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Research Article

Comparing Mean Duration of Post-operative Analgesia in Laparoscopic Cholecystectomy Patients Receiving Intra-peritoneal Bupivacaine/Bupivacaine Plus Buprenorphine

Muhammad Bilal Akbar*, Babar Hameed, Keesa Zahra

General Surgery, NHS Grampian De Grays Hospital, United Kingdom

***Corresponding Author:** Muhammad Bilal Akbar, General Surgery, NHS Grampian De Grays Hospital, United Kingdom.

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Abstract

Laparoscopic procedures are the newest techniques with better outcomes for most upper GI pathologies. As a matter of fact Laparoscopic Cholecystectomy has become the gold standard these days for cholelithiasis. In post op recovery for these patients, Post-operative pain is one of the commonest entity to deal with and there are number of drugs that can be added. Bupivacaine and Buprenorphine have shown promising results.

Objective: To compare the mean duration of post-operative analgesia in laparoscopic cholecystectomy patients receiving intra-peritoneal bupivacaine/bupivacaine plus buprenorphine.

Study design: Randomized controlled trial.

Settings: Surgical department, National Hospital, and medical Centre, Lahore.

Duration of study: 24-02-20to 24-09-20.

Sampling technique: Non probability consecutive sampling**.**

Methodology: In this study the patients of both sex groups with age in the range of 20 to 60 years undergoing laparoscopic cholecystectomy were included. Cases in group A were given Bupivacaine 0.25% and those in group B were given Bupivacaine 0.25% and Buprenorphine. Duration of post operative analgesia was noted.

Results: In this study there were total 60 cases, 30 in each group. There were 14 (46.67%) males in group A and 13 (43.33%) in group B with mean age in group A was 45.67 ± 11.12 vs 44.89 ± 9.66 in group B. Mean duration of post operative analgesia was 3.14 ± 0.71 vs 8.97 ± 1.13 in group A and B with p = 0.001. Mean duration of post operative analgesia in males was 3.19 ± 0.81 vs 9.02 ± 0.91 and in females 3.02 ± 0.67 vs 8,34 ± 0.56 in group A and B with p values of 0.001 and 0.003 respectively. This duration of analgesia was also significantly high in both age groups i.e. 20-39 years and 40-60 years with p values of 0.001 and 0.002 respectively. Post operative analgesia duration was much better in group B regarding BMI less than 30 where this was seen as 9.97 ± 1.23 vs 3.87 ± 1.13 with p = 0.001 and in BMI 30 or more this was 8.11 ± 0.94 vs 2.97 ± 0.43 in group B and A respectively with p = 0.01.

Conclusion: Mean duration of post operative analgesia was significantly better in cases treated with intra peritoneal bupivacaine and buprenorphine as compared to bupivacaine only and this difference is significantly better in all the confounding variable like age, gender and BMI.

Keywords: Bupivacaine; Buprenorphine; VAS

Introduction

Whereas it is true that no operation has been more profoundly affected by the advent of laparoscopy than cholecystectomy has, it is equally true that no procedure has been more instrumental in ushering in the laparoscopic age than laparoscopic cholecystectomy has. Laparoscopic cholecystectomy has rapidly become the procedure of choice for routine gallbladder removal and is currently the most commonly performed major abdominal procedure in Western countries [1]. A National Institutes of Health consensus statement in 1992 stated that laparoscopic cholecystectomy provides a safe and effective treatment for most patients with symptomatic gallstones and has become the treatment of choice for many patients [2]. This procedure has more or less ended attempts at noninvasive management of gallstones.

The initial driving force behind the rapid development of laparoscopic cholecystectomy was patient demand. Prospective randomized trials were late and largely irrelevant because advantages were clear. Hence, laparoscopic cholecystectomy was introduced and gained acceptance not through organized and carefully conceived clinical trials but through acclamation.

