INTRAPERITONEAL AND LOCAL INFILTRATION OF BUPIVACAINE FOR PAIN RELIEF AFTER LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Objective: To compare the effectiveness of intraperitoneal and local infiltration of bupivacaine on pain relief in postoperative period after laparoscopic cholecystectomy.
Study Design: Randomized controlled trial.
Place and Duration of Study: Combined Military Hospital Multan, from Jan to Dec 2014.
Material and Methods: In this study, 72 adult patients of either gender with age between 20 to 60 years having symptomatic gallstones scheduled for elective laparoscopic cholecystectomy were divided into two groups. Patients in group A received intraperitoneal and local infiltration of bupivacaine at the end of surgery. Group B was administered placebo. Postoperatively, intensity of pain was recorded by using 10 points' Visual Analogue Score at 3, 9, 12, 24 hours. A *p*-value ≤0.05 was considered as statistically significant.
Results: In group A, there were 27 male and 9 female patients while in group B, there were 22 male and 14 female patients. Mean age was 37.75 ± 12.49 years and 41.92 ± 12.73 years in groups A and B respectively. The mean postoperative pain score was 8.18 ± 1, 6.36 ± 0.98, 4.98 ± 1.11 and 3.89 ± 1.11 in group A & 8.72 ± 1.05, 6.91 ± 0.96, 5.92 ± 0.96 and 4.47 ± 1.05 in group B at 3, 9, 12 and 24 hours post operatively. The difference in mean pain scores was significant; 0.0286, 0.0188, 0.0001 and 0.0258 at 3, 9, 12 and 24 hours respectively.
Conclusion: Intraperitoneal and local infiltration of 0.25% bupivacaine significantly reduces the intensity of postoperative pain and analgesic requirement in the early postsurgical hours following laparoscopic cholecystectomy.

Keywords: Bupivacaine, Effectiveness, Intraperitoneal injection, Laparoscopic cholecystectomy, Periportal injection, Postoperative pain.

INTRODUCTION

Laparoscopic cholecystectomy (LC) is now a gold standard technique for the treatment of gallstone disease. There are many advantages of laparoscopic cholecystectomy against open procedure which include reduced haemorrhage, smaller incision, shortened recovery time, less hospital stay and expenditure, reduced risk of acquiring infections and blood loss. However, these patients do experience postoperative pain which may be transient or may last for 24 hours upto 3 days. Besides pain, nausea and vomiting are also common complications in early postoperative hours[1].

Wound infiltration with local anaesthetics for postoperative pain relief is a routine practice nowadays in many surgical procedures. Local anaesthetic infiltration of wound is beneficial in open abdominal surgery after minor procedures, such as hernia repair. However, it has shown less benefits in moderate to major procedures. As laparoscopic surgery is a minimally invasive technique and as it is associated with reduced surgical trauma, wound infiltration of local anaesthetics after laparoscopic surgery may provide clinically significant relief from postoperative pain in immediate postoperative period[2].

Administration of intraperitoneal and periportal local anaesthetics employing bupivacaine during surgery is used by many clinicians to effectively decrease postoperative pain. However, the studies have shown mixed results. Therefore, this study was conducted to

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study the role of bupivacaine in postoperative pain management after laparoscopic cholecystectomy.

MATERIAL AND METHODS

This was a randomized control trial conducted at Combined Military Hospital Multan, Pakistan for a period of 1 year from 1st January 2014 to 31st December 2014. The sample size was calculated based on the reported effectiveness of intraperitoneal and local infiltration of bupivacaine using Open Epi software available online at http://www.openepi.com/Sample Size.html. We assumed an alpha error of 0.05 and applied an allocation ratio of 1. A sample size of 36 participants in each group was calculated to provide a 80% power in detecting a difference in pain relief by 30%.

