Ulutas Med J 2019;5(1):26-33
DOI: 10.5455/umj.20190130080233

ORIGINAL ARTICLE OPEN ACCESS

The Effectiveness of Bupivacaine Instillation on Postoperative Pain after Elective Laparoscopic Cholecystectomy: A Prospective Randomized Controlled Trial

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Background: The gold-standard procedure for the surgical treatment of gallstone disease is Laparoscopic Cholecystectomy. With better pain management Laparoscopic Cholecystectomy can be practiced as Day-case surgery by the reduction in post-op pain, reduced analgesia demand, early mobility, and shorter hospital stay.

Materials and Methods: This study was conducted at the department of general surgery, Pakistan Institute of Medical Sciences (PIMS) Complex, Islamabad from July 2016 to January 2018. A total of 164 patients were selected for the study. Patients aged 13 and above who were diagnosed with symptomatic cholelithiasis, gall bladder polyps or sludge were included in the study. Informed consent was taken. The patients were classified into two groups based on the intervention by instillation of Bupivacaine in one group and no intervention in the other.

Results: Out of these 82 (50%) were installed with bupivacaine at the final stage of closure at peritrocar, sub-phrenic and gallbladder bed and in remaining 82 no instillation of any drug at aforementioned sites was done. The outcome was measured between these two groups in terms of time for first demand of analgesia, the frequency of the demand by the patient, time to mobility and post-op hospital stay.

Conclusion: This study showed that there was a significant difference in the outcome of instillation of bupivacaine in subphrenic space, gall bladder bed and peritrocal site on Postoperative Pain after Elective Laparoscopic Cholecystectomy.

Keywords: Laparoscopic cholecystectomy, cholelithiasis, VAS, bupivacaine, postoperative pain

Introduction

Out of abdominal surgeries, cholecystectomy is one of the most common to be performed. Laparoscopic cholecystectomy is considered the "gold standard" procedure for the surgical therapy of cholelithiasis (1). It is considered to be as safe as open cholecystectomy, however, with a certain number of added advantages (2). This procedure has the advantage of better cosmesis, relatively short duration of hospital stay, lesser inability from work and reduced post-operative pain than open cholecystectomy (3). Subsequently, it results in less prominent stress response and metabolic interference when contrasted with open cholecystectomy (4). Meticulous technique, careful case selection,

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Received: Jan 30, 2019 **Accepted**: Feb 25, 2019
Published: Mar 21, 2019

better training, and high standard equipment of central significance is necessary for good outcomes in laparoscopic cholecystectomy (5). Hence, the development of laparoscopic cholecystectomy revolutionized the history of biliary surgery (6). It is safe and effective management of gall stone disease. It has moved the focus of surgery towards reducing the morbidity without compromising on the quality of healthcare (7). Also, it is the most commonly performed laparoscopic procedure in developing countries. While laparoscopic cholecystectomy is, for the most part, thought to be less painful than open surgery, pain is one of the essential reasons behind deferred discharge from the hospital after surgery and overnight stay.

Advancements in the understanding and treatment of gallstones have been rapid amid the previous decade. Decades-long excellent quality of open surgical cholecystectomy as a treatment for gallstones has been tested by gallstone-disintegration methods and shock-wave lithotripsy and has been ousted by laparoscopic cholecystectomy (8). Therefore a laparoscopic cholecystectomy not only provides a standard treatment of cholelithiasis, it is further being improvised so that this procedure not only has less morbidity for the patient but also is more efficient in term of hospital costs and patient turn over. Currently, different studies are being carried out in many parts of the world to still optimize this much-developed procedure so laparoscopic cholecystectomy could be established as a standard day case surgery (9).

The main focus of these studies is to provide better pain management to the patient by effective on-site analgesia, reducing pneumo peritoneum pressure and infiltrating the wound with local anesthetic agents (10). After that, this study was carried out in light with the aim to evaluate the effectiveness of instillation of Bupivacaine at peri-trocar, gall bladder, and sub-hepatic space after elective laparoscopic cholecystectomy on post-op pain, analgesia demand, early mobility, and hospital stay. Determining the outcome in these two groups will allow the surgeons to perform laparoscopic cholecystectomy as a day-case surgery by keeping patient pain free and thus achieving early discharge, early return to function, short hospital stay, a better patient turn-over and after that the costs on hospital resources.

