**RESEARCH**
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# EFFICACY OF ROPIVACAINE WITH AND WITHOUT FENTANYL USING DURAL PUNCTURE EPIDURAL TECHNIQUE FOR LABOUR ANALGESIA–A RANDOMIZED DOUBLE BLINDED CLINICAL TRIAL

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RUNNING TITLE: Ropivacaine with & without fentanyl by dural puncture epidural for labor analgesia.
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**Abstract**
**Introduction:**
Neuraxial technique is considered the gold standard for labour analgesia. Ropivacaine has shown to produce less motor blockade than the bupivacaine. Addition of fentanyl to ropivacaine for epidural analgesia improve the efficacy and quality of analgesia. The present study was done to compare the effectiveness of intermittent boluses of 0.1% Ropivacaine (R)and 0.1% Ropivacaine with fentanyl (RF) by dural puncture epidural labour analgesia on quality of analgesia.
**Methodology:**
By continuous sampling enrolled 100 primigravida with singleton uncomplicated pregnancies who desired labour analgesia. CSE kit was used and dural puncture was performed after identification of epidural space, and needle was removed without administration of any drug. Group R received 0.1% ropivacaine 12ml while Group RF received the same drug as group R with 2mcg/ml fentanyl through epidural catheter as intermittent bolus. Onset, quality and duration of analgesia were the outcome measure. Mode of delivery, APGAR score, hemodynamic and any complications were noted.
**Results:**
Quality of analgesia was comparable between two groups with 62% and 52% in R and RF respectively did not perceive any pain during uterine contraction (p- 0.59). Mean onset of analgesia in Group R and RF was 3.02 ± 0.68 min and 3.03 ± 0.85 min (p- 0.06) respectively. Duration of analgesia in Group R was 108.59 ± 63.70 min and in Group RF was 155.51 ± 118.1mins. 12% in group R and 22% in Group RF underwent caesarean section. Maternal and fetal HR and maternal DBP was high in R compared to RF group. APGAR was 8 at 1 min and 9 at 5 min in both the groups. None of the parturient had PDPH.
**Conclusion:**
0.1% Ropivacaine is found to be comparable and effective as ropivacaine with fentanyl in terms of onset and quality of analgesia, maternal and foetal outcome by dural puncture epidural technique.
Keywords: Dural puncture epidural, Ropivacaine, Fentanyl, labour analgesia.

## INTRODUCTION:

Dural puncture epidural technique (DPE) is a modification of the combined spinal epidural in which the dura is perforated using spinal needle but there will be no administration of intrathecal medication. DPE for labour analgesia has produced rapid onset, improved and consistent block quality, with an

additional advantage of early identification of epidural failure. Studies had compared plain ropivacaine through epidural route and found to be comparable in producing analgesia.[1,2] However epidural opioid improves the quality of analgesia and reduce the number of failed epidurals due to patchy blocks.[3] Kai Wang in his meta-analysis on the effects of epidural/spinal opioids in labour analgesia on neonatal outcomes showed that the commonly administered doses of fentanyl and sufentanil for labour analgesia are safe up to 24 hr after delivery.[4] However C Mardirosoff, in his systematic review concluded that intrathecal opioids for labour increase the risk of foetal bradycardia and maternal pruritus.[5] We assessed the quality of analgesia during uterine contraction with intermittent boluses of 0.1% Ropivacaine and compared with 0.1% Ropivacaine with fentanyl by DPE technique for labour analgesia.

**METHODOLOGY:**

This prospective randomized double-blind study was conducted in Mahatma Gandhi Medical College and Research Institute, Pondicherry, India after obtaining the approval of Institutional ethical committee between September 2019 and May 2020. Parturient who were admitted in the Obstetrics and Gynaecology department for safe confinement formed the study population. Primigravida with uncomplicated singleton pregnancy, admitted with vertex presentation belonging to American Society of Anaesthesiologist Physical Status (ASA PS) I and II were included for the study.

Parturient who refused to participate, hyper sensitivity to study drug, decreased platelet count, local or systemic sepsis, bleeding disorder, CPD, foetal anomaly, spine abnormalities were excluded. 156 parturients who were admitted in the hospital between December 2018 and March 2020 were recruited by continuous sampling. Detail education about epidural labour analgesia and explanation about the study protocol was given to the parturient and her relatives, after which they were subjected to complete pre anaesthetic evaluation. 100 parturient who satisfied our inclusion and exclusion criteria and willing to participate were enrolled in our study. They were explained about pain assessment scale and quality of analgesia and written informed consent was obtained from all the participants.

