Original Research Article

A Clinical Comparison between Plain Ropivacaine V/S Ropivacaine and Clonidine by Caudal Route for Post Operative Analgesia in Children

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Abstract

Background and objectives: Addition of clonidine to ropivacaine (0.25%) can potentially enhance analgesia without producing prolonged motor blockade. The aim of the present study was to compare the post-operative pain relieving quality of ropivacaine (0.25%) and clonidine mixture to that of plain ropivacaine (0.25%) following caudal administration in children.**Method:** After careful pre-anaesthetic check-up children posted for elective sub- umbilical surgeries between age groups of 2-10yrs of ASA I & II were randomly divided into Groups R and RC, of 30 each, injected with Inj. Ropivacaine 0.25% (1ml/kg body weight) and Inj. Ropivacaine 0.25% (1ml/kg) and Inj. Clonidine (2 mcg/kg) combination through caudal respectively prior to start of surgery after induction. Intra-op and post-operative duration of analgesia and motor blockade were noted along with other vital parameters.**Results:** Significantly prolonged duration of post operative analgesia was observed in Group RC. Heart rate and blood pressure was statistically different but not clinically. Neither motor blockade nor post operative sedation varied significantly between the groups.**Conclusion:** The combination of clonidine 2 mcg/kg and ropivacaine 0.25% 1ml/kg was associated with an improved quality of post-operative analgesia compared to plain ropivacaine 0.25% 1 ml/kg. The improved quality and duration of analgesia of the ropivacaine - clonidine mixture was achieved without causing any significant adverse effects or prolongation of motor blockade.

Keywords: Clonidine; Ropivacaine; Caudal; Motor blockade; Analgesia.

Introduction

The provision of adequate analgesia is necessary during peri-operative period and it is all the more important in children.[1]There is a well-defined pathway for sensation in the new-born infant. Nociception is associated with signs of distress even in new-born.[2] The density of nociceptive nerve endings in the skin of new-born infants is similar to or greater than that in adults[3,4].Pain after surgery is inevitable. Relieving pain has been the focus of continuing human effort. However, it has been recognised for some time that the management of acute pain, especially postoperative pain, has been consistently inadequate. If anything, the situation in children has been even worse, who have long been under-medicated for acute pain[3].Bupivacaine is a well-established local anaesthetic agent, first of long acting to be used. Ropivacaine is a pure S-enantiomer. Both the drugs possess similar structure, pharmacology, mechanism of action and physiochemical properties. However, Ropivacaine is believed to have lower incidence of clinical cardiac side effects than Bupivacaine[5] and also has lesser motor blockade compared to Bupivacaine[6].

The potential use of a local anaesthetic agent that could produce equal or greater degree of analgesia with lesser toxicity has prompted the present study.

The use of an additive like Clonidine further helps in reducing the concentration of local anaesthetic and thereby likelihood of toxicity and prolongs the duration of analgesia.

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Our study aims at comparing local anaesthetic Ropivacaine with Ropivacaine and Clonidine combination with respect to quality and duration of post operative analgesia.

Aim & Objectives of the present study

To study and compare the effect of caudally administered Ropivacaine 0.25% (1ml/kg) alone and Ropivacaine 0.25% (1ml/kg) with Clonidine 2 mcg/kg combination in children between 2- 10 yrs, with respect to following parameters:

1. Duration of sensory and motor blockade
2. Quality of analgesia
3. Adverse effects if any.

Materials and Methods

This study was conducted at NRI Medical College, Guntur from October 2018 to October 2019.

Study included 60 children of either sex posted for various sub-umbilical surgical procedures such as inguinal herniotomy, appendectomy, circumcision, orchidopexy, perineal surgeries and urological procedures.

Inclusion citeria

1. Elective sub-umbilical surgeries
2. Age: 2 to 10 yrs, of either sex.
3. ASA grade I & II

Exclusion citeria

1. Emergency cases.
2. Documented allergies to any drugs, especially local anaesthetics.
3. Any abnormalities of spine or meninges
4. Infection at caudal region.
5. Coagulopathy
6. ASA grade III & IV

This study was approved by the Ethics and Standards committee of this institution. Informed consent was obtained from the parents before including the children in the study.

