Comparative Study of 0.2% Ropivacaine & 0.2% Ropivacaine with 0.5 mcg/mL Dexmedetomidine in Epidural Labour Analgesia

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ABSTRACT

BACKGROUND
Labour analgesia is the emerging technique in obstetric anaesthesia. There are various ways to provide painless labour to a mother. The best technique is epidural analgesia and providing a mother with good analgesia without a motor block is best done by ropivacaine and analgesia can be prolonged with addition of adjuvants. We wanted to compare efficacy, safety, quality of analgesia, total drug requirement, effect on the course and duration of labour, neonatal outcome, maternal satisfaction and adverse events if any, of ropivacaine 0.2% + 0.5 mcg/mL of dexmedetomidine with that of 0.2% of ropivacaine alone, for epidural labour analgesia.

METHODS
60 patients were divided in to 2 groups of 30 each RS and RD. RD received 8 mL of ropivacaine with 0.5 mcg/mL of dexmedetomidine while RS group received ropivacaine 8 mL with normal saline through an epidural catheter inserted at lumbar level. haemodynamic parameters were assessed along with APGAR score for neonatal status and maternal satisfaction was documented.

RESULTS
Ropivacaine with dexmedetomidine was found to be a superior combination than plain ropivacaine in providing labour analgesia. The mean drug requirement in RD group (27.46 mL) was less than RS group (30.93 mL). Duration of labour is less in RD group (180.93±21.26 min) compared to RS group (199.49±24.63 min). Neonatal outcome and maternal satisfaction were better in RD group than RS group.

CONCLUSIONS
Maternal satisfaction with better analgesia was seen when dexmedetomidine was added to ropivacaine group owing to significant results in VAS scores in both the groups also duration of labour was reduced in RD group.

KEY WORDS
Labour Analgesia, Ropivacaine, Dexmedetomidine

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BACKGROUND

The pain of childbirth is the most painful experience for many women and maternal request is a sufficient indication for providing her pain relief during labour. The McGill pain questionnaire ranks labour pain scale between cancer pain and amputation of a digit. Labour pain is associated with maternal physiological responses, which are not necessarily beneficial to the foetal well-being. Maternal hyperventilation causes an increase in oxygen consumption, plasma catecholamine concentrations, hypertension and tachycardia. In addition, maternal hyperventilation may reduce foetal oxygenation, resulting in abnormal foetal heart rate patterns and an increased operative delivery.[1-4]

Superficially, obstetric anaesthesia appears to be a simple field with a limited range of interest, but it is a deceptively demanding subspecialty. The dynamic events of normal labour require that the muscles concerned with delivery retain their power and coordination to the full. Attempts to alleviate pain during labour have been made by different researcher & scientists that ranged from psychological, pharmacological, physical or combination of these techniques but all with limited success. In mid-nineteenth century labour analgesia was popularized across Europe and America after John snow administered Chloroform to Queen Victoria for birth of her 8th child, Prince Leopold (1853). Several methods have been practiced & developed since then for labour analgesia.[2]

The contemporary goal of providing maternal labour analgesia is the relief of the suffering and the pain of labour and delivery, while minimizing effects on maternal safety, awareness, motor functions, progress of labour and foetal well-being. Regional anaesthetic techniques are especially well suited for achieving this goal. Over the past ten years there have been remarkable changes in the field of obstetric anaesthesia. Not only newer techniques such as combined spinal-epidural, continuous epidural infusions, walking epidurals and patient controlled epidural analgesia (PCEA) are now available, Epidural analgesia for labour was maintained either by intermittent boluses or by continuous infusion of the local anaesthetics. Each technique had its own advantages and disadvantages though the purpose remains the same: a painless labour and a healthy neonate.[3]

Of all labour analgesia techniques, epidural analgesia is the most effective form of analgesia and has become the "gold standard" in obstetric care. Ropivacaine has been used commonly for epidural labor analgesia, because of less motor block and stable haemodynamics.[5] dexmedetomidine, an alpha 2- agonist for alpha 2-adrenergic receptors, possesses properties of analgesia and sedation without any respiratory depression effect and enhances their effects without increasing the incidence of side effects when added to local anesthetic agents. It has a opioid sparing effect and hence included in labour analgesia to reduce the side effects caused by opiod when added to local anaesthetics.[6]

We wanted to compare efficacy, safety, quality of analgesia, total drug requirement, effect on the course and duration of labour, neonatal outcome, maternal satisfaction and adverse events if any, of ropivacaine 0.2% + 0.5 mcg/mL of dexmedetomidine with that of 0.2% of ropivacaine alone, for epidural labour analgesia.

