

# Comparision of Caudal Ropivacaine, Ropivacaine Plus Ketamine and Ropivacaine Plus Fentanyl Administration for Postoperative Analgesia in Children

Singh J<sup>1</sup>, Hamal D<sup>2</sup>, Karmacharya A<sup>3</sup>

<sup>1</sup>Dr. Jeevan Singh, Assistant Professor, MBBS, MD, Department of Anaesthesia, <sup>2</sup>Dr. Dixa Hamal, Intern, Department of Surgery, <sup>3</sup>Dr. Avish Karmacharya, MBBS, MS, Lecturer, Department of Surgery. All from the Kathmandu University School of Medical Science, Dhulikhel, Kavre, Nepal.

**Address for correspondence:** Dr. Jeevan Singh, E-mail: [drjeevan25@gmail.com](mailto:drjeevan25@gmail.com)

## Abstract

**Introduction:** The purpose of the study was to compare the analgesic quality and duration of Ropivacaine 0.2% with the addition of Fentanyl (1 mcg/kg) with that of Ropivacaine 0.2% and the addition of Ketamine (0.5 mg/kg) and also compare the post complications. **Materials and Methods:** Ninety children, age one to ten years, undergoing sub-umbilical surgery, were prospectively randomized to one of three groups: caudal analgesia with 0.75 ml/kg of 0.2% Ropivacaine in normal saline (Group R) or caudal analgesia with 0.75 ml/kg of 0.2% Ropivacaine with Ketamine 0.5 mg/kg (Group RK) or caudal analgesia with 0.75 ml/kg of 0.2% Ropivacaine with Fentanyl 1 mcg/kg (Group RF). Post-operative pain was assessed for 24 hours using the FLACC scale. **Results:** The mean duration of analgesia was significantly longer in Group RK ( $629.06 \pm 286.32$  min) than other two groups  $P < 0.05$ . The pain score assessed using FLACC scale was compared between the three groups, and children in Group RK had lower pain scores, which was statistically significant. The requirement of rescue medicine was lesser in Group RK. Ketamine in a dose of 0.5 mg/kg added to 0.2% bupivacaine for caudal analgesia, during sub-umbilical surgeries, prolongs the duration of analgesia of Ropivacaine, without any side effects in compare to Ropivacaine alone or Fentanyl. **Conclusion:** We conclude that Ketamine in a dose of 0.5 mg/kg, added to 0.2% Ropivacaine for caudal analgesia and administered as a 0.75 ml/kg mixture in children, for sub-umbilical surgery, significantly prolongs the duration of post-operative analgesia without any side effects.

**Key words:** caudal analgesia, Fentanyl, Ketamine, post-operative analgesia, Ropivacaine, sub-umbilical surgery.

## Introduction

The International Association for Study of Pain (IASP) defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage<sup>1</sup>."

Clinicians have adapted a number of analgesic strategies to minimize the pain during and after surgeries in paediatric patients and caudal epidural is one among them. It is the most popular and commonly performed technique in children<sup>2</sup>. It is widely accepted due to technical simplicity. It is reliable, safe and can be used with general anaesthesia for providing intra-operative and post-operative analgesia in patients coming for sub umbilical surgeries<sup>2</sup>. Control of pain during intra-operative and post-operative period is important in

paediatric patients as poor pain control may result in morbidity and mortality<sup>3</sup>. Caudal epidural anaesthesia / analgesia are the most widely employed technique for various surgical procedures within the distribution of T10 – S5 dermatome<sup>4</sup>.

The main disadvantage of caudal anaesthesia is the short duration of action after a single injection of local anaesthetic solution. Even long-acting local anaesthetic drugs such as Ropivacaine provide only four to eight hours of analgesia. The use of caudal catheters to administer repeated doses or infusions of local anaesthetic solution is not popular, partly because of concerns about infection. So prolongation of caudal analgesia using a 'single-shot' technique has been achieved by the addition of various adjuvant. Adjuvant

drugs are agents that when co-administered with local anaesthetic agents improve the speed of onset, the quality and/or duration of analgesia. A wide range of drugs have been assessed for caudal anaesthesia. For example, Ketamine, Clonidine, Fentanyl, Midazolam, Tramadol etc.