Seventy two adult patients of either gender with age between 20 to 60 years having symptomatic gallstones scheduled to undergo elective laparoscopic cholecystectomy under general anaesthesia were enrolled after seeking approval from the hospital's ethical committee and after obtaining informed written consent from the patients. Patients who had local anaesthetic allergy; chronic pain for reasons other than gall stones; been using opioids, tranquilizers, steroids, NSAIDS or alcohol and patients in whom laparoscopic cholecystectomy had to be converted into open cholecystectomy were excluded from the study. The sample size was taken as such for convenience only. Sampling technique was consecutive in nature. Inclusion and exclusion criteria were strictly followed to control bias. Ethical issues and financial problems were properly addressed.

The patients were divided into two groups by lottery method. At the end of surgery, group A and B received 0.25% inj bupivacaine 10 ml and placebo respectively. Postoperatively intensity of pain was recorded by using 10 points visual analogue score at 3, 9, 12, 24 hrs. Effectiveness was labeled as positive when the frequency of pain was less in patients treated with intraperitoneal bupivacaine and periportal injection of bupivacaine than those who did not receive so.

Data were entered and analyzed using SPSS version 21. At every assessment time, the descriptive statistics of qualitative and quantitative variables were calculated. For quantitative variables i.e. age and pain score, mean and standard deviation were calculated. For qualitative variables i.e. gender and effectiveness, frequency and percentage were calculated. Student t-test was applied to compare the mean postoperative pain scores and chi square test was applied to compare effectiveness of intraperitoneal and local infiltration of bupivacaine in intervention and control groups. Stratification was done on gender and age to see the effect of these modifiers on outcome i.e. effectiveness by applying chi square test or Fisher exact test where appropriate. A p-value <0.05 was considered significant.

RESULTS

In group A, there were 27 (75%) male and 9 (25%) female patients while in group B, there were 22 (61%) male and 14 (39%) female patients. Mean age was 37.75 ± 12.49 years and 41.92 ± 12.73 years in groups A and B respectively. The mean postoperative pain score at 3, 9, 12 and 24 hours is shown in table-I.

In group A, the effectiveness was observed in 15 (41.7%) patients and in 6 (16.7%) patients in group B (p-value 0.035). The mean postoperative pain score was 8.18 ± 1, 6.36 ± 0.98, 4.98 ± 1.11 and 3.89 ± 1.11 in group A & 8.72 ± 1.05, 6.91 ± 0.96, 5.92 ± 0.96 and 4.47 ± 1.05 in group B at 3, 9, 12 and 24 hours post operatively. The difference in mean pain scores was significant; 0.0286, 0.0188, <0.0001 and 0.0258 at 3, 9, 12 and 24 hours respectively. No significant association of effectiveness was observed with male gender (p-value 0.088), female gender (p-value 0.108) and age >38 years (p-value 0.181). Cross tabulations are displayed in table-II.

DISCUSSION

Laparoscopic cholecystectomy surgery was first introduced in late 1980s. After the

introduction of this new technique several studies revealed an increase in cholecystectomy rates of approximately 20%. As a consequence, even small changes in indications for cholecystectomy have major impact on health care costs. Since the introduction of laparoscopic cholecystectomy, many studies have discussed and high-lighted the importance of adequate surgical technique in order to improve the outcome and timing of surgery. Comparisons to open cholecystectomy, with or without minimal incision, have also been highlighted[2].

Open cholecystectomy has largely been replaced by laparoscopic cholecystectomy which has revolutionized the treatment of gall bladder disease and is now gold standard treatment of gall stones and the commonest operation performed laparoscopically worldwide. Most patients are being discharged the same day as day caresurgery or on the first postoperative day[1]. However in 17% to 41% of the patients, pain is the main cause for staying overnight in the hospital on the day of surgery[3]. Injectable analgesics may be required for postoperative pain in 58-70% of patients[3]. Postoperative pain can be transient or may last for 24 hours up to 3 days.

