# Efficacy of Dexmedetomidine as an Adjuvant to Levobupivacaine in Caudal Anaesthesia in Paediatric Patients

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**Abstract**

**Background:** Postoperative pain management is becoming an integral part of anaesthesia care. Single shot caudal block is a common technique for paediatric analgesia but with the disadvantage of short duration of action. Several adjuvants have been used to prolong the duration of caudal analgesia. So we designed this study using dexmedetomidine as an adjuvant with levobupicaine for caudal block to assess analgesic efficacy, duration of postoperative analgesia, hemodynamic stability and any adverse effects in children.

**Methods:** After getting approval by Institutional Ethical Committee and written informed consent from parents, this prospective, double blind trial was carried on 80 children aged between 1 to 12 years scheduled for elective subumbilical surgeries that were allocated randomly into one of two groups. Children in Group A received 0.25% levobupivacaine 1 mL kg-1 body weight with 0.5 mL normal saline and in Group B received 0.25% levobupivacaine 1 mL kg-1 body weight with dexmedetomidine 1µg kg-1 in 0.5 mL normal saline as caudal drug mixture.

**Results:** The mean duration of analgesia in Group A was 324.±55.6 min and in Group B was 678±170.9 min which was statistically significant (p<0.001). The total analgesic requirement over 24 hours and the mean pain score was also lesser in group B.

**Conclusion:** Dexmedetomidine in doses of 1 µg kg-1 as an adjuvant to 0.25% levobupivacaine for caudal block in pediatric infraumbilical surgeries provides significant prolonged postoperative analgesia and better quality of sleep without any increase in adverse effects.

**Keywords:** Caudal block, Levobupivacaine, Dexmedetomidine, Infraumblical Surgeries

## Background

Caudal epidural anesthesia is the most commonly practiced regional technique in children for infraumbilical surgeries. However, the limited duration of analgesia following a single injection of local anesthetics mandates the quest for an adjuvant that may prolong it safely. The use of an indwelling catheter for prolonging the duration of action of local anesthetics is usually not practiced due to concerns about proximity to the anorectal area giving rise to infection and toxicity risks in the young population [1].

In recent years, the addition of adjuvants such as opioids, ketamine, and alpha-agonists to local anesthetics has resulted in prolonging the duration of block, improved pain control, parental satisfaction, and faster recovery. In recent years, the addition of adjuvants such as

opioids, ketamine, and alpha-agonists to local anesthetics has resulted in prolonging the duration of block, improved pain control, parental satisfaction, and faster recovery.

Levobupivacaine is an amino-amide local anesthetic drug belonging to the family of n-alkyl-substituted pipecoloxylidide. It is the S-enantiomer of bupivacaine. It has shown similar potency to bupivacaine with a lower risk of cardiovascular and central nervous system toxicity.

Dexmedetomidine which has analgesic and sedative properties, is an extremely selective α-2 receptor agonist with α-2/α-1 ratio of 1600:1 and due to which it is eight times more potent than clonidine having major advantage over clonidine [2].

Some studies have shown that addition of dexmedetomidine to ropivacaine/ bupivacaine in regional blocks prolongs the duration of analgesia with minimal side effects. However, there is a scarcity of literature on the use of dexmedetomidine as an adjuvant to levobupivacaine for extension of single shot caudal block. So, we planned this clinical trial to evaluate the analgesic efficacy of dexmedetomidine 1 μg kg-1 as an adjuvant to 0.25% levobupivacaine in caudal block in terms of duration of analgesia, pain intensity, level of sedation and side effects.

**Material and Methods**

Following approval by the institutional ethics committee, written informed consent was obtained from the parents of all children, the study was done on 80 paediatric patients of ASA Grade I or II, aged 1-12 years who were scheduled for elective infra-umbilical surgeries under general anaesthesia with written informed consent from their parents. Patients with history of developmental or mental retardation, known allergy to study drugs, coagulation disorders, coexisting medical or neurological diseases, sacral bone abnormality and any sign of infection at the block site were excluded from study.