Pain was assessed by using visual analogue scale (VAS) of 10cm line from 0-10. Quality of analgesia was assessed using 4 scale grading (0- parturient neither perceive pain nor uterine contraction, 1-parturient perceived uterine contraction without pain, 2- parturient perceive uterine contraction with mild discomfort and 4- parturient perceive uterine contraction as very distressing pain)

**RANDOMIZATION & BLINDING**

All cases were randomly assigned to one of the two groups and blinding was done with sealed envelope technique. Group R received 12ml of 0.1% ropivacaine, Group RF received 12ml of 0.1%ropivacaine with fentanyl 2mcg/ml. The study solutions were prepared aseptically by anaesthetist who was not directly involved in this study.

**PROCEDURE**

When the parturient was in active labour they were shifted to operation table, connected the monitors namely ECG, NIBP and pulse oximetry and Ringer lactate on flow was assured. Under aseptic precautions in either L2-L3 or L3-L4, epidural space was identified using loss of resistance (LOR) technique using CSE kit (Smiths) and spinal needle was inserted through the epidural needle. Once Cerebrospinal fluid flow was confirmed, no drug was given through it and the needle was withdrawn. Epidural catheter was threaded keeping 5 cm catheter in epidural space. Epidural test dose with 3ml of 1.5%lignocaine with 15mcg adrenaline was given.

**EPIDURAL ACTIVATION & ASSESSMENT**

The study drug was given through epidural catheter immediately after shifting from labour room in supine position during contraction free period over 2-3mins.The time of the injection of the initial dose was noted and assessments was scheduled

**RESCUE MEASURES**

At any point of time during the study period hypotension was (defined as systolic blood pressure of <90mmHg) was treated with a bolus dose of 6mg intravenous mephenteramine. Bradycardia was defined as a heart rate of < 60 bpm) was treated with a bolus dose of 0.6mg intravenous atropine sulphate. Fetal bradycardia was defined as a heart rate of <110 bpm for more than or equal to 10 min. The study ended when baby delivery occurred or when caesarean section was required. Throughout the period (from the time of labour analgesia activation till baby delivery except when the patient was ambulating) the patient was under continuous monitoring of heart rate, spo2, fetal cardiotocography and NIBP at 10 mins interval. For those patients who required caesarean section epidural anaesthesia was considered with 12-15ml of 2% lignocaine with adrenaline. Neonatal assessment was done with APGAR score at 1 and 5 min. Finally, two hours after delivery maternal satisfaction for labour analgesia was obtained and was graded as (3- excellent pain relief, 2- good pain relief, 1- fair pain relief and 0- poor pain relief).

**SIDE EFFECTS**

Side-effects like pruritus, nausea and sedation, was also assessed in 30min interval throughout the study based on a scale ranging from 0 = none, 1 = mild, 2 =moderate, and 3 = severe. The presence of a post-dural puncture headache (PDPH) was noted at a post procedure visit between 36 and 48 h after delivery

**SAMPLE SIZE AND STATISTICAL ANALYSIS:**

Sample size was calculated based on study by Rani et al[12] which showed 97% effective analgesia with 0.1%ropivacaine and fentanyl given through epidural, and literature proves that dural puncture epidural is superior to epidural technique. We did a pilot study with 0.1% Ropivacaine with fentanyl by dural puncture epidural technique for 10 patients and found to provide excellent quality of analgesia in 99% of patients. We expect 85% effective analgesia with 0.1%ropivacaine without fentanyl by dural puncture epidural technique. To compare the two groups with a power of 0.9 and to detect a difference at a significance level of less than 0.05, sample size required was 45 in each group. We took a sample size of 50 in each group to allow for withdrawals from study during labour.

The collected data was checked for completeness before entering into the Microsoft excel spread sheet. The validation of the data was checked at regular intervals. Data analysis was performed using Statistical Package for Social Sciences (SPSS IBM) 21. The quantitative data was expressed in Percentages. Mann Whitney U test was be applied to compare the scores and p value less than 0.05 was considered significant.

