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Original Research Article

Comparative study between levobupivacaine with clonidine and levobupivacaine with fentanyl in epidural labour analgesia in rural set up

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ABSTRACT

Background: Neuraxial techniques are the gold standard for intrapartum labour analgesia. Neuraxial labour analgesia using new local anaesthetics such as levobupivacaine has become very popular by virtue of the safety and lesser motor blockade caused by these agents. Multiple randomized controlled trials comparing epidural analgesia with systemic opioids, nitrous oxide or both have demonstrated lower internal pain scores and higher maternal satisfaction with neuraxial analgesia. The purpose of this study is to compare fentanyl and clonidine combination with levobupivacaine in terms of effect of epidural labour analgesia on fetal outcome and incidence of instrumental or caesarean delivery and duration of second stage of labour.
Methods: A total of 50 primiparous with singleton pregnancy and vertex presentation and cervical dilatation of 3-5 cm were enrolled for the study in our hospital in department of obstetrics and gynecology. They were divided into group 1 and group 2 (25 patients in each group). Group 1 received 10 ml. of 0.125% isobaric levobupivacaine with 25µg fentanyl and group 2 received 10 ml of 0.125% isobaric levobupivacaine with 60 µg clonidine. Parturients were given epidural analgesia on numerical rating scale (NRS) Score >3. Breakthrough pain supplemented with 3-5 ml of 0.125% levobupivacaine. Data collected were demographic profile of the patients, analgesic qualities, 1st and 2nd stage labour duration, side effects and feto-maternal outcome.
Results: Post treatment mean NRS were almost similar between two groups at all periods except at 15 minutes when it was significantly lower for group 2 (2.64±0.49). Onset of analgesia was earlier in group 2 (13.68±0.94) in comparison to group 1 (15.36±1.18) and was statistically significant.
Conclusions: In conclusion Group 2 (levobupivacaine with clonidine) showed significant difference in early onset of analgesia but did not show any significant difference in duration of labour, maternal and fetal outcome and mode of delivery.

Keywords: Clonidine, Epidural labour analgesia, Fentanyl, Levobupivacaine

INTRODUCTION

Labour pain is the worst and most intense pain a woman might experience in her life time and hence requires adequate analgesia. This distress may harm the mother and fetus. Painful labour often results in excessive maternal stress, increased uterine contractility, hypo perfusion of feto-placental unit, fetal hypoxia and acidosis, increased oxygen demand and mechanical workload resulting in catecholamine release leading to

uterine vasoconstriction.[1] These responses can be managed by providing adequate analgesia during labour. These include nonpharmacological approaches such as hypnosis, acupuncture, hydrotherapy and transcutaneous electrical nerve stimulation as well as administration of nitrous oxide, low dose sevoflurane and parenteral opioids.[2,3] Though some parturients have claimed to have been provided relief by some of these aforementioned methods still there is enough evidence that the only consistently affective method of pain relief during labour is central neuraxial blockade.[4,5]

Physiological benefits of neuraxial analgesia for the mother and fetus are well documented. Neuraxial analgesia has been shown to improve maternal cardiovascular and pulmonary physiology and acid base status of the fetus.[6-9] Levobupivacaine can be used as an epidural local anaesthetic in 0.5% to 0.75% concentrations for surgical anaesthesia, whereas analgesia can be achieved with concentrations of 0.125% to 0.25%.[10-12] Advantages of levobupivacaine is that it is less cardiotoxic compared with bupivacaine.[13,14] Clonidine is an α_2 adrenergic agonist that produces analgesia via a nonopioid mechanism and the combination of epidural bupivacaine with clonidine for labour analgesia has been previously studied.[15-18] Lipophilic opioids like fentanyl and sufentanil can cause some side effects like sedation, pruritus, lower APGAR score and shivering.[15-18]

METHODS

This was prospective, randomized, double blind study conducted in our hospital after approval of ethical committee on 50 primiparous patients with American society of anesthesiologists (ASA) grade I and Π, aged 18-35 years parturients consenting for labour analgesia. The study design was developed in association with the obstetrician of our hospital. The women, included in the study had singleton pregnancy with vertex presentation, cervical dilatation of 3-5cm and had no contraindications to labour analgesia, were randomly allocated in two groups of 25 each using sealed envelopes.

