Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Anesthesiology

A STUDY COMPARING THE EFFECTIVENESS OF LEVOBUPIVACAINE, BUPIVACAINE AND ROPIVACAINE FOR CAUDAL BLOCK IN CHILDREN UNDERGOING INFRA UMBLICAL PROCEDURES.

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ABSTRACT **BACKGROUND**: Caudal Epidural anaesthesia plays a vital role in providing effective intra operative as well as post operative pain relief in paediatric population for infraumbilical surgeries. Though Bupivacaine is the most commonly used drug, the availability of drugs like Levobupivacaine and Ropivacaine with less toxic potentials led us to conduct a study in which we compared the duration of post operative analgesia between these drugs in children after caudal block for below umbilicus surgeries. **AIM:** To compare the effectiveness of Levobupivacaine, Bupivacaine and Ropivacaine in a concentration of 0.25% given with volume of 1ml/Kg in caudal block before skin incision in terms of post operative analgesia and recovery of motor block for surgeries like circumcision and herniotomy in children aged 2-8 years. **MATERIALS AND METHODS**: This study was conducted in the Department of Anaesthesiology Chengalpattu Medical College; Tamilnadu in 90 paediatric patients of ASA grade I. Patients belonged to the age group of 2-8 years of both sexes. These patients were systematically randomized into groups of 30each. Group I received 0.25% Levobupivacaine (0.5 % solution diluted in equal volumes of normal saline). Group II received 0.25% Bupivacaine (0.5 % solution diluted in equal volumes of normal saline). Group III received0.25% Ropivacaine (0.5 % solution diluted in equal volumes of normal saline) through caudal route. **STATISTICAL ANALYSIS:** The data was analyzed by statistical software SPSS 19.0 and XLSTAT 2013. All variables were examined for outliers and non-normal distributions. The Categorical variables were expressed as Frequency and percentage. The Quantitative variables were expressed as mean and standard deviation. Descriptive statistics were used to evaluate baseline characteristics. The Group comparison for the categorical variables were analyzed using Chi square test and Quantitative variables were analyzed using Analysis of Variance (ANOVA).A repeated measures analysis of variance (RMANOVA) was used to determine between group effects, within-subject effects, and interactions between groups and time. **RESULTS**: Three groups were comparable in their base line characteristics like age, sex, weight, height, type and duration of surgery. The duration of post-operative analgesia between these groups were 130.33±11.74min in Group I, 182.83±12.64min in Group II, and 110.17±8.66min in Group III. The time to full motor recovery was significantly lower in Levobupivacaine 0.25% and Ropivacaine 0.25% as compared to the Bupivacaine 0.25%. In Group I it is 180.17±22.76min, in Group II 239.00±21.55min, in Group III 162.00±20.24min. **CONCLUSION**: Caudal block using Bupivacaine 0.25% in a dose of 1ml/kg provided long lasting analgesia when compared to Levobupivacaine 0.25% and Ropivacaine 0.25% in children undergoing infra-umbilical surgeries. The faster recovery of motor block occurred in Levobupivacaine 0.25% and Ropivacaine 0.25% Group when compared to Bupivacaine Group.

KEYWORDS : Caudal anaesthesia, Bupivacaine, Levobupivacaine, Ropivacaine.

BACKGROUND:

Pain is an uncomfortable sensation which has its influences on health and hence it has been called the fifth vital sign. Even infants and young children can perceive pain which can reflect in the child's recovery. Pain is always subjective[1].Caudal block is the most commonly performed procedure in children. The caudal block prior to the incision after general anaesthesia reduces the need of opioids and decreases the requirement of inhalation anaesthetics for the maintenance intraoperatively[2]. But the disadvantage of caudal block is the residual motor block which may be of distress to children in the day care procedures[3]. The drugs which are used commonly are lignocaine, Bupivacaine, Ropivacaine. Levobupivacaine is a recently introduced drug. Bupivacaine is a long acting amide local anaesthetic that provides anaesthesia as well as analgesia with differential motor blockade[4,5]. But accidental intravascular or intrathecal injection of Bupivacaine may cause severe neurological and cardiovascular depression and even leads to death. Ropivacaine is the first local anaesthetic agent to be manufactured as a pure S-enantiomer and it has shown that it is less cardio toxic and neurotoxic than Bupivacaine[6,7]. Studies have shown that the sensory block produced by Ropivacaine is similar to Bupivacaine but the motor block is slower in onset and less intense and shorter duration when compared to Bupivacaine[8,9]. Levobupivacaine is a newer local anaesthetic agent which closely resembles racemic Bupivacaine but is less cardio toxic and less neurotoxic than racemic Bupivacaine. Hence, we conducted a study to compare drugs such as Levobupivacaine, Bupivacaine and Ropivacaine for the duration of post operative analgesia and duration of motor blockade through caudal route in children for infraumbilical surgeries.

MATERIALS AND METHODS:

This was a prospective double blind comparative study conducted in Government Chengalpattu Medical College Hospital. A pilot study was conducted to define the population and to decide on the inclusion and exclusion criteria, and the target population of 30 subjects in each group was decided. Ninety children who were admitted to the paediatric surgery department for elective surgeries were selected for the study.

INCLUSION CRITERIA:

Children of ASA physical status I,Children aged 2-8 years of either sex,Elective lower abdominal or urological surgeries like herniotomy, processes vaginalis sac ligation, circumcision and hypospadiasis were included in the study

EXCLUSION CRITERIA:

Local infection in the caudal region, Delayed developmental history,Pre existing neurological problem, Congenital anomaly of lower back These children who satisfy the selection criteria were randomized into three groups, Group I received 1 ml/kg of 0.25% Levobupivacaine (0.5% solution diluted in equal volumes of normal saline) Group II received 1ml/kg of 0.25 % of Bupivacaine (0.5% solution diluted in equal volumes of normal saline). Group III received 1 ml/kg of 0.25% Ropivacaine (0.5% solution diluted in equal volumes of normal saline)

STUDY METHODS:

All children satisfying the selection criteria were randomized by computer generated randomization table into three groups Group I, Group II and Group III of 30 each. The randomization sequence was prepared in a double blinded manner. The study drug solution was prepared by final year post graduate student who was not involved in the study. Caudal block was done by the Assistant Professor who was also blinded to the study. Monitoring of parameters was done by the author.

All children were transferred to the premedication room along with parents, and baseline parameters recorded. All children were given oral midazolam (0.4 mg/Kg) 45 min before surgery[10].

After premedication children were wheeled into the operation theatre, connected to standard monitors like Pulse oximetry, NIBP, ECG and

base line parameters recorded. Intravenous access started with 22 G cannula, Ringer lactate maintenance fluid started[11]. Child was preoxygenated with 100% oxygen, Inj. Fentanyl 2mic/Kg given, induced with Inj. Propofol 2 mg/Kg and anaesthesia was maintained with N2o:O2 (50:50) with 1% sevoflurane via appropriate size face mask connected to Jackson Ree's circuit. The child was turned to left lateral position with mask holding in situ. With full aseptic precautions, a sterile 22 G hypodermic needle was introduced in the caudal epidural space, after confirming the space study drug 1ml/kg of 0.25% Levobupivacaine or 0.25% Bupivacaine or 0.25% of Ropivacaine was given in slow increments. The child was turned to supine position. Surgeon was allowed to start after 10 minutes of caudal block.

OBSERVATIONS:

1. Heart rate, blood pressure, oxygen saturation just before and after the surgical incision (0 min, 3 min, 5 min) and then every 5 minutes till the end of surgery. If the child responded to incision with 20% increase in heart rate or blood pressure, fentanyl 1mic/Kg supplemented and child was excluded from the study.
2. Quality of post op analgesia assessed by Modified Hannallah objective pain scale for every 15 min for the first 2 hours and every 30 minutes for the next 5 hours
3. The time between the caudal block and administration of the first rescue analgesic was noted. Inj. Fentanyl 1 mic/Kg was given as rescue analgesic when the pain score equals 4
4. To assess the degree of motor block by motor power scale 15 min for first 2 hours and every 30 min for the next 5 hours
5. Complications and adverse events were noted.

