

## COMPARATIVE STUDY TO EVALUATE THE EFFICACY OF COMBINED PARACETAMOL SUPPOSITORY AND CAUDAL BUPIVACAINE WITH CAUDAL BUPIVACAINE IN PAEDIATRIC PATIENTS UNDERGOING SUB-UMBILICAL SURGERY

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### ABSTRACT

#### BACKGROUND

The advantage of Paracetamol by its central effect on the nociceptive process involving central sensitisation provides excellent post-operative analgesia inspired us to conduct a study in which we evaluate the efficacy and duration of post-operative analgesia of Paracetamol rectal suppository in paediatric patients undergoing sub-umbilical surgeries.

#### AIM

To compare the postoperative analgesic effect of paracetamol rectal suppository with caudal bupivacaine and caudal bupivacaine in paediatric patients undergoing sub-umbilical surgeries.

#### METHODS AND MATERIALS

This study was conducted in Chengalpattu Medical College Hospital during the period May 2016 - July 2016. Sixty ASA I children were taken up for a prospective randomised comparative double-blind trial and were grouped into Group C (Caudal bupivacaine) and Group S (Caudal bupivacaine with paracetamol suppository). After getting approval from the Hospital Ethical Committee and informed consent from parents, 60 children undergoing sub-umbilical surgeries, aged from 3 to 8 years weighing less than 20 kg of either gender, ASA 1, who fulfilled the inclusion criteria were included in the study.

#### STATISTICAL ANALYSIS - FLACC, ALDRETE SCORING SYSTEMS

The comparison of efficacy was done based on Mean Rescue Analgesic Time, Mean Pain Score, Recovery Score and the variations of Heart Rate, Respiratory Rate, and SpO<sub>2</sub> in both Group S and C by using FLACC, Aldrete Scoring Systems. Incidence of PONV, rise in temperature and first urine voiding time were also noted.

#### RESULTS

The comparison of Mean Rescue Analgesic Time (Post-operative analgesic duration) is significantly higher in rectal paracetamol group S than the caudal bupivacaine only group C.

#### CONCLUSION

We conclude from the above study that the addition of paracetamol suppository to caudal bupivacaine enhances the quality and extends the duration of post-operative analgesia better than caudal bupivacaine alone in paediatric patients undergoing sub-umbilical surgeries.

#### KEYWORDS

Bupivacaine, Paracetamol Suppository, Caudal Analgesia, Post-Operative Analgesia.

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#### INTRODUCTION

The postoperative pain in paediatric patient is not adequately managed despite its cause of morbidity and even some reported mortality. It is now accepted that pain should be anticipated, safely and effectively controlled in all children, whatever their age, maturity or severity of illness.<sup>1,2</sup> Because of the multiplicity of mechanisms involved in post-operative

pain, a multimodal analgesia regimen with a combination of opioid and non-opioid analgesic drugs is often used to enhance the analgesic efficacy and reduce the opioid requirements and side effects.<sup>3</sup>

Peripheral tissue injury provokes peripheral and central sensitisation.<sup>4,5</sup> These changes contribute to the post-injury pain, hypersensitivity state which manifests as an increase in the responsiveness to noxious stimuli and a decrease in the pain threshold, both at the site of injury and in the surrounding uninjured tissue.<sup>4,5</sup>

Single shot caudal epidural analgesia is a widely used regional technique for intra- and post-operative pain relief during lower abdominal, inguinal and penoscrotal surgeries in paediatric patients.<sup>6</sup> It is technically simple, safe and reliable, and provides effective analgesia for surgery below umbilicus. However, the analgesic effect of caudal bupivacaine lasts for 4-12 hours. Different additives are used to prolong the analgesic period.

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The use of caudal morphine provides excellent analgesia at higher incidence of serious side effects like respiratory depression, nausea, vomiting and urinary retention.<sup>7</sup> Other combinations such as clonidine, tramadol and midazolam have also been used as adjuvant to bupivacaine for caudal analgesia. All of them provide improved analgesia without any serious side effects. However, clonidine, tramadol and midazolam do have potential risk of hypotension, behavioural changes, vomiting and sedation respectively.<sup>8</sup>

Rectal paracetamol suppository preparations are very easy to administer and the therapeutic range is very high and safe to use in paediatric age group and has good analgesic effect. Rectal paracetamol is free from complications of non-steroidal anti-inflammatory drugs such as coagulopathy, nephropathy, gastropathy and asthma.<sup>9,10,11</sup> Studies have demonstrated that mechanical hyperalgesia surrounding the wound in post-operative patients and experimentally heat induced secondary hyperalgesia share a common mechanism and the central neuronal sensitisation contributes to post-operative pain. Paracetamol by its central effect on the nociceptive process involving central sensitisation provides excellent post-operative of analgesia.<sup>12</sup>

In our institution, we chose to study the post-operative analgesic effect of rectal paracetamol in addition with caudal bupivacaine in paediatric patients undergoing sub-umbilical surgeries.