- Group 1 received 10 ml of 0.125% isobaric levobupivacaine with 25 µg fentanyl through epidural route via catheter
- Group 2 received 10 ml of 0.125% isobaric levobupivacaine with 60µg clonidine via epidural catheter.

In current study both the patient as well as the anesthesiologist administering the drug did not know which drug was used. Another anesthesiologist not involved in the study prepared the drug. Exclusion criteria consisted of patients unwilling for procedure, parturients with gravida ≥2, history of allergy to local anaesthetics, history of bleeding disorders, cephalopelvic disproportion, deformity of vertebral column etc. Baseline pain score was assessed using numerical rating scale. (NRS, 0=No pain, 10=worst pain) before the epidural analgesia. An intravenous access was achieved in every parturient and preloading was done with 10 ml/kg bodyweight with lactated Ringer's solution. Then an epidural catheter placement with the help of 18 G Tuohy needle through LOR technique, was performed with parturients in sitting position under all aseptic precautions at L3-L4 level. Test dose not given because administration of traditional epidural test dose causes unwanted loss of proprioceptive and motor functions. Baseline maternal blood pressure, heart rate, oxygen saturation was measured.

Parturients were given epidural analgesia when NRS>3 and then maternal blood pressure, heart rate, oxygen saturation were measured noninvasively every 5 minutes for 15 minutes, then every 15 minutes for 45 minutes then every 30 minutes for 180 minutes or delivery of fetus whichever was early. Breakthrough pain was supplemented with 3-5ml of 0.125% levobupivacaine. Partograph was assessed as an assessment tool to monitor the duration and progress of labour. Time of onset was taken as the time between epidural drug injection till the time when NRS score becomes <3. Time from injection of drug from epidural route to the request of additional analgesia for painful contraction(NRS>3) was taken as duration of analgesia. Highest dermatome sensory block was assessed by using 26G needle for loss of pin prick sensation. Degree of motor block was assessed using modified Bromage scale i.e.

- 0= No motor block
- 1= Inability to raise extended leg; able to move knees and feet
- 2= Inability to raise extended legs and move knees; able to move feet
- 3= Complete block of motor limbs.

Statistical analysis

Continuous data was summarized as Mean±SD. While discrete (categorical) in number and percentage. Continuous data were compared by unpaired student's t test while categorical data were compared by chi-square ($\chi 2$) test. A p-value <0.05 ($p<0.05$) considered statistically significant. All analyses were performed on SPSS software.

RESULTS

A total of 50 patients randomized equally to treat with levobupivacaine 0.125% with fentanyl and levobupivacaine 0.125% with clonidine through epidural were taken. Table 1 shows distribution of age and anthropometric parameters between the groups. The mean age of both groups 1 and 2 ranged from 20-32 years with Mean±SD (24.72±3.06) and (25.80±2.23) respectively with p value of (>0.05). Similarly, mean height, weight and BMI also did not differ (p >0.05) between the two groups.

Table 1: Distribution of age and anthropometric parameters between both the groups.

	Group 1	Group 2	P value (t test)
Age in years	24.72±3.06	25.80±2.23	0.15
Weight in Kg	58.80±5.03	59.12±6.91	0.85
Height in cms	150.44±2.48	152.60±7.77	0.19
BMI in Kg/m^2	25.98±2.16	25.53±3.61	0.60

Table 2 shows comparison of systolic, diastolic, mean arterial pressure, heart rate and NRS. The post treatment systolic, diastolic, mean arterial pressure and heart rate did not differ significantly (p>0.05) between the two groups. The post treatment mean NRS was almost similar between two groups at all periods except at 15 minutes, it was lower in group 2 compared to group 1 and statistically significant (p=0.001).

Table 2: Comparison of systolic BP, diastolic BP, mean BP, heart rate and NRS score across time periods.

