How to Cite:
Manjula, P., Prathima, P., & Rajani, P. (2022). A comparitive study of 0.1% ropivacaine with fentanyl versus 0.125% bupivacaine with fentanyl in epidural labour analgesia. *International Journal of Health Sciences*, *6*(S5), 11906–11918. https://doi.org/10.53730/ijhs.v6nS5.11529

A comparitive study of 0.1% ropivacaine with fentanyl versus 0.125% bupivacaine with fentanyl in epidural labour analgesia

Dr Pathri Manjula
Assistant professor: Department of Obstetrics and Gynecology GMH/Kakatiya medical college, Hanamkonda, Telangana, India

Dr. Prathima
Assistant professor: Department of Obstetrics and Gynecology GMH/Kakatiya medical college, Hanamkonda, Telangana, India

Dr Pilli Rajani
Assistant professor: Department of Obstetrics and Gynecology GMH/Kakatiya medical college, Hanamkonda, Telangana, India

***Abstract*---**Background: Analgesic adequacy during labor along with the avoidance of adverse effects is vital for obstetric conditions. Painful labor can have negative impacts on maternal and fetal physiology. Aim: The aim of the study was to compare the efficacy of ropivacaine with fentanyl and bupivacaine with fentanyl in epidural labour analgesia. Methodology: Seventy ASA I&II parturients with singleton pregnancies who presented in active labour with cervical dilatation of 3-5cm were studied in a prospective, randomized control manner. Patients were randomized into Group A (ropivacaine)-35 patients and Group B (bupivacaine) - 35 patients. Epidural analgesia was performed and various parameters (heart rate, blood pressure, respiratory rate, oxygen saturation, pain score) and complications if any were recorded every 15 minutes in the 1st hour, every 30 minutes in the 2nd hour and every hour later on. Results: The fluctuations in pain were not clinically or statistically significant between the two study groups. The number of patients who required bolus were 7(20%) in both the groups. The spontaneous deliveries were more, 62.9% in Group-A as compared to 54.3% in Group-B. The instrumental delivery rates were less, 25.7% in Group-A as compared to 37.1% in Group-B. Cesarean sections were performed in 4(11.4%) women in Group-A as compared to 3 (8.4%) patients in Group-B. These differences were not statistically significant. The duration of first stage of labour was 467 minutes in both the groups. The mean duration of second stage of labour was 33 minutes in Group-A as compared to 31 minutes in

Group-B. The third stage of labour was 6 minutes in both the groups. No adverse neonatal outcome (because of the drugs used) in the form of low Apgar scores or admission to NICU were noticed in both the groups. Motor block was observed in 3 patients (8.5%) in Group B (bupivacaine) only. There was no clinically observable motor blockade in Group-A(ropivacaine). This difference was not statistically significant. The incidence of complications was minimal and comparable in both groups. Conclusion: From this study it can be concluded that ropivacaine is equipotent with bupivacaine, ropivacaine is as efficacious as bupivacaine in the concentrations used in the study.

***Keywords*---**comparitive study, epidural labour analgesia, fentanyl, bupivacaine.

Introduction

The ASA & ACOG have said that "Labor causes severe pain for many women. There is no other circumstance where it is considered acceptable for an individual to experience untreated severe pain, amenable to safe intervention, while under a physician's care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor. Pain management should be provided whenever medically indicated."[1] The first documented incident of pain relief during labour in USA was for Fanny Longfellow in1847 with ether.[2] The second woman to become famous was Emma Darwin, wife of the eminent naturalist Charles Darwin who was administered chloroform during labour. But the third incident influenced the history of labour analgesia in a profound way. It was the administration of chloroform to Queen Victoria by Dr.John Snow for her 8th confinement to deliver Prince Leopold on April 7,1853.[2] This made pain relief in labour famous as well as more acceptable, since it had a royal patronage. From 1840s to 1960s, different methods of pain relief were tried. This included inhalational agents, systemic agents[opioids, ketamine, Twilight sleep(morphine + scoploamine)], local blocks.