Preanesthetic assessment was done on the day before surgery and parents were asked to ensure child's preoperative fasting (minimum 2 hours for clear liquid and 6 hours for semisolid or solid). On the day of surgery, all the patients were premedicated with oral midazolam 0.5 mg kg-1, 45 minutes before induction of anesthesia. In the operation room, routine monitors including pulse oximetry, electrocardiogram, and noninvasive blood pressure (NIBP) monitoring were instituted and the baseline vitals were recorded. Intravenous (IV) line was placed with appropriate size cannula and IV fluid infused at the rate of 4 mL/ kg/ hr. Intravenous glycopyrrolate 0.005 mg /kg/body weight was administered as premedication. Then standard inhalational anaesthesia technique was used for induction of anaesthesia. Neuromuscular blocking agent atracurium 0.5 mg /kg body weight was given to facilitate endotracheal intubation. Maintenance of anesthesia was done with 40% $O_2$:60% $N_2O$ mixture and sevoflurane 1-2%. After induction of anaesthesia, child was moved to lateral decubitus position for blind caudal block. With a sterile procedure, the caudal space was recognized using standard landmarks technique and a 22 G short, hypodermic needle was inserted into the caudal space. Test aspiration was done and the study drug was injected following confirmation of absence of blood/cerebrospinal fluid.

These patients were randomly divided into 2 groups of 40 each and randomization was done using a computer generated excel spread sheet randomization program. Sequentially numbered sealed opaque envelopes naming the drug to be administered were opened shortly before the induction of anaesthesia. The drugs for use in the caudal space were prepared by an anaesthesiologist who was not contributing in the study and the caudal block was given by another anesthaesiologist who was blinded to the drug that was injected. Children in Group A received 0.25% levobupivacaine in the

dose of 1 mL/ kg body weight with 0.5 mL normal saline and Group B received 0.25% levobupivacaine in the dose of 1 mL/ kg body weight with dexmedetomidine 1 µg /kg in 0.5 mL normal saline as caudal drug mixture. The time of placement of caudal block was recorded and surgery was allowed after 10 minutes of caudal block. In case the block was inadequate as suggested by limb movement on surgical incision or tachycardia, patients were managed with additional fentanyl 1 µg /kg and excluded from the study. Failure of the caudal block was not found in any of our patients. As per standard protocol heart rate, NIBP, oxygen saturation and temperature were recorded before induction and then every 5 minutes for first half an hour and then every 10 minutes until the end of surgery. The manifestation of intraoperative hypotension i.e., fall in systolic blood pressure >20% of the baseline, requiring a fluid bolus and bradycardia requiring atropine was recorded. After completion of surgery, the residual neuromuscular blockage was reversed using intravenous glycopyrrolate (0.002 mg kg-1) and neostigmine (0.05 mg kg-1). After extubation, patients were shifted to recovery and were monitored for vital signs (heart rate, respiratory rate and peripheral oxygen saturation).

Postoperatively the Face, Legs, Activity, Cry and Consolability (FLACC) pain scale was used to assess pain immediately and at 2, 4, 6, 12, 18 and 24 hours of the postoperative period [3]. Intravenous paracetamol 15 mg/ kg was given as rescue analgesia whenever the FLACC score ≥4 was observed. Duration of analgesia and the 24 hours total analgesic consumption were also recorded. Ramsay sedation score was used to assess the level of sedation at 15, 30 and 60 minutes after extubation and thereafter hourly until the sedation score became 2 or less in each patient [4]. Any other side effects like nausea, vomiting and respiratory depression were monitored and managed accordingly. Postoperative respiratory depression was defined as respiratory rate <10/min or fall in $SpO_2$<93% requiring supplement oxygen or assisted ventilation.

