ORIGINAL RESEARCH PAPER

Volume-9 | Issue-5 | May-2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF FETO-MATERNAL OUTCOME IN PAINLESS LABOR BY USING CLONIDINE, DEXMEDETOMIDINE AND FENTANYL AS ADJUVANT WITH ROPIVACINE.AN RCT

Anaesthesiology

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ABSTRACT

Context: Apprehension, anxiety and fear about the labor pains have always existed. Epidural analgesia provides effective pain relief and attenuates the adverse physiological response to pain. PCEA pump allows continuous administration of drug into the epidural space also covers differences in anesthetic requirement as patient can match dose of analgesia to amount of pain as labor progresses.

Aims: Aim of our study is to evaluate and compare the analgesic effect of dexmedetomidine, clonidine and fentanyl. This study is also meant to assess the success rate of vaginal delivery and maternal satisfaction.

Settings and Design: randomized controlled study conducted in 60 parturient at Department of Anaesthesiology (with co operation of Department of Obstetrics & Gynaecology), Sir Sunderlal Hospital, and Banaras Hindu University. It is a randomized control trial

Methods and Material: 60 ASA physical status I&II parturients were divided into three groups with 20 patients in each group. Group A was given PCEA of Ropivacaine 0.1% with dexmedetomidine2mcg/ml. Group B was given PCEA solution of Ropivacaine 0.1% with Fentanyl 2mcg/ml Group C was given PCEA solution Ropivacaine0.1%with Clonidine1.5mcg/ml. Outcomes for motor blockade was noted, time to onset of analgesia, time to onset of maximum analgesia, duration of analgesia, maternal complication, fetal outcome in terms of APGAR score, mode of delivery and fetal complications were noted.

Statistical analysis used: Statistical analysis of data was s performed by u sing SPSS 16.0 statistic s software. Parameters including total duration of labor, total study drug requirement, pulse rate, oxygen saturation and blood pressure measurements were compared by one way analysis of variance test with Post hoc intergroup comparisons using Bonferonni's correction. Nominal data including mode of delivery need of demand boluses and side effects were compared by Fisher's exact test/ chi square test whichever appropriate. The critical value of 'p' indicating the probability of significant difference was taken as <0.05 for comparisons.

Results: motor blockade at 6 hours was 3.44± 0.15 in Group A, 3.90± 0.12 in Group B and 3.90 ± 0.41 in Group C which was not significant. Onset of analgesia was fastest in Group B at 20 min which was 4.50±1.100, in Group A it was 5.35±1.089 and in Group c it was 6.05±1.356 which was highly significant with p-value 0.001. Mean no of demand bolous was least in Group B which was 2.35±0.58 which is significant, whereas in Group A it was 3.40±0.94 and in Group C it was 5.45±1.05. Mean of total infusion volume required, duration of labour, APGAR score and maternal satisfication score and incidences of side effects in all three group were similar and not significant.

Conclusions: most of the parturient (93.33%) showed satisfactory response to patient controlled epidural analgesia PCEA and also wanted to receive same in future pregnancy. P CEA does not increase the incidence of forceps delivery or caesarean section or worsens the neonatal outcome. All the 3 adjuvants used in study (fentanyl, Clonidine and dexmetomedine) have the qualities of being the future in labour analgesia

KEYWORDS

Clonidine, Dexmedetomidine, Epidural Analgesia, Fentanyl, Labor Pain, Pcea

INTRODUCTION

Apprehension, anxiety and fear about the labor pains have always existed. This perception of labor pain is gradually changing with the introduction of labor analgesia for painless labor. In some cases, the labor may be short i.e. 4 to 8 hours, but in other cases it may go on up to 24 hours, especially in first pregnancy. Labor analgesia has been appreciated and acknowledged by all those patients who have opted for this procedure. In United States more then 70 to 80 % expectant mothers opt for this procedure, in India also with increased level of information & awareness more and more would be mothers have started to realize the beauty of this procedure. Experience of childbirth should be joyful and delightful. Therefore maternal request is sufficient justification for pain relief during labor.

An array of regional nerve blocks, systemic analgesic, and nonpharmacologic techniques are currently used for labor analgesia. Neuraxial labor analgesia (most commonly epidural or combined spinal epidural) is the most effective method of pain relief during childbirth, and the only method that provides complete analgesia without maternal or fetal sedation.