Most would agree that the ideal analgesic would be safe for the mother and newborn, would have minimal effects on the progress of labor, and would provide flexibility in changing conditions. Additionally, the ideal technique would provide long- lasting, consistent analgesia titrated to individual. Central neuraxial blocks were introduced in labour in 1950. Pioneering research in this field has lead to great development in the safe and effective practice of neuraxial techniques. Modern neuraxial labour analgesia reflects a shift in obstetrical anesthesia, thinking away from a simple focus on pain relief and towards a focus on the overall quality of analgesia.[3]Central neuraxial analgesia is the most versatile method of labour analgesia and the gold standard technique for pain control in obstetrics that is currently available. The satisfaction of birth experience is

greater with neuraxial techniques.[4] Among this epidural blockade comes close to being the ideal analgesic technique in labour.[4].

Epidural injection of a local anaesthetic combined with an opioid provides a more rapid onset of analgesia with little motor blockade. The pain relief starts sooner and also lasts longer than either drug alone. It allows both the drugs to be used in lower concentration, thereby reducing the risk of local anaesthetic systemic toxicity as well as opioid side effects.[5]Bupivacaine and Ropivacaine are widely used to provide efficient epidural analgesia in labour. The value of bupivacaine is limited by the risks of motor blockade(associated with maternal dissatisfaction and increased instrumental deliveries) and cardiac toxicity. Ropivacaine has the advantage of more sensory motor differential blockade as well as decreased risk of systemic toxicity. There have been conflicting comparisons of ropivacaine and bupivacaine for labour analgesia.[6] Some studies have suggested that ropivacaine produces less motor block than bupivacaine while others found the drugs to be indistinguishable. Dilute solutions of epidural local anesthetics combined with opioids may be used to minimize unwanted motor block. We undertook this study to compare the efficacy of Ropivacaine and Bupivacaine in regards to pain relief, motor block, and labour characteristics.

Materials & Methods

This was a prospective randomized control trial involving 70 parturient (35 in each group) attending the Department of Obstetrics & Gynecology at Chandrakanthiah Memorial Hospital, Warangal).Institutional ethics committee and scientific committee approval was obtained. All patients admitted to the labour room were counseled regarding labour analgesia. The procedure was explained to the patient. Informed consent was obtained. Detailed history of the patient was collected. Routine investigations like blood grouping and typing, hemoglobin and platelet count were done as per our hospital labour protocol. Patients fulfilling the inclusion criteria and who gave consent were then randomly allocated to one of the study groups on the basis of computerized randomized list.

Inclusion Criteria

Normal singleton pregnancies, with age – 18-35 years, ASA status- I & II in patients in active labour with cervical dilatation – 3-5 cm.

Exclusion Criteria

Contraindications to epidural block 2. Pre-term pregnancy, multiple pregnancies and previous cesarean section. An 18G IV cannula was inserted and patient was started on an infusion Ringer lactate solution. The patient was then positioned in Lt. lateral position or sitting position based on the anaesthetist convenience and her back aligned with the edge of the bed. Under strict aseptic precautions, the skin over the lower thoracic and lumbar region was cleaned and area draped. The best interlumbar space between L1 and L4 was identified and infiltrated with 2% lignocaine. The skin was pierced with 18G needle in the interlumbar space. The

epidural needle was inserted with bevel facing upward and pushed till it pierced the interspinous ligament. The stylet was then removed. A 10ml LOR(Loss Of Resistance) syringe filled with either Air or saline was attached to the hub of the epidural needle. The needle was then slowly advanced with pressure exerted on the air/saline column through the plunger of the LOR syringe. The epidural space was identified with LOR to injection of air or saline. Careful aspiration was done to make sure that the duramater was not punctured. If CSF was aspirated, the needle was withdrawn and reintroduced in a different space. If no CSF was aspirated, the LOR syringe was removed. The depth of the epidural space was noted. A 20G fine epidural catheter was threaded through the needle into the epidural space. The epidural needle was removed. The catheter was positioned so that a length of 5cm of catheter remained in the epidural space. Careful aspiration of the cathter was again done to check for CSF or blood.