METHODS

This prospective, comparative study was conducted at Acharya Vinoba Bhave Rural Hospital attached to JNMC, Sawangi, Wardha during the period of August 2017 to September 2019 (principle investigator –Dr. Bhakti Patil), this study was approved by ethical approval from Central Ethics Committee on Human Research (ref no: DMIM (DU)/IEC/Jun-2019/8118) JNMC and AVBRH Sawangi Meghe, Wardha written consent was obtained from all parturients in the study.

Sample Size Calculation

$$n = \frac{(Z\alpha + Z\beta)^2 . 2 . (S)^2}{d^2}$$

Zα: Two tailed significance level 5% = 1.96
Zβ: Power of study 90% = 0.94
(Zα + Zβ) 2= (1.96 + 0.94)2= 8.4
S= 16.4 (S= standard deviation of SBP, d = mean difference of SBP)
d = 15.5

$$n = \frac{8.4 \times 2 \times (16.4 \times 16.4)}{(15.5 \times 15.5)} = 18.8$$

The sample size obtained was 19 for each group which was rounded up to 30 for each group. So final sample size estimated was 60. Reference article for sample size calculation is made based on the study conducted by Zhao Y et al[6] Total of 60 parturients of age group 20-35 yrs., Heights in cm: >150 cms, full term singleton vertex presentation, previous normal vaginal delivery, consented for the study, Primigravida and multigravida of physical status ASA grade I&II, foetus having normal heart rate pattern before induction of Epidural, Cervical dilatation of 3-5 cms were included in group and divided in 2 group using computer generated randomization technique. Group RS received 0.2% ropivacaine epidurally as bolus dose of 8 mL followed by intermittent top ups as and when required and Group RD received 0.2% ropivacaine with 0.5 mcg/mL of dexmedetomidine epidurally 8 mL as bolus dose followed by intermittent top ups as and when required.

A complete history of each patient was obtained, and clinical examination was done. Routine investigations along with coagulation profile was obtained and noted. All baseline parameters like Heart Rate, Blood Pressure, ECG, SpO2, Foetal Heart Rate were recorded. Lignocaine sensitivity test was done. Intravenous access was achieved with 18G intravenous cannula. Preloading was done with ringer lactate solution 10 mL/Kg. With Patient in sitting position, her back was cleaned, painted and draped, to achieve and maintain asepsis. A 2mL Lignocaine 2% of solution was injected locally in L3-L4 space into the skin and subcutaneous tissue. An 18G epidural needle was advanced up to interspinous ligament. A 10cc loss of resistance syringe with 2mL of air in it was attached at the hub of the needle after removing the stylet. The needle was then advanced slowly until loss of resistance felt. Epidural space was confirmed with hanging drop technique. An 18G epidural catheter was threaded through the needle and secured in the epidural space with 5 cms of length into the

epidural space. Following this, needle was removed, and catheter strapped firmLy to the back of the patient with an adhesive tape. Distal end of the catheter was covered with a sterile gauge piece and a cover. During this whole procedure care was taken not to advance either the needle or the catheter during contractions as chance of piercing the dura or a blood vessel is maximum during contractions.