Epidural analgesia provides effective pain relief and attenuates the adverse physiological response to pain. In addition, effective epidural analgesia reduces maternal catecholamine levels, increasing intervillous blood flow and results in improved uteroplacental blood flow. Reduced stress or anxiety of the mother, more focus on pushing the baby, decreased exhaustion, and good for hypertensive patients as stress doesn't add to increase in blood pressure and early mother child bonding are some of the advantages of painless labor.

"Superficially, obstetric anesthesia appears to be a simple field with a limited range of interest, but is a deceptively demanding subspecialty. Not only are two patients involved in each anesthetic administration, but also the dynamic events of normal labor require that the muscles concerned with delivery retain their power and coordination to the full".

-Philip Bromage

Recent advances in the field of anesthesia has made epidural analgesia more effective with minimal side effects researches are still going on to create new dimension to this method. Introduction of PCEA pump is one of them, it does not only allows continuous administration of drug into the epidural space but also covers differences in anesthetic requirement as patient can match dose of analgesia to amount of pain as labor progresses. Also it reduces the need of clinical top-ups, which in total decreases the amount of drug given, and thus decreases the possibility of motor block. However this may be costly and the woman should be willing enough to use it. In this study ropivacaine along with fentanyl, clonidine and Dexmedetomidine is used to give labor analgesia through epidural catheter using a PCEA pump. Aim of our study is to evaluate and compare the analgesic effect of dexmedetomidine, clonidine and fentanyl. This study is also meant to assess the success rate of vaginal delivery and maternal satisfication.

SUBJECTS AND METHODS

This was a prospective, double blind, randomized study which was conducted at the Department of Anaesthesiology (with co-operation of Department of Obstetrics & Gynaecology), Sir Sunderlal Hospital, Banaras Hindu University, Varanasi. After getting institutional ethical approval and written informed consent. 60 ASA physical status I&II, multiparous parturient at term, with spontaneous onset, in active phase of labor(> 3 cm cervical dilation), with vertex presentation, requesting epidural analgesia, enrolled were enrolled in the study. Patient having cardiac disease, fetal distress, cephalopelvic disproportion, morbid obesity, spinal deformities and bleeding disorder were excluded from the study.

The procedure was explained to the parturients and an informed written consent was obtained from the patient and her attendant. Patients were positioned in left lateral decubitous / sitting position according to the suitability for the block and the part was cleaned with spirit and betadine lotion and draped.

The epidural catheter was placed before the active phase of labor because the patients were more comfortable and easily positioned or in active labour when cervical dilatation ≥3cm. Drugs were given only after the labour was well established. The patient's bladder and bowel was evacuated before they were shifted to operation theatre. All were prehydrated with 500 ml of glucose free lactated ringer's solution over 10-15 minutes through a 16 G IV cannula.

The L3-4 interspinous space was chosen for catheter insertion, xylocaine 2% was infiltrated locally to render the procedure painless. Then 18G Tuohy needle was passed through the L3-4 interspace into the epidural space by using loss of resistance technique. A multiport epidural catheter was advanced 5cm into the epidural space with the needle bevel facing in the cephalic direction. The epidural catheter was secured by gauge piece and adhesive tape and its length taped over the back with its end kept over right shoulder and capped with the bacterial filter provided followed by a 3 ml test dose of 2% lignocaine with adrenaline (1:200,000), to rule out intravascular or Intrathecal catheter position after which patients were shifted back to the labour room.

The participants were allocated randomly into one of the following groups according to the drugs used in PCEA pump for continuous infusion:

Group A = PCEA solution of Ropivacaine 0.1% with dexmed etomidine 2mcg/ml.
Group B = PCEA solution of Ropivacaine 0.1% with Fentanyl 2mcg/ml.
Group C = PCEA solution of Ropivacaine 0.1% with Clonidine 1.5mcg/ml.

When labor was well established and was progressing well i.e regular contractions 3-4 minutes apart and lasting about, 1 minute, cervical dilatation 3-4 for multiparous patients and Fetal head was well engaged 10ml bolus of 0.2% ropivacaine alone was given in incremental fashion to all parturient and then connected with their respective PCEA solution. PCEA pump settings were continuous basal infusion @ 6ml/hr and 1.5ml of demand bolus with a 15 min lock out interval (total 6ml/hr).

In 2nd stage (at full cervical dilatation) 10ml bolus of the respective solution is given in sitting position (perineal dose) which helped in episiotomies or any other operative delivery and PCEA was continued up to the completion of delivery. Uterine displacement was maintained continuously and each patient was encouraged to turn from side to side or even move around if required during labour. An anesthesiologist who was unaware of the dose or drug given performed all assessments and data recording. All the patients were monitored continously for painreleive, sedation, progress of labour, hemodynamics, respiratory rate ,spo2 and drug side effects the at 0, 10, 20, 30 min after giving 1st epidural bolus dose and then at 30 min interval for ongoing labor as follows. Pain was assessed by visual analogue scale (VAS), motor blocade was assessed by modified Bromage score and sedation was assessed by Ramsay sedation score.

