

Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study

S Jaiswal, P Ranjan, N Tewari, N Agarwal, S Mathur

Citation

S Jaiswal, P Ranjan, N Tewari, N Agarwal, S Mathur. *Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study*. The Internet Journal of Anesthesiology. 2006 Volume 14 Number 1.

Abstract

Background: In this study Midazolam/Butorphanol was used in combination with Bupivacaine in the epidural space to objectively establish the superiority of the combination, for labor analgesia, effect on conduct of labor and delivery, maternal complication and outcome of the neonate.

Materials and Methods: In a prospective, double blinded, randomized sequential allocated study, 60 ASA I and II physical status patients were divided in three groups of 20 each. 20 patients in active phase of labor not given any sort of analgesia were kept as controls.

Group I received no epidural analgesia. Group-II was treated with 2mg (2ml) preservative free midazolam + 8 ml of 0.25 % bupivacaine. Group-III was treated with 2mg (2ml) preservative free butorphanol + 8 ml of 0.25 % bupivacaine and in Group-IV the patients were given 10 ml of 0.25 % bupivacaine only.

Results and Conclusion: Addition of Midazolam / Butorphanol as an adjuvant with bupivacaine did not have any adverse effects on uterine activity, duration of first or second stages of labor or fetal heart rate parameters. Duration of analgesia was significantly longer in group III (130.85±13.82 min) as compared to Group II (90.55±10.83 min) and group IV(62.75±9.92 min) respectively. Quality of analgesia was significantly better in groups II, and III when compared with group IV. It is concluded that epidural butorphanol and midazolam can be useful and safe adjuncts to bupivacaine used for epidural analgesia during labor.

INTRODUCTION

Neuraxial analgesia is the most effective method of intrapartum pain relief in current practice. Epidural analgesia offers great versatility in extent and duration of effect. Use of low-dose bupivacaine with an opioid is the most popular method of maintaining epidural analgesia for labour. Burnstein et al (1999). The addition of the opioid allows the dose of bupivacaine to be reduced without adversely affecting the quality of analgesia. Chestnut et al (1988). Incidence and severity of maternal blockade can be reduced to a great extent by use of low dose of bupivacaine. Russel et al (1996). Increased mobility during epidural analgesia has been associated with greater maternal satisfaction. Collis et al (1995). But some side effects are seen with the use of opioids, most common of which are pruritus (Russel et al , 1996) and maternal hypoxaemia during second stage of labor. Porter et al (1996).

Butorphanol is a potent analgesic with both opioid agonist and antagonist effect. Its analgesic action is mediated by its interaction with kappa and mu opioid receptors. It has been shown that epidural butorphanol in combination with bupivacaine for labor analgesia, improves the duration and quality of analgesia. The time of onset of analgesia was significantly decreased as compared to plain bupivacaine and no fetal adverse effects were seen except that of a low amplitude sinusoidal fetal heart rate pattern with doses of 3 mg butorphanol. Hunt et al (1989)

Midazolam, is an agonist of the benzodiazepine- γ -aminobutyric acid (GABA)_A receptor complex, and has spinally mediated analgesic effects. Edwards et al (1990). It has been shown that epidural administration of midazolam with bupivacaine is more effective in alleviating postoperative wound pain than bupivacaine alone.

Nishiyama et al, (1995, 1998).

However, to date there has been no direct study of the effects of epidural bupivacaine with midazolam in labor analgesia. In this study Midazolam was used in combination with Bupivacaine and Butorphanol, a synthetic opioid was used in combination with Bupivacaine in the epidural space, to objectively establish the superiority of the combination, for the relief of labor pain and their effect on conduct of labor and delivery, maternal complication and outcome of the neonate.

MATERIAL & METHODS

This research was conducted at the Department of Anesthesiology and Critical Care (with cooperation of Department of Obstetric & Gynecology), Sir Sunderlal Hospital, Banaras Hindu University. After institutional ethical approval and written, informed consent, 60 ASA physical status I or II nulliparous or multiparous parturient at term, with spontaneous onset of labor and requesting epidural analgesia, were enrolled into this prospective, double-blinded, randomized sequential-allocation study. 20 patients in active phase of labor not given any sort of analgesia were kept as controls.

Inclusion criteria were- Patient primipare or gravida two, with no cephalopelvic disproportion or contracted pelvis, vertex presentation, patient in active phase of labor (>3 cm dilation), with no fetal distress prior to the procedure, with no bleeding disorders, with no spinal deformities.

The participants were allocated randomly into one of the groups as per the drugs used.

Group-1 (n = 20): Patient receiving no epidural analgesia.

Group-2 (n = 20): Patient treated with 2mg (2ml) preservative free midazolam + 8 ml of 0.25 % bupivacaine

Group-3 (n = 20): Patient treated with 2mg (2ml) preservative free butorphanol + 8 ml of 0.25 % bupivacaine

Group-4 (n = 20): Patient treated with 10 ml of 0.25 % bupivacaine only

The midazolam and butorphanol injections used were preservative free. Each patient received top-ups of 0.25 % bupivacaine (6 ml) as per individual demand.