Laparoscopic cholecystectomy decreases postoperative pain, decreases the need for postoperative analgesia, shortens the hospital stay from 1 week to less than 24 hours, and returns the patient to full activity within 1 week (compared with 1 month after open cholecystectomy) [3,4]. Laparoscopic cholecystectomy also provides improved cosmesis and improved patient satisfaction as compared with open cholecystectomy. Although direct operating room and recovery room costs are higher for laparoscopic cholecystectomy, the shortened length of hospital stay leads to a net savings. More rapid return to normal activity may lead to indirect cost savings [5]. Not all such studies have demonstrated a cost savings, however. In fact, with the higher rate of cholecystectomy in the laparoscopic era, the costs in the United States of treating gallstone disease may actually have increased. Trials have shown that laparoscopic cholecystectomy patients in outpatient settings and those in inpatient settings recover equally well, indicating that a greater proportion of patients should be offered the outpatient modality [6]. Laparoscopic cholecystectomy has received nearly universal acceptance and is currently considered the criterion standard for the treatment of symptomatic cholelithiasis [6,7]. Many centers have special "short-stay" units or "23-hour admissions" for postoperative observation following this procedure [6].

Material and Methods

Study design

Randomized controlled trial.

Settings

Surgical department, National Hospital, and medical centre, Lahore.

Duration of study

24-02-19 to 24-09-19.

Sample size

Sample size of 60 (30 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.

Sampling technique

Non probability consecutive sampling.

Sample selection

Inclusion criteria

- Patients of both sex groups with age in the range of 20-60 years undergoing laparoscopic cholecystectomy as per operational definition.
- Patients who signed written consent to participate in the study.

Exclusion criteria

- Patients who were sensitive to bupivacaine as per history of the patients
- Patients with history of previous upper abdominal procedures (area between the xiphisternum to the umbilicus).
- Patients with acute Cholecystitis (ultrasound showing pericholycystic fluid, and or gall bladder wall thickening > 5 mm
- Patients with choledocolithiasis (total bilirubin > 1.2 mg/dl and presence of CBD stones on ultrasound), ascending cholangitis (temperature > 38.6 C) as per clinical record.

- Patients with serum bilirubin > 1.2 mg/dl and ultrasound showing common bile duct of > 1 cm.
- Patients with uncontrolled diabetes (fasting blood glucose level > 110 mg/dl), uncontrolled blood pressure (systolic blood pressue > 140 mmHg), ischemic heart disease (ejection fraction < 40%) and pulmonary dysfunction (FEV1 < 70%) of the normal) as per clinical record.

Data collection procedure

After approval from ethical review committee of the hospital, 60 cases that presented in the department of surgical National Hospital, Medical Centre, Lahore and who fulfilled the above criteria were counselled and explained the details of the study. Written informed consent and detailed history was taken from each patients. These patients were then randomly divided in to two groups using computer generated randomization table.

- Group A; Bupivacaine plus buprenorphine
- Group B; Bupivacaine.

Laparoscopic cholecystectomy was performed using 4 ports. At the end of the procedure, bupivacaine 25 ml (0.25% concentration) or bupivacaine 25 ml (0.25%) plus buprenorphine (0.3 mg) were instilled on the upper surface of liver, on the right sub diaphragmatic space and n the gall bladder fossa to allow it to diffuse into the space near and above the hepato-dudenal. Duration of post operative analgesia was noted and recorded into the attached performa along with demographic details of the patients. All the surgeries were performed by the same surgical team involving the candidate to eliminate bias and confounding variable were controlled by exclusion.

Data analysis procedure

All the collected data was entered and analyzed into SPSS version 21.

- Numerical variable i.e. age, BMI and duration of post operative analgesia were presented by mean and SD and rang. T test was applied for comparison of mean duration of analgesia between the two groups.
- Categorical variables i.e. gender were presented as frequency and percentage
- Data was stratified for age, gender and BMI to address effect modifiers. Post stratification independent sample t test were applied taking p value pf < 0.05 as statistically significant.

