, Weterslev I, Dahl JB. Local anesthetic infiltration for postoperative pain relief after laparoscopy: a qualitative and quantitative systematic review of intraperitoneal, port-site infiltration and mesosalpinx block. Anesth Analg. 2000 Apr 1; 90(4): 899-912.
[10] Pascoe GC. Patient satisfaction in primary health care: a literature review and analysis. Eval Program Plann. 1983; 6(3-4): 185-210.
[11] Jensen MP, Martin SA, Cheung R. The meaning of pain relief in a clinical trial. J Pain. 2005 Jun 1; 6(6): 400-6.