Exclusion criteria were: Patients refusal, ASA III and IV, local skin infection at the spinal lumbar region, women

scoring <50 on a visual analog pain scale (VAPS) (0-100 mm), with presenting part below the ischial spines, and those who received opioid analgesic medication.

The epidural catheters were placed in L3- L4 or L2-L3 interspace before the active phase of labor, but drugs were given only after the labor was well established.

Using blinded syringes, all the patients received 10 ml of respective study solution, followed by top up dose of 6 ml of 0.25% bupivacaine on demand. The last dose in most of the cases was given in sitting position (perineal dose) which helped in episiotomies or any other operative delivery. A blinded anesthesiologist who was unaware of the dose or drug given performed all assessments. All the patients were monitored for the following parameters at 0, 5, 10, 15, 30 and 60 minutes interval.

Obstetric factors – Duration of 1st and 2nd stage of labor, mode of delivery, fetal weight, fetal cord blood gas analysis and maternal arterial blood gas analysis.

Anesthesia related factors- Onset of analgesia (minutes), duration of analgesia and sedation, interval between top ups, sensory block (segments), motor block – Bromage scale, assessment of pain by visual analogue score and rupee scale. Chakraborty et al. (2007)

In addition of the above recordings, baseline maternal heart rate and noninvasive blood pressure uterine contraction and fetal heart rate from 30 minutes before the epidural block till the completion of the study were recorded. The occurrence of maternal side effects, such as sedation, pruritus, nausea, and vomiting was recorded. Base line measurement of pain and muscle strength was made in all patients.

Possible complications which were anticipated- Dural tap, sedation, hypotension, weakness, nausea, pain at injection site, retention of urine and headache.

Monitoring of Patient after Delivery: Various maternal and fetal parameters and complications were recorded and appropriate measures were taken.

Reaction of the Patients: Finally the impression of the mother regarding the conduction of the labor was noted on the next day of delivery.

OBSERVATIONS AND RESULTS

Eighty laboring females consented to participate in this study. There were no differences among the four groups in

Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study

demographic data. (Table I)

Figure 1

Table 1: Demographic data

	Group I	Group II	Group III	Group IV
Mean age ± SD (years)	22.55±2.96	23.70±2.20	23.45±3.19	22.96±3.72
Mean weight ± SD (kg)	51.65± 2.87	51.80±2.85	52.40±2.85	52.11±3.36
Mean cervical dilation in cm ± SD	-	4.1500 ± 0.73 (3-5.50)	4.075 ± 0.84 (3-5.50)	3.95 ± 0.81 (3-5.50)

P=NS

The observations have been broadly categorized into five groups.

i) Drugs used, ii) Pain relief, iii) Motor blockade and sensory level,

iv) Course and outcome of labor, v) Arterial blood gas analysis.

A. Drugs:

All the three drugs, midazolam, butorphanol and bupivacaine were analyzed in the form of:

i) Amount of drug required , ii) Drug intervals, iii) Number of top up doses needed, iv) Duration of sedation after first dose, v) The effect on blood pressure.

Figure 2

Table 2: Mean Arterial Pressure variation with time.

Groups	0 minute	5 minutes	10 minutes	15 minutes	30 minutes
I	82.05 ± 5.53	82.65 ± 5.41	83.15 ± 4.09	83.70 ± 5.22	83.75 ± 4.69
II	84.50 ± 4.96	80.50 ± 6.49	75.30 ± 5.17	74.90 ± 5.90	75.90 ± 4.51
III	84.40 ± 5.11	82.40 ± 6.48	79.80 ± 7.04	78.0 ± 7.24	79.30 ± 7.59
IV	82.50 ± 3.72	77.25 ± 4.48	73.80 ± 3.94	73.0 ± 4.38	73.90 ± 4.12
F-value	1.36	4.66**	15.0***	17.33**	15.76***

* p= <0.05, **p= <0.01, ***p = <0.001

Table 2 shows mean arterial pressure of the three study groups and the control group at different time intervals. It reveals that there was significant fall in MAP in all epidural groups during the study period. The fall in MAP was more in bupivacaine group (group IV) as compared to group II, III

and control group. There was no significant difference in MAP in group II and III.

Figure 3

Table 3: Amount of bupivacaine(0.25%)required

	Group II	Group III	Group IV	F-value
Drug amount (ml)	29.20±6.75 (14-38)	22.7±4.11 (14-32)	36.10±5.25 (28-46)	29.88***

*** = p<0.001

Figure 4

Table 3A: Multiple Comparisons (SNK test)

	Groups		
	II Vs III	II Vs IV	III Vs IV
q values	6.83	6.22	6.75
p values	<0.001	<0.001	<0.001

Table 3 shows the amount of bupivacaine required during the study period in the three study groups.