Armamentarium for caudal procedure:

1. 23G needle, 22G 1 inch hypodermic needle.
2. 2 cc syringe (for whoosh test)
3. 5 cc and 10 cc syringes for drug administration.
4. Sterile swabs, bowl, sponge holding forceps, hole towel, betadine paint and spirit.
5. Drugs— Ropivacaine 0.25%, Clonidine, sterile water for dilution of drugs.
6. Anaesthesia work-station.
7. Jackson Rees circuit.
8. Patent I.V line with infusion set

Methods

Pre-anaesthetic check-up

All patients were evaluated one day prior to the surgery with a detailed general physical examination, systemic examination including airway and spine examination. Baseline parameters like heart rate were recorded. Routine laboratory investigations like complete blood picture, urine routine, bleeding and clotting time, HIV HBs Ag status and chest x-ray if needed. Informed consent for the procedure was acquired from the parent with clear fasting guidelines (solid foods stopped 6hrs before, milk 4 hours and water 2-3 hours prior to surgery).

Pre-medication: All children were pre-medicated with oral or nasal midazolam 0.5 mg/kg 30 minutes before surgery.

Monitoring: On arrival into operation theatre, monitors viz pulse oxy-meter, ECG leads and NIBP cuff were connected and baseline parameters were noted.

Procedure

Child was induced with gas, oxygen and volatile agent using Jackson-Ree‘s circuit. 22G I.V cannula was secured. Inj. Glycopyrrolate 0.01mg/kg followed by Inj. Fentanyl 2µg/kg was injected. I.V infusion of ringer lactate was started and fluid administered as per calculated requirements.

Caudal block: Child was put in lateral semi-flexed position. Vitals were recorded with child in spontaneous breathing under mask ventilation. Under strict aseptic precautions, sacral hiatus was identified by running thumb from superior sacral spines towards coccyx.After identifying sacral hiatus, a 22G hypodermic needle with its bevel facing anteriorly was inserted at 45-70 degrees angle till sacrococcygeal membrane was pierced with a clear pop. Confirmation of needle position in epidural space is done with the _whoosh‘ test. After negative aspiration to CSF and blood drug was injected.After injection, needle was removed, site of injection was wiped with betadine swab and child was placed in supine position. There on anaesthesia was maintained with Oxygen, Nitrous oxide and inhalational agent with patient on spontaneous ventilation throughout surgery.

Drug & dosage: Children were randomly divided into 2 groups of 30 each.

- Group R —Ropivacaine 0.25% 1ml/kg into caudal epidural space.
- Group RC—Ropivacaine 0.25% 1ml/kg and Clonidine 2mcg/ kg into caudal epidural space.

Monitoring: Monitoring included pulse-oximetry, NIBP, ECG and respiratory rate. Time of caudal block was noted.

Recovery: Anaesthetic agents were discontinued at the beginning of skin closure. 100% oxygen was administered through face mask. Once the child was awake and vitals were stable, child was sifted and placed in lateral position in recovery room. On arrival to recovery room, child was monitored for another one hour with pulse oximetry and NIBP every 15minutes. After that child was shifted to ward and monitored thereafter.

Parameters studied: Hemodynamic parameters: Child‘s heart rate, blood pressure and respiratory rate after administration of caudal block at 0, 5, 10, 15, 30 minutes and there on every 15 minutes till end of procedure were recorded.

Duration: time of caudal injection, duration of anaesthesia, duration of sensory and motorblockade and time of first dose of rescue analgesia post-operatively were noted.

Motor block was assessed on awakening by using a modified Bromage scale that consisted of 4 points:

0 = full motor strength (flexion of knees and feet), 1 = flexion of knees,

2 = little movement of feet only,

3 = no movement of knees or feet. However, younger children who could not move their legs on command were stimulated by tapping on the legs and feet.

Pain scores were assessed post-operatively after recovery by anaesthesiologist and then by a single person at 1, 2, 4, 8 and 12 h with a 5-point observer pain score (OPS):

1 = asleep or awake and laughing 2 = awake, but no pain

3 = mild pain (irritable/restless)

4 = moderate pain (crying, grimacing restless but consolable) 5 = severe pain (crying/screaming/inconsolable).The duration of absolute analgesia was defined as the time from caudal injection until the pain score was > 2. Rescue analgesic was given for a pain score=/>4.Post-operatively analgesic rescue dose was given based on visual and verbal analogue score with ibuprofen and paracetamol syrup.

