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Original Article

Comparative Analysis of Post-Operative Analgesia Duration in Laparoscopic Cholecystectomy: Intraperitoneal Bupivacaine Versus Bupivacaine/ Buprenorphine Combination

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ABSTRACT

Successful pain management following Laparoscopic Cholecystectomy (LC) is essential for a speedy recovery for patients. Intraperitoneal (IP) administration of analgesics, particularly bupivacaine and buprenorphine, offer promising approach to alleviate post-operative pain with minimized systemic side effects. **Objective:** To compare the duration of post-operative analgesia in patients undergoing laparoscopic cholecystectomy who receive either intraperitoneal bupivacaine alone or a combination of bupivacaine and buprenorphine. **Methods:** The quasi experimental study was conducted at Department of Anesthesiology, Farooq Hospital, Islamabad from April 2023 to September 2023. Patients scheduled for elective laparoscopic cholecystectomy for symptomatic cholelithiasis or other gallbladder diseases were included. The sampling methodology used was convenience sampling, with patients divided into two groups through the lottery method. Patients were assigned into two groups (55 patients in each group). Group A intraperitoneally received 25 ml dilution of bupivacaine (0.25%) in normal saline. Bupivacaine (0.25%) and buprenorphine (0.3mg) dissolved in normal ub6p B compared to Group A (9.26 ± 1.28 vs. 3.08 ± 1.04 hours, $p < 0.001$). **Results:** The mean BMI of participants was 29.79 ± 3.44 kg/m^2 Group A had 36 (65.5%) women and group B 41 (74.5%). The mean duration of post-operative analgesia was much greater in Group B (9.26 ± 1.28 hours vs. 3.08 ± 1.04 hours, $p < 0.001$). **Conclusions:** The combination of bupivacaine and buprenorphine offer post-operative analgesia in laparoscopic cholecystectomy with longer duration as compared to bupivacaine alone which is also statistically significant ($p < 0.001$).

INTRODUCTION

Laparoscopic Cholecystectomy (LC) remains as one of the most important milestones in surgical intervention in the field of surgical disease treatment of the twenty-first century. However, managing the post-operative pain for those patients who had this procedure is still a challenge [1]. It is a major shift from the traditional open method of cholecystectomy and provides patient with minimally invasive methods that clearly have several advantages in terms of post-operative pain management, duration of the hospital stay, rate of recovery and the scarring. Ever since the introduction of the method in the late 1980s, this method has become the standard for addressing symptomatic cholelithiasis and other gallbladder disorders [2, 3]. Laparoscopic cholecystectomy distinguished by employing multiple small incisions that are between 5 to 10mm in average, through which a small camera system and special gadgets inserted into the abdominal cavity [4]. These instruments provide the surgeon with fine control and enhanced magnification of the region being operated; thus enabling the surgeon to extinguish the gallbladder

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effectively without harming other tissues in the region [5]. The techniques applied regarding postoperative pain control in LC patients include systemic, regional, and neural blockade and local anesthetic techniques used during the surgery [6]. Among those, intraperitoneal applications local anesthetics has been emerged as potentially valuable addition to traditional approaches to pain relief [7]. Common to this procedure has been the use of bupivacaine – a long acting local anesthetic which has been used in several volumes of IP administration to manage pain at site of surgery in LC. When performing surgical procedures, surgeons introduce bupivacaine into the peritoneal cavity at the end of the surgery with the purposes of post-operative pain relief and minimizing the need for using systemic opioids [8, 9]. Bupivacaine is a local anesthetics drug that offers prolonged postoperative pain relief, it has a certain duration of action and therefore may require supplemental doses for further analgesia. Buprenorphine, an agonist at μ-opioid receptor is another drug that is given consideration as a contender to be added in combination with budivacaine for prolonging the duration of post-operative analgesia with a reduction in the side effects associated with opioids [10, 11].

This study aimed to expand current knowledge by investigating better pain management options among patients undergoing laparoscopic cholecystectomy by comparing duration of analgesic effect in patients those who receive intraperitoneal bupivacaine alone with those who receive a combination of bupivacaine and buprenorphine. Furthermore, it also answers a particular research question related to Pakistan to provide information on specific pain control measures applicable to the country that will improve on perioperative nursing care studies within the region.