Table 1:MODIFIED HANNALLAH PAIN SCALE

No.	Observation	Criteria	Points
1	Crying	No crying Crying responding to Tender loving care Crying not responding to TLC	0 1 2
2	Movement	None Restless Thrashing	0 1 2
3	Agitation	Asleep/calm Mild Hysterical	0 1 2
4	Swallowing of secretions	Normal uncomfortable unable	0 1 2
5	Verbalisation of pain	Asleep/states no pain Vague/ Can`t localize Can localize pain	0 1 2

Table 2 MOTOR POWER SCALE

Muscle Tone	Flaccid	Hypotonia	Normal
	0	1	2
Muscle Power (Flexion)	Unable	Partial	Normal
Ankle	0	1	2
Knee	0	1	2
Thigh	0	1	2
Ability to stand	0	1	2

STATISTICALANALYSIS

All variables were examined for outliers and non-normal distributions. The Categorical variables were expressed as Frequency and percentage. The Quantitative variables were expressed as mean and standard deviation. Descriptive statistics were used to evaluate baseline characteristics.

The Groups Comparison for the categorical variables was analyzed using Chi square test and Quantitative variables were analyzed using Analysis of Variance (ANOVA).

A repeated measures analysis of variance (RMANOVA) was used to determine between group effects (Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%), within-subject effects, and interactions between groups and time.

The p value of less than 0.05 was considered as statistically significant. The statistical analysis was carried out using statistical software SPSS 19.0

OBSERVATION AND RESULTS

PATIENTS CHARACTERISTICS(table 3)

Patient Characteristics	Levobupivacaine 0.25%	Bupivacaine 0.25%	Ropivacaine 0.25%	P value
Age (years)*	4.22+ 1.54	4.12 + 1.86	4.68 + 1.87	0.420
Sex (Male/Female)	22/8	26/4	23/7	0.420
Weight*	13.70 + 2.55	13.53 + 2.83	14.03 + 2.99	0.248
Height	110.13 + 5.69	108.93 + 5.82	110.50 +	0.495

* values are expressed as mean +2s.dThere is no statistically significant difference between the groups in base line characters such as age, height, weight, sex distribution among Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%.

MEAN HEART RATE

There is no statistically significant difference between the Mean Heart Rate during the surgical procedure between Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%.

MEAN ARTERIAL PRESSURE

There is no statistically significant difference in the MAP during the surgical procedure between Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%

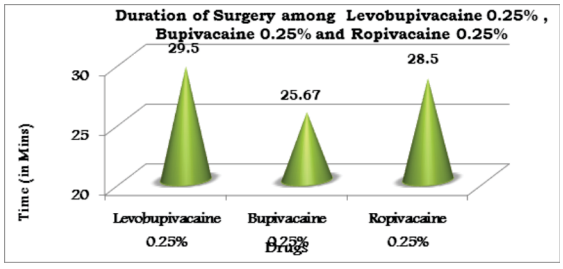

Figure 1

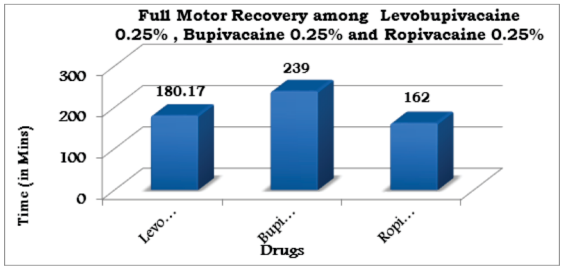

Figure 2

There is statistically significant difference between the three drugs in the full motor recovery (p= 0.000). Inter comparison among the three drugs revealed that the full motor recovery was statistically significantly lower in Levobupivacaine 0.25% and Ropivacaine 0.25% as compared to the Bupivacaine 0.25%.