Outcomes for motor blockade were defined as follows:

Effective: Bromage score < 4 at 30 min of injection on either leg.

Ineffective: Bromage score unchanged or 4 within 30 minutes of injection of both legs.

Progress of Labour:
Duration of 1st stage of labor
Duration of first stage of labor – defined as the interval between cervical dilation of 4 cm to 10 cm.

Duration of 2nd stage of labor
Duration of second stage of labor – defined as interval between diagnosis of full (10 cm) cervical dilation and delivery.

MODE OF DELIVERY
The mode of spontaneously vaginal delivery with or without episiotomy, forceps assisted or caesarean section was all noted.

Fetal APGAR score
Fetal APGAR score at 1 minute and 5 minutes were recorded and analyzed.

Monitoring of Patient post Delivery
Patients were monitored up to 2 hrs after any problem suffered by the mother or her baby was recorded and appropriate measures were taken. Patient were monitored for vital parameters, ability of the mother to pass urine on her own, any motor loss, period during which mothers were free of low abdominal pain following epidural blockade, any cardiovascular or CNS side effects like double vision, numbness of tongue and lips, dizziness, articular difficulties, pressure over chest, muscular fasciculation were noted and if occurred the administration of local anesthetic was suspended.

Overall satisfaction of the patient
Next day of delivery, following question were asked:
- How did she feel about the conduction of her labor?
- How much pain was she expecting and how much did she have?
- Was she satisfied with the whole procedure?
- In multipara – how do they compare this delivery with previous ones?
- Would she like to have this method of pain relief for any future pregnancy?
- Would she recommend it to others?

RESULTS

Table 1: Patient characteristics

	GroupA (n=20)	GroupB (n=20)	GroupC (n=20)	p-value
Meanage (inyears)±SD	23.70±2.20	23.45±3.19	22.96±3.72	
Meanweight(inkgs)±SD	51.80±2.85	52.40±2.85	52.11±3.36	
Gravida 2	14(70%)	13(65%)	12(60%)	
Garvida 3	6(30%)	7(35%)	8(40%)	
Mean cervical dilation (in cm) At beginning of study	4.1500±0.73 (3-5.50)	4.075±0.84 (3-5.50)	3.95±0.81 (3-5.50)	
BaselineVASscore	>7	>7	>7	

Table 2: Visual Analogue Scale (VAS) at regular intervals

VAS	Group A	Group B	Group C	f-value	p-value
Pre-epidural	7.15±1.387	7.75±1.585	7.60±1.046	1.058	0.354
10m	6.20±1.056	6.05±1.356	6.80±0.951	2.448	0.096
20m	5.35±1.089	4.50±1.100	6.05±1.356	8.532	0.001
30m	3.50±0.889	2.85±0.813	3.45±1.356	2.386	0.101
1hr	2.40±0.754	2.65±0.745	2.85±0.988	1.452	0.243
1.30hr	2.25±0.639	2.70±0.801	2.30±1.031	1.727	0.187
2hr	2.30±0.571	2.10±0.553	2.05±0.759	0.869	0.425
3hr	2.15±0.489	2.10±0.553	2.50±0.946	1.980	0.147
3.30hr	2.25±0.639	2.30±0.811	2.40±0.132	0.358	0.700
4hr	2.10±0.551	2.20±0.543	2.05±0.752	0.302	0.740
4.30hr	2.25±0.469	2.20±0.593	2.20±0.949	0.034	0.965
5hr	2.50±0.888	2.15±0.823	2.45±0.352	1.370	0.262
5.30hr	2.35±0.089	2.40±0.100	2.25±0.356	2.519	0.089
6hr	2.15±0.389	2.25±0.587	2.20±0.045	0.310	0.734

There is significant reduction in VAS score after 20min of putting patient on PCEA (P<0.05).when compared VAS score was significantly reduced in group B as compared to group C. This shows a better analgesia attained by fentanyl as compared to clonidine but the overall analgesia in three groups was satisfactory as each of them shows a significant reduction in VAS score

Table 3: Drug requirement, motor blockade, mode of delivery, duration of labour APGAR score and mean maternal satisfaction

