*Original Research Article*

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# Comparison of Morphine with Nalbuphine as an Adjuvant to Caudal Bupivacaine: A Double blinded Randomized Study

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**Abstract**

*Context:* Caudal analgesia is the most preferred technique for pain relief in paediatric population using local anaesthetic drug along with other adjuvants such as morphine, fentanyl, nalbuphine, tramadol, clonidine. *Aim:* To compare the efficacy and assess the complications of morphine and nalbuphine as an adjuvant to caudal bupivacaine for post-operative analgesia. *Settings and Design:* It is a prospective randomized double blind control study , conducted in Melmaruvathur Adhiparasakthi Institute of Medical Sciences & Research over a period of six months from August 2017 to January 2018 after getting ethical approval. *Methods and Material:* Children fulfilling the inclusion criteria were randomly allocated to receive 1ml/kg of caudal bupivacaine 0.25% either with morphine 50ug/kg (group M ) or nalbuphine 0.2 mg/kg (group N) following general anaesthesia. Post operative pain scores assessed using FLACC score and sedation using Modified Wilson scoring. Complications such as respiratory depression, vomiting, & pruritis were also noted. *Statistical analysis used:* Statistical analysis was performed using appropriate test with Graphic prism 5.0 software. *Results:* Two groups are comparable in age, sex & weight. The post operative pain scores were less in group M compared to group N and they are statistically significant ($p<0.05$) only at 0 (0.500±0.124 vs 0.866±0.114), 1 (0.667±0.66 vs 1.200±0.78) & 2 (1.400±0.498 vs 2.000±0.830) hours but they were not statistically significant at 4 (2.133±0.776 vs 2.567±1.006), 8 (3.400±0.959vs 4.200±1.003), & 12 hours (5.733±0.827 vs 6.500±1.841). Requirement of rescue analgesic were significantly longer in group M (11.93±1.98 hrs) compared to group N (9.150±1.29) and they are statistically significant ($p< 0.05$). Post operative sedation score are statistically significant between two groups. *Conclusions:* As an adjuvant to bupivacaine ,morphine has prolonged the duration of analgesia and decreased the use of rescue analgesic for around 12 hours but at this therapeutic dose, it is associated with higher life threatening complications such as respiratory depression, and other complications like nausea and vomiting whereas Nalbuphine has decreased the use of rescue analgesic for more than 8 hours and has not produced above mentioned complication . Hence the usage of morphine as an adjuvant can be replaced with nalbuphine in Pediatric surgeries.

**Keywords:** Caudal Analgesia; Morphine; Nalbuphine; Bupivacaine.

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## Introduction

Pain control is the cornerstone in the management of pediatric anaesthesia as it alleviates patient distress and aids in rapid uncomplicated recovery. The incidence of pain was found to be 44% following surgery in pediatric population, out of which 64% patients had moderate to severe pain [1].

Caudal block is one popular reliable and safe technique that provides intraoperative and

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postoperative analgesia in lower abdominal ,lower limb, and urogenital surgeries in paediatric age groups[2]. Most of the time it is used for analgesia as an adjunct for general anaesthesia than as a sole anaesthesia but associated with one major disadvantage of shorter duration of action.

Various adjuvants were used to prolong the duration of block such as opioids, clonidine, neostigmine, tramadol, ketamine [3-5]. Opiods are commonly used as an adjunct to prolong the duration of block which includes morphine, tramadol, nalbuphine, fentanyl [3]. Morphine a natural opioid which acts on μ, κ, δ receptors used commonly since its discovery. It is associated with various side effects such as nausea vomiting, pruritis, urinary retention and life threatening respiratory depression. Even though it is associated with various adverse effects, the quality and duration of analgesia remains unmatched.

Nalbuphine is a mixed κ-agonist and μ-antagonist opioid of the phenanthrene group [6]. It is related in its chemical structure to the opioid antagonist naloxone. It provides good analgesia with minimal sedation, minimal nausea and vomiting, less respiratory depression and stable cardiovascular functions. Nalbuphine being an agonist- antagonist opioid is less likely to cause side effects such as pruritis, respiratory depression, urinary retention, excessive sedation, because of its action at kappa receptors [7-8]. The aim of this randomized double blind controlled trial was to compare the duration of post-operative analgesia, sedation and other side effects of single shot caudal epidural morphine versus nalbuphine mixed with bupivacaine in childrens in childrens undergoing herniotomy, phimosis repair.