#### METHODS AND MATERIALS (METHODOLOGY)

The study was conducted in Chengalpattu Medical College Hospital during the period May 2016 - July 2016. Sixty ASA I children were taken up for a prospective randomised comparative double-blind trial and were grouped into Group C (caudal bupivacaine) and Group S (caudal bupivacaine with paracetamol suppository).

#### Inclusion Criteria

1. ASA I.
2. Age 3-8 years (<20 Kg).
3. All sub-umbilical surgeries.

#### Exclusion Criteria

1. Children with h/o allergy to local anaesthetics.
2. Undiagnosed diarrhoea.
3. Coagulopathies.
4. Local sepsis.
5. Recent respiratory infection.
6. Abnormalities of sacrum vertebral column and spinal cord.
7. Convulsive disorders and raised intracranial pressure.
8. Children with developmental delay.

After getting approval from the Hospital Ethical Committee and informed consent from parents, 60 children undergoing sub-umbilical surgeries aged from 3 to 8 years weighing less than 20 kg of either gender of ASA 1, who fulfilled the inclusion criteria were included in the study.

Randomisation was done by draw of lots. Pre-operative evaluation included detailed elicitation of significant history, clinical examination, investigations such as Hb, PCV, BT/CT, Urine albumin/sugar. Any relevant specialist's opinion,

investigations and care were obtained. Drawing of lots for randomisation and preparation of study was prepared by a consultant who took no part in further part in study, the rest of the study was conducted by us and an investigator who was blinded to the drug administered.

#### PROCEDURE

Sixty children of ASA I who were scheduled to undergo Sub-Umbilical Surgeries were randomised into either groups, Group C and S. Parents were informed about the study and consent obtained. All the children were examined one day before surgery. Pulse rate, blood pressure and respiratory rate recorded. Fasting guidelines were followed.

**Group C:** Control group with caudal bupivacaine only.

**Group S:** Study group Rectal Suppository 20 mg/kg with caudal Bupivacaine.

**Premedication:** Inj. Glycopyrrolate 10 ug/kg IM 30 mins. before surgery.

Monitoring was done using multiparameter monitor which included ECG, NIBP, SpO<sub>2</sub> and Precordial stethoscope.

#### Anaesthesia

Baseline parameters heart rate, pulse rate, respiratory rate, temperature, blood pressure and pulse oximetry recorded after connecting to the monitor and intravenous line secured with 22-gauge Venflon. After pre-oxygenation, intravenous anaesthesia induced with Inj. Ketamine 2.5 mg/kg and Inj. Midazolam 0.05 mg/kg IV with face mask assisted ventilation with 100% oxygen initially and after establishment of spontaneous ventilation maintained with 50% nitrous oxide and 50% oxygen and 0.5 – 1.0% halothane for first 15 mins.

#### Caudal Epidural

All the 60 children received caudal epidural, 0.25% Bupivacaine 1 mL/kg in left lateral position under aseptic precautions. Thirty children under Group S received rectal paracetamol 20 mg/kg using lignocaine jelly in the same position following caudal epidural. Thirty children under Group C received only caudal epidural anaesthesia. Surgery was allowed to start only after 15 mins. The effectiveness of caudal analgesia was tested and made sure before the onset of surgery in all cases.

#### Parameters Monitored

1. Pre-induction HR, SpO<sub>2</sub>, RR and Temperature.
2. Post-induction HR, SpO<sub>2</sub>, RR and Temperature.
3. Intraoperative continuous monitoring of HR, RR, SpO<sub>2</sub> and Temperature.
4. FLACC pain scale were monitored in all children post-operatively at 2.30, 3.00, 3.30, 4.00, 4.30, 5.00, 5.30, 6.00, 6.30, 7.00 hours and corresponding HR, RR, Aldrete recovery score were monitored at same time intervals.
5. According to pain scoring, rescue analgesics were given when pain score was more than three FLACC pain scale.
6. Presence of nausea and vomiting noted down.
7. The Modified Aldrete Recovery scoring system (Table 1).

Original Criteria	Modified Criteria	Points
<b>Colour</b> Pink Pale or Dusky Cyanotic	<b>Oxygenation</b> SpO2 >92% on Room Air SpO2 >90% on Oxygen SpO2 <90% on Oxygen	2 1 0
<b>Respiration</b> Can Breathe Deeply and Cough Shallow, but Adequate Exchange Apnoea or Obstruction	Breathes Deeply and Coughs Freely Dyspnoea, Shallow or Limited Breathing Apnoea	2 1 0
<b>Circulation</b> BP +/- 20% of Normal BP +/- 20-50% of Normal BP > 50% of Normal	BP +/- 20% of Normal BP +/- 20-50% of Normal BP > 50% of Normal	2 1 0
<b>Consciousness</b> Awake, Alert and Oriented Arousable, but Readily Drifts back to Sleep No Response	Fully Awake  Arousable on Calling Not Responsive	2  1 0
<b>Activity</b> Moves all Extremities Moves two Extremities No Movement	Moves all Extremities Moves two Extremities No Movement	2 1 0

Table 1

- Temperature monitoring done both post-operatively and any rise in temperature above 100°F is noted.
- First urine voiding time is noted post-operatively.

