

# POST OPERATIVE ANALGESIA FOLLOWING OPEN CHOLECYSTECTOMY; IS INTERMITTENT EPIDURAL BUPIVACAIN BOLUS ADMINISTRATION MORE EFFECTIVE THAN CONTINUOUS ADMINISTRATION?

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**ABSTRACT...** **Introduction:** Pain following surgery is a universal phenomenon; it is often underestimated and undertreated. Epidural analgesia is considered to be the best method of pain relief after subcostal cholecystectomy. Epidural is effective technique that offers comparable analgesia and better side effect profile. **Design:** Quasi Experimental study. **Period:** Jan2010 to June 2010. **Setting:** Military Hospital Rawalpindi. **Material and methods:** This is a prospective, randomized control trial. The main objective of this study was to compare the number of rescue doses for postoperative pain relief, after subcostal cholecystectomy under epidural anesthesia, in patients receiving continuous epidural infusion of bupivacain 0.125% with those receiving intermittent boluses. Thoracic epidural catheter was placed for post operative pain relief. Patients were divided into two equal groups. Patient receiving continuous epidural anaesthesia were placed in group A and those receiving intermittent doses were included in group B. **Sampling technique:** Purposive (non probability) sampling. **Result:** Patient who received intermittent boluses (group B) required less rescue doses of nalbuphine as compared to the patients who received continuous infusion of 0.125 bupivacain. **Conclusions:** Intermittent boluses of 0.125% bupivacain are considered a better method of postoperative pain relief than continuous infusion of 0.125 % bupivacain.

**Key words:** Post Operative Analgesia, Open Cholecystectomy

## INTRODUCTION

The original study was based on the hypothesis that intermittent bolus administration of bupivacain is considered superior to continuous infusion of bupivacain in terms of post operative pain relief, for patients undergoing open cholecystectomy under epidural anaesthesia. Objective of study was to compare the number of rescue doses of nalbuphain 5mg intravenous, for post operative pain relief after open cholecystectomy, in patients receiving continuous epidural infusion versus those receiving intermittent bolus administration.

## MATERIALS AND METHODS

This prospective study, extending over a period of six month (Jan2010 to June 2010) was a randomized control trial. Study was conducted in department of anaesthesia at the Military Hospital Rawalpindi after approval of hospital ethics committee.

Purposive non probability sampling technique was employed.

In total hundred patients of both sexes, aged between 18-65 years belonging to ASA grade I and II and weighing between 40-80kg, hence meeting inclusion criteria were recruited to the study.

To control the confounding variables, we excluded patients with history of neuropathies or evidence of sepsis or coagulopathies and/or history of local allergy to local anaesthetics.

## Study Design

Quasi Experimental study

## Data Collection

Informed consent was obtained. Randomization was done by lottery method by using single blind technique, patients were divided into two equal groups. Patients

receiving continuous epidural were included in group A. and those receiving intermittent doses were included in group B. The epidural space was identified using the loss of resistance technique to the injection of Saline with a 16G Tuohy needle inserted between thoracic tenth and eleventh intervertebral space. With the bevel directed cephalad, a three side hole catheter was advanced 3 to 5 cm and secured. A 3 ml test dose of 2% Lignocaine with Adrenaline was injected and followed by 15-20ml of 0.5% Bupivacaine with Tramadol 5mg/ml for surgery and sensory block up to the level of T4 was achieved.

After surgery patients were given 15-20ml of 0.125% Bupivacaine with Tramadol 5mg/ml to achieve the same level and timed zero. Then patients were randomly placed either in continuous or intermittent group. Patients in intermittent group received 12ml of 0.125% Bupivacaine with 5mg/ml Tramadol through epidural catheter every three hours. On the other hand patients in continuous group received the same solution at the rate of 4ml/hour.

If (and only if) patient requested for pain relief, inj. Nalbuphine 5mg i.v. (rescue dose) was given to the patient. Number of rescue doses were documented and compared for first 24 hrs Pain was assessed one hourly.

### Data Analysis Procedure

All the data collected through the Proforma was entered into the SPSS version 12.0 and analyzed through its statistical package.

Mean and SD was calculated for all numerical variables in both the groups and compared using independent sample t-test, including age, weight, height and number of rescue doses.

Frequency and percentages for gender, ASA status and requirement of rescue doses were calculated in both the groups and compared by chi-square test.