## Statistical Analysis

The duration of analgesia was taken as primary outcome measure for the sample size calculation. Based on former clinical data to detect the mean difference of 4 hours between two groups in duration of analgesia and 80% power along with 5% probability of type 1 error, sample size of 80 patients (40 in each group) was considered acceptable. After completion of trial, all the outcomes were evaluated by using IBM SPSS Statistics for Windows, Version 17.0 (Chicago: SPSS Inc.). Numerical variables were analysed using Student's unpaired t-test and Pearson's chi square ($\chi2$) test was used for categorical values. Non parametric numerical variables within the two groups were analyzed by using the Mann-Whitney U test. For all statistical analyses, p value <0.05 was taken as significant.

## Results

In this study, a total of 80 patients were enrolled and screened for eligibility to participate in this clinical trial. All the 80 patients were allocated to one of the two study groups and there was no drop out in the study. Regarding demographic data including age, weight, and sex and duration of surgery (Table I) and type of surgery (Table II), no statistically significant difference was found between the two groups. Intraoperative hemodynamic parameters i.e., HR, NIBP, oxygen saturation and temperature were also comparable in both the groups.

### Table 1: Comparison of demographic data and duration of surgery

| Variables | Group A (n=40) | Group B (n=40) | p value |
|---|---|---|---|
| Age (years) (mean±SD) | 4.28±2.759 | 4.38±2.863 | 0.905 |

| | | | |
|---|---|---|---|
| Weight (kg) (mean±SD) | 16.59±6.2 | 16.83±6.4 | 0.861 |
| Sex (male/female) (n) | 35/5 | 36/4 | 0.723 |
| Duration of surgery (min) (mean±SD) | 45.1±12.8 | 45.1±12.8 | 1.00 |

*p value >0.05 is insignificant

**Table 2: Type of surgeries in two groups**

| Type of Surgery | Group A (n=40) | Group B (n=40) | P value |
|---|---|---|---|
| Chordee (%,n) | 5% (2) | 5% (2) | |
| Hypospadias (%,n) | 25% (10) | 32.5% (13) | |
| Inguinal Hernia (%,n) | 55% (22) | 47.5% (19) | 0.962 |
| Phimosis (%,n) | 5% (2) | 5% (2) | |
| Undescended Testis (%,n) | 10% (4) | 10% (4) | |

*p value >0.05 is insignificant

Duration of analgesia was demarcated as time between administration of caudal block and the time to first request for rescue analgesia. The mean duration of analgesia in group A was 322±53.7 minutes (mean 5.4 hours) with confidence interval of mean 306.19-341.81 while in group B it was 679±169.9 minutes (mean 11.3 hours) with confidence interval of mean 623.34-732.66. The statistically difference in their mean duration of analgesia was found to be highly significant (Table III).

**Table 3: Duration of analgesia**

| Variable | Group A (n=40) | Group B (n=40) | P value | Significance |
|---|---|---|---|---|
| Duration of analgesia(minutes) (mean ±SD) | 322±53.7 | 679±169.9 | 0.000 | HS |