The amount of bupivacaine required in the midazolam and butorphanol group (group II & III) was 29.20±6.75 and 22.7±4.11 ml respectively. However, it was more in bupivacaine group (group IV) as compared to the other two groups. This difference was statistically significant.

Figure 5

Table 4: Interval at which top ups of different drugs were given

	Group II	Group III	Group IV	F-value
Mean interval in minutes ± SD	90.55±10.83	130.85±13.82	62.75±9.92	F=172.83***

** = p<0.001

Figure 6

Table 4A: Multiple Comparisons (SNK test)

	Groups		
	II Vs III	II Vs IV	III Vs IV
q values	11.98	12.36	9.68
p values	<0.001	<0.001	<0.001

Table 4 shows mean intervals at which top up doses were required in the three study groups.

The mean intervals were 90.55±10.83 and 130.85±13.82 minutes in group II & III, while it was 62.75±9.92 minutes in group IV. Comparison among different groups showed that it was significantly less in group IV as compared to other two groups (p<0.001)

Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study

This shows that combination of midazolam and butorphanol with 0.25% bupivacaine increases the intervals between the subsequent drug requirements. Combination of 2 mg butorphanol with 0.25% bupivacaine increases the interval between the subsequent drug requirements even more than that of 2 mg midazolam, it is statistically significant.

Figure 7

Table 5: Number of top ups (including perineal dose)

	Group II	Group III	Group IV	F-value
Mean No. of top ups \pm SD	3.45 \pm 1.05 (1-5)	2.35 \pm 0.58 (1-3)	4.40 \pm 0.94 (3-6)	27.08***

*** = p<0.001

Figure 8

Table 5A: Multiple Comparisons (SNK test)

	Groups		
	II Vs III	II Vs IV	III Vs IV
q values	12.55	10.87	14.85
p values	>0.001	>0.001	>0.001

Table 5 shows the numbers of tops required in the three study groups after the initial epidural dose. The number of top ups required in group IV was comparatively more (mean 4.40 \pm 0.94) as compared to the mean number of top ups in midazolam (mean 3.45 \pm 1.05) and butorphanol group (mean 2.35 \pm 0.58).

The difference in the three groups is statistically significant but in general midazolam and butorphanol groups required less top ups thus less amount of bupivacaine.

Figure 9

Table 6: Duration of sedation after first dose

	Group II
Mean duration of sedation in minutes	14.65 \pm 3.54 (8-20)

Mild to moderate sedation was observed in some patients of group II. The mean duration of sedation in group II was 14.654 \pm 3.52 minutes. Sedation was less in group III (butorphanol) and absent in group IV (plain bupivacaine).

PAIN RELIEF

It was observed that pain relief was 100% in 12, 14 and 8 patients in group II, III and IV respectively; 75% in 6, 4 and 8 patients in group II, III and IV respectively; 50% in 2, 2 and 4 patients in group II, III and IV respectively. None of the patients in any of the groups complained that there was

no relief after drug administration.

At the end of the study 95, 100 and 90 percent patients in group II, III and IV respectively said that they had satisfactory pain relief throughout the period of their labor and delivery. Only 2 patients in group IV and 1 patient in group II experienced unsatisfactory pain relief. Comparison among different groups shows that the three groups were comparable with respect to quality of pain relief and patient satisfaction.

Figure 10

Table 7: Visual Analogue Pain Scores at different intervals

VAPS Interval (minutes)	1 Minute	5 Minute	10 Minute	15 Minute	30 Minute	60 Minute
II	92.75 \pm 6.29 (75-100)	53.50 \pm 14.24 (20-80)	21.50 \pm 6.71 (10-40)	10.30 \pm 4.06 (5-20)	4.45 \pm 4.84 (00-20.0)	3.95 \pm 4.75 (00-20)
III	91.0 \pm 8.20 (80-100)	42.75 \pm 10.81 (30-80)	17.75 \pm 2.55 (15-20)	6.75 \pm 2.45 (5-10)	3.00 \pm 2.51 (00-5.0)	3.00 \pm 2.51 (00-5.0)
IV	93.75 \pm 7.23 (80-100)	72.25 \pm 6.17 (60-80)	55.25 \pm 9.66 (35-70)	28.50 \pm 10.14 (20-50)	11.50 \pm 7.45 (5-30)	42.75 \pm 10.81 (30-80)
F-value	0.730	37.35***	176.66***	65.134***	14.55***	62.21***

*** = p<0.001

Table 7 shows visual analogue pain scores in the 3 groups at different time intervals.

In group II before giving epidural analgesia the mean pain score was 92.75 \pm 6.20, 10 minutes after giving epidural analgesia score became 21.50 \pm 6.71 the range was 10 to 40. At 15 minutes interval the mean pain score was 10.30 \pm 4.06 (5 to 20). The mean pain scores came down to 4.45 \pm 4.84 and 3.95 \pm 4.75 at 30 and 60 minutes time interval respectively.