Materials and Methods

The hospital ethical committee first approved the work plan. All patients admitted with cholelithiasis to the surgical unit of Pakistan Institute of Medical Sciences Islamabad were enrolled in the study as per inclusion criteria. Written informed consent was obtained from the patient. A detailed medical history was obtained from patients in which patients were asked questions about their demographic data, history of presenting illness, past medical history, drug history, history of previous medical and surgical procedures as well as occupational and travel history. The history concluded by a systematic review. History taking followed physical examination. Then investigations were carried out to confirm the diagnosis of symptomatic gall stones, polyp or sludge.

After planning surgery, patients were assessed by the Department of Anesthesiology and other relative departments for co-morbid if present, e.g. diabetes mellitus, hypertension or asthma for optimal fitness for surgery. In Group A, after laparoscopic cholecystectomy, on the final stage of closure, peritrocal, subphrenic and gallbladder bed instillation of bupivacaine

(0.125%) was done. In group B no such intervention was done. After the surgery, a meticulous record of the treatment was kept. The parietal, visceral, and shoulder tip pain was assessed at 4, 8, 12 and 24 hours post operatively using a visual analog scale (VAS). Intravenous tramadol 50mg (1ml) diluted in 9 ml of normal saline was used as analgesia. The time for the first demand of analgesia, the frequency of the demand by the patient, time to mobility in hours after surgery and post-op hospital stay was also recorded. All data were collected by the postgraduate resident and was documented on the Performa.

Statistical Analysis

The data were analyzed using SPSS software version 23. Statistics were calculated for variables such as age, gender, pain score at the set number of hours, the time for first demand of analgesia, the frequency of the demand by the patient, the time to mobility after surgery and post-op hospital stay was analyzed. Relative frequency and percentage were calculated. Results are presented in table-1 along with inference. A p-value <0.05 was considered significant. Independent sample t-test was applied on VAS, time to mobilize after surgery, the total number of analgesia doses and length of hospital stay.

Results

A total of 164 patients included in the study. Out of these, 82 patients who underwent a laparoscopic cholecystectomy as control subjects 14 were male, and 68 were female. While 82 patients who underwent laparoscopic cholecystectomy followed by Bupivacaine instillation 19 were male and 63 were female. The mean age of patients in the control group was 48.46 years with standard deviation of 9.17. The youngest patient was 32 years old and oldest was 68 years old with 53.7% of these patients falling up to 50 years of age. While mean age of patients in the group of bupivacaine instillation was 49.5 with a standard deviation of 7.8; the youngest being 31 years old and oldest 65 years old with 50% of these patients falling up to 50 years of age (Table-1).

Among the control group, upon assessment for pain by VAS at 4 hours, the mean VAS was 3.3 with standard deviation of 1.08 with a max score of 6 and minimum of 1. while in group with bupivacaine instillation mean VAS at 4 hours was 0.94 with a standard deviation of 0.89 with a Maximum score of 3 and Minimum of 0. The mean VAS assessed at 8 hours in the control group was 4.84 with a standard deviation of 1.52 with a maximum score of 8 and a minimum of 1. While in the group with bupivacaine instillation mean VAS at 8 hours was 1.06 with a standard deviation of 0.83 with a maximum score of 4 and a minimum of 0. The mean VAS assessed at 12 hours in the control group was 5.07 with a standard deviation of 1.32 with a maximum of 8 and a minimum of 2. While in a group with bupivacaine instillation mean VAS at 12 hours was 1.39 with a standard deviation of 1.063 with a maximum score of 5 and a minimum of 0. The mean VAS assessed at 24 hours in the control group was 5.76 with a standard deviation of 1.38 with a maximum score of 8 and a minimum of 2. While in a group with bupivacaine instillation mean VAS at 24 h was 1.34 with a standard deviation of 0.96 and a maximum score of 2 and a minimum of 0.

The most common first site of pain in control group was operation site as reported by 55 (67.1%) patients in that group; followed by shoulder pain in 18 (22%) patients, pain at other sites in 6 (7.3%) followed by visceral in 3 (3.7%) patients. The most common first site of pain in

bupivacaine instillation group was operation site as reported by 35 (42.7%) patients in that group; followed by visceral in 30 (36.6%) patients, pain at other sites in 9 (11%) followed by shoulder pain in 8 (9.8%) patients.

During the hospital stay all 82 patients in the control group required analgesia. However, in a group with bupivacaine instillation 33 out of 82 patients required analgesia. The first dose of analgesia required by a patient of the control group was at an average of 7.48 hours after surgery with a standard deviation of 1.39. While in bupivacaine instillation group the first dose of analgesia required was at 6.39 hours with a standard deviation of 5.05 hours. The patients in the control group required their first dose as early as 06 hours and a latest by 10 hours after surgery. Meanwhile, the patients in the control group required their first dose as early as 08 hours and a latest by 24 hours after surgery.