*HS-highly significant, p value <0.01 is considered highly significant

In present study, the FLACC pain scale was measured in PACU at 0 hour and at 2, 4, 6, 8, 12, 16, 24 hours of the post-operative period. FLACC score was statistically non-significant among two groups in PACU at 0 hour. The patients in group A showed increase in FLACC pain score at 4 hours and 6 hours whereas the patients in group B had low FLACC score at above intervals. This difference on statistical analysis was found highly significant. However, in group B, there was increase in FLACC score at 8th hour i.e., 3.10±0.8. After receiving rescue analgesia, FLACC score decreased in both the groups. Thus, the difference between mean FLACC Score was statistically significant at 2, 4, 6, 8, 12 and 16 hours while it was comparable at 24 hours postoperatively among two groups (Figure 1).
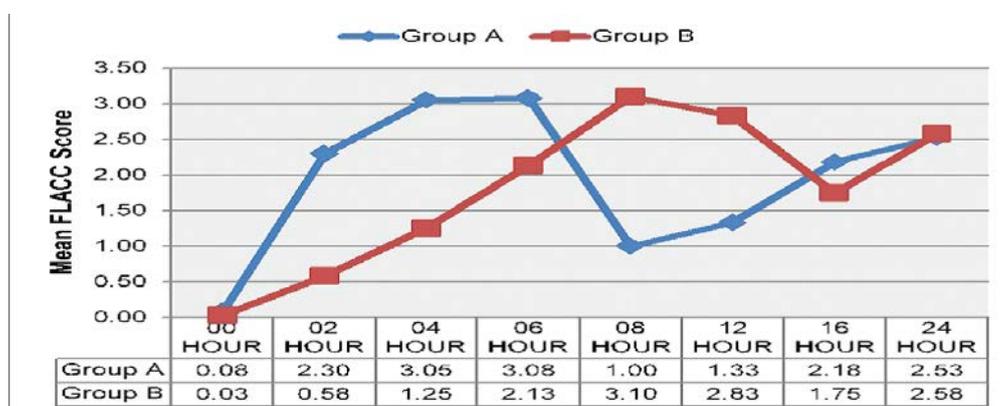


| | 00 HOUR | 02 HOUR | 04 HOUR | 06 HOUR | 08 HOUR | 12 HOUR | 16 HOUR | 24 HOUR |
|---|---|---|---|---|---|---|---|---|
| Group A | 0.08 | 2.30 | 3.05 | 3.08 | 1.00 | 1.33 | 2.18 | 2.53 |
| Group B | 0.03 | 0.58 | 1.25 | 2.13 | 3.10 | 2.83 | 1.75 | 2.58 |

**Figure 1:  Face, Legs, Activity, Cry and Consolability (FLACC) score during postoperative period**

Rescue analgesia was used when FLACC score was ≥4. The mean number of doses of rescue analgesia that was required in group A was 1.60±0.501 and in group B was 1.00±0.00 and the difference was found statistically significant among two groups. Most of the patients in group B (90%) required only single dose of rescue analgesia (except 10% who required second dose in first 24 hours period) whereas in group B, 42.5% patients required single rescue analgesia dose and 55% patients needed two doses of rescue analgesia in 24 hours post-operative period. Only one patient in group A required three doses of rescue analgesia. Mean total analgesic consumption in group A was 392.3±187.5 mg and in group B was 268.9±111.8 mg and the difference among two groups was found statistically significant.

There was also statistically significant difference regarding level of sedation among the two study groups. The mean RSS score in group B was statistically significant higher as compared to group A at 0, 2 and 4 hours postoperatively. But after 4 hours, RSS was comparable between two groups as shown in (Figure 2). In our study, the intraoperative and postoperative period was uneventful in both groups. No episodes of hypotension, bradycardia, or respiratory depression requiring intervention in any of the patients in the two groups were noted.
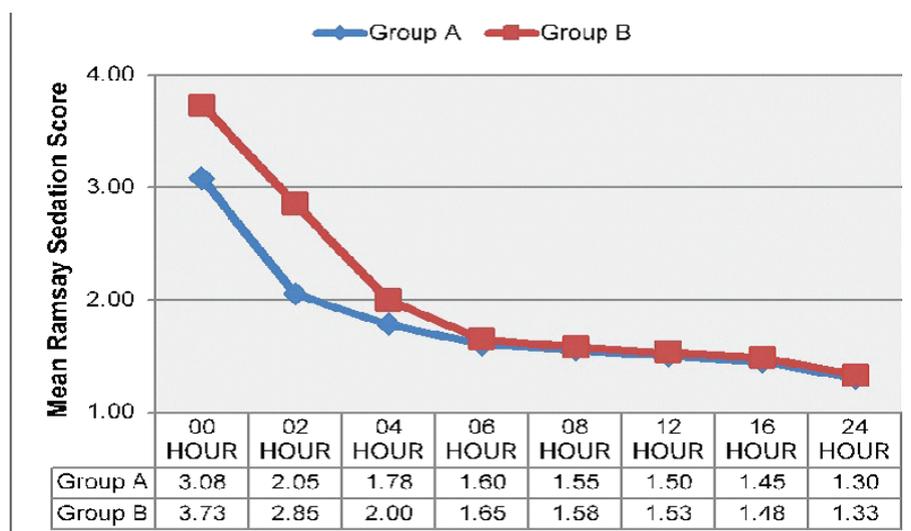