**CONSORT 2010 Flow Diagram**

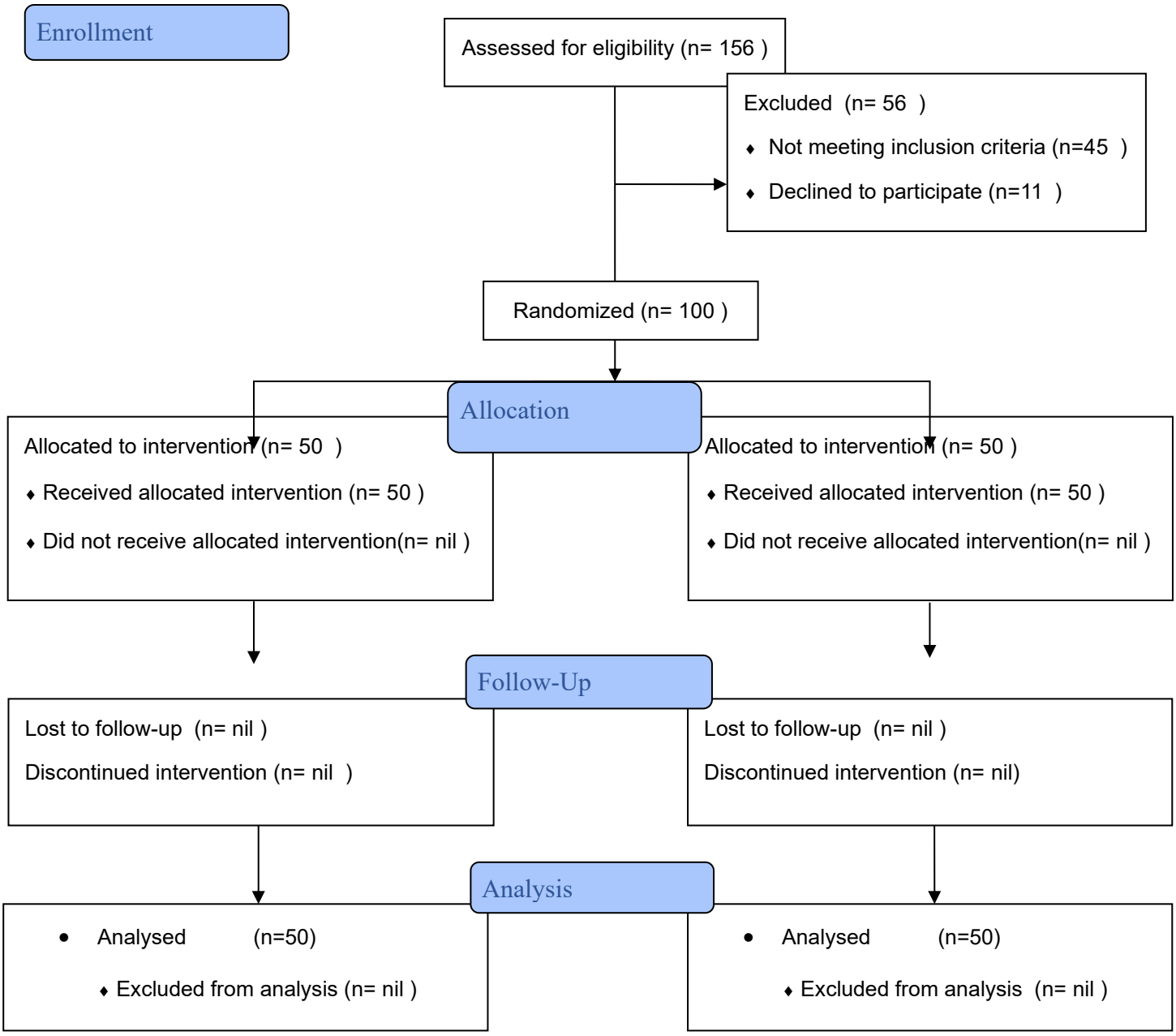


**Figure 1** - CONSORT diagram

**RESULTS**

156 Parturients were enrolled in the study. 37 parturients did not meet the inclusion criteria, 11were not willing for labour analgesia 8 parturient who gave consent for the study were taken for emergency caesarean section in view of fetal heart rate declaration before the DPE technique.100 parturient who were enrolled were analysed and there were no drop outs.

