

**COMPARATIVE STUDY BETWEEN EPIDURAL BUPIVACAINE WITH BUPRENORPHINE AND EPIDURAL BUPIVACAINE FOR POST-OPERATIVE ANALGESIA IN ABDOMINAL AND LOWER LIMB SURGERY**K. S. Nagesh<sup>1</sup>, M. Sathesha<sup>2</sup>, R. S. Prasad<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

K. S. Nagesh, M. Sathesha, R. S. Prasad. "Comparative Study between Epidural Bupivacaine with Buprenorphine and Epidural Bupivacaine for Post-Operative Analgesia in Abdominal and Lower Limb Surgery". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 18, March 02; Page: 3057-3064, DOI: 10.14260/jemds/2015/444

**ABSTRACT:** Epidural administration of various analgesics gained increasing popularity following the discovery of opioid receptors in the spinal cord capable of producing potent analgesia. This effect seems to be greatest when epidural anaesthesia is continued in the post-operative period as epidural analgesia. It is now clear that epidural administration of opioids. Ours was a comparative study between epidural bupivacaine with buprenorphine and epidural bupivacaine for post-operative analgesia in abdominal and lower limb surgery. **METHODS:** 60 patients undergoing lower abdominal and lower limb surgeries of either sex with ASA grade 1 and 2 aged between 20 and 60 years for divided into two groups. After completion of the surgery and when the effect of local anaesthetic wears off and the patients complain of pain the intended study drugs were given when visual analogue pain score touched 5 cm mark. Group – A: Patients received 8ml of 0.25% bupivacaine + 0.15mg of buprenorphine. Group – B: patients received 0.25% of bupivacaine alone. In the post-operative period the following parameters were studied, 1. Onset of analgesia, 2. Duration of analgesia, 3. Vital parameters such as heart beat, blood pressure, respiratory rate, sedation score and visual analogue score were recorded, 4. Side effects like nausea, vomiting, hypotension, respiratory depression, and pruritus allergic reaction were looked for. **RESULTS:** It is observed that onset of analgesia in Group A (0.25% bupivacaine + 0.15mg buprenorphine) was 7.35 min. When compared to Group B which 15.5 min, which is statically significant ( $P < 0.05$ ). Duration of analgesia in Group A is 17.23 hrs compared to Group B, which is 5.2 hrs, this is statically significant ( $P < 0.05$ ). Visual analogue scale was reduced in Group A compared to Group B **CONCLUSIONS:** Addition of buprenorphine to bupivacaine by epidural injection for post-operative analgesia improves the onset, The duration and the quality of analgesia.

**KEYWORDS:** Bupivacaine, Buprenorphine, Post-Operative analgesia, Epidural.

**INTRODUCTION:** The word pain<sup>1,2</sup> is derived from Latin word 'Ponea' which is an unpleasant sensory and emotional experience associated with actual or potential tissue damage and described in terms of such damage.

Chemical mechanical or thermal stimuli of sufficient quantity or intensity to threaten or destroy tissue or to disrupt vascular integrity typically lead to autonomic (Changes in heart rate and blood pressure) or hormonal (Adrenal and pituitary secretion) responses as well as to the subjective sensation of pain. A wide range of options exists to combat pain both pharmacologically and non-pharmacologically.

Morphine has been used epidurally<sup>3,4</sup> for post-operative analgesia but has been associated with delayed respiratory depression. On the invention of buprenorphine which is more potent than

## ORIGINAL ARTICLE

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morphine and is agonist – antagonist with lipid solubility about 5 times greater than morphine has been used epidurally for post-operative analgesia.

A few clinical report shows even though epidural bupivacaine produces analgesia does not cause side effects of epidural opioids.

This study was envisaged and designed to evaluate the effectiveness of relief of pain, on onset of pain relief and side effect due to epidural administration of bupivacaine with buprenorphine mixture and bupivacaine alone in patients undergoing abdominal and lower limb surgery.