After fixing the catheter patient was made to lie down with a wedge placed on her left side to avoid aortocaval compression. After negative aspiration for blood and CSF a test dose of 3 mL of 2% Lignocaine with adrenaline was administered to confirm epidural placement of the catheter. Maternal heart rate every 5 mins in initial half an hour after the drug was administered and thereafter every 30 minutes. Maternal hypotension was considered if fall in blood pressure was 20% or more in comparison to baseline value and it was treated with increased rate of intravenous fluids and if needed injection ephedrine 6 mg bolus. Bradycardia (less than 50 beats/minute).[6] It was treated with atropine given in bolus of 0.6 mg. The intensity of pain was assessed using a 10 cm visual analogue scale. All patients were made familiar with VAS scoring system earlier. The patient was asked to point to the position on the line between 1-10 cm to indicate how much pain they were currently feeling. The far-left end indicates 'NO PAIN' and the far-right end indicates 'WORST PAIN'. 0- no pain, 1-3-mild pain, 4-7 moderate pain, 8- 10 severe pain.

Pain scale was assessed every 5 mins after the drug was given and thereafter every 30 minutes on a scale of 0-10. Sensory level was assessed by absence of sensation to pin prick. foetal heart rate was monitored by obstetrician by using Foetal Doppler. Incidence of motor blockade, hypotension, bradycardia, nausea, vomiting, motor blockade were also looked for and appropriately treated. Neonatal status was assessed by APGAR score at 1 min and 5 mins. using parameters of Heart rate, Respiratory rate, Color of the skin, muscle tone and grimace response to stimulus<7 considered signicant.[7] The assessment of maternal satisfaction was done by asking the parturient about pain relief and acceptance of this technique in view of rural myths and belief.

Statistical Analysis

Statistical analysis was done using descriptive and analytical statistics. The chi square test was used to check differences in proportions. Continuous variables are expressed as mean and standard deviation. The normality of continuous data was analysed by the Shapiro-Wilk test. As the data followed normal distribution, parametric test (t-test) was used to analyse the data. The independent sample t- test was used to check mean difference. The level of significance was kept at p<0.05.

RESULTS

Looking at figure-1, Demographic and obstetric variables were comparable in both the groups and with no statistical significance which was calculated by calculated by independent sample t-test with Levene's test for equality of variances. To assess the neonatal status APGAR score (table 1) at 1 and 5 mins was evaluated. It was found that there was NO statistically significant difference in mean APGAR score at 1 min (p=1.000) and 5 mins (p=0.309).

APGAR	Group RS (n=30)		Group RD (n=30)		P-Value
	Mean	S.D.	Mean	S.D.	
1 min	8.00	0.37	8.00	0.37	1.000, NS
5 mins	8.90	0.30	8.96	0.18	0.309, NS

Table 1. Details of APGAR at Baseline and 5 Mins. of the Study Population

Variable	Group RS (n=30)		Group RD (n=30)		P-Value
	Mean	S.D.	Mean	S.D.	
Stage I	163.96	20.62	159.00	15.27	0.294, NS
Stage II	35.93	8.62	37.23	8.79	0.566, NS
Total	199.40	24.63	180.93	21.26	**0.003, S**

Table 2. Details of Duration of Labor (Mins) among the Study Population

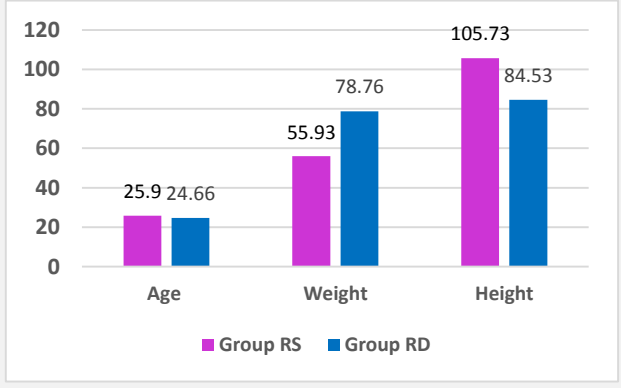

Figure 1. Details of Age (Years), Weight (kg) and Height (cm) of the Study Population