In group III initial mean pain score was 91.0 \pm 8.20. It was 17.75 \pm 2.55 10 minutes after epidural analgesia. At 15 minutes, the mean pain score was 6.75 \pm 2.45. It came down to 3.00 \pm 2.51 at 30 minutes time interval and was same, 60 minutes after epidural analgesia.

In group IV initial mean pain score was 93.75 \pm 7.23. At 10 minutes it was 55.25 \pm 9.66. It became 28.50 \pm 10.14 at 15 minutes time interval. Mean pain scores were 11.50 \pm 7.45 and 53.50 14.24 at 30 minutes and 60 minutes interval respectively.

Comparisons among different groups revealed that there was no significant difference in mean pain scores before giving epidural analgesia in three groups. 5 minutes after giving epidural analgesia mean pain score was significantly less in

Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study

group III as compared to group II ($p < 0.05$) and group IV ($p < 0.001$). Mean pain score in group II at this time interval was significantly less than group IV ($p < 0.001$).

At 10 minutes time interval there was no significant difference between groups' II and III. At 10 and 15 minutes time intervals it was significantly more in group IV as compared to groups II and III ($p < 0.05$). At 30 and 60 minutes time intervals also there was no significant difference between group II and III. It was significantly more in group IV at 30 minutes time interval as compared to group II ($p < 0.01$) and group III ($p < 0.001$). At 60 minutes time interval mean pain scores were significantly less in group II ($p < 0.05$) and group III ($p < 0.01$) s compared to group IV.

Figure 11

Table 8: Distribution of patients according to pain scores at different time intervals

Minutes	Group II				Group III				Group IV			
	VAPS scores				VAPS scores				VAPS scores			
	A	B	C	D	A	B	C	D	A	B	C	D
0	-	-	-	100%	-	-	-	100%	-	-	-	100%
5	-	5%	45%	50%	-	25%	55%	20%	-	-	-	100%
10	5%	90%	5%	-	-	100%	-	-	-	-	40%	60%
15	75%	25%	-	-	100%	-	-	-	-	80%	20%	-
30	95%	5%	-	-	100%	-	-	-	50%	50%	-	-
60	95%	5%	-	-	100%	-	-	-	10%	30%	35%	25%

A: 0-10, B: 11-30, C: 31-50, D: 51-100

MOTOR BLOCKADE AND SENSORY LEVEL

Figure 12

Table 9: Bromage score \pm SD at different time intervals.

Groups	1 Minute	5 Minute	10 Minute	15 Minute	30 Minute	60 Minute
II	4.0 \pm 0.0	4.0 \pm 0.0	3.95 \pm 0.22 (3-4)	3.90 \pm 0.31 (3-4)	3.90 \pm 0.307 (3-4)	4.0 \pm 0.0
III	4.0 \pm 0.0	4.0 \pm 0.0	4.0 \pm 0.0	4.0 \pm 0.0	3.85 \pm 0.37 (3-4)	3.95 \pm 0.22 (3-4)
IV	4.0 \pm 0.0	4.0 \pm 0.0	3.95 \pm 0.22 (3-4)	3.65 \pm 0.49 (3-4)	3.80 \pm 0.41 (3-4)	4.0 \pm 0.0
F-value	-	-	0.500 (NS)	5.835 (NS)	0.377 (NS)	1.00 (NS)

Table 9 shows Bromage scores \pm SD at different time intervals in the 3 groups. The motor-blocking potency was slightly higher in bupivacaine group (group IV), as compared to other two groups. However no significant difference in the three groups was revealed on comparison among them. After 30 minutes interval group IV had 4

patients who had Bromage score of 3 as compared to 2 patients in midazolam group (group II) and 3 patients in butorphanol group.

Figure 13

Table 10: Sensory level achieved in different groups

	Group II	Group III	Group IV	F
Mean sensory level \pm SD (Thoracic segments)	7.35 \pm 1.18 (T5-9)	7.40 \pm 1.23 (T5-9)	7.10 \pm 1.37 (T5-9)	0.323

P = NS.

There was no significant difference in the three groups regarding the upper level achieved for pinprick sensation. It was 7.35 1.18 (5 to 9), 7.40 1.23 (5-9) and 7.10 1.37 (5-9) in group II, III and IV respectively.

OUTCOME AND COURSE OF LABOR

Figure 14

Table 11: Duration of active phase of labor

	Group I	Group II	Group III	Group IV	F-value
Mean duration \pm SD (minutes)	323.90 \pm 7.21	322.90 \pm 8.63	320.10 \pm 10.05	324.40 \pm 7.72	1.027

Since the cases were taken for epidural analgesia when cervical dilatation was 3 to 5 cm, only the duration of active phase of first stage of labor was considered here. (Table 11)

It was noted that patients who received bupivacaine only (group IV) had a slightly longer active phase of first stage of labor, though statistically not significant as compared to midazolam, butorphanol and control groups.

