ORIGINAL ARTICLE

Comparison of Mean Duration of Post-Operative Analgesia in Laparoscopic Cholecystectomy Patients receiving Intra-peritoneal Bupivacaine versus Bupivacaine plus Buprenorphine

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ABSTRACT

Aim: To compare the mean duration of post-operative analgesia in laparoscopic cholecystectomy patients receiving intraperitoneal bupivacaine versus bupivacaine plus buprenorphine.
Design: It was a randomized controlled trial.
Place and duration of study: This study was conducted at the Department of Surgery, Unit-I, Sir Ganga Ram Hospital, Lahore over 6 months period from July 2015 through December 2015.
Methods: This study was a blend of both the genders with 80 patients having age between 20-70 years undergoing laparoscopic cholecystectomy under general anesthesia. Two treatment groups were made by dividing these patients equally. Patients of Group-A (n=40) received intra-peritoneal bupivacaine alone while patients of Group-B (n=40) received intra-peritoneal bupivacaine + buprenorphine. Outcome variable was post-operative analgesia duration which was noted and compared between the two groups. An informed written consent was taken from all the patients.
Results: The patients had a mean age of 47.56±9.24 years. The sample included 24(30%) male and 56(70%) female patients with a female to male ratio of 2.3:1. Both the study groups had no significant difference in reference with age groups (p=1.000), gender (p=0.626) distribution and mean age (p=0.971). The mean duration of post-operative analgesia was significantly longer with intra-peritoneal bupivacaine+buprenorphine (9.43±1.08 hrs. vs. 3.05±1.18 hrs; p=0.000) as compared to intra-peritoneal bupivacaine alone. This difference was significant across all age and gender groups.
Conclusion: The mean duration of post-operative analgesia was long significantly with intra-peritoneal bupivacaine+buprenorphine (9.43±1.08 hrs. vs. 3.05±1.18 hrs; p=0.000) as compared to intra-peritoneal bupivacaine alone regardless of patient's age and gender.
Keywords: Laparoscopic Cholecystectomy, Post-operative Analgesia, Intra-Peritoneal Bupivacaine,

INTRODUCTION

Now a days a rapidly growing specialty of surgery is MIS (Minimally invasive surgery)[1]. The underlying cause of rising frequency of laparoscopic surgeries is lesser postoperative pain and shorter healing time in comparison with the open procedure that gives speedy recovery consequential discharging of patient from the hospital. Postoperative problems like vomiting, nausea, pain though less frequent in comparison with open procedure, are noted to be substantial enough to upset the recovery process and results into deferred discharge from the hospital.[1] Pain is the most impendent and imperative factor determining the recovery time. The typical treatment of pain is parenteral and oral analgesics especially the opioids. Though a quick onset of analgesic effect is offered by these drugs yet they are linked with adverse effects like constipation, somnolence, respiratory depression and PONV (postoperative nausea and vomiting), that results in tardy discharge from hospital.[2] consequently, alternate means for relieving pain have been considered over time to minimize the hospital stay with better satisfaction of the patient.

Intraperitoneal instillation of bupivacaine is a conventional practice to control post-operative pain. Nevertheless, the action period of intraperitoneal bupivacaine was noting to be varying. The results of studies vary from substantial reduction in pain in 24-48 hours after surgery[3,4] to that of no reduction in pain[5,6]. However, a modest reduction in pain was noted by other author and it was only detectable after 2 hours of surgery[7] or up to 6-8 hours after surgery[8,9]. Newer studies are considering the combination of anesthetics for post-operative pain relief[10,11]. Khurana et al. conducted a study on the comparison of duration of post-operative analgesia after laparoscopic cholecystectomy between intraperitoneal bupivacaine versus combination of bupivacaine plus buprenorphine and found that the duration of analgesia was drastically higher in bupivacaine plus buprenorphine group than

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bupivacaine alone (3.07±0.46 hours in bupivacaine group vs. 9.60±2.19 hours in bupivacaine plus buprenorphine combination; p<0.01)[10].

The results of this randomized controlled trial are promising; and combination of bupivacaine plus buprenorphine can thus provide pain relief for longer duration. However, this study is first of its kind and no other local or international arch study was available. Therefore, repetition of this trail for confirmation of role of combination of bupivacaine plus buprenorphine in prolonging mean duration of post-operative analgesia in those patients who were undergoing laparoscopic cholecystectomy in local population.