## Materials and Methods

After obtaining written informed consent from guardian and Research ethics committee approval from the institution this randomized controlled study was conducted in Melmaruvathur Adhiparasakthi Institute of Medical Science & Research over a period of six months from August 2017 to January 2018. Total of 60 patients of ASA classification I, Age 2-6 years old of either sex undergoing elective surgery such as herniotomy, phimosis repair were included in the study. Exclusion criteria includes abnormal coagulation profile, mental retardation, allergic to study drugs, infection at the site of injection, congenital anomaly of the sacrum.

After fulfilling the inclusion criteria patients were randomly assigned into two groups using the lottery method. Group M (n-30) received caudal bupivacaine 0.25% with morphine 50ug/kg and the other group N (n-30) received caudal bupivacaine 0.25% with 0.2 mg/kg nalbuphine. Total volume of 1ml/kg is used in all groups irrespective of the group.

All patients were kept fasting as per ASA NPO guidelines. After checking informed consent patient shifted to operative room and standard monitors such as NIBP, ECG, $SpO_2$, were attached. General anaesthesia induced with sevoflurane 6-8% with $O_2$ 100% and intravenous (iv) line secured. ET tube of appropriate size selected and intubation achieved with succinylcholine 1mg/kg iv. Anaesthesia maintained with $O_2$:$N_2O$ (50:50), Sevoflurane 1-2% with Atracurium at appropriate dose with controlled ventilation.

Patients positioned in lateral decubitus position, using 24G hypodermic needle, after negative aspiration for blood, patients of group M received 1ml/kg of 0.25% bupivacaine with 50ug/kg morphine and group N received 1ml/kg of 0.25% bupivacaine with 0.2mg/kg of nalbuphine. Documentation of $SpO_2$, PR, ECG, NIBP were monitored every 5 minutes until end of the surgery.

Patients with anal wink reflex were presumed to have incorrect drug placement and excluded from the study. Any increase in PR, BP >20% of its baseline value defined as inadequate analgesia. After surgery NM blockade was reversed and patient transferred to postoperative room and observed for 12 hours.

Primary outcome of the study is to know the duration of analgesia and time of rescue analgesia using pain score- FLACC score. FLACC (FACE, LEG, ACTIVITY, CRY, CONSOLABILITY) pain scale (Table 1) is a measurement used to assess pain in children between the age of 2 months and 7 years or in individuals not able to communicate, the score ranges from 0-10. Pain score of >4 is taken as time of first analgesic request, 0 is taken as no pain, and score of 10 as severe pain [9].

Secondary outcome to assess sedation score using Modified Wilsons sedation score (Table 2) and score ranging from 1-4, in which 1 indicates alert and maximum score of 4 indicates asleep, not arousal by verbal contact and complications such as respiratory depression, vomiting, pruritis are noted [3]. Respiratory depression is defined as fall in $O_2$ saturation ($SpO_2$-<92%) and decrease in respiratory rate [3]. Intravenous paracetamol used for rescue pain at a dose of 15mg/kg with minimum 4hours interval.

**Table 1:** FLACC Scale

| Parameters | FLACC Behavioural pain assessment scale Score 0 | 1 | 2 |
|---|---|---|---|
| Face | No particular expression or smile | Occasional grimace or frown, withdraw, disinterested | Frequent to constant frown, cleanched jaw, quivering chain |
| Leg | 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 |
| Crying | No cry(awake or sleep) | 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 |

Score: 0:no pain; 1-3:mid pain; 4-7:moderate pain; 8-10:severe pain, FLACC:face, legs, activity, cry, and consolability.

