

CLINICAL EVALUATION OF CLONIDINE AS AN ADJUNCT TO CAUDAL ROPIVACAINE IN PEDIATRIC INFRAUMBILICAL SURGERIESUrmila Keshari¹, Sonal Awasya², Tripti Vatsalya³**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND: The addition of clonidine as an adjuvant has allowed the use of lower concentration of the local anaesthetic for achieving the same level of anaesthesia but with the prolonged duration of analgesia which increases the margin of safety and reduces the incidence of unwanted motor blockades. With these facts in mind we undertook the study to compare the analgesic properties of 0.25% ropivacaine with the addition of clonidine (1µg/kg) to that of ropivacaine 0.25% following caudal administration in children. **METHODS:** After approval from ethical committee 60 children of age 1-10 yrs of ASA grade I or II undergoing elective sub umbilical surgeries were selected for the study. We gave caudal block with 0.25% ropivacaine 1ml/kg+1ml normal saline for group R or 0.25% ropivacaine 1ml/kg + clonidine 1microgram/kg+1ml normal saline to make volume 1ml for group C. To perform caudal block all patient received IV injection glycopyrolate- 0.01mg/kg, IV injection midazolam- 0.1mg/kg and IV Injection ketamine-1mg/kg. Hemodynamic parameters were observed before, during and after the surgical procedure. Quality of surgical anesthesia & requirement of supplemental midazolam/ketamine were also noted. Duration of Post-operative analgesia, pain scores, level of sedation and side effects if any were looked for and duly recorded. **RESULT:** Duration of analgesia in group R was 6.45±0.52 hrs. and in group C was 13.01±0.89hrs i.e. significantly prolonged in group C (P<0.0001). Post-operative pain score and sedation score were also significantly better in group C (P<0.0001). The quality of surgical analgesia was also significantly excellent in group C. Other vital parameters were not statistically significant in both the groups. **CONCLUSION:** Ropivacaine (0.25%) with clonidine (1µg/kg) in caudal block showed prolong duration of analgesia as well as better quality of surgical anaesthesia than plain ropivacaine (0.25%) in pediatric patients without any significant side effects.

KEYWORDS: Caudal, Clonidine, ropivacaine, pediatric analgesia.

INTRODUCTION: Caudal epidural technique is one of the most popular, reliable, safe and easy method for intra operative and post-operative analgesia especially for sub umbilical surgeries in young children. But its main disadvantage is short duration of action after single injection even with a long acting local anaesthetic.¹ Prolongation of caudal analgesia has been achieved by the addition of various additives. Caudal analgesia could reduce the amount of inhaled and intravenous (IV) anesthetic administration, attenuate the stress response to surgery, facilitate a rapid, smooth recovery, and provide good immediate postoperative analgesia.²

Ropivacaine is one such drug that appears to be associated with a greater safety margin and reduced systemic toxicity. In adults it has been reported to cause less motor block and less cardio toxicity than bupivacaine and produces a similar duration of analgesia.^{3,4} The lower incidence of cardiovascular side effects and neurotoxicity as well as the ability to produce lesser motor blockade has made the ropivacaine a safer choice as compared to bupivacaine for caudal epidural anaesthesia

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especially for day care surgeries.^{5,6} A preliminary evaluation of ropivacaine for caudal analgesia in children suggested increased margin of safety particularly in children.⁷

Clonidine is an imidazoline derivative with alpha 2 agonist activity has been used for sedation, premedication.^{8,9} It is being used nowadays for potentiating the analgesic action of various local anaesthetics administered regionally. It has been used safely in the younger age group for caudal epidural analgesia.^{10,11} After administration into the subarachnoid or epidural space, clonidine provides a substantial antinociceptive effect by acting on the alpha 2 receptors in the dorsal horn of spinal cord and brain stem nuclei implicated in pain. Clonidine has sedative property and it is often a desirable feature by reducing the requirement of hypnotics.^{12,13}

The main interest of our study was to evaluate the clinical efficacy of caudal clonidine when combined with the 0.25% solution of ropivacaine in children undergoing sub umbilical surgeries; in terms of quality of surgical anesthesia and the duration of post-operative analgesia. To observe the side effects if any.

MATERIAL AND METHODS: After taking the institute ethics committee approval, 60 children of American Society of Anesthesiologist (ASA) physical status I and II of either sex in the age range of 1 to 10 years scheduled for elective sub umbilical surgical procedures were selected for this study.

