

## EPIDURAL ADMINISTRATION OF LOW – DOSE BUPIVACAINE WITH BUPRENORPHINE VS BUPIVACAINE WITH MORPHINE FOR POSTOPERATIVE ANALGESIA IN THE CAESAREAN DELIVERY

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### ABSTRACT

Post operative pain after lower segment caesarean segment is almost always severe in nature and its makes very difficult for nursing mother to take care of baby. Its need early ambulation of caring mothers .This randomised double blind control study was carried out among 100 lower segment caesarean section (LSCS) patients, divided into two groups to assess the analgesic efficacy and side effects of epidural analgesia, group I with intermittent topup epidural bupivacaine (0.125%) with buprenorphine (0.060mg) N=50 and group II bupivacaine (0.125%) with morphine (1.5mg) N=50. Patients were under observation for 48 hours post operatively for onset, duration, potency of analgesia and its side effects. The demographic characteristics (age, weight and height) of the two groups were comparable and the differences among age, weight, were statistically significant and among height were not statistically significant. Postoperative pain score, blood pressure, heart rate, respiratory rate were measured at hourly during the first 48 h after operation.

Both the drugs produced significant pain relief (assessed by vas scale).

Onset of analgesia were earlier in group 1 and statistically significant. Duration of analgesia was statistically significant in group I with longer duration of action than morphine as in group II. The incidence of side effects was less in both groups and statistically not significant.

Post operative analgesia was for longer duration in case of epidural buprenorphine than morphine.

**Key Words:** Post operative analgesia, epidural buprenorphine, morphine

### INTRODUCTION

Development of specific opiate receptors in the substantia gelatinosa of the posterior horn gave significant idea to understand its use in postoperative pain management by using epidural opiates.<sup>1</sup>First epidural opiate used in human was morphine, after that several opiates like Pethidine,<sup>2</sup> Fentanyl,<sup>3</sup> Methadone<sup>4</sup> and Diamorphine<sup>5</sup> have been studied extensively. Proposed mechanism of opiates, its act locally and when deposited in epidural space diffuse through dura and bind to specific opiate receptors. The higher lipophilic substance, the greater will be its penetration through dura. The opiates with greater affinity for the receptor sites will produce longer duration of analgesia.<sup>6</sup>

Morphine was one of the preferred opiates because of its long duration of action with low dosage. but, it has certain side effects like pruritis, nausea, vomiting, urinary retention and rarely respiratory depression.<sup>7,8</sup> made clinician to hunt for other safer option. The newer opioid buprenorphine is a thebaine derivative, semisynthetic having both agonist as well as antagonist properties. It is highly lipid soluble and 30-40 times more potent than morphine and has higher affinity for opioid receptor, so the chances of side effects and addiction will be minimal and can be safely used epidurally.<sup>7,9</sup> The aim of study was to evaluate the effect of adding very low dose regimen of continuous epidural bupivacaine with buprenorphine vs bupivacaine with morphine for postoperative analgesia in the caesarean delivery.

### MATERIALS AND METHODS

This study was conducted in KIMS Medical College, Amalapuram. It was designed in the form of a

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prospective, randomized and double blinded study. Approval for the study was obtained from the institutional ethical committee and a written informed consent from each patient was taken before the study. One hundred patients at term (ASA-I and ASA-II), scheduled for lower segment caesarean section under epidural anaesthesia, were selected by the simple random sample technique and divided into two groups. Patients with complicated pregnancy like acute foetal distress and history of hypersensitivity to opioids / local anaesthetics were excluded. In the pre-anaesthetic check-up, all the patients were informed about the study plan and the different visual analogue scales (VAS) to be used in the assessment by the investigators. Respiratory rate, non invasive blood pressure, peripheral arterial saturation and heart rate were monitored throughout the peri-operative period.

Epidural anaesthesia was used for surgery. Subsequently, the epidural route was used for postoperative analgesia also. Intensity of postoperative pain during the first 48 hours postoperatively was assessed at hourly intervals using a visual analogue pain score; 0 denotes 'no pain' while 10 denotes 'worst pain imaginable'. When the patients were asleep, no VAS assessments were made and a VAS of 0 was given. Group I was scheduled to receive bupivacaine (0.125%) and buprenorphine (0.060mg) at 10-hour intervals or when the pain score was 4 or more, or if the patient requested analgesia (whichever occurred earlier). Group II was scheduled to receive bupivacaine (0.125%) and morphine (1.5 mg) at five-hourly intervals or when the pain score was 3 or more, or if the patient requested analgesia (whichever occurred earlier). The observer assessing pain was kept blinded for the epidural medication. If the VAS score failed to decline at least by the first one, even after 30 minutes of epidural injection, the patient was given an injection of tramadol 100mg intramuscularly. Total analgesics required for a 48-hour period was recorded.