**Table 2:** Modified Wilsons sedation score

| Value | Patient state |
|---|---|
| 0 | Awake and alert |
| 1 | Minimally sedated:tired/sleepy, appropriate response to verbal conversation, and/or sound |
| 2 | Moderately sedated:somnolent/sleeping, easily aroused with light tactile stimulation or asimple verbal command. |
| 3 | Deeply sedated: deep sleep, aroused only with sigificant physical stimulation |
| 4 | Arousable |

*Statistical Analysis*

Statistical analysis done using Graphic Prism software version 5. Data's were summarized using mean, standard deviation, median for quantitative variables and frequency, relative frequency for categorical variables. Quatitative variables analysed using Unpaired t-test, and categorical variables using chi square test.

## Results

A total of 60 patients were included in the study, and randomly divided into Group M (n- 30 patients) and Group N (n-30 patients). Two groups were comparable in respect to age, gender, and weight of the patients. The mean age of the patient in group M found to be 4.167±1.25(Mean±SD) and group N 4.067±1.363.The mean weight of the patient in group M & group N are 14.93±2.63 and 14.07±2.53 respectively (Table 3).

Postoperative FLACC pain scores were less in group M compared to group N, and they were statistically significant($p<0.05$) at 0 (0.500±0.124 vs 0.866±0.114), 1 (0.667±0.660 vs 1.200±0.714), & 2 hours (1.400±0.498 vs 2.000±0.714) only but they were not statistically significant at 4 (2.133±0.776vs 2.567±1.006), 8 (3.400±0.959 vs 4.200±1.003), & 12 hours (5.733±0.827 vs 6.500±1.841) (Table 4). Post operative sedation scores were statistically significant ($p<0.05$) between Group M & N at 0, 1, 2, 4, 8, & 12 hours. But 8 patients of group M had

**Table 3:** Demographic data

| | Group M | Group N | p- value |
|---|---|---|---|
| Age (Years) | 4.167±1.25 | 4.067±1.363 | 0.771 |
| Weight (Kg) | 14.93±2.63 | 14.07±2.53 | 0.198 |
| Sex (Male/Female) | 21/9 | 19/11 | - |

Datas are expressed in Mean ± SD (Standard Deviation)

**Table 4:** FLACC pain score

| | Group M | Group N | p-value |
|---|---|---|---|
| 0 HRS | 0.500±0.124 | 0.866±0.114 | 0.034 |
| 1 HRS | 0.667±0.660 | 1.200±0.714 | 0.004 |
| 2 HRS | 1.400±0.498 | 2.000±0.714 | 0.001 |
| 4 HRS | 2.133±0.776 | 2.567±1.006 | 0.066 |
| 8 HRS | 3.400±0.959 | 4.200±1.003 | 0.063 |
| 12 HRS | 5.733±0.827 | 6.500±1.841 | 0.529 |

**Table 5:** Time of analgesic request & complications

| | Group M (n-30) | Group N (n-30) | p-value |
|---|---|---|---|
| Time for rescue analgesics | 11.93±1.98 | 9.150±1.297 | <0.001 |
| Complications (respiratory depression, vomiting, pruritis) | 8 | 0 | - |

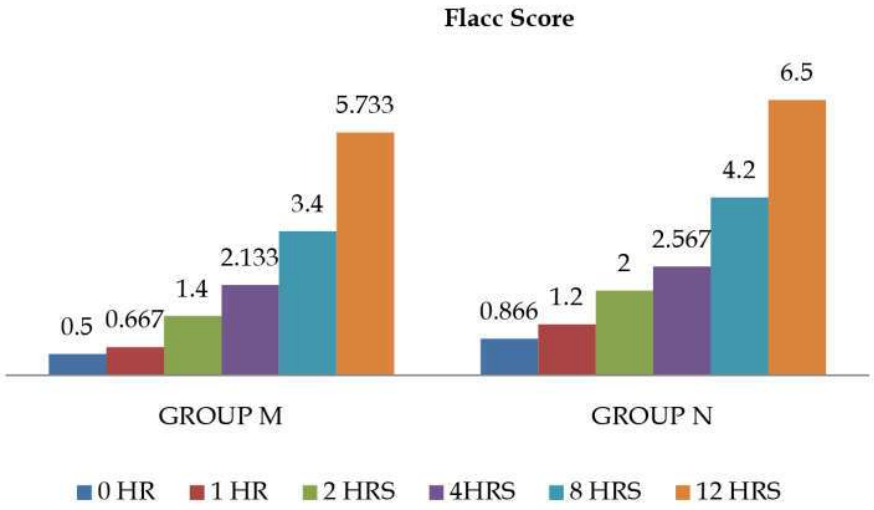


**Fig. 1:** Comparison of FLACC scale in both groups

complications like respiratory depression, vomiting and pruritis whereas none of the patients in group N had complication.