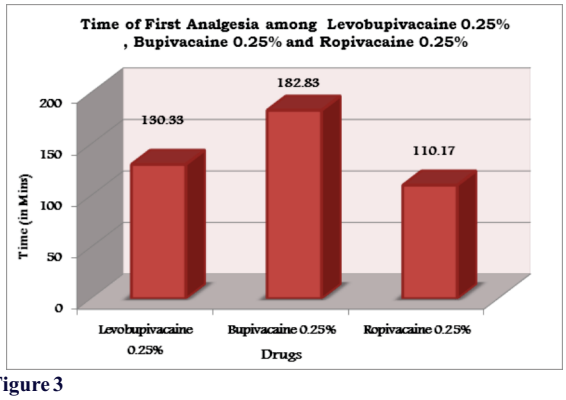

Figure 3

There is statistically significant difference between the three drugs in the time of first analgesia (p= 0.000). Inter comparison among the three drugs revealed that the time of first analgesia was statistically significantly lower in Levobupivacaine 0.25% and Ropivacaine 0.25% as compared to Bupivacaine 0.25%

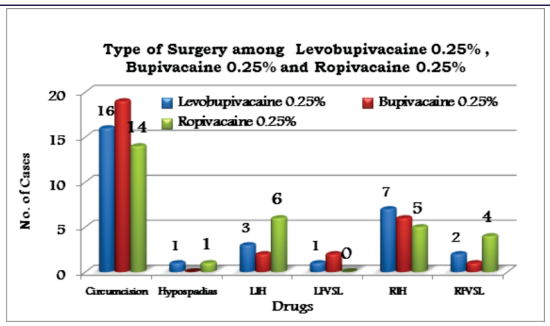

Figure 4

Comparison of Mean Pain Score among Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%

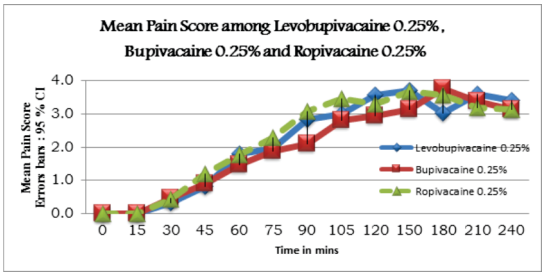

Figure 5

There is statistically significant difference among Levobupivacaine 0.25% , Bupivacaine 0.25% and Ropivacaine 0.25%in the Mean pain scores readings taken in all times except 30 min, and after 210 Min ($p<0.05$).

Comparison of Mean Motor Scale among Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%

There is statistically significant difference among Levobupivacaine 0.25% , Bupivacaine 0.25% and Ropivacaine 0.25%in the Mean Motor Power Scale readings taken in all times except 15 min, 45 Min ($p<0.05$). Inter comparison among Levobupivacaine 0.25% , Bupivacaine 0.25% and Ropivacaine 0.25%revealed that the Ropivacaine 0.25%and Bupivacaine 0.25% differ most of the times significantly.