P-value of <0.05 was considered as significant.

## RESULTS

The present Quasi Experimental study was conducted in the department of Anesthesia at Military hospital

Rawalpindi. A total of 100 patients of ASA -I and ASA- II were included in the study and divided into two groups of 50 patients in each group. In group A the patients were given continuous epidural infusion and in group B patients were given intermittent epidural boluses.

The mean age in group A was  $38.02 \pm 9.301$  years with a minimum of 22 years and maximum of 58 years and in group B the mean age was  $41.78 \pm 9.276$  years with a range of 25 to 55 years as given in (table I).

**Table-I. Age (Years) Distribution of Patients in both groups**

Group	No. of pts.	Min. age	Max. age	Mean age	Std. Deviation
Group A	50	22	58	38.02	9.301
Group B	50	25	55	41.78	9.276

*\*Group A: Continuous Epidural Infusion*  
*\*Group B: Intermittent Epidural Boluses*

There were 12 (24%) males in group A and 8 (16%) in group B. There were 38 (76%) females in group A and 42 (84%) in group B as shown in (fig 1).

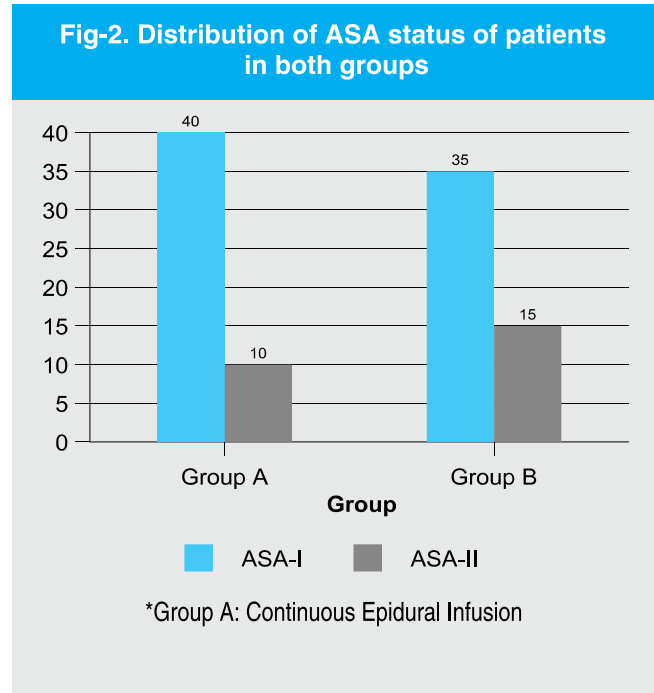
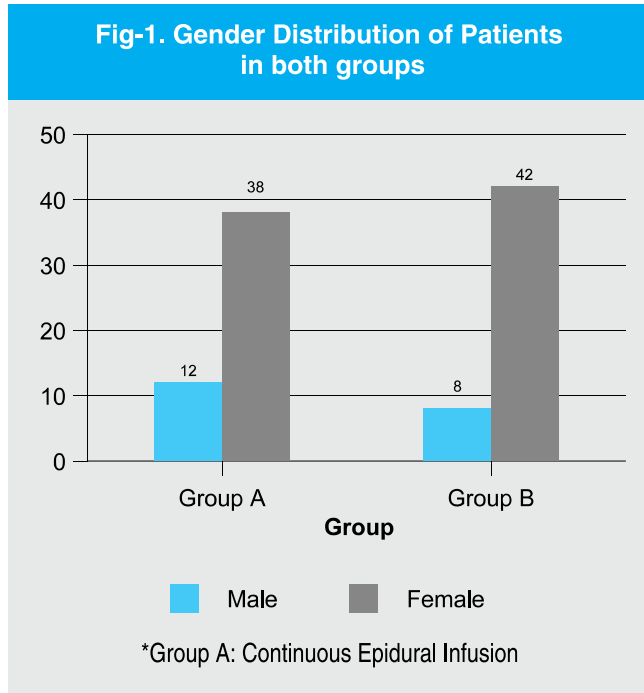
The minimum height in group A was 5 feet and maximum was 6.3 feet with a mean height of  $5.5180 \pm 0.39779$  feet. Similarly in group B the minimum height was 5 and maximum was 6.20 feet with an average height of  $5.564 \pm 0.4251$  feet as given in (table II).