Results

In this study there were total 60 cases, 30 in each group. There were 14 (46.67%) males in group A and 13 (43.33%) in group B as shown in table 1. The mean age in group A was 45.67 ± 11.12 vs 44.89 ± 9.66 in group B (table 2). Mean BMI in group A and B was 29.89 ± 5.34 vs 30.67 ± 5.89 kg/m² as shown in table 03. Mean duration of post operative analgesia was 3.14 ± 0.71 vs 8.97 ± 1.13 in group A and B with p = 0.001 as shown in table 04. Mean duration of post operative analgesia in males was 3.19 ± 0.81 vs 9.02 ± 0.91 and in females 3.02 ± 0.67 vs 8,34 ± 0.56 in group A and B with p values of 0.001 and 0.003 respectively (table 05). This duration of analgesia was also significantly high in both age groups i.e. 20-39 years and 40-60 years with p values of 0.001 and 0.002 respectively as in table 06. Post operative analgesia duration was much better in group B regarding BMI less than 30 where this was seen as 9.97 ± 1.23 vs 3.87 ± 1.13 with p = 0.001 and in BMI 30 or more this was 8.11 ± 0.94 vs 2.97 ± 0.43 in group B and A respectively with p = 0.01 as displayed in table 07.

Gender	Group	
	Group A	Group B
Male	14 (46.67%)	13 (43.33%)
Female	16 (53.33%)	17 (56.67%)
Total	30	30

Table 1: Gender Distribution n = 60 (30 in each group).

	AGE	
	Group A	Group B
Mean	45.67	44.89
Std. Deviation	11.12	9.66
Minimum	20	21
Maximum	60	60

Table 2: Age in study subjects n = 60 (30 in each group).

	BMI (kg/m^2)	
	Group A	Group B
Mean	29.89	30.67
Std. Deviation	5.34	5.89
Minimum	26	28
Maximum	38	37

Table 3: BMI in study subjects n = 60 (30 in each group).

	GROUP		p
	A	B	
Post operative pain	3.14 ± 0.71	8.97 ± 1.13	0.001

Table 4: Post operative analgesia duration with respect to both groups n = 60 (30 in each group).

Gender	Group		p value
	A	B	
Male	3.19 ± 0.81	9.02 ± 0.91	0.001
Female	3.02 ± 0.67	8,34 ± 0.56	0.003

Table 5: Post operative analgesia duration in both groups with respect to gender n = 60 (30 in each group).

Age	Group		p value
	A	B	
20-39	3.23 ± 0.87	9.56 ± 0.98	0.001
40-60	3.11 ± 0.61	8.91 ± 0.45	0.002

Table 6: Post operative pain in both groups with respect to age n = 60 (30 in each group).

BMI	Group		p value
	A	B	
<30	3.87 ± 1.13	9.97 ± 1.23	0.001
30 or more	2.97 ± 0.43	8.11 ± 0.94	0.01

Table 7: Post operative pain in both groups with respect to BMI n = 60 (30 in each group).

Discussion

There is always an ongoing advancement in the field of surgery and so is the finding of laparoscopic surgeries which have greatly reduced the threats, fears and dreadful complications like large incisions, amount of blood loss and the degree of post operative pain and morbidity, but yet they are not devoid of complications. The most common complications associated after laparoscopic surgeries include pain which is most at abdomen, shoulder region and back and need to be addressed as it can add to overall morbidity and can halt the process of early mobilization and enhanced recovery and on the other hand reduced risk of atelectasis and deep vein thrombosis.

A number of modalities have been tried in the past to reduce this pain after laparoscopic cholecystectomy and these included the different pressure used for insufflating gas, application of local anesthetic to the site of surgery, infiltration of local anesthetic to the skin and muscle wounds and usage of appropriate NSAIDS. Along with local anesthetic agents, different combination therapies have also been tried with different degree of success to relief any degree of pain.