**METHODS:** After obtaining approval from the institutional ethics committee and inform consent 60 patients undergoing general surgery gynecological and orthopedic surgeries were selected at random. All the patients were aged between 20 and 60 during the preoperative visit detailed preoperative evaluation was done. Laboratory investigations included routine blood (Hb% TC, DC & ESR) urine, blood urea, creatinine, Sugar, ECG, HIV and HBSAG. The procedure was explained to the patient and consent obtained. In the visual analogue scale patients were shown a scale of 10 cm length. Zero end of the scale was taken as ‘No Pain’ and 10cm mark as ‘Maximum Pain’. Intensity of the pain increase gradually from 0 to 10 patients was instructed to point the intensity of pain on the scale.

For the purpose of assessing the pain:

- 0- 2.5 cm taken as no pain
- 2.5-5 cm taken as mild pain
- 5-7.5 cm taken as moderate pain
- 7.5 – 10 cm taken as severe pain

Intraoperative anaesthesia and analgesia<sup>5,6</sup> was achieved with lignocaine 2% with adrenaline 1:2, 00, 000, 16-20 ml through the epidural catheter and anaesthesia was topped up with 5ml of 1% lignocaine hydrochloride every 30 min till the end of the surgery.

After completion of surgery patient observed in the recovery room till the level of analgesia wears off to the spinal segment T<sub>12</sub> before shifting to post-operative ward.

When the effect local anaesthetic wears of and the patient complains of pain, first assessment of intensity of pain was done by VAS and later study drugs were given when the VAS score touched 5 cm mark.

Group – A: Patients received 8ml of 0.25% bupivacaine + 0.15mg of buprenorphine.

Group – B: patients received 0.25% of bupivacaine alone.

In the post-operative period the following parameters were studied:

- a. Onset of analgesia: it was taken as time duration between injection of drug and onset of pain relief.
- b. Duration of analgesia: This was calculated from the time when the first dose of analgesia were give post operatively and followed up till patient complained of pain. Time at which patients complained of pain more than 5 cm on VAS scale was noted.
- c. Vital parameters such as heart rate, blood pressure respiratory sedation score and visual analogue were recorded.
- d. Side effects like nausea, vomiting, hypotension, respiratory depression, and pruritus allergic reaction were looked for.

## SEDATION SCORE: Grade 1 to 6:

1. Deep sleep – does not respond to verbal commands.
2. Sleepy – responds to verbal commands.
3. No complaint or body movement-calm.
4. Complaints with body movement – But calm.
5. Substantial complaining and body movement – not calm.
6. A great degree of complaining and body movement accompanied by some excitement.

Statistical analysis was done using Chi-square test, student t-test (paired and unpaired t-test), A P value of < 0.05 was considered significant, <0.01 – highly significant, <0.001 – very highly significant, > 0.05 not significant.

## RESULTS:

1. **On set of Analgesia:** It is observed that onset of analgesia in Group A (0.25% bupivacaine + 0.15mg buprenorphine) was 7.35 min. when compared to Group B (0.25% bupivacaine) which was 15.50 min, which is statistically significant (P<0.05) it shows bupivacaine with buprenorphine has faster onset of pain relief when compared to bupivacaine alone given epidurally.
2. **Duration of Analgesia:** Duration of analgesia in Group A is 17.23 hrs compared to Group B which is 5.2 hrs. This is statistically significant (P<0.05)
3. **VAS Score-** when compared to two groups the VAS score was reduced in Group A when compared to Group B.
4. **Sedation Score:** It was found that there was highly significant increase in sedation score with Group A.

There was no significant change in heart rate, blood pressure, respiratory rate between the two groups.

**SIDE EFFECTS:** Side effects like nausea, vomiting, hypotension, respiratory depression, and pruritis and hypotension was studied. We observed that nausea, vomiting, and retention of urine was more in Group A.

**DISCUSSION:** In the post-operative period when the effect of anaesthetic disappears, the tissue injury persists and pain introducing substances which liberated during the operation greatly reduce the normally high threshold of the nociceptors,<sup>7,8</sup> so that innocuous stimulation produces pain, moreover the cut ends of axons further contributed to nociception.

Traditionally epidural bupivacaine was used for post-operative analgesia. Epidural bupivacaine 0.05% causes motor, sensory and sympathetic blockade, 0.25% causes sensory and autonomic blockade and 0.125% causes autonomic blockade only.