Side effects

Children were monitored for any intra or post-operative complications. Hypotension: Defined as a decrease in mean arterial pressure of greater than 30% of baseline value. Treated with IV infusions and Inj. Ephedrine 0.1-0.3 mg/kg.Nausea and vomiting-any episode noted.Any other sequelae like urinary retention were noted.

Statistical analysis

The results of continuous variables are given as mean ± SSD and preparation as percentage. The difference between the two groups was assessed by student‘s _T‘ test and chi-square test. For all the tests a _p‘ value of 0.05 or less was considered for statistical significant.

Results and Observations

A total of 60 children in age group of 2-10 years belonging to ASA I & II were enrolled in this study. They were divided into two groups:

- Group R : received caudal injection ropivacaine 0.25% (1ml/kg)
- Group RC: received caudal injection ropivacaine 0.25% (1ml/ kg) and clonidine (2mcg / kg) combination.

Table 1:Age Distribution

Age in years	Ropivacaine with Clonidine		Ropivacaine	
	No	%	No	%
1-2	2	6.7	2	6.7
3-5	18	60	14	46.7
6-10	10	33.3	14	46.7
Total	30	100	30	100
Mean SD	4.83 ± 2.00		5.36 ± 2.22	

Mean age in Group RC was 4.83 ± 2.00 and in Group R was 5.36 ± 2.22. Samples are matched with p>0.34, i.e. did not differ significantly with respect to their age.

Table 2: Gender Distribution

Gender	Ropivacaine with Clonidine		Ropivacaine	
	No	%	No	%
Male	29	96.7	29	96.7
Female	1	3.3	1	3.3
Total	30	100	30	100

Samples are gender matched with p>0.10.

Table 3: Weight Distribution

Weight	Ropivacaine with Clonidine		Ropivacaine	
	No	%	No	%
1-10	7	23.3	3	10
11-20	22	73.3	26	86.7
21-30	1	3.3	1	3.3
Total	30	100	30	100
Mean SD	12.83 ± 3.23		14.2 ± 3.33	

The weight of the children in Group RC was 8-22 kgs, with a mean weight of 12.83±3.23. In Group R weight ranged from 8-25 kgs with mean weight being 14.2 ± 3.33. The two groups did not differ significantly with respect to the weight (P>0.83)

Table 4: Types of Surgical Procedures

Surgery	Ropivacaine withClonidine		Ropivacaine	
	No	%	No	%
Herniotomy	18	60	15	50
Hypospadiasis Repair	2	6.7	4	13.3
Orchidopexy	4	13.3	4	13.3
Circumcision	6	20	6	20
Open Appenicectomy	0	0	1	3.3
Total	30	100	30	100

The different surgical procedures performed during the study in the two groups are shown in table 4.In our study herniotomy accounted for 18 (60%) of cases in Group RC and 15(50%) in Group R. Circumcision accounted for 6 (20%) in Group RC and 6 (20%) in Group R. Orchidopexy accounted for 4 (13.3%) in both Group RC and Group R, whereas Hypospadiasis repair accounted for 2(6.7%) in Group RC and 4(13.3%) in Group R. One appendicectomy was done in Group R.

Table 5: Heart Rate

Heart Rate	Ropivacaine withClonidine	Ropivacaine	P Value
Baseline	105.20 ± 4.25	103.83 ± 6.41	0.03
0 mins	100.33 ± 4.10	100.03 ± 6.59	0.29
5 mins	96.0 ± 4.16	96.10 ± 6.03	0.03
15 mins	91.60 ± 4.46	93.23 ± 5.40	0.37
30 mins	87.46 ± 4.09	90.60 ± 5.82	0.17
45 mins	85.06 ± 2.91	89.86 ± 4.61	0.01
1 hr	83.06 ± 1.94	88.43 ± 4.93	0

In Group RC the mean baseline heart rate was 105.20±4.25 which gradually decreased to 83.06 ± 1.94 by the end of 1 hour from caudal administration. In Group R the baseline heart rate was 103.83 ± 6.41 which gradually decreased to 88.43 + 4.93 at the end of 1 hour from caudal administration.And there was significant difference in heart rate at the end of 1 hour (p=0) as shown in table 5.