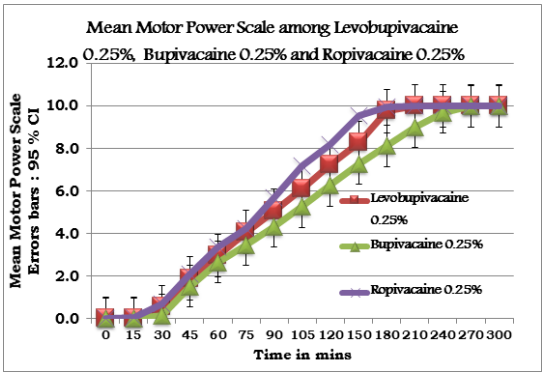

Figure 6

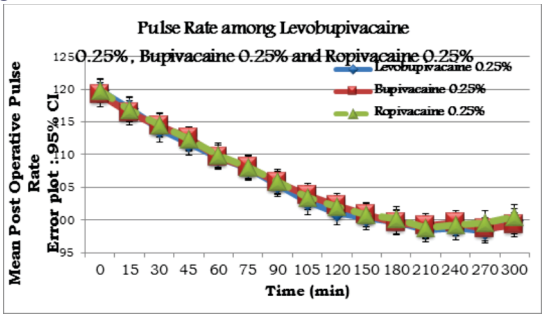

Figure 7

There is no statistically significant difference in the postoperative pulse rate,sbp,saturation between Levobupivacaine 0.25%, Bupivacaine 0.25% and Ropivacaine 0.25%.

DISCUSSION

The aim of instituting adequate pain relief in pediatric day care surgery is of prime importance as it ensures pain relief not only in the intra operative period but also take cares of the post-operative analgesic requirements. Pain has got long term behavioural changes in children. Various studies showed that the effect of analgesia might vary between patients, which depend on the type of the surgery, patient's age, type and volume of the local anesthetic agent.

Our study shows that a single pre-surgical caudal injection of bupivacaine after induction of anesthesia provides good quality of analgesia both during intraoperative period and the postoperative period than levobupivacaine and ropivacaine in patients undergoing infraumbilical surgeries.

POSTOPERATIVE ANALGESIA:

Locatelli et al[12] compared 0.25% bupivacaine, levobupivacaine, ropivacaine in a dose of 1ml/kg for orchidopexy and hernia repair. For phimosis 0.5ml/kg was used. They reported that bupivacaine had longer analgesic effect than other two drugs. In our study we compared the similar drugs in the same concentration and as standardized procedure all patients received 1ml/kg of the test drug. The results from our study are comparable with views supported by Locatelli et al. in terms of postoperative analgesia.

Kaya z et al[13] studied 0.25% of bupivacaine, levobupivacaine for sub-umbilical surgeries in a dose a 0.5ml/kg. He found that bupivacaine produced significant analgesia when compared with levobupivacaine. These results were similar to the results of our study.

Breschnan et al compared 0.20% of bupivacaine, levobupivacaine, and ropivacaine in a dose of 1ml/kg for infraumbilical surgeries he found that there was no significant difference in the post-operative analgesia provided. Pablo M Ingelmo[14] et al also compared similar drugs who found that there was no significant difference between the study drugs in terms of analgesia but the effectiveness of caudal block was more with bupivacaine and levobupivacaine than ropivacaine. Astuto et al[15] also found no significant difference between 0.25% levobupivacaine, and ropivacaine in terms of mean duration of onset of caudal block and time of first analgesic administration.

G Ivani et al[16,17] did two different studies comparing levobupivacaine and ropivacaine. In one study he compared 0.20% ropivacaine and 0.25% levobupivacaine and in the other he compared 0.20% ropivacaine and 0.20%levobupivacaine where he found that there was no significant difference between the mean time of onset of the caudal block and time of first analgesic administration.

In contrary to our study, Manjushree et al[18] when comparing 0.25% bupivacaine and ropivacaine found that ropivacaine provided effective analgesia and less motor block than bupivacaine.

Dobereiner et al[19] showed in his study that there was no difference seen with the use of high dose of local anesthetic agents on the quality of postoperative analgesia.

G.Ivani et al found that the mean onset time of caudal 0.20% ropivacaine was 9 min with that of 12 min for 0.25% bupivacaine. Since our aim was not to compare the onset times, we used a fixed time of 10min after caudal block for incision for all the groups. In our study, this was found to be adequate for all the test drugs, with no child requiring fentanyl supplementation.

RESIDUAL MOTOR BLOCK:

Different studies have shown that postoperative motor block intensity and duration varies. With regard to this, Locatelli et al[12] and Ivani et al[16,17] in their investigations found that bupivacaine had longer duration of motor blockade when compared to levobupivacaine, but this effect was reduced in the subsequent hours of follow up.