Pain following LC is multifactorial in etiology: 1) Pain arising from incision sites being somatic pain 2) Pain from the gallbladder bed being mainly visceral in nature 3) Shoulder pain is mainly due to the residual CO_2 irritating the diaphragm[4]. Some studies report visceral pain to be major component of early postoperative pain. Others suggest that incisional sites play main role in causing major component of the total abdominal pain after that pneumoperitoneum and then cholecystectomy. This sequence of pain components is refuted by studies which report that infiltration of trocar sites with local anaesthetic does not provide significant local analgesia. Most of the patients, ranging from 35% to 63% complain of shoulder pain after laparoscopic procedures but the cause of that type of pain is still not clear. Proposed mechanisms consists of partial injury of the phrenic nerve like neuropraxia, irritation of diaphragmatic muscle because of stretching of the fibers due to pneumoperitoneum and peritoneal damage from chemical, ischemic or traumatic injury. After 24-48 hours, most of visceral and parietal pain subsides but shoulder pain may remain problematic. In our study, we sought to evaluate the efficacy of the total pain control of the patient atvarious time intervals but

Table-I: Mean postoperative pain score.

Time	Group A	Group B	*p*-value
3 hours	8.18 ± 1	8.72 ± 1.05	0.0286
9 hours	6.36 ± 0.98	6.91 ± 0.96	0.0188
12 hours	4.89 ± 1.11	5.92 ± 0.96	<0.0001
24 hours	3.89 ± 1.11	4.47 ± 1.05	0.0258

Table-II: Comparison of pain relief in intervention and control groups by age and gender.

Variable	Group	Effectiveness		*p*-value
		Yes	No	
Male Gender	Bupivacaine	11	16	0.088
	Control	4	18	
Female Gender	Bupivacaine	4	5	0.108
	Control	2	12	
Age ≤38 years	Bupivacaine	9	9	0.041
	Control	4	17	
Age >38 years	Bupivacaine	6	12	0.181
	Control	2	13	

not the various types of pain and their various intensities[2].

Many ways have been used to decrease postsurgical pain for example local anesthetic infiltration, gasless technique, low pressure pneumoperitoneum, saline washout and instillation of a local anesthetic agent in the subdiaphragmatic area[4-6].

Instillation of a local anesthetic agent at the trocar sites and in the subdiaphragmatic region as a method for pain control has been evaluated in many trials. In their systematic review, Yari Ahn et al[2] of usage of local anaesthesia in LC in thirteen trials[3-15] showed intraperitoneal was beneficial in seven of nine trials[5-12]. However, in their Cochrane database review, Gurusamy et al[13] included 12 randomized controlled trials on use of intraperitoneal local anaesthetics in patients undergoing elective laparoscopic cholecystectomy. They found that none of the trials reported good quality of life, early return to normal activity, or early return to work. The variations in proportion of patients who were discharged as same day of surgery and duration of hospital stay were imprecise in all the trials of comparisons. There were few variations in the pain scores on the visual analoguescale (1 to 10 cm) but these were neither consistent nor robust to fixed effect versus random effects meta analysis or sensitivity analysis.

Which local anaesthetic should be used for local intraperitoneal instillation is also a matter of debate. Ingelmo et al[14] concluded that Ropivacaine nebulization before or after surgery reduced postoperative pain and reduced morphine requirements. Khan el al[15] concluded that bupivacaine and lignocaine (lidocaine) are both safe and equally effective at decreasing postoperative pain after LC.

Karaaslan et al[12] and Marks et al. showed better control of postoperative pain with early instillation of intraperitoneal local anaesthetics compared with instillation at the end of the surgery. Alkhamesi et al[9] showed injected intraperitoneal LA is less effective than aerosolized LA. The timing, volume and way of administration of drug are responsible for difference in observations. Some authors believe that most of the patients could not get enough pain relief because of decreased contact time of drug with surgical site due to intraperitoneal influx. Ahmad et al[16] applied a 2x3 inches bupivacaine soaked surgical guaze at the gall bladder bed for pain control and got better result without significant complications because of increased contact time of the drug.