**OBSERVATION AND RESULTS**

The study constituted of sixty children undergoing sub-umbilical surgeries. They were evaluated for post-operative pain score using FLACC pain scale, rescue analgesic time, the Aldrete recovery score, raise in temperature, post-operative nausea and urine voiding time were compared between Group S (Rectal paracetamol with caudal bupivacaine) and Group C (Caudal bupivacaine alone).

The Mean Rescue Analgesic time in the Group S is 353±6.0 mins. and in the control Group C is 253±3.9 mins., (p<0.0001, T value 13.9). There is significant increase in the post-operative analgesia time and quality and there is less pain score in the study Group S when compared to the control Group C. The incidence of fever and post-operative nausea and vomiting is higher in the control Group C. The average urine voiding time is higher in the study Group S. The variables age, weight, pain scores, rescue analgesic time, heart rate, respiratory rate, Aldrete recovery score and urine voiding time were analysed using Levene’s test for equality of variances and T-test for equality of means.

Comparison of FLACC pain score in both the rectal paracetamol Group S and caudal bupivacaine Group C.

Minimum pain score - 0, Maximum pain score - 10

Five criteria Crying, Facial expression, Legs position, Activity and Consolability were considered and each criteria was given 0, 1 and 2 scores for absent, moderate and severe response to pain respectively.

At all post-operative intervals, the pain score is significantly low in the study Group S (Rectal paracetamol) than in control Group C. The quality of post-operative analgesia is better in the study Group S (Rectal paracetamol) than in control Group C. There are many other pain scoring scales like Modified Observational pain score, CHEOPS pain score, Visual analog scale, etc., but in our study FLACC score is more appropriate for age group 3-8 yrs.

Time	Mean±Std (Max, Min)	P value (T-value)
Study	353±6.0 (300, 420)	0.0001 (13.9)
Control	253±3.9 (210, 285)	

Table 2: Mean±Standard Deviation (Minimum, Maximum) of Rescue Analgesic Time in Minutes

There is a highly significant difference between the study group and control group on mean Rescue Analgesic Time (t=13.9, p < 0.0001).

Comparison of Heart rate and Respiratory rate at different post-operative intervals in both rectal paracetamol Group S and caudal bupivacaine Group C.

Heart Rate in Mins	Group S	Group C
150	112.7	123.2
180	111.5	122.3
210	109.8	119.7
240	106.5	117.5
270	105.6	117.6
300	105.7	116.4
330	104.8	116.5
360	103.9	116.1
390	104.3	115.9
420	103.7	114.4

Table 3: Distribution of Heart Rate at Different Interval of Time

Respiratory Rate in Mins	Group S	Group C
150	16.5	20.2
180	16.6	19.5
210	15.8	19
240	15.7	18.9
270	15.8	18.8
300	15.6	18.9
330	15.7	18.4
360	15.5	18.2
390	15.1	17.9
420	15.8	17.4

Table 4: Respiratory Rate at Different Interval of Time

There is significant difference in heart rate and respiratory rate in both the rectal paracetamol Group S and caudal bupivacaine Group C. Both heart rate and respiratory rate is significantly low in rectal Paracetamol group than the caudal bupivacaine group at all post-operative time intervals, which reflects that the quality of post-operative analgesias better in the rectal paracetamol Group S.

#### **Aldrete Recovery Score at Different Post-Operative Time Intervals**

At all time intervals, the Aldrete recovery score is higher but it is not statistically significant in the Control Group C than the rectal suppository Group S.

Time in Mins	Study Group S	Control Group C
150	6.1	6.4
180	6.4	7.2
210	6.8	7.4
240	7.2	8.1
270	7.5	8.4
300	7.8	8.5
330	7.9	9
360	8.1	9.3
390	8.4	9.7
420	9	9.7

**Table 5**

#### **DISCUSSION**

Rescue analgesic time, FLACC pain scale HR, RR, SpO<sub>2</sub>, Aldrete recovery score, incidence of PONV, rise in temperature and first urine voiding time were monitored in both Group S and Group C.

In our study the FLACC pain score, at all post-operative intervals up to 7 hours were significantly lesser in Group S than group C.