PATIENTS AND METHODS

It was a randomized controlled trial. Research was conducted at Department of Surgery Sir Ganga Ram Hospital, Lahore. Duration of study was 6 months from July 2015 through December 2015. With 5% significance level, sample size was consisted of 80 cases (40 in each group) was calculated with 80% power of test, 5% level of significance and taking mean duration of post-operative analgesia to be 3.07±0.46 hours in bupivacaine group and 9.60±2.19 hours in bupivacaine plus buprenorphine[10]. Selection of patients was made on by Non-probability, Consecutive Sampling. Patients of both sex groups with ages in the range of 30-70 years suffering cholelithiasis (gallbladder showing single or multiple calculi as per abdominal ultrasound) were included in the study.

Exclusion criteria: Patients who were sensitive to local anesthetics, had previous upper abdominal procedures (area between the xiphisternum to the umbilicus) or endoscopic retrograde cholangio-pancreatography (ERCP) with or without endoscopic sphincterotomy (ES) as per history and clinical record of the patient. Patients with acute cholecystitis (Ultrasound showing peri-cholecystic fluid, and/or gallbladder wall thickening>5mm), choledocho-lithiasis (total bilirubin>1.2 mg/dl and presence of CBD stones on ultrasound), ascending cholangitis (temperature>38.6°C, serum bilirubin> 1.2mg/dl and ultrasound showing common bile duct diameter of > 1cm), uncontrolled diabetes (fasting blood glucose level >1l0mg/dl), uncontrolled systolic blood pressure >140 mmHg), ischemic heart disease (ejection fraction <40%) and pulmonary dysfunction (FEV1<70% of the normal) were also excluded.

Data collection procedure: Laparoscopic cholecystectomy was performed. Bupivacaine 25ml (0.25% concentration) or bupivacaine 25 ml (0.25%) plus buprenorphine (0.3mg) was instilled on liver's upper surface, on the right sub-diaphragmatic space and in the gall bladder fossa for allowing its diffusion in space near and above the hepatoduodenal ligament after extraction of the gall bladder. Duration of post-operative analgesia was noted. Attached performa was used for noting and recording of all the data, along with patient's demographic details. All surgeries were performed by the same surgical team and all the durations of the pain relief were assessed on the same chart to eliminate bias and confounding variables were controlled by exclusion.

Data Analysis: Numerical variables; duration of post-operative analgesia and age have been shown by mean±SD. For comparing mean duration of post-operative analgesia between the 2 groups taking p≤0.05 as significant, independent sample t-test was used. Categorical variables; presentation of gender has been made as percentage and frequency. Data has been stratified for gender and age to redress effect modifiers. By taking p-value ≤0.05 as significant, post-stratification independent sample t-test has been applied.

RESULTS

The patients had an age range of 35-65 years with a mean of 47.56±9.24 years. Number of male patients was 24(30%) while females were 56(70%) female patients with a female to male ratio of 2.3:1. Summary of findings is given in Table 1.

Table 1: Baseline Characteristics of the Study Cohort

Characteristics	**Participants (n=80)**
Age (years)	47.56±9.24
Age groups	
• 35-45 years	40(50%)
• 46-55 years	20(25%)
• 56-65 years	20(25%)
Gender	
• Male	24(30%)
• Female	56(70%)

No significant difference was observed in the two study groups in terms of mean age (p=0.971), age groups (p=1.000) and gender (p=0.626) distribution as shown in Table 2. Mean duration of post-operative analgesia was radically long with intra-peritoneal bupivacaine + buprenorphine (9.43±1.08 hrs. vs. 3.05±1.18 hrs; p=0.000) as compared to intra-peritoneal bupivacaine alone. This difference was significant across all age and gender groups as shown in Table 3.

Table 2: Baseline characteristics of the study groups

Characteristics	Intra-peritoneal Bupivacai	Intra-peritoneal Bupivacaine + Buprenorphin
Age* (years)	47.53±9.32	47.60±9.27
Age group (p value 1.000)		
• 35-45 years	20(50%)	20 (50%)
• 46-55 years	10(25%)	10 (25%)
• 56-65 years	10(25%)	10 (25%)
Gender (P value0.626)		
• Male	11(27.5%)	13 (32.5%)
• Female	29(72.5%)	27 (67.5%)

*P value=0.971

Independent sample t-test and chi-square test, observed difference was statistically insignificant

Table 3: Comparison of Mean Duration of Post-Operative Analgesia (hours) between the Study Groups

Characteristics	n	Intra-peritoneal Bupivacaine	Intra-peritoneal Bupivacaine + Buprenor-phine	P value
Overall	40/40	3.05±1.18	9.43±1.08	0.000*
Age Groups (years)				
• 18-23	20/20	3.05±1.36	9.45±1.09	0.000*
• 24-29	10/10	3.10±0.99	9.50±1.08	0.000*
• 30-36	10/10	3.00±1.05	9.30±1.16	0.000*
Gender				
• Male	11/13	3.09±1.30	9.54±1.13	0.000*
• Female	29/27	3.03±1.15	9.37±1.08	0.000*