Exclusion criteria included: Patients with infection at site of injection, neurological diseases, and neurological deficits, bleeding disorders, skeletal deformities, systemic infection, bleeding disorder, hepatic or renal disease and any known allergic diathesis.

During the preoperative visit, all patients were evaluated and assessed. The study protocol was explained to the parents and written informed consent was taken from them. It was a Double blinded study. The anesthesiologist administering anesthesia and doing data collection were blinded to the drug administered. The drugs were prepared and coded by anesthesiologists who were not involved in patient management or data collection.

In the operation theatre after connecting the patient to the monitors, an intravenous line was established. Patients were hydrated with a multiple electrolytes infusion 6ml kg / hr. all patients received following drugs:

Injection Glycopyrrolate- 0.01 milligram per kilogram,

Injection midazolam- 0.1 milligram per kilogram,

Injection ketamine- 1 milligram per kilogram.

Patients were randomly allocated to one of the two groups of 30 patients each.

GROUP R (n=30): Caudal with 0.25% Ropivacaine (1ml/kg) +1 ml Normal saline.

GROUP C (n=30): Caudal with 0.25% Ropivacaine (1ml /kg) with clonidine.

(1 microgram/kg) + Normal saline to make volume 1ml.

Caudal block was performed under all aseptic precautions, using 23 G hypodermic needle, after negative aspiration either 0.25% ropivacaine (1ml/kg)+1ml Normal saline i.e. group R or 0.25% ropivacaine (1ml/kg) with clonidine (1 micg/kg)+1ml Normal saline i.e. group C was administered.

No surgical stimulus was allowed for the next 10 mins i.e. the onset time for sensory block to occur, after which surgery was performed under the residual effect of ketamine and caudal block only.

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Pin prick method was used to assess the level of sensory anesthesia and the Bromage Scale for assessing the degree of motor blockade. If a child responded to the incision with an increase in heart rate (>10 beats/min) was considered as inadequate block. These patients were received supplemental doses of ketamine + midazolam.

Heart rate, SPO₂, ECG were recorded throughout the operation at an interval of five minutes. In PACU, vital parameters, severity of pain and sedation was recorded at an interval of one hour. Quality of surgical anesthesia & requirement of supplemental Midazolam / Ketamine were also noted.

Quality of Surgical Anesthesia was assessed as:

1. **Excellent:** if no response to surgical stimulus.
2. **Good:** if patient showing sad facial expressions & moving upper half of body, but is allowing surgery without pain/cry; & requires supplemental Inj. midazolam for sleep.
3. **Poor:** not allowing surgery at all & requires supplemental dose of Inj. ketamine and midazolam for anaesthesia.

Level of Sedation:

Sedation was assessed by 4 point scale.¹⁴

1. Barely arousable (Sleep, needs shaking or shouting to arouse)
2. Asleep (Eyes closed, arousable with soft voice or light touch)
3. Sleepy (Eyes open but less active and responsive)
4. Awake.

The sedation score was used to quantify sedation and to help to identify side effects, such as respiratory depression from excess sedation.

Pain was assessed by CRIES scale.¹⁵

	0	1	2
Crying	No	High pitched	Inconsolable
Requires O ₂ for SPO ₂ >95%	No	< 30% of O ₂	> 30% of O ₂
Increased vital Signs	No increase in HR and MAP	Increase in HR and MAP < 20%	Increase in HR or MAP >20%
Expression	None	Grimace	Grimace / Grunt
Sleepless	No	Wakes at Frequent Intervals	Constantly awake

Table 1: Cries Scale

A score of 0 signifies excellent analgesia whereas a score of 10 indicates ineffective analgesia. Patients were given rescue analgesia (syrup paracetamol 15 mg/kg) when pain score is 4 or more.

The time in minutes from the caudal block to the time when rescue analgesic was first administered was considered duration of analgesia.

All the above assessments were made at 30 min interval for 1st hr., At 1 hourly interval for next 6 hrs. At 8th, 12th, 24th hour., Side effects if any, were duly recorded.

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After completion of the study, the data was analyzed statistically. Data was described as mean±SD and percentages. The intergroup comparisons for the data were done by unpaired T test and the p values <0.0001 were considered statistically significant.

RESULTS: We studied 60 children that were randomly selected 30 each in group.