Figure 15

Table 12: Duration of second stage of labor

	Group I	Group II	Group III	Group IV	F-value
Mean minute \pm SD	29.80 \pm 6.50	29.45 \pm 4.18	27.35 \pm 4.28	30.30 \pm 2.75	2.37

Similar pattern as the first stage was seen in 2nd stage. The four groups were comparable with respect to the duration of second stage of labor. (Table 12)

Figure 16

Table 13: Mode of delivery in difference groups

Mode of delivery	Group I	Group II	Group III	Group IV
SVD	16 (80%)	18 (90%)	19 (95%)	18 (90%)
Cesarean	4 (20%)	2 (10%)	1 (5%)	2 (10%)

$\chi^2 = 2.379$ (NS)

The delivery pattern of the 60 cases in this series is

Comparative Study Of Epidural Midazolam And Butorphanol As Adjuvant With Bupivacaine For Labor Analgesia: A Double Blind Study

compared to 20 cases in the non epidural (control group). In the five patients who ultimately needed a caesarean section, the reasons were not related to the technique used. Two were due to fetal distress the cause for which turned out to be tight loops of cord round the neck (per operative finding), two were due to scar (due to previous caesarean section) tenderness, and the remaining one was for cephalopelvic disproportion (due to big size baby). (Table 13)

Figure 17

Table 14: Apgar score – 1 minute and 5 minutes

Apgar score (minute)	Group I	Group II	Group III	Group IV	F-value
1	7.90 ± 0.64	8.0 ± 0.65	8.05 ± 0.51	8.05 ± 0.69	0.26 NS
5	9.10 ± 0.55	9.04 ± 0.45	9.05 ± 0.51	9.05 ± 0.51	0.13 NS

There was no case of fetal distress during first stage or second stage of labor in all the four groups.

There was not a single case of newborn where Apgar score was less than 7 at 5 minutes. There were 5 babies who had Apgar score of 7 at one minute. They improved after suctioning and giving oxygen through a mask. The subsequent Apgar scores at 5 minutes were 9/10 in all the newborns. (Table 14)

Subsequently after delivery none of the babies had any problem in the ward and till discharge. These results are comparable with that of the controls.

ARTERIAL BLOOD GAS ANALYSIS

The various parameters which were studied were – pH, Pco₂, PO₂, SaO₂, and HCO₃. The pH of cord blood in the three groups (mean 7.29 ± .09) was more than that of the control (mean 7.15 ± 0.11) and was statistically significant. The results revealed that in the epidural groups there was significantly less acidosis as compared to the control group as shown in Table 15.

Figure 18

Table 15: Cord blood gas analysis

Group	Ph	PaCO ₂	PaO ₂	SaO ₂	HCO ₃
I	7.15 ± 0.11 (6.90-7.30)	30.45 ± 12.43 (24-32)	34.40 ± 2.62 (30-38)	45.05 ± 6.29 (35-55)	14.75 ± 1.20 (12-16)
II	7.30 ± 0.09 (7.15-7.42)	32.10 ± 2.83 (28-38)	48.75 ± 3.14 (44-54)	59.50 ± 3.0 (53-64)	18.80 ± 1.99 (15.0-22.0)
III	7.29 ± 0.08 (7.15-7.45)	34.50 ± 2.72 (30-39)	52.25 ± 1.41 (50-54)	63.30 ± 0.80 (62-64)	19.0 ± 1.95 (15-22)
IV	7.305 ± 0.107 (7.15-7.50)	31.15 ± 2.30 (28-34)	50.85 ± 2.03 (45-54)	62.85 ± 1.35 (60-64)	17.75 ± 3.20 (16-20)
F	10.70***	1.426	2.37041***	115.43***	15.77***

* = p < 0.05, ** = p < 0.01, *** = p < 0.001.

The levels of PaCO₂ in group II, III and IV were more

towards normal as compared to control group. This is explainable as there was almost no hyperventilation in the epidural groups.

PaO₂ levels showed an increase in group II, III and IV i.e. towards normal (mean 50.61 ± 2.69) as compared to non epidural group (mean 34.40 ± 2.62). This is explained as there was less pain and the patient was not hyperventilating or restless at any time so there was less oxygen consumption.

The bicarbonate levels showed a slight increase in group II, III and IV (mean 18.52 ± 2.47) as compared to the control (mean 14.75 ± 1.20). The normal bicarbonate levels are 20-22 and thus levels of group II, III and IV are comparable with the normal.

MATERNAL ARTERIAL BLOOD GAS ANALYSIS

The pH changes in the mother were almost normal to mild alkalosis (mean pH 7.4 ± 0.03) in the three epidural groups.

This is due to the break in the hyperventilation – hypoventilation cycle by epidural analgesia which prevents maternal respiratory alkalosis and metabolic acidosis development. pH in the epidural groups was significantly higher than that of control. The three epidural groups were comparable with regard to maternal pH.