*Independent sample t-test, *The observed difference was statistically significant*

DISCUSSION

Treating acute postoperative pain is said to be highly important health-care subject. In the last twenty years or so, the under treatment of acute pain has been widely recognized as a chief issue in health care. It has been held by the researchers that that only one in four surgical patients receive adequate relief of acute pain[11]. A number of detrimental acute can be produced by postoperative pain (i.e., chronic effects (i.e., delayed long-term recovery and chronic pain) and adverse physiologic responses) particularly when poorly contorlled[12]. In order to avoid negative outcomes viz-a-viz hypertension, tachycardia, poor healing of wound, decreased alveolar ventilation, myocardial ischemia, deep venous thrombosis and immobility. Therefore, it is necessary to have good pain control after surgery[12,13].

Minimally invasive surgery (MIS) is one of the rapidly growing fields of surgery[1]. The underlying cause of increasing number of laparoscopic surgeries is lesser postoperative pain and shorter time of healing time when making its comparison with open procedure resulting in speedy recovery and discharge from the hospitals. Postoperative problems such as pain, nausea, and vomiting though less frequent as equated to open procedure, have been found to be substantial enough to upset the recovery process and deferred discharge from the hospital[1,14]. In predicting recovery time, pain is most vital and independent factor. Normally, oral and parenteral opioids are used for managing pain. Despite of the fact that a rapid onset action is provided by these drugs yet they are linked with delayed discharge owing to some common side effects like PONV (postoperative nausea and vomiting), constipation, somnolence, and respiratory depressionge[15].

Therefore, study on substitute means of pain relief has been made with the passage of time for limiting stay at hospital with improved patient satisfaction. Intraperitoneal instillation of bupivacaine is a conventional practice to control post-operative pain. However, the action duration of intraperitoneal bupivacaine is found varying. The results of studies varies considerably in reduction of pain over 24-48 hours after surgery[16,17] upto no noticeable reduction in pain[10,19]. A modest reduction in pain was noted by other authors detection of which was detectable only 2 hours after surgery[7] or up to 6-8 hours after surgery[20,12]. Newer studies are considering the combination of anesthetics for post-operative pain relief[13,21].

In the present study, the mean age of the patients was 47.56±9.24 years. There were 24(30%) male and 56(70%) female patients with a male to female ratio of 1:2.3. The mean duration of post-operative analgesia was significantly longer with intra-peritoneal bupivacaine+buprenorphine (9.43±1.08hrs vs 3.05±1.18hrs; p=0.000) as compared to intra-peritoneal bupivacaine alone regardless of patients age and gender. The results of the present study are matching with the results of Khurana et al. who studied 90 patients undergoing laparoscopic cholecystectomy with a mean age of 48.87±11.41 years and with female to male ratio of 2.3:1. A significantly long duration of analgesia was reported by them in bupivacaine plus buprenorphine group than bupivacaine alone (9.60±2.19 vs. 3.07±0.46 hours; p<0.01)[10]. Chakravarty et al. conducted a similar study on 30 patients with a mean age of 46.5±10.6 years and female to male ratio of 2.5:1. They observed similar mean duration of post-operative analgesia; 3.07±0.82 hours with intraperitoneal bupivacaine alone[22]. Sharma et al. however reported relatively longer mean duration of post-operative analgesia of 4.6±3.7 hrs. with bupivacaine alone. A possible cause for this conflict can be the relatively younger age of patients (34.6±12.5 years) in their series[23].

The present study is fist of its kind in local population and adds to the limited existing evidence on the role of combination therapy comprising of intra-peritoneal bupivacaine + buprenorphine in post-operative analgesia after laparoscopic cholecystectomy. The results of the study confirm that this combination regimen has more prolonged post-operative pain relief so decreased the post-operative analgesic requirement with the associated complications and morbidity. It can be thus advocated that future patients undergoing laparoscopic cholecystectomy should be given intra-peritoneal bupivacaine + buprenorphine at the end of procedure to get prolonged post-operative analgesia.

There is a strong limitation to the present study and that is we didn't compare the complications/ side effects of this combination therapy which is an important aspect of management and should be considered in future studies.

CONCLUSION

The mean duration of post-operative analgesia was significantly longer with intra-peritoneal bupivacaine + buprenorphine (9.43±1.08 hrs. vs. 3.05±1.18 hrs.; p=0.000) as compared to intra-peritoneal bupivacaine alone regardless of patient's age and gender.

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