

# A Comparative Clinical Study Of Interpleural Bupivacaine And Interpleural Bupivacaine With Morphine For Post Operative Analgesia For Laproscopic Cholecystectomy

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## Abstract

The purpose of the study was to evaluate and compare the role of interpleural bupivacaine and bupivacaine with morphine for postoperative analgesia in patients of laparoscopic cholecystectomy. A clinical randomized study was done on 45 adult patients, of both sexes, belonging to ASA Grade I and II, undergoing laparoscopic cholecystectomy under general anaesthesia. All patients were divided in three groups of 15 each, to receive 20ml of saline, 20ml 0.5% bupivacaine (B) and 20ml 0.5% bupivacaine with 3 mg morphine (BM) interpleurally. Onset of analgesia was 15min in BM group where as it was 30min in B group and control group do not show any analgesia. Quality of analgesia was much better in BM group. Mean duration of analgesia was 12.4hrs in BM group and it was 8.2hrs in B group. Incidence of postoperative complications like nausea and vomiting were similar in both the groups.

## INTRODUCTION

The relief of postoperative pain is a subject, which is receiving increasing attention in the past few years because effective pain control is essential for optimal care of surgical patients<sup>1</sup>. Cholecystectomy is now commonly performed by laparoscopic technique because it provides distinct advantages over open cholecystectomy.<sup>2,3</sup> The pain produced by laparoscopic cholecystectomy is mainly visceral. Recent reports have demonstrated that many patients experience considerable pain after laparoscopic cholecystectomy, which is a relatively new procedure, so there is no general agreement on effective postoperative pain control.<sup>4,5</sup> The various methods used with variable success include NSAID suppository, infiltration of wounds with local anaesthetics, intermittent intramuscular narcotics, intraperitoneal local anaesthetics and interpleural block.

Reiestad et al (1984) published their results of continuous intercostals nerve block for postoperative pain relief and presented their modification of technique, which is now termed as "interpleural analgesia".<sup>6</sup>

Visceral pain after laparoscopy usually occurs till 24Hr.<sup>4</sup> Shoulder pain due to irritation of phrenic nerve usually occurs on 2nd postoperative day.<sup>7</sup> Pain due to persistent

pneumoperitoneum occurs till 3rd postoperative day.<sup>8</sup>

Analgesia with single shot bupivacaine is of range of 6-10hrs, is not sufficient to cover the period of maximum pain after laparoscopic cholecystectomy. So we planned this study to see the effect of addition of morphine to single shot of bupivacaine interpleurally, on duration and quality of analgesia.

## MATERIAL AND METHODS

Forty-five adult patients of either sex belonging to ASA I and II, admitted in surgical ward for elective laparoscopic cholecystectomy were selected for this study. After thorough pre-anaesthetic checkup and informed consent, patients were randomly divided into three groups of 15 each. All the patients were explained details of visual analogue scale and how to rate it on the scale of 0-10. All patients were given diazepam tablets 5mg and tablet ranitidine 150mg before sleep and made to fast overnight. Anaesthesia was standardized, consisting of glycopyrrolate 0.2mg and midazolam 0.1mg/kg body weight IV as premedication, induction with thiopentone sodium 5mg/kg and succinyl choline 2mg/kg IV, followed by maintenance with isoflurane and nitrous oxide 60-70% in oxygen. After spontaneous reversal from succinyl choline, neuromuscular block was maintained by atracurium. At the end of surgical procedure,

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just before reversal patients of control group received 20ml saline, (C) and other two groups received 20ml bupivacaine with adrenaline (B) and 20ml bupivacaine with adrenaline and 3 mg morphine (BM) through interpleural route.

**Interpleural technique:** Just before reversal under strict monitoring of SpO<sub>2</sub> 19 G Tuohy needle used to make puncture in the right 8<sup>th</sup> intercostal space in midaxillary line perpendicular to skin with bevel turned cephalad just below the 8<sup>th</sup> rib with all the aseptic precautions. Needle was attached with loss of resistance syringe having 2ml of sterile water and loss of resistance was identified in usual manner as in epidural. A first loss of resistance is felt as the intercostal membrane is pierced, and a second one occurs when the parietal pleura is traversed with the characteristic click. Local anaesthetic injected in pleural space while air penetration avoided with use of triway.