	Group R	Group C	P value
Age (yrs.)	4.5±1.8	3.8±2.2	0.12 (>0.0001)
Weight (kg)	14.3±3.8	15.1±2.7	0.35 (>0.0001)
Height (cm)	95±4.2	96.2±1.9	0.15 (>0.0001)
Gender distribution (M/F)	22/8	24/6	-
Surgical duration (mins)	34.4±14.3	38.9±16.3	0.26 (0.0001)

Table 2: Demographic Profile in both the groups did not show any significant variations

Duration of analgesia in group R was 6.45±0.52 hrs. and in group C was 13.01 ±0.89 hrs. which is statistically extremely significant. (P value <0.0001)

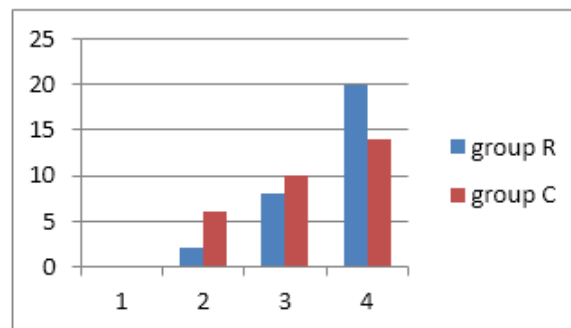


Fig. 1: Sedation score comparison in both the groups

Sedation score was 3.6±0.33 in group R and 3.26±0.24 in group C statistically extremely significant (P value < 0.0001).

	Group R	Group C	P value
Pre-operative HR	116.3 ±13.6	118.4 ±12.6	0.53 (>0.0001)
Intraoperative HR	103.4± 8.2	101.5 ±5.03	0.28 (>0.0001)
Postoperative HR	96.4 ±4.5	94.6± 8.6	0.31 (> 0.0001)
Pre-operative SpO ₂	97 ±2.38	97 ±2.4	1.0 (>0.0001)
Intraoperative SpO ₂	98 ±1.48	98± 1.54	1.0 (>0.0001)
Postoperative SpO ₂	96 ±1.89	96 ±2.43	1.0 (>0.0001)

Table 3: Vital Parameters

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	Group R	Group C
Excellent	10	20
Good	18	09
Poor	02	01

Table 4: Quality of Surgical Analgesia

	Group R	Group C
Not required	5	18
Single dose in 24 hrs.	12	09
Second dose in 24 hrs.	13	03

Table 5: Rescue Analgesia required in both groups are

Time intervals when pain score >4	Group R	Group C
2 hrs.	02	01
4 hrs.	00	00
6 hrs.	18	00
8 hrs.	10	00
10 hrs.	00	09
12 hrs.	00	20

Table 6: Pain Score > 4 at different time interval prior to rescue analgesia

In our study, we used clonidine in the dose of $1\mu\text{g kg}^{-1}$ along with 0.25% ropivacaine and did not observe significant incidence of side effects like bradycardia and hypotension

DISCUSSION: Since its first description by Campbell in 1933.¹⁶ for pediatric urological interventions, caudal block has evolved to become the most popular regional anaesthetic technique for use in children.

One of the major limitations of the single-injection technique is the relatively short duration of postoperative analgesia (4–6 h) even with the long-acting local anaesthetics. And to further prolong post op analgesia most frequently used method is to add different adjuncts to local anaesthetics. Several local anaesthetic agents (e.g. bupivacaine, ropivacaine etc.) have been used for caudal block.

The efforts to use the relatively safer drugs and lower concentration are growing day by day. Ropivacaine is one such drug that appears to be associated with a greater safety margin and reduced systemic toxicity although such toxicity has been reported in adults following various regional anaesthetic techniques.^{3,4} Clonidine is an effective adjuvant to local anaesthetic agents when administered for caudal block. Addition of clonidine has been found to increase the duration of analgesia without any increase in the side effects.¹⁷

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The duration of study was 24 hours, to assess the maximum duration of analgesia provided by clonidine and local anesthetic Ropivacaine combination. Ropivacaine when used in a reduced concentration below 0.2% in children is hardly effective and that is the reason we adhered to a concentration of 0.2%.¹⁷ And clonidine 1 mg/kg-1 as there is no added advantage of increasing the dose of clonidine to 2 mg/kg-1 from 1 mg/kg-1 Klimscha et al also concluded from their study that the analgesic efficacy does not seem to be enhanced by increasing the dose of clonidine from 1 mg/kg-1 to 2 mg/kg-1. In a study by Upadhyay and Colleagues,¹⁸ they used 1µg/kg-1 of clonidine as adjuvant with 0.25% bupivacaine in children undergoing sub umbilical surgery and observed a significant prolongation of postoperative analgesia without any significant incidence of side effects.