For the measurement of pain we used the FLACC scale, The Face, Legs, Arms, Cry, Consolability scale or FLACC scale is a measurement used to assess pain in children between the ages of 1–10. The scale has 5 criteria which are each assigned a score of 0, 1 or 2<sup>5</sup>. (Table 1) We chose the FLACC score as it is easy to use, is validated and gives us an objective evaluation. The other pain score that can be used are Oucher pain scale, Children's hospital of Eastern Ontario pain scale (CHEOPS), Observational pain/ discomfort scale (OPS) etc<sup>6</sup>.

## Materials and Methods

This is a prospective randomized control trial conducted in the department of anaesthesia from January, 2011 to September, 2012, after approval from the Institutional Review Committee. Convenient sample of 90 patients was taken. Written informed consent was taken from parents and the patients were allocated into three groups according to random allocation number table each group containing 30 patients. Patients with ASA grade I and II coming for below umbilical surgeries that are under the age group age one to ten years weighing approximately between five to twenty kilograms were included in the study groups. Infection at the site of injection, bleeding disorders, patients who are on anticoagulant therapy, congenital anomalies of the spinal cord, congenital disorders, patients allergic to anaesthetic drugs, surgeries extending more than 90 minutes, surgeries requiring anaesthesia above T10 level, active CNS disorders and convulsive disorders were excluded from the study.

All patients were pre-medicated with inj. atropine 0.02 mg/kg orally half an hour prior to surgery. In the operation theatre all patients were induced with halothane and oxygen and delivered through Jackson Rees modification of Ayres T piece. Standard monitoring was done using the pulse oximeter, heart rate, non-invasive blood pressure, ECG, and oxygen saturation after taking the baseline reading and continuous monitoring was done at every five minute interval for the first 30 minutes and there by every 10 minutes till the end of surgery. After securing appropriate gauge IV cannula, Midazolam 0.1 mg/kg and Propofol 2 mg/kg body weight was given and patient's airway was secured with reusable Laryngeal Mask Airway (LMA) of appropriate size. The patients were maintained on oxygen 3 litres/minute and Isoflurane 1 to 2 % and patients were kept in spontaneous ventilation. They were carefully placed in left lateral position with both the legs flexed at hip at 90 degrees and at knee joints. Under strict aseptic precautions sacral hiatus was identified by palpating sacral cornu. 23 gauge hypodermic needle was introduced at 90 degree until a pop is felt and then angled down to enter the sacral hiatus in the cephalic direction. After negative aspiration for blood and CSF, the study drugs were introduced into the caudal space according to allocation. Group R received 0.75 ml/kg of 0.2% Ropivacaine in normal saline, Group RK received 0.75 ml/kg of 0.2% Ropivacaine with Ketamine 0.5 mg/kg and Group RF received 0.75 ml/kg of 0.2% Ropivacaine with Fentanyl 1 mcg/kg. The caudal anaesthesia was given by anaesthesia technicians, who were blinded about the drugs being used. The patients were repositioned supine and after reconfirmation of bilateral ventilation, surgery was started. No other analgesics were given. At the end of the surgery Isoflurane was discontinued; LMA was removed in deep level of anaesthesia and thereafter suctioning of the oral cavity done. Duration of surgery and parameters were recorded and entered in performa sheets.

**Table 1:** The FLACC scale for pain assessment in children. There are five parameters, each given a score of 0–2 and the total score is taken to assess pain

Category	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Each of the five categories is scored from 0–2, resulting in total range of 0-10, FLACC = Face, Leg, Activity, Cry, Consolability.