Table 6: SBP

SBP	Ropivacaine with Clonidine	Ropivacaine	P Value
Baseline	88.60 ± 1.49	90.26 ± 4.60	0
0 mins	85.73 ± 2.81	87.93 ± 4.31	0.17
5 mins	84.13 ± 2.09	85.53 ± 3.81	0.01
15 mins	83.53 ± 1.63	85.06 ± 3.62	0
30 mins	83.13 ± 2.55	84.73 ± 3.68	0.37
45 mins	82.46 ± 1.71	85.06 ± 3.62	0.001
1 hr	81.86 ± 2.02	84.86 ± 3.30	0.003

In Group RC mean SBP was 88.60 ± 1.49. It decreased gradually to 81.86 ± 2.02 by the end of 1 hour. In Group R mean SBP was 90.26 ± 4.60. It gradually decreased to 84.86 ± 3.30 by the end of 1 hr. At the end of 1 hour there was significant difference in the mean SBP between both groups (p=0.003)

Table 7: DBP

DBP	Ropivacaine with Clonidine	Ropivacaine	P Value
Baseline	51.93 ± 4.25	53.40 ± 6.03	0.004
0 mins	47.73 ± 3.88	50.86 ± 6.39	0.001
5 mins	45.20 ± 2.49	48.60 ± 5.12	0
15 mins	43.60 ± 2.06	47.86 ± 4.16	0.001
30 mins	43.33 ± 2.24	47.93 ± 4.62	0.002
45 mins	43.00 ± 3.00	48.26 ± 4.44	0.31
1 hr	42.26 ± 1.46	47.63 ± 4.07	0

In Group RC mean DBP was 51.93 ± 4.25. It gradually decreased to42.26±1.46 by the end of 1 hour. In Group R mean DBP was 53.40±6.03. It gradually decreased to 47.63 ± 4.07 by the end of 1 hour. At the end of 1 hour there was significant difference in the mean DBP between both groups (p=0).

Table 8: Duration of Surgery

Duration of Surgery (in mins)	Ropivacaine withClonidine		Ropivacaine	
	No	%	No	%
<30	6	20	6	20
30-50	20	66.7	19	63.3
>50	4	13.3	5	16.7
Total	30	100	30	100
Mean SD	40.83 ± 13.52		41.83 ± 14.70	

Surgeries in both groups lasted for 25-80 minutes with a mean in Group RC 40.83±13.52 minutes and those in Group R 41.83 ± 14.70 minutes.

Table 9: Pain Scale in Two Groups of Patient Studied

	Ropivacaine with Clonidine	Ropivacaine	P Value
Immediate	1.00 ± 0.00	1.00 ± 0	
1 hr	1.00 ± 00	1.13 ± 0.34	0
2 hr	1.40 ± 0.49	2.10 ± 0.30	0
3 hr	2.00 ± 0	2.16 ± 0.37	0
4 hr	2.00 ± 0	3.10 ± 0.30	0
8 hr	3.00 ± 0	4.06 ± 0.36	0.002
12 hr	4.33 ± 0.47	4.63 ± 0.55	0.41

Pain scores at various time intervals is depicted in the following charts. The was significant difference between Group RC and Group R at 1st, 2nd, 3rd and 4th hour as the p value equals zero. Pain scores at the end of 8th hour in Group RC is 3.00 ± 0 and in Group R is 4.06 ± 0.36. Thus it shows significant difference (P=0.002).

Table 10: Motor Blockade in Two Groups of Patients Studied

	Ropivacaine with Clonidine	Ropivacaine	P Value
Immediate	1.63 ± 0.14	1.50 ± 0.50	0.14
1 hr	1.66 ± 0.47	1.63 ± 0.49	0.59
2 hr	1.16 ± 0.37	1.10 ± 0.30	0.13
3 hr	0.76 ± 0.43	0.70 ± 0.46	0.25
4 hr	0	0	0

Motor blockade at various intervals: Immediate post recovery motor blockade in Group RC as expressed in modified scale was a mean value of 1.63 ± 0.14 and in Group R was 1.50 ± 0.50. The difference of motor blockade between groups were insignificant (p value = 0.14). The motor blockade at the end of 4th hour was zero in both groups.