Klimscha et al. had studied the effectiveness of caudal clonidine in potentiating the post-operative analgesic effect and found that in small children with a mean age of 3 years who underwent an elective day care surgery for hernia operations, the addition of clonidine 1–2 µg/kg to bupivacaine 0.25% significantly prolonged the median duration of analgesia and reduced the total dose of post-operative analgesics compared with bupivacaine alone or bupivacaine plus epinephrine 5 µg/ml ($P < 0.05$).¹³ Neogi et al.¹⁴ compared clonidine 1µg/kg and dexmedetomidine 1µ/kg as adjuncts to ropivacaine 0.25% for caudal analgesia in pediatric patients and concluded that addition of both clonidine and dexmedetomidine with ropivacaine administered caudally significantly increases the duration of analgesia. And we also observed similar results in our study as the duration of analgesia in group R was 6.45 ± 0.52 hrs and in group C 13.01 ± 0.89 hrs and without any significant side effects. Caudally, its interaction with local anaesthetics has been explained by three possible mechanisms. First, clonidine blocks A δ and C fibres as a consequence of an increase in potassium conductance in isolated neurons, thus intensifying local anaesthetic conduction block.¹⁹ Secondly, clonidine may cause local vasoconstriction, thus decreasing local anaesthetic spread and removal around neural structures. This effect is mediated by drug action on post-synaptic α_2 receptors, although there is little evidence of this mechanism with clinical doses.²⁰ Thirdly, clonidine combined with spinal local anaesthetics or used in peripheral blocks intensifies and prolongs analgesia.²¹ Spinal α_2 adrenergic agonists may also induce analgesia by activating spinal cholinergic neurons resulting in acetylcholine release.²²

Bradycardia and hypotension are considered to be the most prominent adverse effects of α_2 -adrenoreceptor agonists, but appear to be less pronounced in children than in adults.¹³

Eisenach et al found hypotension and bradycardia as the most common side effect with caudal clonidine in a dose dependent manner, the incidence being less with 1 mg/kg-1.²³ Some studies,^{24,25} report a marked decrease in heart rate after epidural clonidine while others do not. We did not observe any significant bradycardia in our study.

This study confirms that there was no significant decrease in heart rate and respiratory rate from the base line with the use of clonidine with ropivacaine in caudal epidural analgesia.

Sedation: Clonidine causes dose-dependent post-operative sedation in children as demonstrated by Lee and his colleagues in their study on adding 2 µg/kg clonidine to caudal bupivacaine.²⁶

Lee et al.²⁷ noted significant sedation when 2 mcg/kg clonidine was added to caudal bupivacaine and concluded that the sedative effects in children reflected the improved quality of analgesia offered by clonidine. Various other studies have however shown the absence of significant

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sedation with use of clonidine at 2 mcg/kg in the caudal space.^{28,29} In our study we observed that the children had mild sedation.

One major difference between the above studies and this study was that, in all these patients general anaesthesia were given in conjunction with caudal analgesia, with use of volatile anaesthetic gases or muscle relaxant. Whereas in our study, we use minimal dose of ketamine which was given prior to caudal block to make the patient co-operative; patients were on spontaneous respiration throughout, without use of any volatile anaesthetic gases.

This probably decreased the incidence of side effects and complications associated with general anaesthesia and helped in earlier post-operative mobilization of our patient.

Similarly, Brenner S. C. et al.³⁰ investigated 512 infants and children. In their study Caudal block was performed with ropivacaine 1mlkg⁻¹ (0.2% or 0.35%). after Premedication with midazolam, sedation was induced with i. v. nalbuphine 0.1mgkg⁻¹ and propofol 1mgkg⁻¹, and maintained with propofol 5mgkg⁻¹ h⁻¹ in children, if necessary. They concluded that Caudal block under sedation is a safe and effective procedure for pediatric sub umbilical surgery with low incidence of adverse events.

CONCLUSION: Ropivacaine (0.25%) with clonidine (1µg/kg) in caudal block showed prolong duration of analgesia as well as better quality of surgical anaesthesia than plain ropivacaine (0.25%) in pediatric patients without any significant side effects. It also offers good quality of surgical anaesthesia with significant post-operative pain relief.

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