The mean weight of group A was 63.88 Kg with standard deviation of 8.319 Kg with a minimum weight of 51 and maximum of 78 kg. Similarly in group B the minimum weight was 46 kg and maximum weight was 76 kg with a mean weight of  $60.52 \pm 8.262$  kg as elaborated in (table III).

**Table-II.. Distribution of Height (Feet) in both groups**

Group	No. of pts.	Min. Height	Max. Height	Mean age	Std. Dev.
Group A	50	5.00	6.30	5.5180	.39779
Group B	50	5.00	6.20	5.5640	.42511

*\*Group A: Continuous Epidural Infusion*  
*\*Group B: Intermittent Epidural Boluses*



**Table-III.. Distribution of Weight (Kg) in both groups**

Group	No. of pts.	Min. Weight	Max. Weight	Mean aga	Std. Dev.
Group A	50	51	78	63.88	8.319
Group B	50	46	76	60.52	8.262

\*Group A: Continuous Epidural Infusion  
\*Group B: Intermittent Epidural Boluses

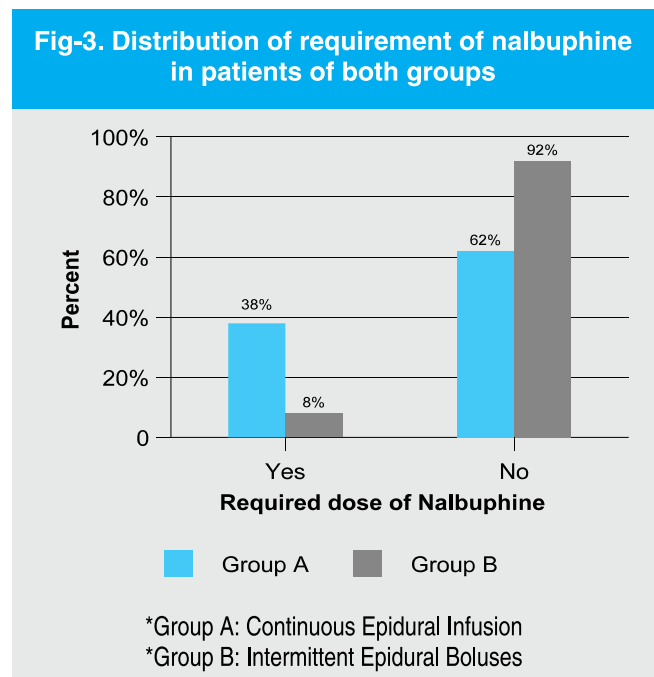


Fig 2 elaborates that there were 40 (80%) patients of ASA-I status in group A and 35 (70%) patients in group B and 10 (20%) patients of ASA-II status in group A and 15 (30%) in group B of ASA-II as shown in (fig. 2).

During first 24 hours post operatively 19 (38%) patients in group A complained of pain and had to be given Nalbuphine for pain relief and in group B 4(8%) patients required Nalbuphine. Remaining 62% in group A and 92 % in group B had satisfactory pain relief with respective treatment given as shown in (fig 3).

In group A the 19 patients who were given Nalbuphine 4 patients complained of pain once, 6 twice, 7 three times and 2 complained four times of pain and required Nalbuphine for pain relief. Similarly in group B, 3 patients

complained of pain once and 1 patient twice in 24 hours post operatively as elaborated in (table IV).

There were 40 ASA-I and 10 ASA-II patients in group A and 35 ASA-I and 15 ASA-II patients in group B. The comparison of ASA status in both groups shows that there was no statistically significant (P-value > 0.05)

**Table-IV. Distribution of Number of rescue doses in both groups**

Group	No. of rescue doses	Frequency	Valid Percent	Cumulative Percent
Group A	1	4	21.1	21.1
	2	6	31.6	52.6
	3	7	36.8	89.5
	4	2	10.5	100
Total		19		
Group B	1	3	75	75
	2	1	25	100
Total		4		

*\*Group A: Continuous Epidural Infusion*  
*\*Group B: Intermittent Epidural Boluses*

difference in both groups as shown in (table V).

Results show that the requirement of rescue dose of Nalbuphine was significantly higher in group A as compared to group B (19 vs. 4 out of 50, P-value < 0.000) as given in (table VI).