Once the cathter was satisfactorily sited, the puncture site was cleaned and an occlusion dressing applied over it. A bacterial filter was attached to the hub of the cathter. A small test dose of local anesthetic (3ml of 2% Lignocaine with Adrenaline) was injected via the catheter to rule out intravascular or intrathecal placement of catheter. If there were no signs of motor block (intrathecal placement) or tachycardia(intravascular placement) after 5 minutes the patient was turned supine. A bolus dose of the test drug was given followed by the infusion. The bolus and infusion protocol of each study group were as follows:

GROUP -A 6ml of 0.2% Ropivacaine 6-8ml/hr of 0.1% Ropivacaine with 2µg/ml Fentanyl
GROUP- B 6ml of 0.25% Bupivacaine 6-8ml/hr of 0.125% Bupivacaine with 2µg/ml fentanyl

Breakthrough pain was managed with 6ml of either 0.2% Ropivacaine or 0.25% Bupivacaine depending on the study group they were involved. Various maternal parameters were continuously monitored and noted every 15 minutes in the first hour, every 30 minutes in the second hour and every hourly thereafter. Continuous fetal heart monitoring was also done.

Parameters monitored

1. Maternal Heart rate
2. Maternal Blood pressure
3. Maternal respiratory rate & oxygen saturation.
4. Pain relief by 11 point verbal numerical rating scale (VNRS) 5. Motor block by Bromage score (0-3)

Clinical outcome studied

1. Pain relief
2. Motor block
3. Duration of labour
4. Mode of delivery - Vaginal - Spontaneous / Assisted - Cesarean section
5. Neonatal outcome - APGAR score, NICU admission.

Sample size

Sample size has been calculated to detect a 40% difference in the occurrence of motor block between the two groups. The optimal sample size required would be 35 in each group (70 in total) with 80% power and 5% level of significance. The incidence of significant motor block (2 or 3 on a 0–3 scale) was assumed to be 30%. (Owen 1998).

Statistical analysis

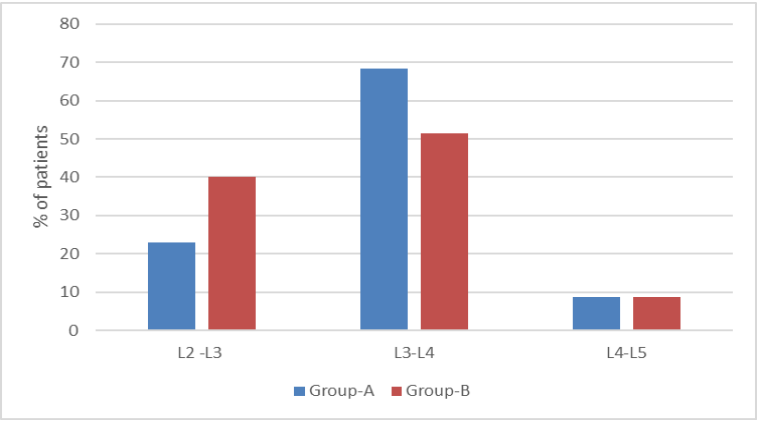
All statistical analysis were performed using SPSS(Statistical package for social sciences) version 17 for windows. The profile of the cases were compared with the treatment allocation in order to check if there was any significant imbalance. Descriptive statistics are presented as mean± 1SD. Component bar and line diagrams were drawn as and when required. Chi-square test for association was used to compare categorical variables between treatment allocations.