All 82 (100%) patients in the control were administered analgesia within 06-10h. However out of 33 (40.2%) patients that required analgesia in bupivacaine instillation group 15 (18.3) required analgesia within 16-20 hours, 7(8.5%) in 21-25 hours, 6 (7.3%) in 06-10 hours, and 5 (6.1%) patients in 11-15 hours. 44 (68.3%) patients in control group required up to 05 doses of analgesia after surgery. Twenty-six patients (31.7%) required six doses in control. While in bupivacaine instillation 50 patients (61%) required no analgesia. 19 (23.2%) patients required 1 dose of analgesia. 13 (15.9%) patients required 2 doses. No patient required more than two doses of analgesia in bupivacaine instillation group. Hence the number of doses of analgesia required by Control Group were 5.15 with a standard deviation of 0.72 minimum being 3 and maximum being 6. While a mean number of doses of analgesia required by Bupivacaine İnstillation group was 0.55 with standard deviation 0.76, the minimum requirement is 0 doses and a maximum of 2 doses. Mean time taken by patients in the control group to mobilize after surgery was noted to be 8.15 hours with a standard deviation of 1.78 while for bupivacaine instillation group to mobilize after surgery mean noted to be 5.02 hours with a standard deviation of 1.75. In the Control group, 10 (12.2%) patients were mobilized by 4 hours. 46 (56.1%) patients were mobilized in 8 hours, and 26 (31.7%) were mobilized at 10 h. In Bupivacaine instillation group, 61 (74.4%) patients were mobilized by 4 hours. 21 (25.6%) patients were mobilized in 8 h after surgery.

In the control group, mean hospital stay noted was 36.97 hours with a standard deviation of 6.08; a minimum of 24 hours and a maximum of 48 h. While in bupivacaine instillation group, mean hospital stay noted was 25.9 hours with a standard deviation of 2.35; a minimum of 22 hours and a maximum of 32 h. In control group 62 (75.6%) patients took more than 30 hours till discharge from hospital and 17 (24.4%) were discharged within 30 h of admission. However, in Bupivacaine İnstillation Group, 79 (96.3%) were discharged within 30 h of admission, and 3.7% were discharged after 30 h.

Discussion

Laparoscopic cholecystectomy is one of the most ordinary day-case surgeries (11). The post-operative pain associated with this minimally invasive procedure is generally less intense and lasts a shorter time than that follow open cholecystectomy but it remains prevalent

Table-1. Patients' data table including demographics and clinical findings

Variables	Control Group	Study Group	P value
Gender			
▪ Female	63 (76.8%)	68 (82.9%)	
▪ Male	19 (23.2%)	14 (17.1%)	
Age	48.4±9.1 (32-68)	49.5±7.8 (31-65)	
VAS after Surgery			
▪ VAS (4 Hours)	3.3±1.08 (1-6)	0.94±0.89 (0-3)	0,03
▪ VAS (8 Hours)	4.84±1.519 (1-8)	1.06±0.83 (0-4)	0,0001
▪ VAS (12 Hours)	5.07±1.322 (2-8)	1.39±1.063 (0-5)	0,02
▪ VAS (24 Hours)	5.76±1.38 (2-8)	1.34±0.95 (0-2)	0,009
First Site of Pain			
▪ Operation Site	55 (67.1%)	35 (42.7%)	
▪ Shoulder Tip	18 (22%)	8 (9.8%)	
▪ Visceral	3 (3.7%)	30 (36.6%)	
▪ Other	6 (7.3%)	9 (11%)	
First Dose of Analgesia			
Total Patients Requiring Analgesia	82 (100%)	33 (40.2%)	
Mean Hours	7.48±1.39 (6-10)	16.3±5.04 (8-24)	0,0001
▪ 0-5 Hours	0	0	
▪ 6-10 hours	82 (100%)	6 (7.3%)	
▪ 11-15 hours	0	5 (6.1%)	
▪ 16-20 hours	0	15 (18.3%)	
▪ 21-25 hours	0	7 (8.5%)	
Total of Analgesia Doses	5.15±0.72 (3-6)	0.55±0.75 (0-2)	0,05
Mean Time to Mobilize	8.15±1.79 (4-10)	5.02±1.75 (4-8)	0,051
Mobilized after Surgery			
▪ 4 Hours	10 (12.2%)	61 (74.4%)	
▪ 8 Hours	46 (56.1%)	21 (25.6%)	
▪ 10 Hours	26 (31.7%)	0	
Duration of Hospital Stay			
▪ Less than 24 Hours	3 (3.7%)	36 (43.9%)	
▪ 25 Hours to 30 Hours	17 (20.7%)	43 (52.4%)	
▪ More than 30 Hours	62 (75.6%)	3 (3.7%)	