Time (in minute)	Systolic B.P. Group 1/Group 2	Diastolic B.P. Group 1/Group 2	Mean B.P. Group1/ Group 2	Heart rate Group 1/Group 2	NRS Group 1/Group 2
0	123.6±8.28/126.48 ±3.47	86.8±5.09/89.12±3.6	98.84±5.06/101.76± 2.75	107.36±5.52/108.2 4±4.79	8.44±0.58/8.52±0. 58
	P value 0.11	P value 0.06	P value 0.06	P value 0.55	P value0.63
5	120.12±8.37/121.2 8±4.39	85.04±6.58/86.16±6. 5	97.4±6.97/97.8±4.42	104.4±5.91/104.96 ±5.13	6.88±0.92/6.52±0. 51
	P value 0.54	P value 0.54	P value 0.81	P value 0.72	0.09
10	111.76±7.19/110.4 8±4.77	85.32±6.03/83.36±4. 53	97.76±7.20/96.8±3.6 0	91.16±8.36/93.16± 7.52	4.68±0.47/4.68±0. 47
	P value 0.46	P value 0.20	P value 0.33	P value 0.37	P value 1.00
15	106.36±6.61/107.3 6±4.68	82.36±8.68/79.76±5. 84	94.12±5.36/91.92±4. 29	89.04±7.46/89.64± 6.51	3.36±0.63/2.64±0. 49
	P value 0.54	P value 0.22	P value 0.09	P value 0.76	P value 0.001*
30	107.60±6.58/106.0 8±3.85	80.24±7.33/77.12±5. 35	89.52±4.50/87.08±5. 22	87.12±8.36/90.00± 6.11	2.60±0.50/2.64±0. 49
	P value 0.32	P value 0.11	P value 0.08	P value 0.13	P value 0.77
45	109.44±9.02/106.0 0±3.26	83.44±5.90/83.56±5. 94	92.12±4.10/90.96±4. 21	88.16±7.64/89.04± 6.35	2.56±0.50/2.64±0. 49
	P value 0.08	P value 0.94	P value 0.32	P value 0.64	P value 0.57
60	109.92±8.21/106.8 ±2.79	83.80±6.44/84.28±6. 01	92.40±4.23/91.28±4. 05	87.96±7.14/90.08± 6.33	2.56±0.50/2.64±0. 49
	P value 0.07	P value 0.78	P value 0.34	P value 0.37	P value 0.57
90	109.44±9.01/106.3 2±3.44	83.92±7.12/84.60±6. 50	92.52±5.22/91.32±4. 82	88.24±7.15/88.96± 5.38	2.60±0.50/2.64±0. 49
	P value 0.11	P value 0.72	P value 0.40	P value 0.65	0.77
120	110.28±9.41/106.2 4±2.53	83.36±8.24/83.76±7. 90	92.52±6.11/90.84±5. 56	87.96±9.93/88.72± 4.61	2.60±0.50/2.64±0. 49
	P value 0.4	P value 0.86	P value 0.31	P value 0.63	P value 0.77
150	109.84±7.91/107.2 ±2.51	81.92±7.84/82.64±7. 06	91.20±6.04/90.20±5. 05	88.00±5.90/88.48± 3.22	2.60±0.50/2.68±0. 47
	P value 0.11	P value 0.73	P value 0.52	P value 0.71	P value 0.56
180	109.28±6.87/106.4 ±2.94	82.56±5.50/82.80±5. 17	91.92±3.89/90.20±3. 74	88.88±6.41/89.72± 4.39	2.56±0.50/2.64±0. 49
	P value 0.06	P value 0.87	P value 0.11	P value 0.53	P value 0.57

NRS score is significant (P value=0.001) at 15 minutes, but mean NRS value, systolic BP, diastolic BP, mean BP, heart rate is insignificant (P value >0.05).

Table 3 shows comparison of onset of analgesia, sensory dermatome blockade level and modified Bromage scale between the groups. Onset of analgesia was earlier in group 2 and was statistically significant (p=0.001). Comparing the post treatment frequency (%) of sensory levels and modified Bromage motor scale of two groups were statistically insignificant (p>0.05). Table 4 shows comparison of duration of 1st stage and duration of 2nd stage of labour between the groups. Mean duration of first stage of labour and 2nd stage labour in both the groups are comparable and are statistically insignificant (p>0.05).

Table 3: Comparison of onset of analgesia, blockade of sensory dermatome level and modified Bromage scale between the groups.

	Onset of analgesia		Sensory dermatome level						Modified motor Bromage scale	
		P value	T5	T6	T7	T8	T9	P value		P value
Group 1	15.36±1.8 (Mean±SD)	0.001*	4%	52%	20%	20%	4%	0.18	0.60±0.50 (Mean±SD)	0.40
Group 2	13.68±0.94 (Mean±SD)		0%	28%	32%	20%	20%		0.48±0.51 (Mean±SD)	

Significant difference for onset of analgesia (p value=0.001) between the groups, but no significant difference for sensory dermatome level blockade and motor blockade (p value >0.05) between the groups.