Patients were then shifted to observation ward after they were awake and breathing room air and then to their respective wards. In the post-operative period vital parameters like pulse rate, respiratory rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation were monitored for 2 hours at 30, 60 and 120 minutes respectively. Sedation was assessed by using sedation score. Assessment of sedation was done by sedation score at every hour for the first 8 hours. Pain score was evaluated using objective pain score scale (FLACC) by a trained nurse for 24 hours or till discharge whichever was the first. Intra-operative or post-operative decrease in systolic blood pressure and heart rate more than 30% of the baseline values were considered as severe hypotension and bradycardia respectively. It was treated with IV fluids followed by inj. atropine IV, if necessary. Respiratory depression was considered if oxygen saturation less than 93% on breathing room air and if so supplemental oxygen via face mask was given at 4 litres per minute. The respiratory rate was however not considered for the pain scoring. The duration of analgesia is defined as the time between the caudal anaesthesia and the first complaint of pain. If the score is more than 4 or if the patient complains of pain they were given oral Paracetamol 10 mg/kg as rescue analgesia in the form of syrup/drops. Patient sedation score was defined as 1: Asleep, not arousable by verbal contact 2: Asleep, arousable by verbal contact, 3: Drowsy, not sleeping, 4: Alert/ awake<sup>7</sup>. The time of first micturation, post-operative nausea and vomiting, itching or any other symptoms were noted before discharge.

Changes in the hemodynamic variables, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP),

between the three groups were analysed with ANOVA (analysis of variance) using general linear model for repeated measures (SPSS- 17, Multi language) and by Student's t-test with Bonferroni's corrections. Changes in the hemodynamic variables within the groups were analysed with multiple paired t-tests with Bonferroni's corrections. Demographic data and baseline hemodynamic values of were analysed using either student's t-test or chi-square test. A p value  $\leq 0.05$  was considered statistically significant. Values are presented as mean  $\pm$  standard deviation.

**Results**

The results were analysed in relation to age, weight of the patients, duration of anaesthesia in minutes, recovery to first analgesia time (Table: 2), systolic, diastolic and mean arterial pressure, heart rate, respiratory rate and pain scale in 24 hours in postoperative period and post-operative complications like nausea, vomiting, hypotension, hypertension, pruritus, constipation, bradycardia and urinary retention.

All three groups were comparable in relation to age and weight without any significant differences. Duration of anaesthesia was also similar (Table: 2).

While comparing all three groups, the mean duration of analgesia was significantly longer in Group RK (621.00  $\pm$  142.73 min) than in Group RF (507.74  $\pm$  122.12 min) and Group R (380.07  $\pm$  141.21 min); P < 0.05. The duration of analgesia provided range from 3.91 hours to 8.68.4 hours for 0.75 ml/kg of 0.2% Ropivacaine in normal saline (Group R), 7.8 hours to 12.73 for 0.75 ml/kg of 0.2% Ropivacaine with Ketamine 0.5 mg/kg (Group RK) and 6.42 hours to 10.5 for 0.75 ml/kg of 0.2% Ropivacaine with Fentanyl 1 mcg/kg (Group RF).