| | 00 HOUR | 02 HOUR | 04 HOUR | 06 HOUR | 08 HOUR | 12 HOUR | 16 HOUR | 24 HOUR |
|---|---|---|---|---|---|---|---|---|
| Group A | 3.08 | 2.05 | 1.78 | 1.60 | 1.55 | 1.50 | 1.45 | 1.30 |
| Group B | 3.73 | 2.85 | 2.00 | 1.65 | 1.58 | 1.53 | 1.48 | 1.33 |

**Figure 2: Mean Ramsay Sedation Score (RSS) at different time intervals during postoperative period**

## Discussion

Caudal epidural analgesia is most common, dependable, and safe method in paediatric anaesthesia that can provide satisfactory analgesia for a variety of infra-umbilical surgeries. The main drawback of caudal block is the shorter duration of analgesia after a single injection. The use of repeated doses or infusions of local anaesthetics through caudal catheter is not common in clinical practice due to risk of infection. So, prolongation of single shot caudal analgesia technique has been accomplished by the use of different adjuvants with local anaesthetics [5].

In present study, we used levobupivacaine in dosage of 1 mL/ kg of 0.25% levobupivacaine i.e., 2.5 mg/ kg. Clinically, its use in paediatric regional anaesthesia is well established. A study conducted by Frawley *et al*. [6] had concluded that levobupivacaine at a recommended dose of 2.5 mg/ kg is an effective drug for caudal anaesthesia in children and the faster onset of action was

suitable for achieving surgical anaesthesia and this postoperative analgesia was established in greater than 97.5% of patients.

Ivani *et al.* [7] compared caudal block characteristics using three different concentrations of levobupivacaine 0.125%, 0.2%, and 0.25% in children undergoing infraumbilical surgery. They reported that 0.125% levobupivacaine provides a short duration of analgesia but allows more rapid return of motor functions and 0.2% levobupivacaine provides both significant analgesia and quick motor recovery. We noted a prolonged duration of analgesia with 0.125% levobupivacaine with dexmedetomidine 1 µg/kg. This increase in the duration of postoperative analgesia can be temporally attributed to the addition of dexmedetomidine.

Dexmedetomidine is a highly selective alpha 2 adrenoceptor agonist. It possesses a selective affinity for alpha 2 adrenoceptor subtype A, which causes it to be much more effective sedative and analgesic without undesirable side effects from alpha 1 receptor activation [8]. Dexmedetomidine enhances the effects of local anesthesia without increasing the incidence of side effects [9].

Saadawy *et al.* [10] evaluated the analgesic effect of addition of 1 µg/kg of dexmedetomidine to 0.25% bupivacaine in infraumbilical surgeries in pediatric patients and demonstrated that time to first rescue analgesia was 18 h in dexmedetomidine group compared to 6 h in the bupivacaine group. Our study also observed an efficacious postoperative analgesia with addition of dexmedetomidine.

We used dexmedetomidine in dosage of 1 µg kg-1 as an adjuvant because it has a favorable safety profile with better haemodynamic stability which is in concordance with the reports published by several authors [11,12]. In recent study on different doses of dexmedetomidine (1 µg/ kg and 2 µg/ kg) as an adjuvant to caudal analgesia done by Al Zaben *et al.* [13] had found that use of higher doses of dexmedetomidine had increased the incidence of side effects without any additional prolongation in duration of analgesia.