**Consort diagram:**

**Profile of the study participants:**

Table 1: Demographic profile of the parturients.

| Variables | Group R | Group RF | P value |
|---|---|---|---|
| Age (yrs) | 26.14 ± 3.29 | 25.66 ± 3.50 | 0.25 |
| Weight (kg) | 71.08 ± 7.0 | 69.70 ± 8.55 | 0.45 |
| Height (cms) | 164.1 ± 4.6 | 158.94 ± 7.11 | 0.00 |
| Gestational age (weeks) | 38.03 ± .33 | 38.49 ± 1.21 | 0.09 |

The mean age, height, weight and gestational weeks of the study participants are given in the table.1.

**Maternal outcome:**

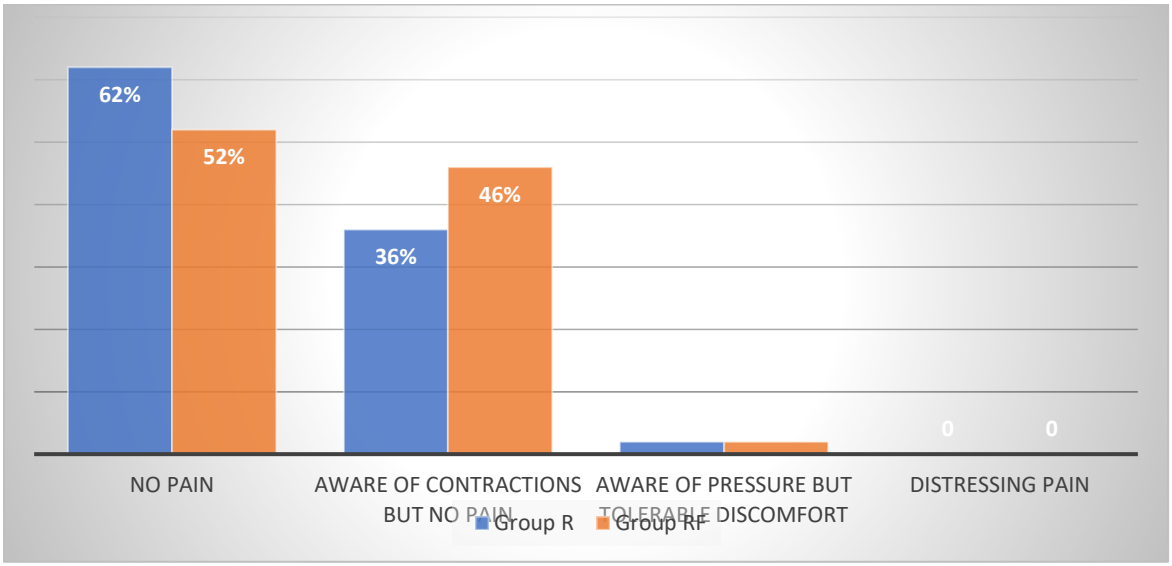


Fig 2: Quality of analgesia among both the groups.

The quality of analgesia was comparable between the groups (p = 0.592). None of the parturient had suffered distressing pain in both the groups.

Table 2: comparison of maternal & fetal outcomes between the two groups.

| | Group R | Group RF | P value |
|---|---|---|---|
| Onset of analgesia (mins) | 3.02 ± 0.68 | 3.03 ± 0.85 | 0.732 |
| Duration of analgesia (mins) | 108.59 ± 63.70 | 155.51 ± 118.1 | 0.067 |
| Duration of labour (mins) | 110.92 ± 65.57 | 152.20 ± 110.01 | 0.073 |
| No. of parturients had SVD | 44/50 | 39/50 | 0.183 |
| No. of parturients had instrumental delivery | 4/44 | 5/39 | - |
| APGAR (1 minute) | 8.12 ± 0.3 | 8 ± 0.2 | 0.054 |
| APGAR (5 minutes) | 9.1 ± 0.3 | 9 ± 0.2 | 0.092 |

Onset and duration of analgesia and duration of labour were comparable. The satisfaction score was comparable between the groups (p = 0.102).