Breschann et al[20] in their investigations compared levobupivacaine, ropivacaine, and bupivacaine and found that ropivacaine and levobupivacaine had lower motor block than that of bupivacaine in the first two hours but this difference was lost after two hours. Kaya z et al[13]

had also reported similar results in his studies where they compared levobupivacaine and bupivacaine, bupivacaine caused more duration of motor blockade and there was no residual motor block in both the groups after 150 minutes.

Our study results were comparable to the above studies, where bupivacaine produced a longer duration of motor blockade than levobupivacaine and ropivacaine.

In contrary to the above studies, Ingelmo et al compared the effects of ropivacaine 0.2%, bupivacaine 0.2% and levobupivacaine 0.2% on motor block, similar results were obtained for all groups in terms of motor block both during wakeup and after waking up.

Frawley et al[21] reported that there was no significant difference between groups in terms of motor block in their study where they compared 1 ml/kg of bupivacaine 0.25% and levobupivacaine 0.25%. After 150 min there was no residual motor blockade observed between the groups. There are studies that showed that motor block is proportional to the dose of the local anesthetic used.

Only one child in ropivacaine and two children in levobupivacaine group had vomiting postoperatively that was treated with Inj. Ondansentron 0.01mg/kg i.v. This may be due to the effects of general anesthetics.

SUMMARY

Bupivacaine is the most commonly used local anesthetic for caudal anesthesia in children that provides reliable and long-lasting anesthesia and analgesia. Ropivacaine and levobupivacaine are newer local anesthetic agents which provides pain relief lesser than that of bupivacaine with less motor blockade.

The aim of the study was to compare Caudal levobupivacaine 0.25%, Caudal Bupivacaine 0.25%, and Caudal Ropivacaine 0.25% in terms of the quality and duration of analgesia, motor and sensory block for infra-umbilical surgeries.

In a randomized double-blinded comparative study, 90 children aged 2-8 years of ASA I physical status were randomly allocated to receive a single presurgical caudal injection of 1ml/kg of either Caudal levobupivacaine 0.25%(Group I) or 0.25% Bupivacaine (Group II) or 0.25% Ropivacaine (Group III) after induction of anesthesia. Apart from monitoring the vital parameters, all children were assessed for postoperative analgesia by Modified Hannallah pain scale and for motor blockade by Motor power score.

The groups were comparable for age, sex, weight, height, vital signs, duration and type of surgery. The quality and duration of postoperative pain relief between the groups were 130.33$\pm$11.74 min in Group I, 182.83$\pm$12.64 min in Group II and 110.17$\pm$8.66 in Group III with a $P<0.001$. The time to full motor recovery was significantly less in ropivacaine group than in levobupivacaine and bupivacaine group. In Group I(180.17$\pm$22.76 min), in Group II(239.00$\pm$21.55 min) and in Group III(162.00$\pm$20.24 min) with a $P<0.001$.

Postoperative vitals were stable in all the children. Apart from minor adverse events such as nausea and vomiting, no major adverse events were observed.

CONCLUSION

We conclude that in our randomized, prospective, double blinded study comparing Caudal Bupivacaine 0.25%, Levobupivacaine 0.25%, Ropivacaine 0.25%, for post-operative analgesia, Caudal Bupivacaine 0.25% in a dose of 1ml/kg provided reliable and long lasting analgesia when compared to Levobupivacaine 0.25%, and Ropivacaine 0.25% in children undergoing infra-umbilical surgeries The faster recovery of motor block occurred in Levobupivacaine 0.25% and Ropivacaine 0.25% Group when compared to Bupivacaine Group

Acknowledgement:

We are very grateful to the professors and assistant professors of the Department of Paediatric Surgery. We are extremely thankful to the assistant professors and the postgraduates of the Department of Anaesthesiology for their help in carrying out this study.

We are thankful to the institutional ethical committee for their guidance and approval for this study. Last but not the least we thank all our patients for willingly submitting themselves for this study. We also wish to state that no financial or material support was obtained for this study.

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