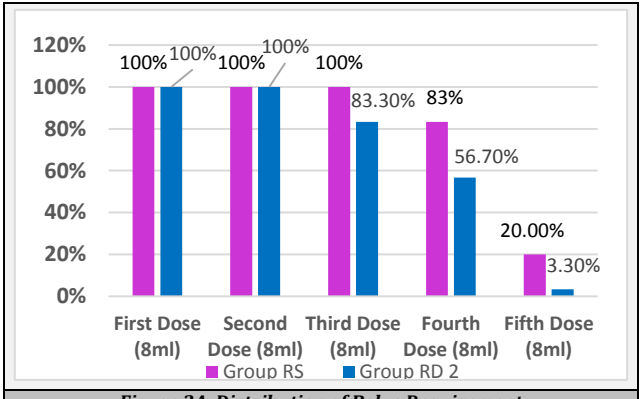

Figure 2A. Distribution of Bolus Requirement among the Study Population

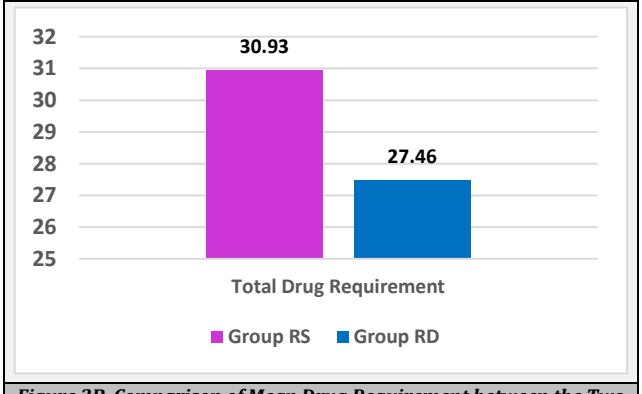

Figure 2B. Comparison of Mean Drug Requirement between the Two Groups

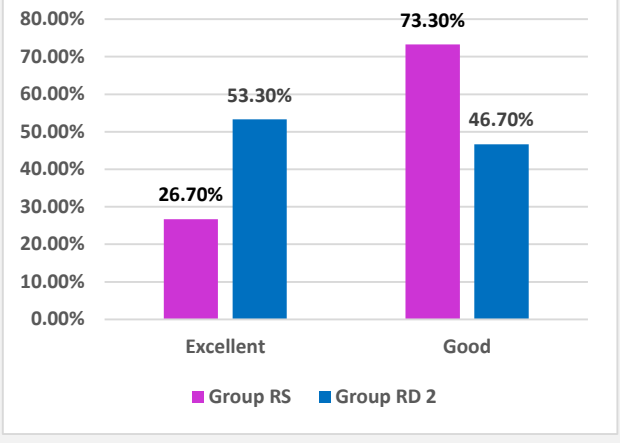

Figure 3. Comparison of Maternal Satisfaction between the Two Groups

The highest sensory level in both groups was observed at T6 (p=0.190). Total drug requirement in both groups was calculated. All the subjects 30 (100%) in both the groups required first and second dose of bolus. While third bolus was required only for 25 (83.3%) subjects of RD groups compared to 30 (100%) of RS group. Fourth bolus was required only for 17 (56.7%) subjects of RD groups compared to 25 (83.3%) of RS group. Fifth bolus was required only for 1 (3.3%) subjects of RD groups compared to 6 (20.0%) of RS group. There was statistically significant difference between the two groups for third (p=0.020), fourth (p=0.024) and fifth bolus (p=0.044). The total drug requirement for RS group (32.27+- 4.91) was significantly higher than the RD group (27.46 +or- 6.53), p value of 0.021 (figure 2A and 2B)

The duration of labor (mins) between the two groups was compared. It was found that the mean labor time for stage I and stage II did NOT show any statistical significance difference between the two groups. The total labor duration of RD group (180.93+-21.26) was significantly lower than the RS group (199.40+-24.63), (p=0.003) (table 2) The haemodynamic parameters i.e. the mean heart rate, systolic blood pressure, mean arterial pressure, SPO2 did not show any statistical significance in both the groups. The mean VAS score between the two groups at various time intervals did NOT show any statistically significant difference for mean VAS score at 5 min (p=0.209), 30 min (p=0.447), 120 min (p=0.140) and 210 min (p=0.579) between the two groups (p>0.05).