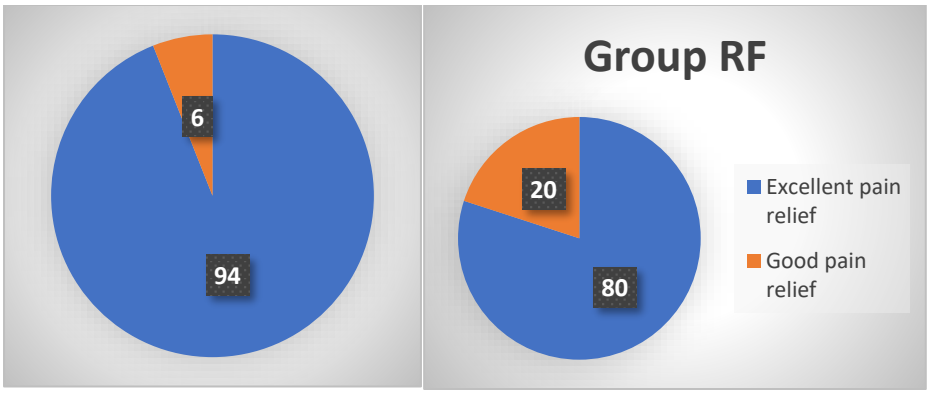


Fig 3: satisfaction score between the two groups.

98% of parturient had no motor blockade (grade 0) and 2 % were not able to do straight leg raise (grade 1) in both the group (p= 0.320). None of our parturient in both the groups had post-dural puncture headache.