Results and Observation

The patient's age ranged from 17-36 years. The average age did not differ between the two groups. The mean age of women in Group-A was 25.37±3.85 years and that of group-B was 25.23±3.623.The difference was not statistically significant.(P=0.874) The patient's weight ranged from 46-89 kgs at the time of presentation. The average weight of the women allocated to group-A was 68±8.86 kgs and that of those in Group-B was 64.29±9.03 kgs. This difference in weight between the two groups was statistically not significant.(P=0.087)

Gravid a (p=0.200) and parity(p=0.122) of the women between two Groups were not statistically significant. Overall, out of the 70 pregnant women, 65(92.9%) had ASA grade I pregnancy, the rest 5(7.1%) had ASA grade II pregnancy. The distribution of patients was not statistically significant.(p=0.643) Group-A and Group-B each had one women(2.9% in each group) with GDM(Gestational Diabetes Mellitus). PIH(Pregnancy Induced Hypertension) was present in one women(2.9%) in group-A and two(5.8%) women in group-B. Their distribution among groups was not statistically significant.(p=0.840) . The average vaginal dilatation of the whole group was 3.44±0.65 cm. The vaginal dilatation in group-A was 3.37±0.54 cm and in group was 3.51±0.74 cm. This variable did not have any statistically significant difference.(p=0.206)

Figure-1: Level of epidural placement



More than 50% of the patients in both the groups received epidural in the L3-4 interspace. The distribution of level of epidural catheter placement among both the groups did not have any statistical significance.(p=0.287)

Table-1: Comparison of systolic blood pressure between the two groups during their labour

Time	Group-A	Group-B	t value	p value
.Baseline	115.6±10.5	114.8±11.2	0.308	0.759
15 mins	114.4±8.1	115.4±7.8	-0.538	.0.592
30 mins	114.2±6.8	115.1±10.1	-0.442	0.660
.45 mins	112.9±8.2	115.4±7.8	-1.314	0.193
1 hr	116.4±7.9	116.5±7.6	-0.092	.0.927
.1.5 hr	117.2±6.1	117.1±7.8	0.068	0.946
2 hr	114.4±7.8	114.5±6.8	-1.060	0.293
3 hr	114.5±5.5	115.4±10.1	-0.469	0.640
.4 hr	114.7±6.3	113.8±7.7	0.538	.0.592
5 hr	113.4±7.7	116.3±9.5	-1.009	.0.320
6 hr	112±7.8	117.5±7.1	-1.537	0.144
7 hr	110±0.0	103.3±5.7	2.000	0.116

All the periods of systolic BP are insignificant

Table-2:Comparison of mean dyastolic blood pressure

.Time	Group-A	Group-B	t value	p value
.Baseline	76.2±7.8	74.2±6.9	1.122	.0.266
15 mins .	74.7±7.9	75.4±6.1	.-0.405.	0.087
30 mins	74.4±7.9	74.2±6.9	0.112	0.911
.45 mins	74.6±7.7	71 ±12.4	1.319	.0.192

.1 hr	75.8±7.9	72.5±7.8	1.747	.0.085
.1.5 hr	77.2±6.8	74.5±6.1	1.69	0.095
2 hr	74.4±7.8	72±7.9	1.303	0.197
3 hr	77.6±6.7	75.4±6.5	1.39	0.167
4 hr	75.7±7.6	73.1±7.8	1.363	0.177
5 hr	76.5±5.9	74.2±5.1	1.290	0.205
6 hr	71.4±3.2	73.7±5.1	-1.176	0.257
7 hr	73.3±5.7	73.3±5.7	1.000	1.000

Comparison of mean diastolic blood pressure between ropivacaine and bupivacaine groups are insignificant

Table-3: Comparison of respiratory rate between the two groups during their labour

Time	Group-A	Group-B	t value	p value
.Baseline	21.9±3.2	20.8±4.0	1.267	0.209
15 mins	17.4±2.4	18.1±1.7	-1.407	0.164
30 mins	17.1±1.9	17.7±1.4	-1.534	0.130
45 mins	17.7±2.3	17.7±1.4	-0.100	.0.951
1 hr	16.7±2.4	17.6±1.5	-1.745	.0.085
1.5 hr	17.4±5.8	17.6±1.4	-0.198	0.849
2 hr	16.8±2.2	17.5±1.3	-1.612	0.112
3 hr	16.8±2.4	17.7±1.6	-1.794	0.077
.4 hr	17.4±2.1	18.1±1.5	-1.480	0.144
5 hr	17.6±2.0	17.7±2.2	-0.180	0.882
6 hr	16.6±2.0	17±2.8	-0.307	.0.762
.7 hr	15.3±1.1.	15.3±1.2	0.000	1.000