The first time requirement of postoperative analgesics was significantly longer in Group M (11.93±1.98) compared to group N (9.150±1.297) and they are statistically significant (p value<0.05) (Table 5).

## Discussion

Caudal block is one of the most commonly perfomed blocks in paediatric population [3]. Local anaesthesia drugs are commonly used in caudal block for postoperative analgesia purpose. To decrease the toxicity of local anaesthesia drugs and to prolong the duration of analgesia, various adjuncts are used, especially opiods like morphine, fentanyl, nalbuphine, tramadol etc [4].

Two groups were comparable in respect to age, gender, and weight of the patient. The present study compares the use of caudal bupivacaine with adjuvants morphine and nalbuphine for postoperative analgesia using FLACC pain score and the time needed for rescue analgesics. Previous studies have demonstrated use of various dose of morphine for analgesic efficacy and their associated complications. Nalbuphine is also used as adjunct in caudal block and their efficacy has been studied. So this study was made to compare the efficacy of morphine and nalbuphine in caudal block and at the same time comparing the incidence of complication produced by these drugs at their therapeutic effect.

Assessment of pain scores in children is difficult, as they are unable to explain their feelings

especially in infantile age groups. Therefore in children no scale is considered as universal, so we used FLACC score to assess pain similar to Salama et al. [2].

In this study we found the pain scores in nalbuphine group were substantially more after 4 hours of surgery and their analgesic effect lasted for more than 8 hours, whereas in morphine group the analgesic effect lasted more than 12 hours. This results are similar to other study conducted by Salama et al. [2] a randomised control study in which they compared group LN receiving 0.125% levobupivacaine with nalbuphine 0.2mg/kg 1ml/kg and group L receiving 0.25% levobupivacaine 1ml/kg. The analgesic effect in group LN is similar to our study that lasted for more than 6 hours. Baduni et al. [3] used three different doses of morphine in three groups as 30ug/kg (GROUP I), 50ug/kg (GROUP II) and 70ug/ kg GROUP III) and the duration of analgesia in group II ( 50ug/ kg) is similar to our study. At the same time in our study complications associated with caudal opioids such as respiratory depression, nausea/vomiting is especially higher in opioid agonist group such as morphine as compared to agonist- antagonist drugs such as Nalbuphine [6]. Respiratory depression, the most deleterious side effect of caudal morphine increases with increase in dose of morphine as reported by Budani et al.[3] in which 3 patients had respiratory depression which is similar to our study. In our study 8 patients of group M had complications like respiratory depression, vomiting and pruritis whereas none of the patients in group N had complication like these. Similar to our study Vetter et al.[11] had compared single dose of caudal morphine 50ug/kg, clonidine 2ug/kg and hydromorphone 1ug/kg and they have found that morphine provides sustained initial analgesia, though with a higher incidence of postoperative nausea, vomiting and respiratory depression.

## Conclusion

In conclusion we found that, as an adjuvant to bupivacaine, morphine has prolonged the duration of analgesia and decreased the use of rescue analgesic for around 12 hours but at this therapeutic dose, it is associated with higher life threatening complications such as respiratory depression, and other complications like nausea and vomiting whereas Nalbuphine has decreased the use of rescue analgesic for more than 8 hrs and has not produced above mentioned complication. Hence the usage of morphine as an adjuvant can be replaced with nalbuphine in Pediatric surgeries.

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*Key Messages*

**E**venthough morphine and nalbuphine are good adjuvants for bupivacaine, the incidence of complications are higher in patients receiving morphine . Hence the morphine usage can replaced with nalbuphine in pediatric surgeries

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