**Hemodynamic parameters**

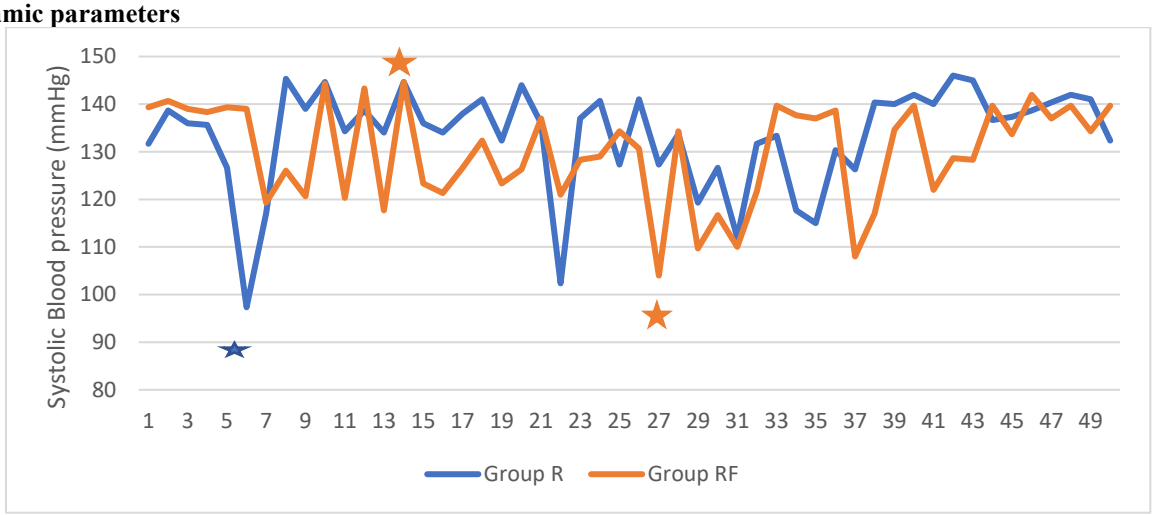


Fig 4: Systolic blood pressure changes among the groups

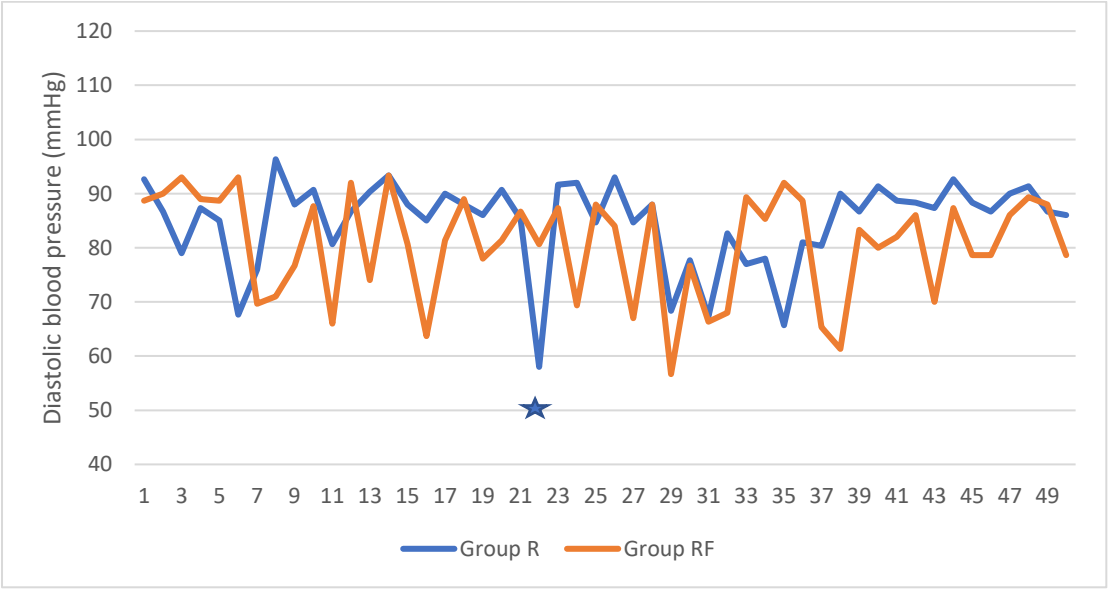


Fig 5: Comparison of Diastolic blood pressure changes among groups (p<0.05)

The maternal heart rate was stable in both the groups. The difference in systolic blood pressure was statistically insignificant. The mean diastolic blood pressure in group RF was lower than the group R and was statistically significant (p value <0.05) at baseline and minimum.

The mean baseline fetal heart rate was 148.12 ± 6.93 per minute and 147.36 ± 5.25 in R and RF group respectively and it was statistically significant. (p value <0.05)

## DISCUSSION

There are differing views regarding superiority of DPE technique over conventional epidural technique for labour analgesia. Bernards et al.[7] proposed intrinsic diffusion capacity of local anaesthetics to be a factor influencing passage of drugs through dural hole. Thomas et al.[8] and Gupta et al.[9] in their study showed that DPE technique did not provide superior labour analgesia when compared with a traditional epidural technique. Cappiello et al.[10] and Chau et al[11] suggested that DPE technique may benefit parturient by improving sacral spread, onset and bilateral nature of epidural labor analgesia as compared to standard epidural analgesia. In our study the parturients who received 0.1% ropivacaine (R) alone had better quality of analgesia compared to RF group. 62% perceived uterine contractions without pain and 36% with minimal discomfort in R group. Only 2% parturient perceived contractions with tolerable discomfort among both the groups and none of the parturient had distressing pain by DPE technique. Ahirwar et al[2] and Wang et al[1] observed comparable pain relief with 0.125% ropivacaine alone through epidural labour analgesia. In our study 52% and 46% of parturients had no pain and minimal discomfort during uterine contractions respectively with 0.1% ropivacaine with fentanyl whereas Yadav et al[13] had observed excellent quality of analgesia with DPE technique using 0.2% ropivacaine with fentanyl.

Many studies favoured the use of intermittent epidural bolus than continuous epidural analgesia and Hussain N et al[14] in his meta-analysis stated that intermittent epidural bolus enhanced maternal satisfaction, shortened labour duration, decreased motor block, and reduced local anaesthetic consumption. In our study we used intermittent bolus local anaesthetic administration whenever parturient complained pain with VAS >3. In our pilot study none of our patients had good pain relief with intermittent bolus of 0.1% ropivacaine by epidural method but Ahirwar et al[2] showed satisfactory result with 0.125% ropivacaine alone which may be attributed to PCEA infusion as maintenance.

25, 26 and 27 G pencil point spinal needles were used in DPE and found to produce good result in terms of faster onset, sacral spread and good quality of analgesia. 27G Whitacre spinal needle was used in our study which comes as component of single CSE kit. Free flow of cerebrospinal fluid (CSF) was confirmed before withdrawal of spinal needle. In our study the onset of analgesia was rapid and effective with good sacral spread and was comparable between both the groups.