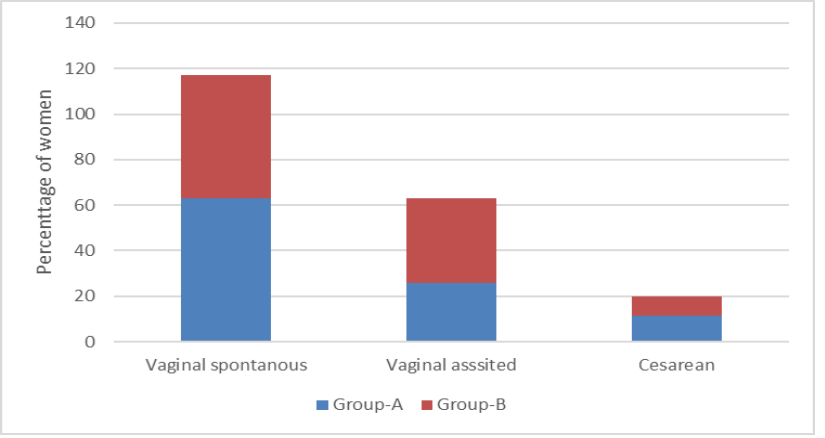
There was no statistically significant difference in the hemodynamics of patients among both groups including heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate. The oxygen saturation (SPO2) among both groups of patients also did not vary significantly.

Table-4: Bolus requirement

Time	Group-A	Group-B	P value
1.5 hr	1	nil	0.314
3 hr	1	2	0.55
4 hr	2	nil	0.151
5 hr	2	3	0.631
6 hr	1	2	0.396

7 women in both groups required boluses during their labour. The proportion of women requiring boluses was comparable in both the groups. All other periods did not require blous.

Figure-2: Mode of delivery in study



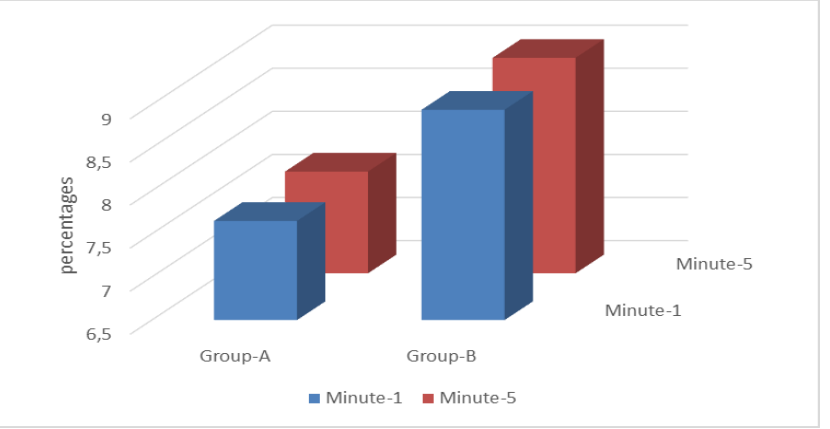
There were more spontaneous vaginal deliveries in Group-A (62.9%) compared to group-B(54.3%). Assisted vaginal deliveries were less in group- A(25.7%) compared to group-B(37.1%). Four patients in group-A(11.4%) and three patients in group-B(8.6%) had cesarean deliveries.

Table-5: Average duration of 1^{st},2^{nd} and 3^{rd} stage of laour were comparable.