Eight trials observed the effect of incisional LA, including to which together with intraperitoneal LA[5,9,11,17-21]. Out of these, only two trials[5,11] failed to give adequate benefit with incisional LA and one[9] of these infiltrated it after surgery. Before giving incision LA was superior to post-incisional administration[19].

One of the main reason of using bupivacaine intraperitoneally is to increase the concentration of drug in plasma because peritoneum is good systemic absorber. Raetzell et al[22] reported an increase of concentration of bupivacaine in plasma exceeding the threshold value of 2mg/L after intraperitoneal administration of 50ml of 0.25% bupivacaine during laparoscopic cholecystectomy. But the main drawback which was found in these patients in the postoperative period, was significant compromise of respiratory function and recurrent episodes of hypoxemia (SpO<92%). However in our study, we did not calculate the exact concentration of bupivacaine in plasma but not a single patient in our study, reported with any respiratory, neurogenic or cardiac problem in postoperative period, likely due to administration of safest possible dose of intraperitoneal bupivacaine.

Some authors have experimented with addition of different agents to intra-peritoneal bupivacaine regimen and study their effects on pain relief. In their study Golubovic et al[23] reported that intraperitoneal administration of bupivacaine or tramadol or combined form of both are effective procedure for control of pain after laparoscopic cholecystectomy and they

decrease the usage of postoperative analgesic and antiemetic medications significantly.

Upadaya et al[24] compared the effectiveness of intra-peritoneal bupivacaine (group I) versus intravenous paracetamol (group II) and came to the conclusion that post-operative pain, as assessed by visual analog scale, was equivalent in both groups at 1st and 4th hours. However VAS was significantly raised in group I as compared to group II at 8, 12 and 24 postoperative hour.

CONCLUSION

Intraperitoneal and local infiltration of 0.25% bupivacaine significantly reduces the intensity of postoperative pain and analgesic requirement in the early postsurgical hours following laparoscopic cholecystectomy.