Gupta A[9], Capeillo[10], Chau[15], Wilson[16] and Yadav[13] demonstrated faster onset through DPE technique using bupivacaine with fentanyl and in our study ropivacaine alone produced equivalent result. However, the mean duration of analgesia was longer in RF group than the R group. It is known that fentanyl intensifies the analgesic action of local anaesthetics and it was explained by Ahriwar et al[2] showing decreased consumption of ropivacaine in combination of fentanyl compared to ropivacaine alone.

98% of parturient had no motor weakness as assessed by modified Bromage scale similar to Ahirwar et al[2] in terms of comparison between ropivacaine with ropivacaine and fentanyl. Ropivacaine is an alternative to epidural bupivacaine, with greater selectivity for sensory fibres than motor fibres, thus producing less motor blockade as compared to bupivacaine.

In the present study, the maternal and the foetal heart rate was stable in both the groups but there was statistical difference between the groups. R group had high heart rate in both mother and fetus compared to RF group which was like Ahirwar.[2] Similarly diastolic blood pressure of the parturient was higher in R group than RF. This can be explained with the finding of Li HX[17] which showed decreased stress hormone release in ropivacaine and fentanyl group and Zhang et al[18] which demonstrated increased inflammatory markers in ropivacaine group. Studies have proved that fentanyl and sufentanil with commonly used dose are safer and have less negative impact on neonates however it is always a concern for obstetrician regarding the use of opioid during labour.

Few studies have demonstrated higher incidence of pruritis in the mother and hence we want to study the efficacy of ropivacaine without opioid as additive through DPE technique. Although there was a statistical difference in feto-maternal heart rate between the group, it was clinically insignificant by means of mode of delivery and APGAR of the new born. In our study 88% in R group and 78% in RF group had spontaneous vaginal delivery (SVD). Ropivacaine only (R) had a higher percentage of SVD similar to Ahirhar et al.[2] Yadav et al[13] observed better maternal expulsive effort and mode of delivery with intermittent bolus of 0.2% ropivacaine with fentanyl by DPE. The indication of cesarean section was unengaged head, fetal distress in both the group 4(8%) and 5(11%) parturient had instrumental vaginal delivery in group R and RF respectively. The indication of instrumental vaginal delivery was decreased maternal effort.

Brancato et al[19] in his meta-analysis showed that during the second stage of labour, delayed pushing can encourage passive descent of the foetal head and thereby significant positive effects on raised incidence of the spontaneous vaginal deliveries, reducing the instrumental vaginal deliveries and shortened pushing time when compared with early pushing in labouring women with epidural analgesia. Different obstetricians were involved in the management of labour during this study and decision on mode of delivery was subjective.

APGAR score was observed at 1st and 5th minute after delivery. Though mean APGAR score was good and comparable at both the time point, it was better in R group than RF group similar to Wong et al.[12] The mean total duration of labour was 110.92 ± 65.57 and 152.20 ± 110.01minutes in group R and RF respectively which was statistically insignificant. In our study demographic variables were comparable between the groups and epidural analgesia was activated when the parturient was in active labour and Visual Analogue Scale was > 3 irrespective of cervical dilatation. Since we did not correlate cervical dilatation with the activation of labour analgesia, we are unable to comment on it. Maternal satisfaction was measured using a 3-point Likert scale. It showed that 94% and 80% of the study participants had excellent pain relief in Group R and RF respectively. Even though there are innumerable methods of established pain relief epidural is the most popular and efficient methods[20, 21]. We accept that we did a real time study of pain and not a reported pain sometime later.

None of the parturient had side-effects such as pruritis, nausea, vomiting during the study. Parturient were followed for next 48 hours and enquired regarding PDPH and no parturient reported regarding it. In our study we found DPE technique was beneficial with ropivacaine alone compared to ropivacaine with fentanyl to produce comparable results in quality, onset and duration of analgesia, maternal and fetal outcome.

## CONCLUSION

0.1% Ropivacaine alone is found to be effective in terms of onset and quality of analgesia, maternal and foetal outcome by dural puncture epidural technique compared to ropivacaine with fentanyl.

Ethical issues – approval – Yes
No financial aid
No conflict of interest for any author.
CTRI registration – Yes

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