Buprenorphine<sup>9,10</sup> was 30 times more potent than morphine and has high lipid solubility and which has been used epidurally with lower incidence of respiratory depression.<sup>11,12</sup>

Onset of analgesia is taken as time interval between the blood administration and the time when patient started getting pain relief mean time of onset of analgesia is Group A was 7.53 min and Group B was 15.50 min.

## ORIGINAL ARTICLE

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The onset of analgesia was significant faster in Group A compared to Group B.

Zenz M, Pipenbrocks S,<sup>13</sup> did a double blind comparison of epidural buprenorphine and epidural morphine for postoperative pain relief. Both substances produce analgesia with a short latency of 6.8 min. which is close to our observation of 7.53 min.

Duration of analgesia in our study the main duration of analgesia in Group A was 17.23 hrs which significantly higher compared to Group B of mean duration of analgesia of 5.2 hrs. The rapid onset of action and long duration of analgesic effect of buprenorphine can be explained by high liquid solubility of buprenorphine and it's high affinity to opioid receptors.

**ON CARDIO VASCULAR SYSTEM:** The objective parameters of analgesia like mean arterial pressure and heart rate were compared and reduction in MAP was statically significant in Group A compared to Group B.

In Group A MAP from base line 98.3 mmHg fell to 90.8 mmHg at 30 min then picked up to 94.92 at 11<sup>th</sup> hour remained same throughout the study. In Group B MAP from baseline 93.97 mmHg fell to 8.43 mmHg at 10 min then picking up slowly to 93.7 mmHg at 1<sup>st</sup> hour thereafter remained significantly high throughout the study. The mean HR reduction indicating analgesia was also significant in Group A compared Group B. The mean base line heart rate in Group A was 94.3 min<sup>-1</sup> reduced gradually to 80.66 at 1hr and remained low throughout the study. The mean base line heart rate which was in Group B 81.76 min<sup>-1</sup> went up to 87.3 at 10 min<sup>-1</sup> then significantly remained higher throughout the study.

The study done by Cahill J<sup>14</sup> and others showed epidural buprenorphine had no serious haemodynamic derangements.

**ON RESPIRATORY RATE:** In Group A mean base line respiratory rate from 17.7 min<sup>-1</sup> fell to around 15.9 in 30 min gradually reducing to 12.56 by 7<sup>th</sup> hr, picking up slightly by 11<sup>th</sup> hr again falling to 12.76 by 15<sup>th</sup> hr and gradually raise to 14.26 by 21<sup>st</sup> hr. Zenz M and Coworker<sup>13</sup> when comparing epidural buprenorphine and epidural Morphine observed decrease respiratory rate and increase tidal volume however there was no severe respiratory depression.

In Group A there was slight delayed minimal respiratory rate fall this correlates to the above mentioned study.

In Group b baseline respiratory which was 15.2 fell to 14.76 at 20<sup>th</sup> min remaining stationary throughout the study.

**SEDATION:** In Group A patients had moderate drowsiness (Grade II). All the patients woke up when pulse and bold pressure were recorded. The sedative effect of buprenorphine was desirable in the immediate post-operative period.

**SIDE EFFECTS:** In our study the incidence of nausea and vomiting in Group A was 16.5% and the Group B was 3.3%. no. patients reported Pruritus or hypotension or urinary retention.

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## ORIGINAL ARTICLE

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	No. of Patients	Mean onset of analgesia (in min)	SD	t	Significance
Group A	30	7.52	2.71	2.38	P<0.05. significant
Group B	30	15.50	1.50		

**Table 1: Onset of Analgesia**

	No. of Patients	Mean onset of analgesia (in min)	SD	t	Significance
Group A	30	17.23	2.8	2.80	P<0.05. S
Group B	30	5.20	0.66		