The main outcome of our study was the prolongation of caudal analgesia with addition of dexmedetomidine to caudal levobupivacaine with mean duration of 11.3 hours as compared to levobupivacaine alone (5.4 hours). Tandale *et al.* [14] also found the significant prolongation in duration of analgesia with mean of 12.8 hours in patients with caudal levobupivacaine 0.25% with dexmedetomidine and 7.3 hours with levobupivacaine 0.25% alone. Our findings were also supported with study done by Fares *et al.* [15] who found mean duration of analgesia of 8.38 hours and

19.2 hours in patients receiving caudal bupivacaine 0.25% alone and in combination with dexmedeto-midine 1 µg kg-1 respectively.

Nasreen *et al.*, [16] also showed prolongation in duration of analgesia with use of dexmedetomidine (1 µg/ kg) as an adjuvant to caudal levobupivacine (0.75 mL/ kg of 0.125% levobupivacaine). Mean duration of analgesia was statistically prolonged ($1299 \pm 145$ min) in Group B (dexmedetomidine with levobupivacaine) as compared to Group A (levobupivacaine) ($348 \pm 36$ min). Comparable analgesic duration with lower concentration of levobupivacine could be attributed to the harness of ultrasound in this study, leading to precise deposition of drug.

Moreover, the mean number of rescue analgesic doses and total analgesic requirement were also significantly lower in group B as compared to Group A in present study and these results were also in agreement with study done by Goyal *et al.* [17] and Kamal *et al.* [18].

In our study, pain intensity was measured by usingFLACC Scale. FLACC scale is easy to use, reliable and valid which has been recognized in miscellaneous settings and in different patient population [19]. In present study, the difference of mean FLACC score among two groups was statistically significant at 2, 4, 6, 8, 12 and 16 hours except at 0 hour and at 24 hours in PACU. Similar results were also observed by Nasreen *et al*. [16] where the mean FLACC score was >4 in patients of Group A (levobupivacaine alone) after 5 hours as compared to group B (dexmedetomidine & levobupivacaine) and the two groups showed a statistically significant difference of FLACC score at all times in the postoperative period. Tandale *et al*. [14] also observed a significant reduction in the FLACC scale among patients receiving dexmedetomidine with levobupivacaine.

In this present clinical trial, mean sedation score was more in the group B at 0, 2 and 4 hours postoperatively as compared to Group A but all the patients were easily arousable by verbal contact and none of them experienced any respiratory depression. Some other authors also noted higher sedation scores in patients receiving dexmedetomidine as caudal additive in the postoperative period [14,15].

In our study none of the patient in either group had any side effects like nausea/vomiting, hypotension, bradycardia and respiratory depression within the observation period. A study conducted by Kamal *et al*.,[18] also found no episodes of clinically significant postoperative complications with use of dexmedetomidine 2 µg /kg as adjuvant to ropivacaine (0.25%).

There are few limitations in this present study. Firstly, the enrollment of children with wide range of age group (1 to 12 years) who has variable thresholds for pain and capability to communicate pain, could have led to difference in the pain measurement. Secondly, due to difference in degree of surgical trauma (variable surgical procedures) might have led to variability in pain score in this study. Thirdly, as with use of all adjuvants in regional blocks, the analgesic action of dexmedetomidine through systemic absorption cannot be entirely ruled out from present study since we did not include intravenous dexmedetomidine as control group. Lastly, although we did not encounter even a single block failure, it will be safer and precise to conduct the procedure under ultrasound guidance.

## Conclusion

Hence, we conclude that dexmedetomidine is an effective adjuvant to levobupivacaine for caudal block in pediatric infraumbilical surgeries in terms of prolonged postoperative analgesia, decreased rescue analgesic consumption and better quality of sleep without any adverse effects. This can contribute significantly to better patient comfort and safety.

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