In postoperative period blinded observers observed patients, at regular interval for hemodynamic parameters, pain scores and peak expiratory flow rate (PEFR). Postoperative pain was assessed according to visual analogue scale, that is 10cm scale, which represents varying intensity of pain from 0cm (no pain) to 10cm (worst possible pain) and verbal rating scale, 0= no pain, 1=mild pain, 2=moderate pain and 3=severe pain.<sup>9</sup> Rescue analgesic given to patients complaining pain exceeding 7 on VAS scale or severe pain/3 on VRS scale and patients who received rescue analgesic were then dropped from our study. Rescue analgesic used was 50mg tramadol IM. Pulse and blood pressure were assessed at regular interval. Postoperative nausea vomiting and other side effects were also noted and treated accordingly. 4mg Ondansetron was given IV to patients complaining nausea and vomiting.

All the clinical data was collected, tabulated and analyzed with Microsoft excel 2000 and Statgraphic Plus 3.0. Statistical analysis was performed using Chi-square test for categorical data (with Yates's correction for 2x2 contingency tables). Whenever the data had values less than 5 the p-values were cross-checked using Fisher's exact test. In case of numerical data or continuous data parametric tests like student 't' test for two groups and analysis of variance (ANOVA) for more than two groups. In case of ordinal data Kruskal-Wallis test was used for comparison of multiple groups and Mann-Whitney U test for two-group comparison.

## RESULTS

The three groups did not differ with respect to age, weight,

height, gender, peak expiratory flow rate (PEFR) base line and hemodynamic parameters (table1). Onset of analgesia was quicker in BM group (15min) where as it was 30min in B group. Mean duration of analgesia (mean time for rescue analgesic) was about 12.4hrs in BM group where as it was 8.26hrs in B group (table 2,3)

Mean pain score at 15min showed significant difference between the three groups  $p=0.0$  ( $p \leq 0.05$  is significant) (table 2). All the patients in control group required rescue analgesics by 30 min and hence were deleted from study. Where as all the patients of B group required rescue analgesic by 10hrs and that of BM group needed rescue analgesic by 14hrs (table 2, fig 2). Quality of analgesia was better in bupivacaine with morphine group (fig 1).

Peak expiratory flow rate improved more in BM but there was no significant difference ( $p \leq 0.05$ ) fig 3. Heart rate and blood pressure, showed numerically slight but significant decrease in groups that received B and BM compared with control group (Table 4). But this decrease was not significant between the two study groups.

Perioperative complications were similar in both groups with no significant difference in incidence of nausea and vomiting. One patient in BM group had localized subcutaneous emphysema that resolved itself.

## Figure 1

Table 1. PREOPERATIVE PARAMETERS

	Control	Bupivacaine with adrenaline	Bupivacaine with adrenaline + morphine	p-value
Age(yrs)	42.73±8.32	43.07 ± 8.06	44 ± 7.30	0.54
Weight (kg)	56.27±10.21	59.87 ± 8.63	57.27 ± 6.92	0.51
Height (cm)	156 ± 9.11	157 ± 8.60	155.3 ± 7.07	0.88
M:F ratio	3:12	3:12	4:11	0.87
SBP(mmHg)	125 ± 4.35	120 ± 8.53	125 ± 5.93	0.08
DBP(mmHg)	78 ± 4.36	80 ± 4.92	80 ± 4.11	0.37
PR per min	81 ± 5.59	81 ± 3.59	78 ± 4.23	0.29
PEFR(L/min)	378 ± 37.83	387 ± 52.32	383 ± 37.93	0.86

$p < 0.05$  is significant.

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**Figure 2**

Table 2. MEAN PAIN SCORES (VRS,VAS)

Time	Control		Bupivacaine with adrenaline		Bupivacaine with adrenaline+morphine	
	VRS	VAS	VRS	VAS	VRS	VAS
15min	2.80±0.41	7.87±1.13	1.13±0.74	4 ± 2.13	0±0.59*	1±1.4*
30min	3±3.80	9±4.5	0.2±0.41	1± 1.20	0±0.35*	0±0*
1hr			0±0	0.3 ± 0.62	0±0	0±0
2hr			0±0	0 ± 0	0±0	0±0
4hr			0.13±0.36	1 ± 0.92	0±0	0±0
6hr			1.13±1.13	4 ± 3.02	0±0	0±0
8hr			2.33±0.89	7 ± 2.42	0±0.50*	1±1.3*
10hr			3±0.0	9 ± 0.71	1±1.08	3±3.15*
12hr					2±0.78	6±3.09
14hr					3±0	9±0.55

\* p< 0.05 which is significant

**Figure 3**

TABLE 3

	control	Bupivacaine with adrenaline	Bupivacaine with adrenaline + morphine
•Onset of analgesia (time in min)	-	30	15
••Duration of analgesia (time in hrs)	-	8.26±1.49	12.4±1.35

- Time of onset is the at which mean pain score reached( VRS=0, VAS=0,1)
- Duration of analgesia is period starting when patients became pain free to the time when they further required the top up dose.