**Table-VI. Comparison of requirement of rescue dose of Nalbuphine in both groups**

Group	ASA Status		Total
	Yes	No	
Group A	19	31	50
Group B	04	46	50
Total	23	77	100

*\*Statistically not significant at 5% level of significance*  
*\*\*Group A: Continuous epidural infusion*  
*\*\*Group B: Intermittent epidural boluses*  
*Chi-square = 12.705 df = 1 P-value: 0.000*

The number of mean doses of Nalbuphine in both groups was significantly different. In group A the mean number of rescue doses was significantly higher (2.37±0.955 vs. 1.25±0.500, P-value < 0.05) as compared to group B as given in (table VII).

**Table-V. Comparison ASA status in both groups**

Group	ASA Status		Total
	ASA-I	ASA-II	
Group A	40	10	50
Group B	35	15	50
Total	75	25	100

*\*Statistically not significant at 5% level of significance*  
*\*\*Group A: Continuous epidural infusion*  
*\*\*Group B: Intermittent epidural boluses*  
*Chi-square = 1.333 df = 1 P-value: 0.248*

**Table-VII. Comparison of Number of Doses in both groups**

	Group	N	Mean	Std. Deviation	P-value
No. rescue doses	Group A	19	2.37	.955	0.035*
	Group B	04	1.25	.500	

*\* Statistically Significant at 5% level of Significance*  
*\*\*Group A: Continuous Epidural Infusion*  
*\*\*Group B: Intermittent Epidural Boluses*

**DISCUSSION**

This study was designed to compare intermittent and continuous approach for post-operative analgesia in post-cholecystectomy patients. Two groups were created and equal amount of bupivacaine was given in both the groups over 24 hours. In group A continuous while in B, intermittent approach was adopted. Results showed that the requirement of rescue dose of Nalbuphine was significantly higher in group A, as compared to group B (19 vs. 4 out of 50). This difference is statistically significant (P value < 0.05). So, this study determines that; intermittent epidural analgesic technique is more effective in providing post-operative analgesia in post-cholecystectomy patients.

Pain following surgery is a universal phenomenon, yet it is often underestimated and under treated. Post-operative pain relief is an important factor defining the outcome of surgery and the post-operative hospital stay. The aim of postoperative pain management is to relieve

pain so that normal functions, including ventilation, gastrointestinal function, coughing, and mobility, are minimally impaired. For this purpose epidural analgesia is a powerful treatment modality<sup>5</sup>. Local anaesthetics administered by the epidural route are the only drugs that suppress the stress response in patients who have undergone lower-body operations<sup>6</sup>.

Effective post-operative pain management has a humanitarian role besides additional medical and economic benefits of rapid recovery and early discharge from hospital. Recent advances in pain control provide greater potential for effective post-operative pain management<sup>7</sup>.

Any post-operative analgesia technique should meet three criteria viz; effectiveness, universal applicability and safety<sup>4</sup>. Regional techniques have received much attention because they are associated with less sedation and early ambulation with preservation of lung functions and effective pain control<sup>1,2</sup>.

Epidural analgesia with bupivacaine prevents the use of opioids and NSAIDS<sup>6</sup>. Studies have confirmed that epidural analgesia is far superior to the parenteral use of opioids for post-operative pain relief. Epidural analgesia can be administered intermittently, continuously or as PCA<sup>3</sup>.

Administration of dose in the catheter is not free from complications. The dose administration leads to fall in blood pressure which requires preloading the patient with fluids or an administration of vasoconstrictors. Moreover migration of epidural catheter in the epidural venous plexus and subarachnoid space is a well-known entity. Top up doses are administered after confirming the correct placement of the epidural catheter. In the case of continuous drug administration with an infusion pump, regular placement of catheter cannot be confirmed. Continuous cardiovascular monitoring is therefore mandatory<sup>7</sup>. This requires more staff commitment.

Bupivacaine is the most commonly used local anesthetic during postoperative epidural analgesia. Its use in combination with sufentanil provides better pain relief at

rest and during mobilization than bupivacaine alone<sup>8</sup>. Commercially available bupivacaine is a racemic mixture of S (-) and R (+) enantiomers. The greater toxicity of R (+) bupivacaine may be partly attributed to the increased binding of R (+) enantiomer to the sodium channels of neural or cardiac tissues<sup>9,10</sup>.