Figure 19

Table 16: Maternal arterial blood gas analysis

Group	Ph	PaCO ₂	PaO ₂	SaO ₂	HCO ₃
I	7.2115 ± 0.10 (7.01-7.57)	29.45 ± 3.10 (24-35)	70.10 ± 4.90 (62-78)	89.15 ± 3.83 (80-95)	14.95 ± 1.15 (14-17)
II	7.40 ± 0.033 (7.31-7.43)	35.05 ± 2.54 (30-40)	86.95 ± 2.42 (79-90)	93.50 ± 1.47 (91.0 ± 0.95)	18.90 ± 1.89 (16-21)
III	7.42 ± 0.016 (7.38-7.44)	38.25 ± 1.48 (34-40)	88.10 ± 1.29 (86-90)	94.10 ± 0.64 (93-95)	19.05 ± 0.76 (18-20)
IV	7.39 ± 0.035 (7.32-7.44)	34.650 ± 2.37 (30-380)	85.25 ± 3.23 (80-90)	93.80 ± 0.95 (92.0 - 95)	17.45 ± 1.70 (15-20)
F-value	48.60***	44.397	134.835***	25.286***	34.609***

* = p < 0.05, ** = p < 0.01, *** = p < 0.001.

PaCO₂ in group II, III and IV (mean 35.98 ± 2.69) showed values towards normal as compared to control group (mean 29.45 ± 3.10).

PaO₂ and oxygen saturation showed an increase in epidural groups (mean 86.76 ± 2.67) as compared to the control (mean 70.10 ± 4.90) and statistically significant.

HCO₃ is towards normal in group II, III and IV (mean 18.47 ± 1.67) as compared to control group (mean 14.95 ± 1.15).

SOME GENERAL OBSERVATIONS

1. No major problems were encountered while passing the epidural catheter.
2. None of the patients had any sharp fall in blood pressure.
3. None of the sixty cases involved in the study showed any adverse reaction to the drugs used eg. Respiratory depression, anaphylactic shock, seizures etc.
4. All babies were born alive with no fetal distress, no intrapartum accident was noted.
5. The mothers were in general well co-operative with us during labor (irrespective of their literacy status) in understanding the procedure and in telling about their interpretation of degree of pain relief.
6. No immediate postpartum complication of epidural blockade like headache and weakness in the legs were noted in the study groups.
7. It was also observed that of all the spontaneous vaginal deliveries (n=55), 32 patients required episiotomies. Of these 26 patients had received the last dose (perineal dose) just prior to full dilatation and thus they required no additional analgesia or local anesthetic for episiotomy. This group of patients was also very comfortable post delivery.
8. There was no alteration in the intensity, frequency or duration of uterine contraction in patients who received epidural analgesia rather it was a general observation that the patients who were having uncoordinated pattern of contractions, delivered normally. If these patients would not have been given epidural analgesia, these patients would definitely have ended up with a caesarean section (due to fetal distress).
9. In our study some degree of somnolence was observed in patients receiving midazolam the degree of somnolence was less in butorphanol group.
10. Nausea was notice in some cases in the butorphanol group.

DISCUSSION

Epidural analgesia using various drugs alone and in combination with local anaesthetics have long been used to produce analgesia for labor and delivery.

Among the drugs used in our work some studies have already been done with bupivacaine and butorphanol trying them in combination as well as separately in different concentrations, but there is no published documentation on the use of midazolam for labor analgesia. Although the efficacy of epidural midazolam in post operative pain, low backache, etc. have been studied by many researchers. In our study we have tried to compare the efficacy of combination regimen of butorphanol and midazolam with bupivacaine as compared to bupivacaine alone in the relief of labor pain, and also to find out any adverse effects of any of the regimen.

1. Maternal systolic blood pressure and epidural midazolam, butorphanol and bupivacaine: The absence of hypotension in the 60 laboring females was probably due to The preloading with ringer lactate solution prior to administration of drugs in epidural space and the use of local anesthetic in lower concentration and low dose.

In a similar study in 1991 by Nishiyama T. et al where he studied the hemodynamic changes for 120 minutes after epidural midazolam, it was found that the blood pressure, heart rate, respiratory rate did not change from preinjection values.

Sedation: Some sedation was observed in patients treated with epidural midazolam and butorphanol, but there was no sedation in the group IV (bupivacaine alone).

Nishiyama T. et al. (1991, 1995, 1988) reported that the incidence of sedation following epidural midazolam is significant when used for postoperative pain relief. Our study corroborated their findings.

Pain Relief: Best results evidenced by the subjective and objective pain relief were observed in patients who received epidural butorphanol (group III) as compared to midazolam (group II) or who received bupivacaine alone (group IV).

But the pain relief was almost comparable in group II and III. Almost 80% patients had excellent pain relief in butorphanol group as compared to 70% in midazolam group, but it was only 50% in bupivacaine group.

Few studies in literature are about the use of epidural butorphanol for labor analgesia, but there is no published literature regarding use of epidural midazolam for labor analgesia.