	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value
Mean no o f demand bolous ± SD	3.40±0.94	2.35±0.58	5.45±1.05	S
Mean of total infusion volume required (in ml)± SD	48.45±9.934	44.70± 8.504	42.00±7.691	NS

Motor blockade				
at 0 min	4.0±0.0	4.0±0.0	4.0±0.0	NS
at 6 hour	3.44± 0.15	3.90± 0.12	3.90 ± 0.41	NS
Duration of labour (in hours)				
Total duration first stage	5.25±1.106	4.95± 1.234	5.70±1.720	NS
Total duration in second stage	50.50±9.445	49.50± 14.681	42.50±12.085	NS
APGAR score				
at 1 min	8.0 ± 0.65	8.05 ± 0.51	8.05 ± 0.69	NS
at 5 min	9.0±0.45	9.05 ± 0.51	9.05 ± 0.51	NS
Satisfaction score	86.25±6.664	88.00± 7.504	87.25±7.860	NS

The number of demand boluses required in group C was comparatively more (mean 5.45±1.05) as compared to the mean number of demand boluses in other two groups. The difference in the three groups is statistically significant with lowest demand boluses required in group B as compared to group A and C.

The motor-blocking potency was slightly higher in group A as compared to other two groups. However, on comparison among different groups there is no significant difference.

Total duration of labour was comparable in all the three groups. This shows that none of these drugs significantly prolong the duration of labour.

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. Subsequently after delivery none of the babies had any problem in the ward and till discharge.

The mean maternal satisfaction above 85% in each group, and on comparison the difference was found insignificant among the different group.

Table 4: Mode of delivery in difference groups

Mode of delivery	Group A (n=20)	Group B (n=20)	Group C (n=20)	p-value
SVD	17(85%)	19(95%)	17(85%)	NS
Forceps assisted delivery	1(5%)	0	1(5%)	NS
Caesarean	2(10%)	1(5%)	2(10%)	NS

Table 5: Side effects among the groups

Side effect vs group	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
0 no side effect	14	70	15	75	13	65
1 nausea	0	0	1	5	0	0
2 vomiting	3	15	0	0	1	5
3 pruritus	0	0	4	20	0	0
4 hypotension	1	5	0	0	4	20
5 shivering	0	0	0	0	2	10
Total	20	100	20	100	20	100

p = 0.008,There are group specific side effects seen in the different study groups like incidence of pruritus and nausea was more in fentanyl group whereas hypotension and shivering was seen mostly in clonidine group, and vomiting was the complain of some patients in dexmedetomidine group so in these terms the p value is significant but if we see the percentage of these side effects none of these occurred in more than 20% patients of that group which is very less to label a drug toxic or inappropriate to be used as an analgesic

DISCUSSION:

Epidural analgesia is the most common method applied for combating pain during delivery. Patient remains conscious and aware of the activities going on, but without feeling pain. Epidural analgesia also makes it easy for any instrumental delivery and ceaserian section if required. Lot of work have been done on ropivaine, fentanyl and clonidine. In this study we added dexmedetomidine to establish, its role as adjuvant in epidural analgesia in pain less labour and to compare its effect with fentanyl and clonidine. Ropivacaine causes less motor weakness by the epidural route while still providing effective analgesia.

The study groups were full term mutigravida without significant difference in terms of age, height, weight, initial cervical dilatation, blood pressure pre epidural, heart rate, spO2, VAS, MBS, and RSS.

As reported by Guffud et al [1] significantly fewer women experienced pain during the procedure or required supplemental analgesia who received epidurally administered 0.5% bupivacaine plus fentanyl 100 mcg compared with women who received bupivacaine alone. Similarl findings were presented by Preston et al [2] who used epidural fentanyl 1 µg/kg plus lignocaine than lignocaine alone.

Preliminary data from a study done in 60 patients indicate that75µg of clonidine with bupivacaine 0.125% is an optimal combination for enhanced quality of epidural analgesia during labour. Another dose ranging study in 45 patients indicated that epidural clonidine given initially as a bolus dose (25µg in 100ml saline) followed by continuous infusion (19 µg/h) provided effective adjunctive analgesia to bupivacaine 0.125%. [3]

VAS is relatively easy to use, minimally intrusive, conceptually simple and its rational scale properties allow meaningful interpretation of percentage difference in VAS measurements. [4] In the parturient, Plummer and Brownridge [5] found that the patients who reported satisfactory pain relief had a median VAS score of 2 (interquartile range, 2 4). In clinical practice, a VAS ≤ 1 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 VAS exceeds 3. [6,5]