**Figure 4**

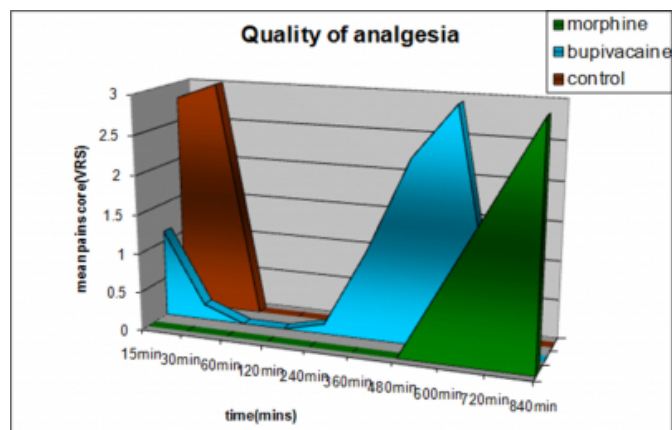
TABLE 4. HEMODYNAMIC PARAMETERS

Time	Control			Bupivacaine with adrenaline			Bupivacaine with adrenaline+morphine		
	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP
preop	81± 5.6	124± 5.0	80± 4.9	81± 3.5	120± 8.5	78± 5.4	78± 4.2	125± 5.93	80± 4.10
15min	95± 5.32	132± 5.92	83± 5.16	86± 3.80	123± 8.67	80± 5.63	81± 3.67*	125± 6.90 *	81± 4.32
30min	94± 4.0	133± 4.0	82± 4.76	82± 3.06	120± 7.74	80± 5.54	79± 4.80*	125± 5.93*	80± 4.10
1hr				81± 3.41	120± 8.37	80± 5.57	77± 5*	123± 6.20	79± 5.09
2hr				81± 2.83	120 ± 8.37	80 ± 5.57	77± 5.04*	123± 5.99	79± 4.91
4hr				83± 2.89	120 ± 8.30	79± 5.24	77± 5.04*	123± 5.99	79± 4.91
6hr				86± 3.76	124 ± 8.92	79± 5.34	78± 4.97*	124± 6.47	79± 5.92
8hr				86± 4.11	128 ± 8.24	81± 4.90	79± 5.49*	125± 7.57	79± 6.23
10hr				86± 3.67	132 ± 6.54	81± 2.12	83± 6.77	128± 7.59	80± 4.97
12hr							88± 5.74	132± 6.77	81± 4.29
14hr							89± 8.77	131± 12.10	80± 5.59