In clinical practice, a VAPS ≤ 10 mm is a lower level of analgesia than is required for clinical comfort, because it has been reported that parturients request further intervention during epidural analgesia only when the VAPS exceeds 30 mm (Brownridge et al., 1992).

The VAPS is probably the most frequently used scale in research studies, including those in anesthesia. It is relatively easy to use, minimally intrusive, conceptually simple, and its rational scale properties allow meaningful interpretation of percentage difference in VAPS measurements (Bodian et al 2001). Although there are some data on maternal satisfaction with analgesia, they are related only to pain relief and not specifically to other characteristics of the block. The area of overall maternal satisfaction deserves further attention.

OUTCOME AND CONDUCT OF LABOR

ACTIVE PHASE OF FIRST STAGE OF LABOR

No statistically significant difference was observed in the duration of active phase of first stage of labor though group IV noted slight prolongation (mean 324.40 7.72 minutes) as compared to control group (mean 323.90 7.21) or the midazolam and butorphanol groups (mean 322.90 8.63 and 320.10 10.05 minutes respectively). This slight increase in the duration in group IV is due to the increased amount of drug (due to more no. of top ups) used rather than the concentration of the drug (0.25%) used.

Duration of second stage: Duration of second stage of labor was comparable in all the groups. The duration is almost similar in all groups and is comparable with controls (mean 29.80 3.650 minutes).

Mode of delivery: It was observed in our study that 91.66% patients in the study groups had a spontaneous vaginal delivery as compared to control group and no patients had instrumental delivery which is similar to the results in the control group where the incidence of forceps delivery was 0%. We also did not observe any malrotation in the study group. Our results are in support the results of the following researchers- Porter et al (1996), Philips et al (1987)

Results of our study are in contrast to those of Studd et al(1980), Bromage et al (1969),

The rates of caesarean section in study groups were 8.33% and were found to be comparable with the control of 20%. The results are in support of studies by Evan et al (1975), who reported a caesarean section rate of 10% with epidural infusion of 0.25% bupivacaine .

Our results showed that the low incidence of difficult deliveries needing any forceps assistance could very well be due to insistence on early induction (all patients had been induced at cervical dilatation < 5.5 cm) of epidural analgesia. Our observations were supported by the finding of Fraser et al. (2002), the risks of difficult delivery were increased with late induction of epidural analgesia in labor (≥ 6 cm) than induction between 3 to 5 cm.

Fraser et al (2002) found that an interval between epidural induction and full dilatation increased the risk of difficulty delivery. This seems to tally with our results where induction – dilatation interval was between 315 to 335 minutes (i.e. not more than 360 minutes as studied by Fraser et al (2002).

Fetal Outcome: None of the indicators of neonatal well being were different among the four groups. This included the incidence of low umbilical artery cord pH and Apgar scores at 1 and 5 min.

The study demonstrated that midazolam, butorphanol or bupivacaine used for obstetric epidural analgesia, do not have any adverse affect on the fetus and later, on the newborn, as has been seen through Apgar scores studies which basically has been the main concern of the patients and the obstetricians to avoid taking and giving epidural analgesia.

Majority of the studies have revealed that either outcome is unaffected or at times even better in patients who received epidural analgesia. Our findings are supported by - Matouskova et al (1974), Evans et al (1975), Jouppila et al (1984), Studd et al (1980).

Some of the past studies did reveal that fetal or neonatal outcome was affected in the babies of mothers with epidural block. Scanlon et al (1974)

ARTERIAL BLOOD GAS ANALYSIS

The results of maternal arterial blood gas analysis and baby cord blood gas analysis are slightly better in our study groups. The fetal metabolic acidosis in the study groups (7.29 ± 0.09) was comparatively less than the control group

(7.15 ± 0.12). The oxygen saturation and PaO₂ are better in both baby and mother of epidural groups (baby; SaO₂ 61.88 ± 2.57, PaO₂ 50.85±2.03, mother; SaO₂ 93.80 ± 0.95, PaO₂ 86.75 ± 2.67) as compared to baby and mother of control group (baby; SaO₂ 45.05 ± 6.29, PaO₂ 34.40 ± 2.62, mother's SaO₂ 89.15 ± 3.83, PaO₂ 70.10 ± 4.90). Mother had almost normal pH or slight alkalosis as compared to control group who had metabolic acidosis. The PaCO₂ level was also more towards normal of epidural groups as compared to that of control group (mean 29.45 ± 3.10).

Scherer R. et al. (1995) studied the influence of epidural analgesia on fetal and neonatal well being and their fetoplacental blood flow seems to be improved by epidural analgesia with local anesthetics and fetal and neonatal acid base balance and gas exchange are not adversely affected by epidural analgesia.