Duration(in minutes)	Group-A	Group-B	t value	p value
Stage-I	467.4±95.8	467.6±87.8	-0.007	0.995
Stage-II	33.5±8.5	31.1±8.9	1.116	0.269
Stage-III	6.8±1.7	6.1±1.2	1.769	0.082

Average duration of 1^{st},2^{nd} and 3^{rd} stage of laour were comparable which are insignificant

Figure-3: Neonatal outcome in present study



The neonatal outcome was rated with Apgar acore at 1 & 5 minutes. The average Apgar score during 1st minute assessment was 7.65±0.59 and 7.68±0.47 in group-A and group-B respectively. At 5 minutes, the Apgar score was 8.94±0.23 and 9 in group-A & B respectively. The difference in mean values were not statistically significant at both 1 minute (p-0.460) and 5 minutes(0.221). Five neonates(14.3%) in group-A and three neonates(8.6%) in group-B were admitted in NICU. The difference was not statistically significant (p- 0.845). The indications for admission in NICU in group-A were cord around the neck, IUGR, respiratory distress and meconium stained liquor. Corresponding indications in group-B were cord around the neck, respiratory distress and meconium stained liquor. Motor blockade of Bromage score-1 was observed in 3 persons belonging to group-B. This was observed during the 5th hour in all 3 patients. There was no clinically observable motor blockade in Group-A. However this was not statistically significant(p-=0.071). Numbness was seen in 2 patients in group-B and compared to none in group- A. It was seen in 6th and 7th hour. The numbness rate was not statistically significant. Pruritis was not seen in any patients in both the groups.

Discussion

In our study we have compared bupivacaine with ropivacaine for labor epidural analgesia. Bupivacaine is a proven drug for effective labor analgesia. We decided to compare bupivacaine with ropivacaine, which is marketed as a levo-enantiomer because ropivacaine has a better sensory-motor differentiation and less cardiotoxic potential compared to bupivacaine. We decided to compare 0.1% ropivacaine with fentanyl and 0.125% bupivacaine with fentanyl to see whether ropivacaine offers the same pain relief and if it offers any significant advantage over bupivacaine at this concentration. The parturients were comparable in regards to age, weight, gravida, parity, vaginal dilatation in both groups.

Pain is a subjective phenomenon and it is difficult to measure.. In our study we used VNRS as the pain scoring system because it was easy to use along with patients' understanding and compliance being better. In our study we found that

the mean pain level was 7.8±0.7 in ropivacaine group and 7.6±0.8 in bupivacaine group. After epidural it came down to 0.31 in ropivacaine and 0.17 in bupivacaine group before epidural. The pain score went upto 0.42 in ropivcaine and 0.52 in bupivacaine group at the end of 5 hours. There was no clinically demonstrable difference in the onset of pain relief. Though our study used a less potent concentration of ropivacaine, there was no statistically significant difference in the pain relief offered.

When Halpern et al [7] did a meta-analysis comparing ropivacaine and bupivacaine he found that 19 out of 23 studies favoured ropivacaine to have minimal motor block and 5 of those studies were statistically significant. In our study, only 2 patients in bupivacaine group had demonstrable Bromage score-I motor block. There was no clinically demonstrable motor block in the ropivacaine group. This difference was not clinically significant. The incidence of motor block in our study was low in ropivacaine and also significantly lower than bupivacaine in many of the comparative studies(Gautier 1999,Fischer 2000,Meister 2000,Campbell 2000)[8] This may be because the volume of drug used in our study was low(6 ml bolus and 6-8ml/hr infusion) thereby resulting in a lesser concentration of drugs.

The duration of labour is determined by the intensity of uterine contraction, the dilatation of cervix and the descent of the presenting part of fetus. A meta-analysis by Halpern et al[9] concluded that epidural analgesia prolonged 1st stage of labour by 42 minutes The results of our study correlate well with the above mentioned studies According to ACOG guidelines, second stage of labour is said to be prolonged when the duration was more than 3 hours for primipara and more than 2 hours for multipara with regional anaesthesia. A metanalysis done by Halpern et al[9] on 2400 parturients who received either epidural analgesia or parenteral opioid analgesia found that the second stage of labour was prolonged by 14 minutes. A recent Cochrane review[10] on epidural versus non-epidural or no analgesia in labour found that women who had epidural were more likely to have a longer second stage of labour. In our study there was no difference in the duration of second stage of labour in both groups. The mean duration was 33.5 min in ropivacaine group and 31.1 min in bupivacaine group. This difference was not statistically significant. Our result coincides well with the meta-analysis done by Halpern et al in 2003[11] which took into account 23 studies comparing ropivacaine and bupivacaine for labour epidural analgesia. They found that neither bupivacaine nor ropivacaine group had any difference in the duration of second stage of labour.