The onset of analgesia was defined as the time from injection of the study medication to the first reduction in pain intensity by at least 1 in VAS; and the duration of analgesia was defined as the time between the onset of analgesia and either a return to baseline VAS or the time when additional pain medication was requested,

whichever occurred first. The occurrence of nausea and vomiting, itching, shivering and respiratory depression (respiratory rate < 12 / minute), and sedation and hypotension was noted for up to 48hours following administration of the study medication. The collected data was analyzed using (Statistical Analysis System) 9.2 Software. Independent T Test / Mann-Whitney U test was used based on the normality assumption to compare the groups. For Categorical variables, Chi-square/Fisher's exact test was used to compare the groups. The observer analyzing the data was kept blind about the groups to avoid bias in analysis and results.

## RESULTS

A total of 100 patients were studied, with two Groups of each 50 patients. The demographic characteristics (age, weight and height) of the two groups as mean, standard deviation and range are depicted in Table 1. The demographic characteristics (age, weight and height) of the two groups were comparable and the differences among age, weight, were statistically significant and differences among height were not statistically significant.

**Table 1 : Demographic characteristics of patients**

Characteristics	GROUP 1(N=50)	GROUP 2(N=50)	P value
Age in years {Mean ± SD (Range)}	26.90 ± 4.93 (19-35)	24.06 ± 3.17	0.0043*
Height in cm {Mean ± SD (Range)}	151.78 ± 4.56 (140-163)	154.76 ± 4.26 (140-163)	0.0005*
Weight in kg {Mean ± SD (Range)}	58.78 ± 4.25 (50-69)	59.18 ± 5.29 (50-75)	0.8789*

Table 2 gives the comparison of post-operative analgesia in the two groups of patients. Mean onset of analgesia was significantly earlier in group 1 and duration of analgesia longer in group 1 patient receiving buprenorphine. (Figure1). The mean highest pain score (VAS scale) was equal in both the groups and statistically not significant. These differences in the three groups were found to be statistically significant. The tramadol one injection required in group one was 6%, in group two also 6% and two injections were required in group one was 1% and group two was 2% and no injections required in group 1 was 46% and in group two was 45% statistically not significant.

**Table 2 : Comparison of post-operative analgesia in the two groups**

Characteristics	GROUP 1(N=50)	GROUP 2(N=50)	P value
Duration of analgesia (in hours) (Mean $\pm$ SD (Range))	10.78 $\pm$ 1.54 (8-12)	5.62 $\pm$ 0.64 (4-7)	<0.0001*
Onset of analgesia (minutes) (Mean $\pm$ SD (Range))	7.66 $\pm$ 1.91 (5-10)	10.88 $\pm$ 2.11 (5-15)	< 0.0001*
Highest pain score on VAS scale (0 – 10) (Mean $\pm$ SD (Range))	0.50 $\pm$ 0.97 (0-3)	0.64 $\pm$ 0.96 (0-3)	0.2136*
Additional injections needed			
1 injection	3 ( 6.0%)	3 ( 6.0%)	1.0000 <sup>®</sup>
2 injection	1 ( 2.0%)	2 ( 4.0%)	
No injection	46 ( 92.0%)	45 ( 90.0%)	

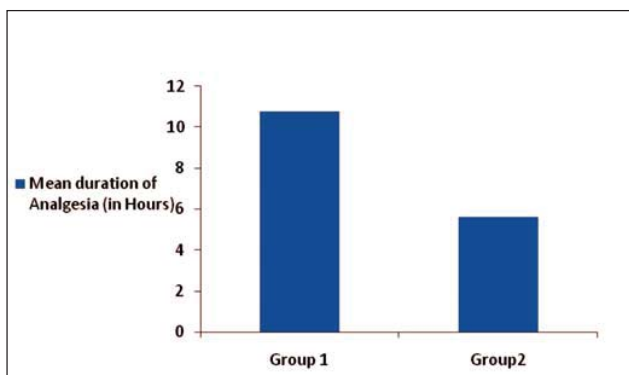
Test done at 5% Significance level and  $P \leq 0.05$  indicates Significance.

<sup>&</sup>Chi-Square /<sup>®</sup> Fisher's exact test to calculate the p-value.

<sup>^</sup>Independent T Test/ \*Mann-Whitney U test used based on the normality assumption to compare the two groups

The data was analyzed using SAS 9.2 Software. Independent T Test / Mann-Whitney U test was used based on the normality assumption to compare the groups. For Categorical variables, Chi-square/Fisher's exact test was used to compare the groups.

#### Comparison of post-operative analgesia in the two groups

**Figure 1: Mean duration of analgesia in Group1 and Group2**

Side effects: Table3 enumerates the side effects observed. It is seen that nausea, vomiting, urinary discomfort, itching were statistically not significant were equal in both buprenorphine and morphine group.