In our study, children 3-8 years of age weighing less than 20 kg were included. The FLACC pain score is more sensitive in this age group. The mean rescue analgesic time in rectal Paracetamol group is significantly prolonged in Group S (353 mins. +/- 6.0) than Group C (253 mins. +/- 3.9) with P value <0.0001 and T value 13.9.

According to Bertolini A and Ferrari A,<sup>13</sup> it has been demonstrated that paracetamol may exert its analgesic effect via molecular targets distinct from COX. In the brain and spinal cord, Paracetamol is conjugated with arachidonic acid to form N-arachidonoyl phenylamine (AM 404). AM 404 is a known capsaicin receptor and the Cannabinoid CB 1 receptor system, both of which confer analgesia in the central nervous system. This pathway also account for the antipyretic effect of paracetamol, known to cause inhibition of prostaglandin synthesis in brain.

Steve Golladay and Sue Hutter et al<sup>14</sup> used either rectal Paracetamol 30 mg/kg or caudal bupivacaine alone in 32 children undergoing peritoneoscopy and found that 54% children in the rectal Paracetamol group did not require any further analgesia in 24 hours post-op period, confirms the post-operative analgesia of paracetamol used when alone.

In our study the rectal Paracetamol when combined with caudal bupivacaine as in Group S, the quality and duration of post-operative analgesia is enhanced. Caudal bupivacaine takes care of immediate post-operative pain relief and the rectal Paracetamol take care of late post-operative period.

Paracetamol is known for its safety in paediatric patients. Following rectal administration of suppository, the therapeutic levels of 10 ug/dL is achieved within 1-2 hours with a rectal bioavailability of 75-99%. In therapeutic doses, the incidence of liver cell failure is (1;5,00,000) and the next rare contraindication is known for hypersensitive reactions to Paracetamol.

Neeru Gupta and Anjali Mehtha et al<sup>15</sup> found in their study that the duration of post-operative analgesia with caudal bupivacaine 0.25% only was 8.2 hours and AR Wolf, Hughes D, Wade A et al study revealed 7 hours of post-operative analgesia. In our study, the caudal bupivacaine Group C had post-operative analgesia up to 4 hrs. 13 mins. This was lesser than the above study and this could be due to differences in surgery performed method of assessing pain score, bupivacaine dose and volume, and calculation of analgesic time.

The Rescue analgesic time is prolonged in 10-12 kg group by 1 hour 17 mins., 13-15 kg group by 1 hour 20 mins. in rectal paracetamol group when compared to control group. The Rescue analgesic time is prolonged in 16-18 kg group by 1 hour 49 mins., 18-20 kg group by 2 hours 4 mins. in Rectal paracetamol Group S when compared to Control Group C.

In the elder children under our study weighing 16-20 kg had higher post-operative analgesia in Rectal Paracetamol Group S 35-45 mins. than the children weighing 10-15 kg in the same group. This can be explained by the better pain tolerance in the elder children and effectiveness of the reassurance by the parents according to Goddard and Pickup SE et al.<sup>16</sup>

The Mean First Rescue analgesic time in our study is prolonged in both groups in children, who underwent circumcision than the children with herniotomy. In Group S by 20 mins. and in Group C by 18 mins. This is mainly because in our study we are using 1 mL/kg of 0.25% bupivacaine for caudal analgesia, whereas for a block up to L1-L2 for circumcision, only 0.5 mL is required according to Armitage, Gary R. Strichartz and Charles B. Berde et al.<sup>17</sup>

At all post-operative time intervals there is 10-11% increase in the Heart rate in the control Group C than the rectal paracetamol Group S in our study. According to study conducted by Maunkaseva Eeva et al,<sup>18</sup> there was 20% increase in heart rate. There is 20-25% increase in respiratory rate in control Group C than Group S, which is consistent with the above Maunkaseva Eeva et al study.

The Aldrete recovery score is comparatively higher in the caudal bupivacaine Group C, but not statistically significant and probably due to less analgesia in this group the child feeling pain recovers faster.

The incidence of post-operative nausea and vomiting is 33% in Group C and 0% in Group S when compared to 7% of Jan Muhammad Shaik and Sikanderli Mughal et al<sup>19</sup> study, where 143 were given only caudal bupivacaine. The incidence of rise in temperature was 16.6% in Group C and 0% in Group S.

In our study, the mean first urine voiding time is significantly prolonged in Group S (5 hrs. 42 mins.) than the Group C (4 hrs. 48 mins.) and P value is <0.05. Jan Muhammad Shaik and Sikanderli Mughal et al<sup>19</sup> study, the time to micturition is 161.79+/-83.9 and on an average the child passed urine in 6-8 hours.

**CONCLUSION**

The addition of paracetamol suppository to caudal bupivacaine enhances the quality and extends the duration of post-operative analgesia better than the caudal bupivacaine alone in paediatric patients undergoing sub-umbilical surgeries.

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