Abbreviations. **VAS**, Visual Analog Score. All continues variables were given as mean±standard deviation with minimum to maximum values.

the problem of the early post-operative period and may delay discharging patient, especially in day-case departments (12). The origin of pain after laparoscopic cholecystectomy is multi-factorial and is comprised of three different components: incisional pain (somatic), visceral pain, and shoulder pain (referred visceral pain). Pain after laparoscopic cholecystectomy demonstrates a high inter-individual variability in intensity as well as duration and is also mostly unpredictable (13). The intensity of pain is highest on the day of surgery and the following day, subsequently declining to low levels within 2-3 days and is most frequently reported at the site of incisions for trocar placement (14).

In the present study effectiveness of instillation of 0.25% bupivacaine at all three components contributing to post-op pain were infiltrated and it was found more effective than using at either site or none, as demonstrated in other studies (15). It significantly decreased the postoperative analgesia requirements, promoted early mobilization and therefore indirectly lead to significant benefits including reduced potential for deep vein thrombosis and pulmonary embolus, lesser incidence of atelectasis and respiratory infection, and minimal motor deconditioning.

Shorter hospital stays added to significance of using bupivacaine as an active practice in the number of prospects. Similar reports exist in the literature. A study conducted in the United Kingdom concluded that patients in the bupivacaine group had less pain in the early postoperative period and a lower incidence of pain in the right hypochondrium after instillation of Intraperitoneal bupivacaine (16). A randomized controlled trial conducted in Iran evaluated Postoperative pain, oral analgesic consumption, peak expiratory flow rate, and presence of nausea or vomiting was recorded at baseline and 4, 8, and 24 hours after surgery (17). Patients who received IP bupivacaine showed a significantly lower pain score and improved peak expiratory flow rate and received lower doses of ibuprofen within the first 24 hours after surgery. Likewise, the presence of nausea/vomiting was significantly lower in bupivacaine groups 1 and 4 hours after surgery. A Croatian study stated that pain was more intense in the saline group at each time point (15). Significant differences between the groups were present for up to 8h. Analgesic consumption was significantly lower in the bupivacaine group. No side-effects occurred. A study carried out in India also demonstrated that a moderate dose of intraperitoneal analgesia with a local anesthetic (ropivacaine and bupivacaine) is simple to use and effective method with minimal side effects (18). Use in the combination of the incision and intra-peritoneal local anesthetic infiltration after Laparoscopic Cholecystectomy resulted in significantly reduced immediate postoperative pain and may explain the reduced use of analgesia and early discharge of patients (19). However, a randomized, placebo-controlled and double-blind study conducted in Sweden stated that intraperitoneal bupivacaine does not effectively reduce pain after laparoscopic cholecystectomy (20).

The sample size was small, and only those patients were recruited in the study who presented to Pakistan Insititute of Medical Sciences, Islamabad. Patients with cholelithiasis who did not come to this hospital were not inducted. This study was a comparative study, yet no effort was made to breakdown etiologic factors in both groups, and no analysis was therefore possible. Only two broad categories

were defined: One, patients with cholelithiasis who underwent cholecystectomy followed by bupivacaine instillation and, two, those with cholelithiasis who underwent cholecystectomy followed by no intervention. Our data cannot be generalized at the national level. Though the outcome of instillation of bupivacaine is comparable with previous evidence, to address these shortcomings, we suggest that large scale, randomized trials be conducted to identify the possible difference in the outcome of bupivacaine instillation to reduce frequency of the analgesia demand by the patient, time to mobilize after surgery and post-op stay.

In future comparative trails of ropivacaine can be evaluated in comparison to bupivacaine as a drug for pain management after elective laparoscopic cholecystectomy. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibers, resulting in a relatively reduced motor blockade. The reduced lipophilicity is also associated with the decreased potential for central nervous system toxicity and cardio-toxicity as it is metabolized extensively in the liver and excreted in urine (21).