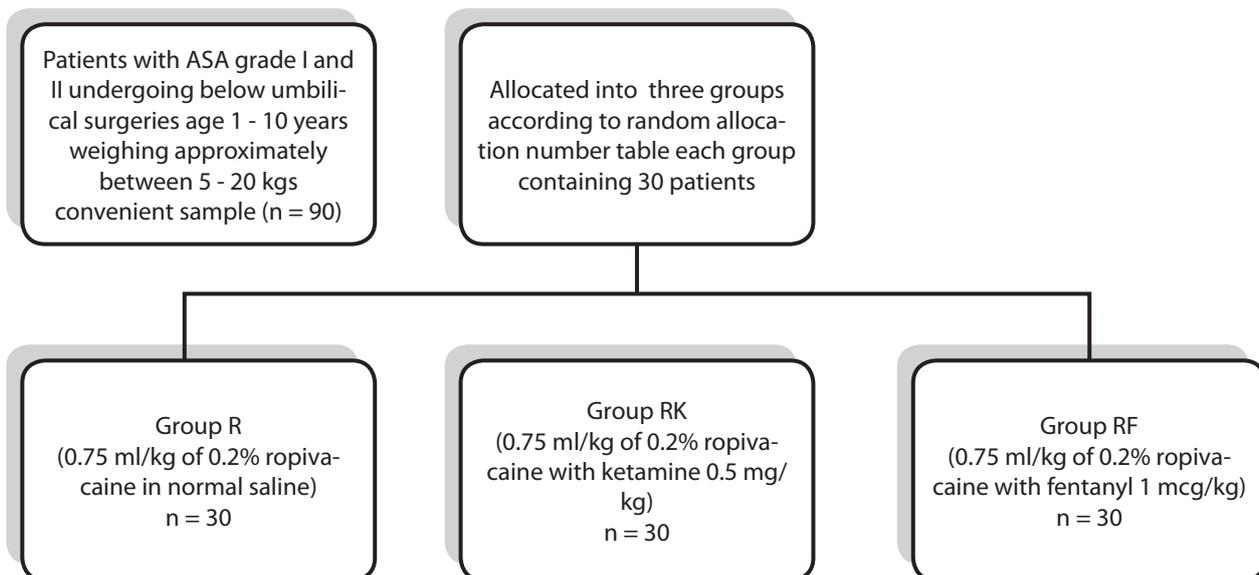


Fig 1: Randomization flowchart

**Table 2:** Different variables of the patient.

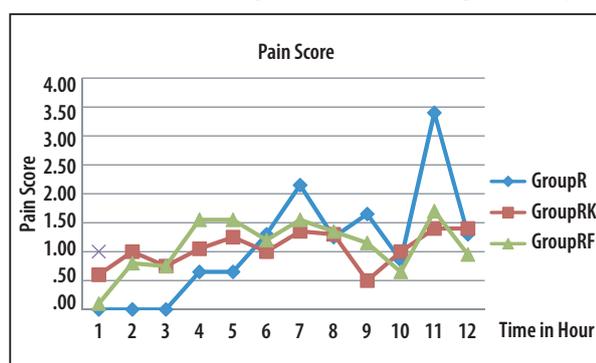
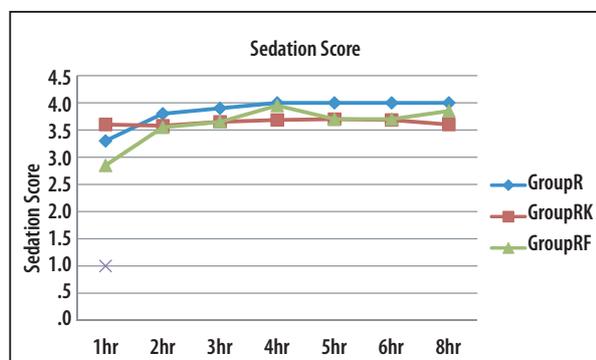
	Group R	Group RK	Group RF	p value
	(n=30)	(n=30)	(n=30)	
Age in Years	5.20±1.8	5.10±1.2	5.10±1.6	0.512
Weight in kg	14.20±2.13	14.85±2.12	14.15±1.34	0.35

Values are mean ± SD. Significance value is regarded as p value <0.05

**Table 3:** Duration of anaesthesia and analgesia in all groups

	Group R	Group RK	Group RF	p value
	(n=30)	(n=30)	(n=30)	
Duration of Anaesthesia in minutes	45.00±10.2	47.15±12.23	46.32±11.12	0.131
Recovery to 1 <sup>st</sup> analgesic in minutes	380.07±141.21	621.00±142.73	507.74±122.12	0.001

Values are mean ± SD. Significance value is regarded as p value <0.05

**Fig 2:** Pain Score**Fig 3:** Sedation Score

The pain score assessed using FLACC scale was compared between the three groups and children in Group RK had lower pain scores, which was statistically significant ( $p < 0.05$ ). The requirement of rescue medicine was lesser in Group RK. Ketamine in a dose of 0.5 mg/kg added to 0.2% Ropivacaine for caudal analgesia, during sub-umbilical surgeries, prolongs the duration of analgesia of Ropivacaine, without any side effects.

Sixty percentages of the patients in the Group RK, thirty percentages Group RF and twenty percentages in each Group R did not require any analgesia. There were no statistically significant differences in systolic blood pressure, diastolic blood pressure, mean blood pressure,

heart rate and level of pain score observed in the 24 hours postoperative period among all the four groups (Figure 2,3).

Post operatively nausea and vomiting occurred in 16.6% and 10% of the patients in the Ropivacaine-Fentanyl group and Ropivacaine group respectively. Urinary retention occurred in one of the patients in Ropivacaine group and two in the Ropivacaine Fentanyl group. There was one episode of itching in both RF group and R group and one episode of hypertension in R group. However other complication like respiratory depression, hypotension, bradycardia and constipation did not observed in any of the groups.