The mean VAS score was significantly lower for RD group compared RS group at 10 min (p<0.001), 15 min (p=0.023), 60 min (p=0.015), 90 min (p<0.001), 150 min (p=0.009) and 180 min (p=0.033) (figure 3) The maternal satisfaction was higher in RD group (53.3%) than in RS group (26.7%) (figure 4). There were 1 case of each – hypotension, Bromage I and nausea in both the groups. There was no statistically significant difference in adverse effects between the two groups (p=1.000).

DISCUSSION

Labour analgesia is a challenging journey with gratifying end points. Any drug or intervention of the parturient is automatically experienced by the foetus. Labour analgesia has grown from chloroform to the queen in the 19th century[8] to automated central neuraxial delivery devices of the 21st century.[9] The search for an ideal technique or drug continues as it has to produce effective pain control to the mother without any effect on foetus.

Ropivacaine has been introduced into obstetric anesthetic practice with the proposed advantage of causing less motor blockade. Previous studies proved that dexmedetomidine could extend the duration of local anesthetics when added as a adjuvant for epidural analgesia.[10] In our study, we found that dexmedetomidine could decrease the total drug requirement when combined with ropivacaine for labor analgesia without increasing side effects.

The present study compared the quality of analgesia, total drug requirement, effects on course and duration of labour, neonatal outcome (APGAR Score), adverse events if any and maternal satisfaction while using intermittent epidural bolus doses of 0.2% ropivacaine and 0.2% ropivacaine plus 0.5 mcg/ml dexmedetomidine. S. Fyneface-Ogan et al,[11] studied the role of dexmedetomidine in labour outcome when added as adjuvant with intrathecal bupivacaine in comparison with fentanyl in bupivacaine. There was no significant difference in APGAR score and umbilical venous blood pH in both the groups also foetal heart rates and maternal blood pressure were unchanged after injection of drug in both the groups. Similar trends of foetal heart rate were seen in our study.

Yu et al[12] in their in vivo study evaluated role of dexmedetomidine in cesarean section under general anaesthesia and its effects on foetus, placental transfer and foetal metabolism was noted to provide a reference for the clinical use of dexmedetomidine. The rate of placental transfer of dexmedetomidine was 0.76, as dexmedetomidine is retained in placenta and hence very negligible amount is transferable. In our study most significant findings were less total drug requirement in ropivacaine with dexmedetomidine group than in plain ropivacaine group. Tao Zang et concluded that dexmedetomidine is better than sufentanil in terms of analgesic effect and low drug requirement.

Zang li et al[13] investigated the effective median concentration EC50 of epidural ropivacaine for labour analgesia when combined with 0.5 mcg/mL of dexmedetomidine. The study inferred that effective analgesia was decided by VAS score <3 within 30 mins after epidural infiltration and next patient concentration of ropivacaine was divided by analgesic effect of previous patient under epidural anesthesia. EC50 of epidural ropivacaine for labour analgesia with or without 0.5 mcg/mL dexmedetomidine were 0.062% and 0.0835% respectively that is the concentration of ropivacaine is decreased when combined with dexmedetomidine without any side effects. In our study we found the duration of labour was less in RD group as compared to RS group.

Similar study was performed by Wang Jun et al[14] where 0.1 % ropivacaine plus 0.5 mcg/mL dexmedetomidine and 0.1 % ropivacaine with normal saline for labour analgesia was compared, setting background infusion of 10 mL/hr. after 1st bolus dose of 10 mL bolus drug of study group. They found that total duration of labour was shorter in ropivacaine plus dexmedetomidine group than plain ropivacaine group as dexmedetomidine intensifies contractions of uterus and helps in rapid progression of labour.

MA Khan et al[15] compared the duration of labour in population of normal parturients in which half received regional labour analgesia and other half was control group. They concluded that epidural analgesia decreases the duration of active first stage and second stage of labour. Similarly, apart from active labour protocol, epidural analgesia could also contribute in decreasing the duration of labour as was found in our study.