Conclusion

We have found that the instillation of bupivacaine is an effective method of providing adequate analgesia to the patient after elective laparoscopic cholecystectomy. All the cases were observed during their hospital stay until satisfactorily discharged from the hospital. It is mandatory to conduct large scale studies on this topic to validate the conclusions. We can suggest after laparoscopic cholecystectomy, on the final stage of closure, peritrocal site, sub-phrenic space and gallbladder bed instillation of bupivacaine (0.12%) can significantly reduce the frequency of the analgesia demand by the patient, time to mobilize after surgery and post-op hospital stay.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of the article.

Reference

1. Csikesz NG, Singla A, Murphy MM. Surgeon volume metrics in laparoscopic cholecystectomy. Dig Dis Sci 2010;55:2398-99.
2. Muhammad NM. Experience of Laparoscopic Chole cystectomy Pak Armed Forces Med J 1996;46(2):59-61.
3. Soper NJ, Stockmann PT, Dunnegan DL, Ashley SW. Laparoscopic cholecystectomy. The new 'gold standard'? Arch Surg 1992; 127:917-20.
4. Kamran A, Mohammad Z, Mohammad AW. Comparison of operative stress after open & Laparoscopic Cholecystectomy.Pak J Surg 2008;24(2):83-6.
5. Adnan M, Muhammad AN, Shizan HF, Haroonur R. Laparoscopic cholecystectomy: an audit of 500 patients.J Ayub Med Coll Abbottabad 2011;23(4):88-90.
6. Yamakawa T, Fukuda N.History of surgery for cholelithiasis: from era of cholecystostomy to laparoscopic surgery. Nihon Geka Gakkai Zasshi. 2000; 101(12):877-81.
7. Muhammad Iqbal. Future of Minimally Invasive Surgery in Pakistan. Rawal Med J 2008;33(2):130.
8. David EJ, and Marshall MK. Pathogenesis and Treatment of Gallstones. EnglJMed 1993; 328:412-421.
9. Mohamed I. S, Shawkat S.G, Khalid S.S. Laparoscopic Cholecystectomy as a Day Surgery Procedure: Is it Safe?—An Egyptian Experience. Saudi J Gastroenterol. 2011; 17(4):277–279.
10. Singla S, Mittal G, Raghav.Pain management after laparoscopic cholecystectomy-a randomized prospective trial of low pressure and standard pressure pneumo peritoneum. J Clin Diagn Res. 2014 Feb;8(2):92-4.
11. Stinton LM, Myers RP, Shaffer EA. Epidemiology of gallstones. Gastroenterol Clin North Am.2010;39:157-169.
12. Tamhankar F, Mazari J. Postoperative Symptoms, After-Care, and Return to Routine Activity After Laparoscopic Cholecystectomy. JSLS. 2010 Oct-Dec; 14(4): 484–489.
13. Choi G. Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic choecystectomy. World Journal of Gastroenterology. 2015;21(47):13386.
14. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg. 2001;167 (2):84-96.
15. Jljri V, Kogler-Majeric. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy.Acta Anaesthesiol Scand 1997; 41:193-196.

16. Chundrigar T, Hedges AR, Morris R. Intraperitoneal bupivacaine for effective pain relief after laparoscopic cholecystectomy. Ann R Coll Surg Engl. 1993;75(6):437-9.
17. Ebrahimifard F, Nooraei N. Postoperative pain after laparoscopic cholecystectomy: a randomized clinical trial comparing intraperitoneal bupivacaine versus intravenous pethidine. Surg Laparosc Endosc Percutan Tech. 2013 Feb;23(1):88-92.
18. Sharma CS, Singh M, Rautela RS, Kochhar A, Adlakha N. Comparison of intraperitoneal and periportal bupivacaine and ropivacaine for postoperative pain relief in laparoscopic cholecystectomy: a randomized prospective study. Anaesth Pain & Intensive Care 2014;18(4):350-54.
19. Chun-NY ,Chun-YT, Chi-TC. Pain relief from combined wound and intraperitoneal local anesthesia for patients who undergo laparoscopic cholecystectomy. BMC Surg 2014; 14:28.
20. Susanne M. Intraperitoneal Bupivacaine Does Not Effectively Reduce Pain After Laparoscopic Cholecystectomy: A Randomized, Placebo-Controlled and Double-Blind Study.Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 2000; 10(6) : 357-359.
21. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth 2011; 55(2):104-110.

How to cite?

Arshad R, Bajwa KM, Sikander M, Rashid R. The Effectiveness of Bupivacaine Instillation on Postoperative Pain after Elective Laparoscopic Cholecystectomy: A Prospective Randomized Controlled Trial. Ulutas Med J. 2019;5(1):26-33

DOI: 10.5455/umj.20190130080233