\* p< 0.05 which is significant

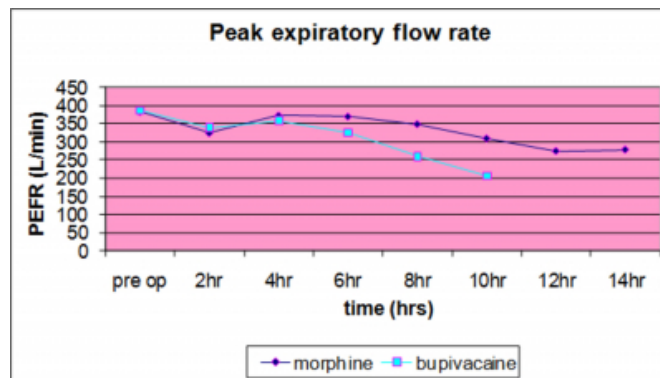
**Figure 5**

Fig 1 Quality of Analgesia



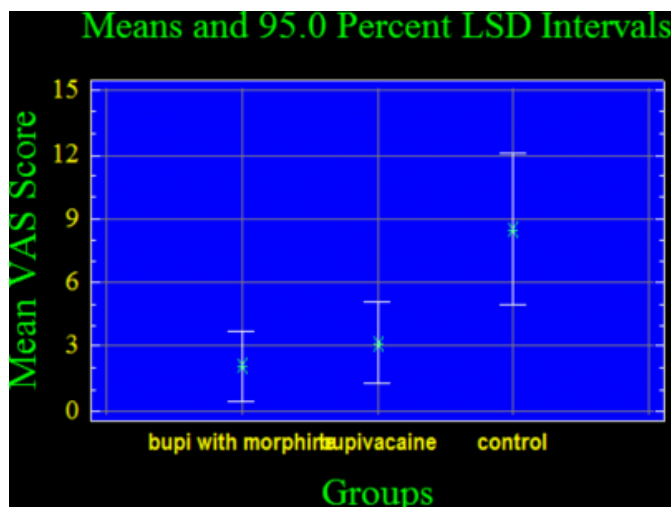
**Figure 6**

Fig 2 Peak Expiratory Flow rate



**Figure 7**

Fig 3 Mean Pain Score



## DISCUSSION

This clinical research has shown the analgesic effect of both 20ml 0.5% bupivacaine with adrenaline in 1:2,00,000 concentration and 20ml .05% bupivacaine with adrenaline plus 3 mg morphine through interpleural route for postoperative analgesia in cases of laparoscopic cholecystectomy compared to saline. In BM group, the mean time to rescue analgesic was significantly prolonged (12.4 hours compared to 15min and 8.26 hours for control and B groups, respectively).

Interpleural regional analgesia is the percutaneous introduction of the local anaesthetic into thoracic cage between parietal and visceral pleural. Analgesia is thought to occur as a result of

- Local anaesthetic diffuses through the parietal pleura and the innermost intercostal muscles to reach the intercostal nerves where blockage occurs.
- Blockage of the intrathoracic sympathetic chain and
- Direct action of local anaesthetic on nerve endings within the pleural<sup>10,11</sup>

Addition of morphine to local anaesthetic in axillary block provides improved postoperative analgesia without increased frequency of side effect or major complications.<sup>12</sup> This is because it has been discovered along with central, opioids also have peripheral receptors such as on peripheral nerves.<sup>13,14</sup> By acting on these nerves they activate opioid

receptors where they can modulate both afferent and efferent neuronal functions and result in antinociception.<sup>15</sup> Opioid agonists produce a local anesthetic –like effect on the surface of excitable cell membranes that does not involve a stereospecific receptor and may contribute to some of their actions.<sup>16,17</sup>

In our study control group did not have any analgesia and all the patients of (C) group required rescue analgesics by 30 min. Mean time of onset of analgesia was 30min in (B) group, mean time for rescue analgesic or duration of analgesia was 8.26hr and there was gradual improvement of PEFR and hemodynamic parameter also came down to preoperative value by 1hr. These findings in our study after a single shot of bupivacaine with adrenaline are consistent with study of Stromskag et al (1988) which showed complete relief of pain by 15-30min, mean duration of analgesia with 20ml 0.5% was 8hrs and patient required rescue analgesic before 7hr.<sup>18</sup> Murphy et al (1983) found that after administration of interpleural bupivacaine peak expiratory flow was significantly better {212(19) L/min} than before its administration {154(14) L/min}.<sup>19</sup>

Our study also shows that addition of morphine to bupivacaine improved the onset time of analgesia (15min), mean duration of analgesia (12.4hr)(p=0.00), improvement in PEFR but that has no significant difference with bupivacaine alone group (p<0.05). Overall over the duration of 12hrs quality of analgesia was better with (BM) group. There were no increased incidences of side effects with BM group. Though little work has been done on interpleural bupivacaine with morphine and analgesia by interpleural route in cases of laparoscopic cholecystectomy, our results were consistent with other studies showing analgesic effect of morphine through peripheral route without increased incidence of side effects. Demian AD et al (2003) used 2mg morphine along with 0.5% bupivacaine and concluded that this technique provides satisfactory analgesia.<sup>20</sup> Bourke DL et al (1993) conclude in their study that addition of morphine 0.1mg to bupivacaine produced improved analgesia without significant side effects.<sup>12</sup>

To conclude, morphine is a good adjuvant to interpleural block for postoperative analgesia in cases of laparoscopic cholecystectomy without increased incidence of adverse affects.

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