METHODS

The current study was quasi experimental study. The work in this single center research took place in the Department of Anesthesiology, Farooq Hospital, Islamabad over a period of six months from April 2023 to September 2023. Approval was obtained from the institutional review board (FH/IRB/75). Any adverse events or protocol deviations were documented and reported promptly to the IRB. Informed consent was obtained from all participants prior to enrollment in the study. A sample size of 110 cases was determined using WHO calculator (www.openepi.com) with 55 patients allocated to each group, based on an 80% power of the test, a 5% level of significance, and an assumed mean duration of post-operative analgesia. In the bupivacaine group, the mean duration was estimated to be 3.07 ± 0.46 hours, while in the bupivacaine plus buprenorphine group, it was anticipated to be 9.60 ± 2.19 hours [11]. The study inclusion consisted of adult patients (aged 18 years and above) scheduled to undergo elective laparoscopic cholecystectomy for symptomatic cholelithiasis or other gallbladder pathologies. Patients with contraindications to laparoscopic surgery, known allergies to study medications, history of chronic pain syndromes, or significant comorbidities compromising surgical outcomes were excluded from the study. The sampling methodology used was convenience sampling, with patients divided into two groups through the lottery method. Patients in Group A intraperitoneal received 25 ml dilution of bupivacaine (0.25%) in normal saline. Patients in Group B received intraperitoneal infiltration of bupivacaine (0.25%) plus buprenorphine (0.3mg) diluted in normal saline. The primary outcome measure was the mean duration of post-operative analgesia, defined as the time from completion of surgery to the first request for rescue analgesia (opioid analgesics). The data were entered into SPSS version 25.0, and the results were analyzed. Descriptive statistics, including mean values with standard deviations (mean ± SD), were used to analyze numerical variables like age and post-operative analgesic duration. An independent sample t-test and Mann-Whitney U test were used to compare post-operative analgesia duration between groups, with a significance level of $p < 0.05$. Gender frequencies and percentages were given using the Chi-square test. Data were stratified by age and gender to adjust for effect modifiers. Post-stratification independent sample t-tests were performed, with a significance level of $p < 0.05$.

RESULTS

This study has shown that in Group A, the mean age was 47.2 ± 8.4 years while Group B had a slightly higher mean age of 48.5 ± 7.6 (p value=0.62). The distribution of gender within the groups was fairly balanced, with Group A consisting of 39 males (45.88%) and 46 females (54.11%), while Group B had 44 males (51.76%) and 41 females (48.23%). Group A had a mean BMI of 27.5 ± 7.6, whereas Group B had a slightly lower mean BMI of 26.3 ± 6.4. In Group A 31 individuals (36.47%) were diagnosed with hypertension , while in Group B had 26 individuals (30.59%) with the condition, as shown in table 1.

Table 1: Demographic Characteristics between Group A and Group B

Variables	Overall N (%)/ (Mean ± SD)	Group A N (%)/ (Mean ± SD)	Group B N (%)/ (Mean ± SD)	p-Value
Gender				
Female	77 (70.0%)	36 (65.5%)	41 (74.5%)	0.298[a]
Male	33 (30.0%)	19 (34.55)	14 (25.55)	
Age Groups (Years)				
25-35	13 (11.8%)	6 (10.9%)	7 (12.7%)	0.756[b]
36-45	43 (39.1%)	22 (40.0%)	21 (38.2%)	0.542[b]
46-55	39 (35.5%)	19 (34.5%)	20 (36.4%)	0.853[b]
56-65	15 (13.6%)	8 (14.5%)	7 (12.7%)	0.771[b]
Age (Years)	45.67 ± 9.61	45.93 ± 9.58	45.42 ± 9.71	0.782[b]
BMI (Kg/m^2)	29.79 ± 3.44	29.27 ± 3.20	30.32 ± 3.62	0.085[c]

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a Chi-square test; b Independent sample t-test; c Mann-Whitney U test.

The mean duration of post-operative analgesia was much greater in Group B (9.26 ± 1.28 hours vs. 3.08 ± 1.04 hours, p < 0.001), as shown in table 2.

Table 2: Between Group Comparison of Mean Duration of Post-Operative Analgesia

Variables	Group A (Mean ± SD)	Group B (Mean ± SD)	p-Value
Duration of Analgesia (Hours)	3.08 ± 1.04	9.26 ± 1.28	< 0.001[a]

a Mann-Whitney U test.

Subgroup analysis based on gender, age, and BMI further supported the significant difference in the duration of post-operative analgesia between the two study groups, as depicted in table 3. Regardless of gender, age group, or BMI, patients in Group B experienced a substantially longer duration of post-operative analgesia compared to those in Group A (p < 0.001)(Table 3).

Table 3: Between Group Comparison of Mean Post-Operative Analgesia Hours with Respect to Gender, Age, and BMI

Variables	Group A N (%)/ (Mean ± SD)	Group B N (%)/ (Mean ± SD)	p-Value
Gender			
Female	2.97 ± 1.01	9.30 ± 1.37	< 0.001
Male	3.27 ± 1.08	9.12 ± 1.00	< 0.001
Age Groups (Years)			
25-35	3.05 ± 0.82	9.22 ± 0.80	0.001
36-45	3.07 ± 1.10	9.31 ± 1.66	< 0.001
46-55	3.13 ± 1.06	9.25 ± 1.11	< 0.001
56-65	2.96 ± 1.12	9.15 ± 0.99	< 0.001
BMI (Kg/m^2)			
< 30	3.07 ± 1.08	9.37 ± 1.43	< 0.001
≥ 30	3.10 ± 0.96	9.05 ± 0.97	< 0.001

a Mann-Whitney U test.