Significant reduction is seen in VAS score after 20min of putting patient on PCEA (P<0.05). When compared VAS score was significantly reduced in fentanyl group as compared to clonidine group. A comparison among the other group (dexmedetomidine) was not significant. This shows a better analgesia attained by fentanyl as compared to clonodine but the overall analgesia in three groups was satisfactory as each of them shows a significant reduction in VAS score. Celleno D et al, Topcu I et al [7] had similar observation that combination of fentanyl or clonidine with local anaesthetics produces similar and prolonged analgesia as compared to local anaesthetics alone. Pain relief as assessed subjectively by the patients was nearly equal for all the groups. None of the parturient complained poor or no analgesia in any of the group as seen by the mean VAS score after 20mins was significantly reduced (p=0.001) showing the effect of the epidural infusion. The mean VAS score after 30 min was in range 2 3, 3-3.5, 3-3.5 respectively among the fentanyl, clonidine and dexmedetomidine groups which further reduced after 1hr of the course of labour.

Motor block was assessed by the Modified Bromage score. There was no significant decrease and none of the patients in any group observed significant motor block. The motor blocking potency was slightly higher in dexmedetomidine group as compared to other two groups. However, comparison among different groups did not reveal significant difference in the three groups. After 2 hrs interval dexmedetomidine group had 4 patients who had Bromage score of 3 as compared to 2 patients in fentanyl group and 2 patients in clonidine group, but this score was not associated with significant motor block as the patient were able to ambulate easily with some assistance. None of them complained inability to stand or walk. In this study we did not observe significant difference in the course of labour and fetal outcome in the groups.

Sedation as assessed by the Ramsay sedation score showed more sedation in dexmedetomidine group compared to clonidine and fentanyl. However, all the parturients were arousable on verbal command. Our study results are contrary to Previous studies [8,9] which supported that sedation is more with clonidine. The difference in result might be because in previous studies clonidine was used as a bolus dose while we are using in a continuous low doses infusion. It was also reported that combination of fentanyl with ropivaicane causes more sedation than fentanyl or clonidine with bupivacaine. [10,11]

In this study, 55 parturients (91.66%) had a spontaneous vaginal delivery, out of which 2 (3.3%) needed instrumental assistance (forcep or ventouse assistance) while five patients (8.33%) needed caesarean section. The reasons were not related to the technique used. Caesarean sections were due to fetal distress (tight loops of cord round the neck per operative finding), previous caesarean section scar tenderness, and

cephalopelvic disproportion (due to big size baby). There was no significant difference in mode of delivery (either SVD or caesarean) in between the groups. Our results were in support of studies done by Evan et al [12] who reported a caesarean section rate of 10% with epidural infusion of bupivacaine while they are in contrast to some early workers[13,14]who reported decreased incidence of spontaneous vaginal deliveries and a twenty fold increase in the incidence of forceps deliveries. The study of *Hault et al* [15] further confirmed these findings and quoted an instrumental delivery rate of about 70% and 40% in epidural and non epidural groups respectively. This high incidence seems odd considering that we had 3.3% incidence among all our patients who received PCEA. Our results showed that the low incidence of difficult deliveries needing any forceps assistance could be attributed to insistence on early induction (all patients had been induced at cervical dilatation < 5 cm) of epidural analgesia. Our observations were also supported by the finding of Fraser et al [16] who observed an increase risks of difficult deliveries with late induction of epidural analgesia in labor (≥ 6 cm) than induction between 3 to 5 cm. Fraser *et al* [16] 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.

There was no statistically significant difference (p>0.05) in the duration of active phase of first stage of labour in this study. It is supported by Paech MI et al, [17] Lyons G et al. [18] Duration of second stage of labour was almost similar in all the groups in our study. Mean duration of second stage of labour was confined between 40 50 min. It has been postulated that an increase in duration of second stage of labour more than 1 hr may lead to fetal acidosis because spells of hyper and hypoapnea in the mother during this phase. When we give analgesia to labouring patients this cycle reduces and thus prevents fetal acidosis and a better APGAR score. We maintained a good posture of the patient which prevents aortocaval compression and fetal acidosis. In previous studies Philips [19] & Crawford et al [13], Hault *et al* [20], Jouppila *et al* [21] and Pearson and Davies [22] reported increased number of instrumental deliveries and prolongation of second stage of labour by epidural analgesia in contradiction to our observation. This may be because in our study we used low concentration of drugs in a continuous infusion at a slow rate which helped preventing these side effects.

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