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CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Alper I, Ulukaya S, Yuksel G, Uyar M, Balcioglu T. Laparoscopic cholecystectomy pain: Effects of the combination of incisional and intraperitoneal levobupivacaine before or after surgery. Agri: Agri (Algoloji) Dernegi'nin Yayin organidir. J Turkish Society Algology 2014; 26(3): 107-12.
2. Ahn Y, Woods J, Connor S. A systematic review of interventions to facilitate ambulatory laparoscopic cholecystectomy. HPB: J Intl Hepato Pancreato Biliary Assoc 2011; 13(10): 677-86.
3. Ahmad A, Faridi S, Siddiqui F, Edhi MM, Khan M. Effect of bupivacaine soaked gauze in postoperative pain relief in laparoscopic cholecystectomy: A prospective observational controlled trial in 120 patients. Patient Saf Surg 2015; 9(1): 31.
4. Yari M, Rooshani B, Golfam P, Nazari N. Intraperitoneal bupivacaine effect on postoperative nausea and vomiting following laparoscopic cholecystectomy. Anesth Pain Med 2014; 4(3): e16710.
5. Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-regional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: A randomized, double-blinded, placebo-controlled study. Anesth analg 1999; 89(4): 1017-24.
6. Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. Anesth analg 1995; 81(2): 379-84.
7. Chundrigar T, Hedges AR, Morris R, Stamatakis JD. Intraperitoneal bupivacaine for effective pain relief after laparoscopic cholecystectomy. Ann Royal Coll Surg Engl 1993; 75(6): 437-9.
8. Rademaker BM, Kalkman CJ, Odoom JA, de Wit L, Ringers J. Intraperitoneal local anaesthetics after laparoscopic cholecystectomy: Effects on postoperative pain, metabolic responses and lung function. Br J Anaesth 1994; 72(3): 263-6.
9. Alkhamesi NA, Peck DH, Lomax D, Darzi AW. Intraperitoneal aerosolization of bupivacaine reduces postoperative pain in laparoscopic surgery: A randomized prospective controlled double-blinded clinical trial. Surg Endosc 2007; 21(4): 602-6.
10. Mraovic B, Jurisic T, Kogler-Majeric V, Sustic A. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy. Acta Anaesthesiol Scand 1997; 41(2): 193-6.
11. Louizos AA, Hadzilia SJ, Leandros E, Kouroukli IK, Georgiou LG, Bramis JP. Postoperative pain relief after laparoscopic cholecystectomy: A placebo-controlled double-blind randomized trial of preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25%. Surg Endosc 2005; 19(11): 1503-6.
12. Karaaslan D, Sivaci RG, Akbulut G, Dilek ON. Preemptive analgesia in laparoscopic cholecystectomy: A randomized controlled study. Pain prac 2006; 6(4): 237-41.
13. Gurusamy KS, Nagendran M, Toon CD, Guerrini GP, Zinnuroglu M, Davidson BR. Methods of intraperitoneal local anaesthetic instillation for laparoscopic cholecystectomy. Cochrane Database Syst Rev 2014; 25(3): Cd009060.
14. Ingelmo PM, Bucciero M, Somaini M, Sahillioglu E, Garbagnati A, Charton A, et al. Intraperitoneal nebulization of ropivacaine for pain control after laparoscopic cholecystectomy: A double-blind, randomized, placebo-controlled trial. Br J Anaesth 2013; 110(5): 800-6.
15. Khan MR, Raza R, Zafar SN, Shamim F, Raza SA, Pal KM, et al. Intraperitoneal lignocaine (lidocaine) versus bupivacaine after laparoscopic cholecystectomy: results of a randomized controlled trial. J Surg Res 2012; 178(2): 662-9.
16. Ahmad A, Faridi S, Siddiqui F, Edhi MM, Khan M. Effect of bupivacaine soaked gauze in postoperative pain relief in laparoscopic cholecystectomy: A prospective observational controlled trial in 120 patients. Patient safety surgery 2015; 9(1): 31.
17. Liu YY, Yeh CN, Lee HL, Wang SY, Tsai CY, Lin CC, et al. Local anesthesia with ropivacaine for patients undergoing laparoscopic cholecystectomy. World J Gastroenterol 2009; 15(19): 2376-80.
18. Hasaniya NW, Zayed FF, Faiz H, Severino R. Preinsertion local anesthesia at the trocar site improves perioperative pain and decreases costs of laparoscopic cholecystectomy. Surg Endosc 2001; 15(9): 962-4.
19. Cantore F, Boni L, Di Giuseppe M, Giavarini L, Rovera F, Dionigi G. Pre-incision local infiltration with levobupivacaine reduces pain and analgesic consumption after laparoscopic cholecystectomy: A new device for day-case procedure. Int J Surg 2008; 6(Suppl-1): S89-92.
20. Papagiannopoulou P, Argiriadou H, Georgiou M, Papaziogas B, Sfyra E, Kanakoudis F. Preincisional local infiltration of levobupivacaine vs ropivacaine for pain control after laparoscopic cholecystectomy. Surg Endosc 2003; 17(12): 1961-4.
21. Ure BM, Troidl H, Spangenberger W, Dietrich A, Lefering R, Neugebauer E. Pain after laparoscopic cholecystectomy. Intensity and localization of pain and analysis of predictors in preoperative symptoms and intraoperative events. Surg Endosc 1994; 8(2): 90-6.
22. Raetzell M, Maier C, Schroder D, Wulf H. Intraperitoneal application of bupivacaine during laparoscopic cholecystectomy risk or benefit? Anesth Analg 1995; 81(5): 967-72.
23. Golubovic S, Golubovic V, Cindric-Stancin M, Tokmadzic VS. Intraperitoneal analgesia for laparoscopic cholecystectomy: bupivacaine versus bupivacaine with tramadol. Coll Antropol 2009; 33(1): 299-302.
24. Upadya M, Pushpavathi SH, Seetharam KR. Comparison of intraperitoneal bupivacaine and intravenous paracetamol for postoperative pain relief after laparoscopic cholecystectomy. Anesth Essays Res 2015; 9(1): 39-43.