## Discussion

The key finding of this study is that the addition of 0.5 mg/kg of Ketamine to caudal Ropivacaine 0.2% significantly decreases the need for rescue analgesia in the immediate postoperative period and the quality of postoperative analgesia is equivalent to that produced with caudal Fentanyl 1 mcg/kg. Our study shows that Ketamine prolongs post-operative analgesia significantly.

Administering regional anaesthesia before surgery is a safe and widely accepted, providing adequate pain relief, reducing general anaesthesia requirements and allowing a calm and satisfactory awakening<sup>8</sup>. Various studies report that caudally administered Ropivacaine provides satisfactory anaesthesia/analgesia in children<sup>9,10</sup>. The effect of Ketamine is thought to be the result of N-methyl-D-aspartate (NMDA) receptor antagonism, opioid  $\mu$  receptor agonism, and voltage-sensitive sodium channel interaction<sup>11,12</sup>. Caudally administered Ketamine is known to provide good postoperative analgesia with minimal morbidity in children. Naqib et al reported that caudal administration of Ketamine 0.5 mg/kg in children lead to satisfactory postoperative analgesia after hernia repair<sup>13</sup>. Semple et al showed that when

Ketamine was used to prolong the duration of caudal epidural blockade in children, doses of 0.5 and 1 mg/kg are significantly more effective than 0.25 mg/kg<sup>14</sup>. De Negri et al found that the addition of S-Ketamine 0.5 mg/kg to Ropivacaine 0.2% resulted in an improvement in postoperative analgesia compared with Ropivacaine alone<sup>15</sup>. On the other hand, Lee et al suggested that the medium duration of analgesia was significantly longer in a Ketamine (0.25 mg/kg) plus Ropivacaine (0.2%) group (12 h) than in a Ropivacaine group<sup>16</sup>.

Several adjuvants have been used to prolong the duration of analgesia of Ropivacaine for caudal analgesia in children. Opioids, Ketamine and midazolam are some of the commonly used drugs<sup>17</sup>. The use of opioids is associated with an increased incidence of pruritus and post-operative nausea and vomiting<sup>18</sup>. The advantage of Ketamine is that it prolongs the duration of analgesia without an increase in the incidence of respiratory depression, pruritus and urinary retention which are commonly seen with neuraxial opioids<sup>19</sup>.

We chose the FLACC scale to evaluate pain post-operatively as it is easy to use, is validated and gives us an objective evaluation<sup>6</sup>. We chose to monitor our patients for a period of 24 hours post-operatively. This is in contrast to a few other studies where there was only a six-hour period of observation post-operatively and the rest of the assessment was done by parents<sup>20</sup>. Assessment by parents could introduce some inconsistency as parents differ in the way they perceive their children to be in pain and the threshold for administering rescue medications varies between parents.

A meta-analysis of 18 trials by Curatalo et al in 2008 comparing epidural Fentanyl, adrenaline and clonidine as adjuvants to local anaesthetics concluded that addition of Fentanyl decreased the incidence of pain quantitatively during surgery and is a safe<sup>21</sup>.

Campbell FA et al in 1991 compared the analgesic efficacy and safety of a single caudal injection of bupivacaine Fentanyl mixture in a prospective, controlled, triple blinded study of 34 children, aged one to 11 years and ASA grade I& II, undergoing urological surgery<sup>22</sup>. They did not found any complications like nausea, vomiting, retention of urine and constipation, which is in contrasts to our study showing 6.6% percentage of retention in RF group and 3.3% percentage in R group. Similarly 16.6% of the patients in RF group and 10% of the patients in R group had nausea and vomiting which was in contrasts to their study.

The study is done in small scale in a single institution, a larger scale study in multiple institution is required to authenticate the data.

## Conclusion

We conclude that Ketamine in a dose of 0.5 mg/kg, added to 0.2% Ropivacaine for caudal analgesia and administered as a 0.75 ml/kg mixture in children, for sub-umbilical surgery, significantly prolongs the duration of post-operative analgesia when compared to 0.75 ml/kg of 0.2% Ropivacaine in normal saline or with 0.75 ml/kg of 0.2% Ropivacaine with Fentanyl 1 mcg/kg without any side effects.

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**Conflict of Interest:** Nil

**Permission from IRB:** Yes

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