#### DISCUSSION

The epidural analgesia is one of the commonly used regional techniques for postoperative pain management. Several opiates has been successfully used for epidural

**Table 3 : Comparison of side effects in two groups of patients**

Side Effects	GROUP 1(N=50) n (%)	GROUP 2(N=50) n (%)	P value
Itching	1 ( 2.0%)	3 ( 6.0%)	0.7065 <sup>®</sup>
Nausea	3 ( 6.0%)	3 ( 6.0%)	
Urinary discomfort	1 ( 2.0%)	2 ( 4.0%)	
No side effects	45(90.0%)	42 (84.0%)	

Test done at 5% Significance level and  $P \leq 0.05$  indicates Significance.

post operative analgesia.<sup>4,10</sup> The efficacy of epidural morphine is well known.<sup>7,11</sup> But it's undesirable side effects which have led to clinician search for other safe opioids for epidural administration.<sup>4,12</sup> Buprenorphine which is highly lipid soluble and high affinity for opioid receptors gave certain advantages.<sup>9,13</sup>

In our study the onset of action was earlier in group 1 (7.66  $\pm$  1.91) buprenorphine compared to group 2 morphine ( 10.88  $\pm$  2.11) and this was statistically significant (p < 0.0001\*). Buprenorphine provided a longer duration of analgesia (10.78  $\pm$  1.54 ) compared to morphine ( 5.62  $\pm$  0.64)and this was statistically significant (P<0.001). Its longer duration of action can be explain on the basis of high lipid solubility and high affinity of buprenorphine for opiate receptors.<sup>13</sup>

Abboud and etal, using higher doses of buprenorphine (1 to 4 mg) alone, epidurally, observed complete pain relief in 22  $\pm$  2.4 minutes, but a remarkably longer duration of post-operative analgesia than that of our combination group.<sup>[14]</sup> Investigators have demonstrated that by using buprenorphine alone epidurally, in doses of 1 to 4 mg, varying durations of pain relief ranging from 2.5 to 9 hours are observed. As one can expect, with the use of lower doses of buprenorphine, the duration of pain relief in our study falls on the lower side of the reported range.<sup>[15]</sup>

Both drugs studied explained insignificant alteration in heart rate and blood pressure. The respiratory changes between the study groups were statistically comparable with insignificant. No patient developed any post procedure respiratory depression in both the study groups. The side effects of opioid in our study were

itching, urinary retention, nausea and vomiting. And were mild in nature and were equal in both the study groups.

### CONCLUSION

Epidural buprenorphine along with bupivacaine in its lower doses produces earlier onset, longer duration and better analgesia than morphine combined with bupivacaine and additional benefit is its safe in lower segment caesarean section patients for post-operative analgesia.

### REFERENCES

1. Synder Solomon H. Opiate receptors in the brain. The New England Journal of Medicine 1977; 296: antiaociceptiv agent. Br J Pharmac 1977; 60: 537- 545. 266-270.
2. Cousins MJ, Mather LE, Glynn CJ, Wilson PR Graham JR. Selective Spinal Analgesia. Lancet 1979; 1: 1141.
3. Woulfe MJ, Davies GK. Anaalgesic action of extradural fentanyl. Br J Anaesth 1980; 52: 357.
4. Bromage P, Comporesi E, Chestnut D. Epidural narcotics for postoperative analgesia. Anesth Analg 1980; 59: 473.
5. Houlton PG, Reynolds F. Epidural Diamorphine and fentanyl for post operative pain. Anaesthesia 1981; 36: 1144.
6. Bromage PR. Mechanism of action of extra dural analgesia. Br J Anaesth 1975; 45: 199.
7. Koshy T, Afzal L and Kaur B. A comparison of epidural Morphine and epidural Buprenorphine for post operative Analgesia: A double blind study. Ind J Anaesth. 1994; 42: 305
8. Behar M, Magora F, Olshwang D and Davidson JT Epidural Morphine in treatment of pain. Lancet, 1997; 10: 527.
9. Cowan A, Lewis JW, Macforlane IR. Agonist and antagonist properties of buprenorphine –A newantiaociceptiv agent. Br J Pharmac 1977; 60: 537- 545
10. Torda TA and Pybus DA. Comparison of four Narcotic Analgesics for extradural analgesia. Br J Anaesth 1982; 54: 291.
11. Pybus DA & Torda TA. Dose Effect relationships of extradural morphine. Br J Anaesth 1982; 54: 1259.
12. Kay B. A double blind comparison of morphine and buprenorphine. In the prevention of pain after operation. Br J Anaesth 1978; 50: 605
13. Cahill J, Murphy D, O'Brien D, Mulhall J and Fitzpatrick G. Epidural buprenorphine for pain relief after major abdominal surgery. Anaesthesia 1983; 38: 760-764.
14. Abboud TK, Afrasiabi A, Zhu J, Mantilla M, Reyes A, D'Onofrio L, et al. Epidural morphine or butorphanol augments bupivacaine analgesia during labor. Reg Anesth. 1989; 14: 115-120. [PubMed]
15. Saxena AK, Arava SK. Current concepts in neuraxial administration of opioids and non-opioids: An overview and future perspectives. Indian J Anaesth. 2004; 48: 13-24.
16. Abdul Hakim et al J. Anesth Clinial Pharmacology 2007; 23 (2) : 155-158.
17. Kiran Agarwal et al Indian J. Anaesth, 2010 Sep/Oct 54 (5); 453-457.