Halpern et al [11] in their meta analysis found that women with epidural were twice as likely to have an instrumental vaginal delivery as compared to control groups. Cambic and Wong [12] in their review on labour analgesia and obstetric outcomes concluded that effective second stage analgesia might be associated with an increased rate of instrumental vaginal delivery. In our study we had an instrumental delivery rate of 25.7% in ropivacaine group and 37.1% in bupivacaine group which was not statistically significant. In majority of cases, maternal failure was the cause of instrumental delivery. Our study results

coincide with the study done by Finegold et al 13, which used a similar concentration of drugs as our study. They had a instrumental vaginal delivery rate of 18% in ropivacaine group and 28% in bupivacaine. In both our studies though the instrumental delivery rates were less in ropivacaine, the differences were not statistically significant. The meta-analysis of 23 studies comparing ropivacaine and bupivacaine in 2003 by Halpern et al [11] also did not find any difference in the mode of delivery between the two drugs. However a meta-analysis of 6 studies comparing 0.25% ropivacaine and 0.25% bupivacaine done by Writer et al[14] in found that there were fewer instrumental vaginal deliveries in the ropivacaine group. This may be because of the higher concentration of bupivacaine used and difference in the motor blocking potency of ropivacaine.

In our study, we had a cesarean delivery rate of 11.4% in ropivacaine and 8.6% in bupivacaine group. The main reasons for the cesarean delivery among both groups were failure to progress, fetal distress due to cord around the neck and meconium stained liquor. Beilin et al in 2007[16] compared ropivacaine with bupivacaine and their effect on outcome of delivery. Bupivacaine group had a cesarean rate of 33% against a 30% rate in ropivacaine group. The meta-analysis by Halpern et al 2003[11] also found no difference in cesarean delivery rates between ropivacaine and bupivacaine when used for labor epidural. In our study the fetal heart rate during the process of labour analgesia was within normal limits. There was no incidence of post epidural fetal bradycardia. The mean APGAR score was 7.65 & 7.68 in ropivacaine and bupivacaine groups respectively. At 5 minutes it averaged to 8.94 & 9 respectively. There was no significant difference in NICU admission in both groups Beilin and Halpern in 2010[16] did a focused review with various studies that compared bupivacaine and ropivacaine and concluded that there was no evidence that neonatal outcome is adversely affected when ropivacaine or bupivacaine is used for labor analgesia. Writer et al.[14] found a difference in the neurologic and adaptive capacity score, favoring ropivacaine, at 24 hours after birth, but not at 2 hours after birth. But recent evidence suggests that the neurologic and adaptive capacity score is unreliable. The incidence of low Apgar scores at 5 minutes is approximately 2% for both drugs. In addition, the umbilical artery and vein pH are well maintained regardless of which local anesthetic is used. Also, the incidence of need for neonatal resuscitation is low and similar with both drugs. The incidence of complications were very minimal in both groups.

Conclusion

Obstetric analgesia strives at making childbirth, a pleasurable and painless event. As a means toward this end, we should ideally adopt the best possible technique, something that would provide excellent analgesia with minimal side effects and absolute safety to the mother and child. The observations of this study show that pain relief offered by epidural ropivacaine is as good and effective as epidural bupivacaine. Also the duration of labour, mode of delivery, neonatal outcome and complications are comparable between the two groups. From this study it can be

concluded that though ropivacaine is equipotent with bupivacaine, ropivacaine is as efficacaious as bupivacaine in the concentrations used in our study.