In the present study, Mean duration of post operative analgesia was 3.14 ± 0.71 hours with Bupivacaine only as compared to 8.97 ± 1.13 hours in group A and B with p = 0.001. These results were close to the findings of the previous studies which have also shown that combination therapy has shown relatively better results. Mraovic B., *et al*. in their study compared the Bupivacaine with the placebo and it was seen that Bupivacaine 0.5% resulted in significantly better results as compared to placebo where 15 ml of 0.9% normal saline was given in cases undergoing cholecystectomy.

In a study carried out by Khurana S., *et al*. on cases of laparoscopic cholecystectomy, they compared the three groups. One was offered 25 ml of 0.9% saline, the other was given 0.25% Bupivacaine and third was treated with 0.25% Bupivacaine with 0.3 mg of Buprenorphine and were assessed for mean post operative analgesia. It was found that mean post operative analgesia was lowest with saline and was seen for 8 hours, while this was even seen up to 24 hours with combination therapy. This variation of results can be explained by the factor that they used higher volume and also the higher strength of the Bupivacaine for analgesia.

Moreover, the Khhurana S., *et al*. studied the comparison of these groups in terms of number of variables i.e. mean post operative score on visual analogue scale not only on the basis of time but also with cough where again the combination of Bupivacaine and Buprenorphine was found statistically significantly better ($p < 0.05$).

According to another study done by Hernández-Palazón J., *et al*. it was found that intraperitoneal instillation of combination therapy i.e. by Bupivacaine combined with Morphine has also led to significantly better results in terms of pain management ($p < 0.05$). The reason of the better analgesic properties of Bupivacaine in all these studies can be explained by the lipophilic nature of the buprenorphine which leads to its slow and sustained release and hence provide better analgesia for longer duration of times.

In another study done by Gul A., *et al*. compared Bupivacaine with placebo and it was seen that in their two groups of Bupivacaine and placebo the mean post operative pain was better with Bupivacaine where it was seen as 3.61 ± 0.67 vs 3.83 ± 0.66 with p value of 0.03 and on further stratification they did not find any significant difference in terms of gender where it was 3.75 ± 0.707 and 3.90 ± 0.737 in males and 3.607 ± 0.677 and 3.80 ± 0.663 respectively in females with p value of 0.513.

This was in contrast to the results of the present study where Mean duration of post operative analgesia in males was 3.19 ± 0.81 vs 9.02 ± 0.91 and in females 3.02 ± 0.67 vs 8,34 ± 0.56 in group A and B with p values of 0.001 and 0.003 respectively and furthermore this duration of analgesia was also significantly high in both age groups i.e. 20-39 years and 40-60 years with p values of 0.001 and 0.002 respectively as in table 06. Post operative analgesia duration was much better in group B regarding BMI less than 30 where this was seen as 9.97 ± 1.23 vs 3.87 ± 1.13 with p = 0.001 and in BMI 30 or more this was 8.11 ± 0.94 vs 2.97 ± 0.43 in group B and A respectively with p = 0.01.

These results were also supported by the studies done by Candido KD., *et al*. where they found that the pain relief can be controlled better after surgery in cases where Buprenorphine was added to the local anesthetic drugs like Bupivacaine. This can be explained by the fact of multimodal analgesia where each drug carries its own benefits.

According to another study done by Pasqualucci A., *et al*. also found Bupivacaine as better agent for the analgesia and they also further described that there were no significant side effect profiles in local instillation and also had no impact on respiratory rate as well as the changes in hemodynamic i.e. blood pressure and heart rate.

There were few limitations of these study as this study did not compare the both groups in terms of mean pain on visual analogue scale and majority of the studies did and furthermore, they also did not compare the use of an add one analgesic agent which was assessed in standard practices of the various studies done in the past.

However, there were many strengthening points as well, as this study highlighted the most under rated part of the surgical cases i.e. post operative analgesia and also used the drugs which are usually considered the part of the anesthesia.

Conclusion

Mean duration of post operative analgesia was significantly better in cases treated with intra peritoneal bupivacaine and buprenorphine as compared to bupivacaine only and this difference is significantly better in all the confounding variable like age, gender and BMI.

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