DISCUSSION

The mean duration of post-operative analgesia is a critical aspect in assessing pain management efficacy following laparoscopic cholecystectomy. Intraperitoneal bupivacaine administration has traditionally been utilized to mitigate post-operative pain in this procedure, while combining bupivacaine with buprenorphine shows promise for extending analgesic duration and improving patient outcomes [12, 13]. The efficacy of intraperitoneal bupivacaine alone versus bupivacaine plus buprenorphine is analyzed, considering their respective roles in optimizing post-operative pain control and patient satisfaction. Our study participants exhibited a mean age of 45.67 ± 9.61 years, with a majority being female (70.0%). This is in concordance with the findings of Chaudhary SM *et al.*, who found the mean age to be almost similar at 47 years. 56 ± 9.24 years and female patients are more in number as compared to male patients (70%) [14]. Current results are consistent with the study by Khurana S *et al.*, who reported that the mean age was 48.87 ± 11. Laparoscopic cholecystectomy was done in 90 patients, and the average age was 41 years [11]. Such consistent demographic characteristics across various studies add to the external validity of our results and indicate homogeneity in the patient population receiving this surgical intervention [11, 12]. The results of the present study showed that there was a statistically significant difference in the mean duration of post-operative analgesia between both the groups, and the mean duration was found to be significantly longer in the group that received bupivacaine combined with buprenorphine compared to the group that received intraperitoneal bupivacaine alone (9.26 ± 1.28 vs 3.08 ± 10) findings are in line with the studies of Khurana S *et al.*, in 2016 and Chaudhary SM *et al.*, in 2017, where they also found that the combination of bupivacaine and buprenorphine has significantly increased analgesia duration as compared to bupivacaine only [11, 14]. More specifically, Khurana S *et al.*, observed a mean duration of analgesia of 9.60 ± 2.19 hours in the combination group as compared to control group to be 3.07 ± 0.46 [11]. Similar results were found in study of Chaudhary SM *et al.*, in 2014, where the mean duration of post-operative analgesia was significantly longer with intraperitoneal bupivacaine combined with buprenorphine (9.43 ± 1.08 hrs) compared to intraperitoneal bupivacaine alone (3.05 ± 1.18 hrs; p=0.000) [14]. These consistent findings across studies support the effectiveness of adding buprenorphine to bupivacaine to prolong the postoperative pain relief in patients who underwent laparoscopic cholecystectomy [10, 13]. The patients in the study were considerably younger (34.6 ± 12.5 years) than the general population of patients who undergo surgery and anaesthesia; the mean duration of anaesthesia after surgery was 4.6 ± 3.7 hours with bupivacaine only as mentioned by Sharma CS *et al.*, in 2014 [15]. Similarly, a randomized clinical trial done by Williams *et al.*, conclusively demonstrated greater pain reductions after administrating bupivacaine along with buprenorphine as compared to the plain BPV group (mean difference 1.8 points, 95% confidence interval 0.6 to 3.0, P = 0.003). These findings align with our results, reinforcing the enhanced analgesic efficacy of combining bupivacaine with buprenorphine over bupivacaine alone [16]. his finding aligns with Manan A *et al.*, in 2020, who reported a mean post-operative analgesia duration of 0.99 ± 0.51 hours in the normal saline group and 16.53 ± 2.65 hours in the bupivacaine group (p < 0.001) [17]. Further, the study of Mahajan L *et al.*, in 2020 revealed that there were statistically significant differences in the post-operative analgesia duration between the groups; the bupivacaine combined with buprenorphine group had the longest duration of 11.5 ± 0.9 hours, the bupivacaine only group had 7.5 ± 0.9 hours [18]. Similarly, Arabzadeh A *et al.*, in 2021 found a similar pattern, where the postoperative analgesic

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durations were significantly longer in the bupivacaine with buprenorphine group compared to the bupivacaine-only group, thus supporting the repeatability of this finding in prior studies [19]. Moreover, Deshmukh P *et al.*, in 2021 demonstrated prolonged analgesic duration with the buprenorphine-bupivacaine combination, supporting our findings and providing further evidence for its efficacy in extending post-operative pain relief [20]. A notable limitation of the present study was the lack of comparison in terms of the complications or side effects linked to the combination therapy, which is an essential component of patient care.

CONCLUSIONS

This study demonstrates the efficacy of intra-peritoneal bupivacaine plus buprenorphine in extending the post-operative analgesia duration in patients who have undergone laparoscopic cholecystectomy as highlighted by the large difference in the mean durations between the treatment groups 9.26 ± 1.28 hours versus 3.08 ± 1.04 hours; $p < 0.001$.

Authors Contribution

Conceptualization: HAH

Methodology: HAH, RS[1], KI, AZ, RS[2]

Formal analysis: RS[1], TA

Writing, review and editing: KI, AZ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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