Table 11: Duration of Caudal Analgesia in Two Groups of Patients Studied

Time of rescueanalgesia	Ropivacaine with Clonidine	Ropivacaine
Mean SD	544.83 ± 12.83	268.00 ± 10.22

Duration of caudal analgesia was calculated as time from caudal injection administration to rescue analgesia administration. It was a mean value of 544.83 ± 12.83 minutes in Group RC and 268 ± 10.22 minutes in Group R.

Table 12: Adverse Effects in Two Groups of Patients Studied

Adverse effects	Ropivacaine withClonidine		Ropivacaine	
	No	%	No	%
NIL	27	90	28	93.3
Urinary retention	3	10	2	6.6
Total	30	100	30	100

Urinary retention was noticed in 3 patients in Group RC and in 2 patients in Group R. No other side effects were noted in either of groups.

Discussion

Caudal epidural block has been a popular technique to provide intra and post- operative analgesia in children as it is easy to perform and safe. Ropivacaine is being increasingly used even in pediatric age group by caudal route because of its less motor blockade and systemic toxicity[7,8].Clonidine is an alpha-2 adrenoceptor agonist, which was widely used as an anti-hypertensive in 70‘s and 80‘s and presently it has been increasingly used for sedation, premedication and as an adjuvant to local anesthetics in neuraxial block. [9]Co-administration of clonidine with local anesthetics has shown to improve the quality of peripheral nerve block[10].

Ivani G et al reported that 2ml/kg of 0.2% ropivacaine is sufficient to obtain sensory block for lower abdominal or for genital surgery in children. Pharmacokinetic studies of ropivacaine shows that 1ml/kg 0.25% of ropivacaine by caudal route produces a maximal plasma concentration of 0.72 ± 0.24 mg/lit, which is much lower than the maximal tolerated plasma concentration of ropivacaine in adult volunteers (2.2 ± 0.8mg/lit)[12]. Therefore, we have chosen 0.25% 1ml/kg ropivacaine[11].In our study, we have seen that caudal ropivacaine alone provided excellemt analgesia in early post operative period, but the effect wore off a few hours (268 ± 10.22 mins) after an operation, and supplemental analgesics were required. An addition of clonidine prolonged analgesia significantly (544.83 ±

12.83 mins). There was no significant prolongation of motor blockade with addition of clonidine.Regarding hemodynamics, we did observe significant difference in mean HR, SBP, DBP between the two groups which shows discordance to the study result obtained by Sukhminder Jit Singh Bajwah et al but this difference was clinically insignificant. There was no undesirable side effects like hypotension and bradycardia.No difference was found regarding post operative sedation between two groups, which matched with our study.

Da Conceicao & Coelho reported a significantly shorter duration of motor block with 0.375% ropivacaine as compared to bupivacaine, which matched with our study[14].

Bajwa et al found in a study that caudal block with 0.25% of isobaric ropivacaine 0.5ml/kg combined with 2 mcg/kg of clonidine provides efficient analgesia intraoperatively and prolonged duration of analgesia postoperatively[13]

Coming to adverse effects, the only adverse effect we encountered was urinary retention which was comparable in both the groups. We did not encounter any nausea and vomiting as encountered by other studies possibly due to shorter duration of surgery and hence lesser exposure to nitrous oxide and thus, cannot be commented about with respect to the drugs.There are some limitations of our study. First it had a small sample size. ASA 1 and 2 might be another limitation of the study, because the cardiovascular effects are more pronounced or easier to see with children having heart disease and high ASA grade.

Nevertheless, this study confirms that addition of clonidine to ropivacaine increases the duration and improves the quality of post operative analgesia without causing any significant adverse effects.

Conclusion

This study suggests that addition of clonidine (2 mcg/kg) as an adjuvant to 0.25% ropivacaine (1 ml/kg) through caudal route increases the duration of post operative analgesia without unnecessary prolongation of motor blockade or production of any other adverse effects.

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