CORRESPONDENCE TO

S. Jaiswal, M.D Department of Anesthesiology Institute of Medical Sciences Banaras Hindu University Varanasi .India
E-mail- drsushiljswl@rediffmail.com

References

1. Burnstein R, Buckland R, Pickett JA. A survey of epidural analgesia for labour in the United Kingdom. *Anaesthesia* 1999; 54: 634-640
2. Chestnut DH, Owen CL, Bates JN, Ostman LG, Choi WW, Geiger NW. Continuous infusion epidural analgesia during labor: a randomized, double-blind comparison of 0.0625% bupivacaine/0.0002% fentanyl vs. 0.125% bupivacaine. *Anesthesiology* 1988; 68: 754-759
3. Russel R, Reynolds F. Epidural infusion of low-dose bupivacaine and opioid in labour. *Anaesthesia* 1996; 51: 266-273
4. Collis E, Davies DWL, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labour. *Lancet* 1995; 345: 1413-16
5. Porter JS, Bonello E, Reynolds F. The effect of epidural opioids on maternal oxygenation during labour and delivery. *Anaesthesia* 1996; 51: 899-903
6. Hunt CO, naulty JS, Malinow AM, Datta S and Ostheimer GW. Epidural butorphanol -bupivacaine for analgesia during labor and delivery. *Anesth and Analg.* 1989; 68: 323-327
7. Edwards M, Serrao J.M , Gent J.P and Goodchild C.S. On the mechanism by which midazolam causes spinally mediated analgesia. *Anesthesiology* 1990; 73: 273-277.
8. Nishiyama T. The post-operative analgesic action of midazolam following epidural administration. *Eur J Anaesthesiol* 1995; 12 : 369-374.
9. Nishiyama T, Yokoyama T and Hanaoka K. Midazolam improves postoperative epidural analgesia with continuous infusion of local anaesthetics. *Can J Anaesth* 1998; 45: 551-555.
10. Chakrabarty A., Mathur S.K. Rupee scale : for measurement of pain in India. *The Internet Jour.of Anesth.* 2007;12 (2).
11. Nishiyama T., Odaka Y., Hiraqaki A., Mikane T., Kohayashi O., Scto K., Epidural administration of midazolam with saline or bupivacaine for postoperative pain. *Masui*, 1991; 40: 1525-1530.
12. Brownridge P., Plummer J., Mitchell J., Marxhall P. An evaluation of epidural Bupivacaine with and without Meperidene in labour. *Reg. Anesth.* 1992;17: 15-21.
13. Bodian CA, Freedman G, Hossain S, et al. The visual analog scale for pain: clinical significance in postoperative patients. *Anesthesiology* 2001; 95: 1356-61.
14. Phillips G. Epidural sufentanil/bupivacaine combinations for analgesia during labour: effect of varying sufentanil doses. *Anesthesiology* 1987;67:835-838.
15. Studd J.W.W, Crawford J.S , Duignan N.M, Rowbotham C.J.F, Hughes A.O. The effect of lumbar epidural analgesia on the rate of cervical dilatation and the outcome of labour of spontaneous onset. *Br. J. Obs. Gyn.* 1980;87:1015-1021.
16. Bromage, P. R.: An evaluation of bupivacaine in epidural analgesia for obstetrics. *Canad. Anaesth Soc.J* 1969;16:46-56
17. Evans, J.M , Gauci C.A. and Watkins G. Horner's syndrome as a complication of lumbar extradural block. *Anaesthesia* 1975;30: 774 -777
18. Fraser W.D, Cayer M, Soeder B.M, Turcot L, Marcoux S. Risk factors for difficult delivery in nulliparas with epidural analgesia in second stage of labour. *Obstet. Gynecol.* 2002 ; 99: 403-418.
19. Matouskova et.al. An improved method of epidural analgesia with reduced instrumental delivery rate. *Acta Obstet. Gynecol Scand.* 1974; 83: 9-13.
20. Jouppila R., Puolakka J., Kaupila A., Vuori J. Maternal and umbilical cord plasma noradrenaline concentration during labour with and without segmental extradural analgesia and during cesarean section. *Br. J. Anaesth.* 1984; 56: 251-255.
21. Scanlon, J. W., Brown, W. U., Weiss, J. B., and Alper, M. H.: Neurobehavioral responses of newborn infants after maternal epidural anesthesia. *Anesthesiology* 1974;411:121
22. Scherer R, Holzgreve W: Influence of epidural analgesia on fetal and neonatal well-being. *Eur J Obstet Gynecol Reprod Biol* 1995; 59:17-29

Author Information

S. Jaiswal, M.D.

Junior Resident, Department of Anesthesiology, Institute of Medical Sciences, Banaras Hindu University

P. Ranjan, M.D.

Reader, Department of Anesthesiology, Institute of Medical Sciences, Banaras Hindu University

N. Tewari, M.Sc.

Junior Research fellow, Department of Anesthesiology, Institute of Medical Sciences, Banaras Hindu University

N. R. Agarwal, M.D.

Professor, Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University

S.K. Mathur, M.D.

Reader, Department of Anesthesiology, Institute of Medical Sciences, Banaras Hindu University