**Table 2: Duration of Analgesia**

## ORIGINAL ARTICLE

Time Interval	HR				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
0	94.3	6.34	81.76	7.44		
10 Min	88.13	6.66	87.13	5.81	0.54	P>0.05 NS
20 Min	88.66	4.99	87.4	7.00	0.642	P>0.05 NS
30 Min	84.86	5.34	86.9	6.88	0.21	P>0.05 NS
1 Hour	80.66	6.15	86.2	6.97	0.002	P>0.05
3 Hour	80.33	6.43	85.0	6.59	0.01	P>0.05 NS
5 Hour	82.00	7.20	85.87	7.29	0.04	P>0.05
7 Hour	81.86	7.20	87.53	7.49	0.004	P>0.05 NS

**Table 3: Mean of mean heart rate in between Group A & Group B**

SD: Standard Deviations, NS: Not Significant

Time Interval	MAP				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
0	98.3	5.45	93.97	9.47		
10 Min	96.5	5.82	83.47	6.97	1.04	P>0.05 NS
20 Min	92.97	6.85	87.7	7.09	0.005	P>0.05 NS
30 Min	90.8	6.78	89.37	7.56	0.44	P>0.05 NS
1 Hour	90.53	8.74	93.7	6.41	0.12	P>0.05 NS
3 Hour	91.77	6.89	97.5	4.99	0.0005	P>0.05 NS
5 Hour	91.93	7.74	97.9	4.82	0.0006	P>0.05 NS
7 Hour	93.33	7.42	99.23	5.33	0.001	P>0.05 NS

**Table 4: Mean of MAP in between Group A & Group B at different time intervals**

SD: Standard Deviations, NS: Not Significant

Time Interval	RR				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
0	17.7	1.29	15.2	1.374		
10 Min	16.96	1.35	15.133	1.136	6.46	P<0.05 S
20 Min	16.2	1.09	14.766	1.651	6.11	P<0.05 S
30 Min	15.9	1.15	15.33	1.268	0.08	P<0.05 S
1 Hour	16.3	1.54	15.6	1.28	0.15	P>0.05 NS
3 Hour	14.73	1.98	14.83	1.80	0.84	P>0.05 NS
5 Hour	13.03	2.00	14.87	1.33	0.0001	P>0.05 NS
7 Hour	12.56	1.79	14.67	1.86	3.99	P<0.05 S

**Table 5: Mean Respiratory Rate in between Group A & Group B at different time intervals**

SD: Standard Deviations, NS: Not Significant, S: Significant

## ORIGINAL ARTICLE

Time Interval	VAS				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
0	5.13	0.63	5.9	0.88		
10 Min	4.23	0.72	5.55	0.65	4.78	P<0.05 S
20 Min	3.33	0.63	4.10	0.92	0.0006	P>0.05 NS
30 Min	2.7	0.89	2.68	0.855	0.941	P>0.05 NS
1 Hour	1.12	0.715	2.93	0.45	5.17	P<0.05 S
3 Hour	1.3	0.59	4.0	0.91	1.09	P>0.05 NS
5 Hour	1.68	0.61	5.4	0.56	2.49	P>0.05 NS
7 Hour	2.53	0.75	5.76	0.50	3.45	P<0.05 S

**Table 6: Comparison of VAS in between Group A & Group B**

SD: Standard Deviations, NS: Not Significant, S: Significant

Time Interval	SEDATION SCORE				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
0	4.16	0.69	4.03	0.490		
10 Min	3	0.371	3.9	0.80	6.84	P<0.05 HS
20 Min	3.03	0.18	2.97	0.614	0.57	P>0.05 NS
30 Min	2.53	0.50	3.03	0.414	9.87	P<0.05 HS
1 Hour	2.9	0.48	2.87	0.571	0.81	P>0.05 NS
3 Hour	3	0	3.2	0.484	0.03	P<0.05 S
5 Hour	3	0	3.57	0.678	2.58	P>0.05 NS
7 Hour	3	0	3.17	6.38	0.02	P<0.05 S

**Table 7: Mean Sedation Score**

SD: Standard Deviations, NS: Not Significant, S: Significant, HS: Highly Significant

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**FINANCIAL OR OTHER**

**COMPETING INTERESTS:** None

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Date of Submission: 17/02/2015.  
Date of Peer Review: 18/02/2015.  
Date of Acceptance: 20/02/2015.  
Date of Publishing: 27/02/2015.