Table 4: Comparison of duration of first and second stage of labour.

Group 1		Group 2	P value
Duration of 1st stage of labour (minutes) Mean±SD	323.20±14.94	325.44±10.91	0.54
Duration of 2nd stage of labour (minutes) Mean±SD	112.60±3.87	114.76±6.16	0.14

Table 5 shows comparison of APGAR score across the time periods between the groups.

Comparing the mean APGAR score of two groups t-test revealed p>0.05.

Table 5: Comparison of APGAR score between the groups across the time periods.

Time periods	Group 1	Group 2	P value
At 1 minute	6.32±1.19	6.44±1.22	0.71
At 5 minutes	8.64±0.56	8.64±0.56	1.00

No significant difference seen for APGAR score between both the groups.

Table 6: Comparison of type of delivery between the groups.

Type of delivery	Group 1 (n=25)		Group 2 (n=25)		P value
	No.	%	No.	%	
Caesarean section	1	4.0	2	8.0	
Instrumental	4	16.0	4	16.0	0.83
Normal	20	80.0	19	76.0	

Table 6 shows comparison of type of delivery between the groups. Comparing the frequency (%) of mode of delivery of two groups $\chi 2$ test revealed similar (p>0.05) mode of delivery between the two groups.

DISCUSSION

Although neuraxial techniques provide excellent pain relief during parturition but may affect the progress and outcome of labour. Obstetrician and anaesthetists have always feared the increased incidence of instrumental deliveries in women receiving labour analgesia as compared to those who do not receive it.[23] Systolic, diastolic and mean blood pressure did not show any significant difference between the groups (p value>0.05). Baseline heart rate of both the groups were same and statistically insignificant (p value>0.05). Chhetty et al, Ropivacaine 0.125% versus 0.2% with fentanyl for labour analgesia found no significant difference in haemodynamic variables. Mean arterial pressure as compared between the groups was (85.48±8.74 versus 86.60±7.72) (p value>0.05).[24] Difference between NRS score was statistically significant at 15 minutes with (p=0.001) on comparison between the groups. But mean NRS score was statistically insignificant.

Onset of analgesia was earlier in group 2 and was statistically significant (p value=0.001), which did not correlate with previous studies. Syal K et al, in their study using clonidine 60µg and bupivacaine 0.125% and bupivacaine 0.125% alone in epidural analgesia found no significant difference in NRS score (3.24±6.0 versus 2.52±0.77) between the groups.[25] In present study, at none of the time intervals a significant difference in proportion of patients with sensory blockade and modified Bromage score≥2 was observed (p>0.05) between the groups. Syal K et al in their study using clonidine 60µg and bupivaine 0.125% and bupivacaine

0.125% alone in epidural labour analgesia concluded no significant difference in sensory and motor blockade in their study. Shah N et al using three groups ropivacaine 0.2%, levobupivacaine 0.125%, bupivacaine 0.125% reported no significant difference in modified Bromage scale among study groups.[26]

In present study comparing the mean duration of 1st stage labour (323.20±14.94 versus 325.44±10.91) (p value=0.54) and 2nd stage of labour (12.60±3.87 versus 14.76±6.16) (p value=0.14) of the two groups, t-test was statistically insignificant. P.D.W. Fettes et al in their study of intermittent vs continuous administration of epidural ropivacaine with fentanyl for analgesia during labour found no significant prolongation of duration of labour. [99.2 (66.2) versus 102.8 (62.6)] (p=0.87).[27] In present study comparison of APGAR score at different time intervals in both the groups did not show any statistical difference. Saroj et al in a low dose epidural analgesia during labour: comparison between patient controlled epidural analgesia with basal continuous infusion and intermittent bolus technique showed no significant difference in APGAR score (8.37±1.03 versus 8.43±0.93) (p-value=0.814).[28]

CONCLUSION

In present study, low dose epidural analgesia showed significant difference in early onset of analgesia in group 2 (levobupivacaine with clonidine), but did not show any significant difference in duration of labour, maternal and fetal outcome and mode of delivery. Further randomized controlled trials with large sample size and study duration are needed to clarify the efficacy of the agents.

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