References

1. COG-Committee on Obstetric practice–Committee Opinion– Number 295, July 2004
2. WongCA. Advances in labour analgesia, Int J Womens Health 2009;1:139-54.
3. HawkinsJL. Epidural analgesia for Labour and delivery. N EnglJMed 2010;362: 1503-10.
4. PolleyLS,ColumbMO,NaughtonNN,WagnerDS,vandeVenCJ. Relative analgesic potencies of ropivacaine and Bupivacaine for epidural analgesia in labor: implications for therapeutic indexes. Anesthesiology 1999; 90: 944-50.
5. Capogna G, Celleno D, Fusco P, Lyons G, Columb M. Relative potencies of Bupivacaine and ropivacaine for analgesia in labour. Br J Anesth 1999; 82: 371-73.
6. Halpern SH, Walsh V. Epidural ropivacaine versus bupivacaine for labor: a meta-analysis. AnesthAnalg. 2003 May;96(5):1473-9
7. Finegold H, Mandell G, Ramanathan S. Comparison of ropivacaine 0.1%-fentanyl and bupivacaine 0.125% -fentanyl infusions for epidural labour analgesia. Can J Anesth 2000 / 47: 8 / pp 740–745
8. Halpern SH, Leighton BL, Ohlsson A, Barrett JF, Rice A. Effect of epidural vs parenteral opioid analgesia on the progress of labor: a meta-analysis. JAMA. 1998 Dec 23-30;280(24):2105-10.
9. Anim-Somuah M, Smyth R, Howell C. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2005 Oct 9;(4):CD000331. Review. Update in: Cochrane Database Syst Rev. 2011;(12):CD000331
10. Halpern SH, Walsh V. Epidural ropivacaine versus bupivacaine for labor: a meta-analysis. AnesthAnalg. 2003 May;96(5):1473-9
11. ambic CR, Wong CA. Labour analgesia and obstetric outcomes. Br J Anaesth.2010 Dec;105 Suppl 1:i50-60.
12. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. Drugs. 2000 Nov;60(5):1065-93.Dresner M, Freeman J, Calow C, Quinn A, Bamber J: Ropivacaine 0.2% versus bupivacaine 0.1% with fentanyl: a double blind comparison for analgesia during labour. Br J Anesth. 2000 Dec; 85(6):826-9.
13. Writer WD, Stienstra R, Eddleston JM, Gatt SP, Griffin R, Gutsche BB, Joyce TH, Hedlund C, Heeroma K, Selander D. Neonatal outcome and mode of delivery after epidural analgesia for labour with ropivacaine and bupivacaine: a prospective meta-analysis. Br J Anaesth. 1998 Nov;81(5):713-7.
14. WANG Li-zhong, CHANG Xiang-yang, LIU Xia, HU Xiao-xia and TANG Bei-lei. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient-controlled epidural analgesia during labor: a randomized clinical trial. Chin Med J 2010;123(2):178- 83.
15. Beilin Y, Halpern S. Focused review: ropivacaine versus bupivacaine for epidural labor analgesia. AnesthAnalg. 2010 Aug;111(2):482-7.

16. Halpern SH, Littleford JA, Brockhurst NJ, et al. The neurologic and adaptive capacity score is not a reliable method of newborn evaluation. Anesthesiology 2001;94:958–62.
17. Negara, I. K. S., Agung, A. A. G., Candiasa, I. M., & Dantes, K. R. (2022). Development of digital instruments for measuring the effect of open selection, job satisfaction, transformational leadership and work motivation on the performance of civil servants. *International Journal of Health Sciences*, *6*(2), 661–681. https://doi.org/10.53730/ijhs.v6n2.7580
18. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. *International Journal of Health Sciences*, *5*(3), x-xv. https://doi.org/10.53730/ijhs.v5n3.2938
19. Sawali, L. (2018). Drills forehand training strategy on the stroke of forehand drive ability in tennis. *International Journal of Physical Sciences and Engineering*, *2*(2), 11–20. https://doi.org/10.29332/ijpse.v2n2.133
20. ASA newsletter–September1997,Volume69,Number9.