Sia AT et al[16] in their study of invitro effects of clonidine and dexmedetomidine on human myometrium came to inference that dexmedetomidine has increased contractility activity on uterus at a concentration lesser than that of clonidine. Jamie Fernandez et al[17] compared 0.0625% bupivacaine with fentanyl and 0.1% ropivacaine with fentanyl for continuous epidural labour analgesia and found no statistically significant difference in any of the maternal haemodynamic parameters. Anim Somuah et al,[18] in his study of 38 parturients observed that the epidural analgesia leads to maternal hypotension, increased instrumental deliveries as compared to the parturients not receiving analgesia. Similar study was done by Mouse et al[19] and concluded that there was no significant difference in haemodynamic parameters and neonatal outcome in epidural group than in non-epidural group, also no significant difference in instrumental deliveries in both the groups.

Pain is a subjective phenomenon and it is difficult to assess its severity in labour. Visual analogue score has been reported to be a reliable method of scoring pain in labour. In our study VAS was <3 at 30 mins in both groups. The mean VAS score was significantly lower for RD group compared to RS group at 10 min ($p<0.001$), 15 min ($p=0.023$), 60 min ($p=0.015$), 90 min ($p<0.001$), 150 min ($p=0.009$) and 180 min ($p=0.033$). The results resembled study by Wang Jun et al[20] who demonstrated lower VAS scores in ropivacaine and dexmedetomidine group than plain ropivacaine group which led to conclusion that dexmedetomidine provided better quality of analgesia in parturients and less requirement of drug. Kiran et al[21] observed postoperative analgesia of epidural ropivacaine with additives fentanyl and dexmedetomidine in patients undergoing infraumbilical surgeries of postoperative analgesia along with improved VAS scores in dexmedetomidine. The study concluded that there was reduced need of top ups and increased duration than in fentanyl group.

It was observed from the ratings given by the parturients in group RD had excellent satisfaction compared to of parturients in RS group. Adjuvant added to local anaesthetic that increase the duration of analgesia with minimal side effects provides better maternal satisfaction. Intermittent epidural bolus slightly reduces local anesthetic usage and improve maternal satisfaction when used for labour analgesia. Selim et al,[22] in his evaluation of bupivacaine with two adjuvants fentanyl and dexmedetomidine on uterine and umbilical artery Doppler velocimetry found that the haemodynamics were stable in mother in dexmedetomidine group than in fentanyl group also the maternal satisfaction was more in dexmedetomidine group than in fentanyl group,

The incidence of nausea and hypotension was seen in both the groups. The hypotension may be due to vasodilatation because of neuraxial blockade[23] and nausea is common symptom in labour, and it does not worsen in epidural blockade if hypotension is prevented.

Naaz et al,[24] in his review of dexmedetomidine in current anesthesia practice observed that the adverse effects of this drug is due to the selective alpha-2- agonistic action leading to vagomimetic action on heart causing bradycardia and hypotension. Dexmedetomidine was tolerated in healthy population with plasma concentrations from 1.8 to 13 times the upper boundary of therapeutic range.

Wang ping et al[25] ascertained the optimal dose of 0.5 mcg/mL of dexmedetomidine when used in labour analgesia did not show any side effects like hypotension, uroschesis, bradycardia, respiratory depression and provided a adequate analgesia.

CONCLUSIONS

Epidural labour analgesia is considered to be a gold standard for pain management during labour, when ropivacaine along with dexmedetomidine is used. Many studies have been conducted to prove the use of dexmedetomidine in obstetric anesthesia in optimal doses. This wonder drug provides excellent maternal satisfaction and good progress of labour with minimal side effects to mother and foetus.

Limitations and Recommendations

Inclusion of both primigravida and multigravida into the sample population masks varying pain intensities. Also, the potential limitation of this study could be the need of a larger sample size to provide a broader perspective. The techniques and drugs available to the present-day obstetrics anaesthesiologist are vastly superior to what existed previously. The future of obstetric anaesthesia lies in refining these techniques and advent of better drugs to make obstetric anaesthesia safer and more effective. So, we recommend addition of dexmedetomidine to improve the quality analgesia, to reduce the duration of labour and gain excellent maternal satisfaction at a dose of 0.5 mcg/mL in epidural labour analgesia.

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