The analgesic efficacy and other benefits of epidural infusion for postoperative analgesia are well established. The efficacy of patient-controlled epidural analgesia (PCEA) compared with continuous epidural infusion (CEI) has been studied extensively in obstetrics. There are few published studies comparing intermittent with continuous epidural infusion for postoperative analgesia. Those that have been published have involved a small number of patients and have not demonstrated a difference in pain scores between treatment modalities<sup>12</sup>.

In this study the primary outcome measure was a summary pain score and administration of rescue systemic analgesia (Nalbuphine) to relieve the pain. Overall pain scores in both groups were low, providing further evidence for the efficacy of epidural analgesia for the treatment of postoperative pain. But requirement of rescue dose of Nalbuphine was significantly higher in group A, as compared to group B; show highly significant differences between groups.

These data may therefore be interpreted as suggesting that intermittent dosing of epidural analgesics offers a clinically significant improvement in analgesic efficacy over continuous epidural infusions.

We have confirmed the conclusion of Mann and colleagues,<sup>11</sup> and our findings agree with those of van der Vyver and colleagues<sup>12</sup>. We have confirmed the efficacy of postoperative intermittent epidural analgesia. Our results are also compatible with other international studies with similar objects<sup>13</sup>. No local data available for comparison of our findings.

In a study by Lim Y et al compared the analgesic efficacy of two drug delivery systems: regular intermittent epidural boluses and continuous infusion and assessed the incidence of break through pain for labor analgesia. They



found the decreased incidence of break through pain and increased maternal satisfactions in intermittent boluses group<sup>13</sup>.

However another study conducted by Shafer, showed that continuous epidural infusion when used appropriately may produce better analgesia than conventional boluses method of pain relief<sup>14</sup>.

The effective concentration of bupivacain that would optimize pain relief and minimize side effects was found to be 0.125% to 0.375%. Sebanathan et al claimed better pain relief and pulmonary function with 0.25% bupivacain compared with placebo after thoracotomy<sup>15</sup>.

The quality of pain relief and incidence of side effects was compared by using two technique of epidural analgesia after major abdominal surgery by Standl t et al, the study showed that the patient controlled epidural analgesia reduces analgesic requirement compared to continuous epidural infusion. Patient control epidural analgesia in comparison to proceeding continuous epidural infusion provides equivalent analgesic with lower local anaesthetic doses and plasma levels and without blocking side effects<sup>16</sup>.

De Eccher et al found no difference between patient controlled and intermittent boluses of epidural analgesics in term of pain control, during labor<sup>17</sup>.

Salim R et al compared continuous with intermittent epidural infusion on the duration of labour and patient satisfaction in nuliparous women. This study provide evidence that both continuous and intermittent epidural infusion produced comparable analgesia achieving equivalent maternal satisfaction with no difference regarding the duration of labour between them. However patient receiving epidural analgesia experience longer labor compared with control<sup>18</sup>.

The effect of anesthetic and postoperative analgesic techniques on perioperative outcome varies with the type of operation performed. Overall, epidural analgesia provides better postoperative pain relief. Epidural anesthesia and epidural analgesia improve the overall

outcome and shorten the intubation time and intensive care stay in patients undergoing abdominal aortic operations<sup>19</sup>. Intermittent epidural analgesic technique is also superior during labour analgesia, abdominal surgeries, and orthopedic procedures<sup>18</sup>.

We did not notice any severe side effects such as respiratory depression or cardiovascular instability during the study.

Our study has certain limitations. First of all it is based on patient's subjective feeling of pain and different patients can have different pain threshold. Secondly it was performed on elective patients and so study cannot be applied to emergency conditions.

We have not followed up patients until their discharge from hospital. As this was an open labeled study, a potential for patient and investigator bias exists. Despite its shortcomings this study provides good but limited evidence to supports the superiority of intermittent over continuous epidural analgesic technique.

## CONCLUSIONS

It has been concluded that both intermittent boluses and continuous epidural techniques provide effective postoperative analgesia after open cholecystectomy. However administration of intermittent blouses of 0.125% bupivacain is better than continuous infusion of 0.125% bupivacain for post-operative pain relief.

Intermittent boluses of 0.125% bupivacain is therefore safe and effective method of pain relief and recommended to be used widely for postoperative pain relief.

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