Analgesic efficacy of dexamethasone as an adjuvant to caudal bupivacaine for infraumbilical surgeries in children: A prospective, randomized study

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Abstract
Background and Aims: Provision of adequate perioperative analgesia in children is important to attenuate the stress response to surgery. Caudal analgesia using local anesthetics is a traditionally used technique but provides a limited duration of analgesia. Several adjuvants can be added to local anesthetics to increase the duration of action. This study was undertaken to evaluate the efficacy of dexamethasone added to bupivacaine for caudal block in children.

Material and Methods: This was a prospective, double-blinded trial on 130 children aged between 6 months and 6 years of age allocated randomly into one of two groups for elective subumbilical surgeries. Children in Group C received caudal bupivacaine and those in Group D received caudal bupivacaine with 0.1 mg/kg of dexamethasone.

Results: The mean duration of analgesia when dexamethasone was added to caudal bupivacaine was 1044.92 (±48.66) min, while it was 435.85 (±17.95) min with plain bupivacaine. The number of doses of rescue analgesics required and the mean pain score was also lesser in this group.

Conclusion: The addition of 0.1 mg/kg of dexamethasone to caudal bupivacaine increases the duration of analgesia of caudal bupivacaine without any side effects in children undergoing subumbilical surgeries.

Keywords: Caudal anesthesia, dexamethasone, local anesthetics, postoperative analgesia

Introduction

Inadequately and inappropriately managed pain in children can lead to long-term physical, psychosocial, and behavioral sequelae.[1] Under treatment of pain in children is common and has been due to the fear of opioid-induced respiratory depression and difficulty with pain assessments in very small children.[2] However, provision of adequate perioperative analgesia in children has improved in recent years due to the increased awareness about the adverse effects of untreated pain and also due to the availability of novel techniques and new drugs.

Single-shot caudal blockade continues to be one of the traditionally opted perioperative pain management strategies in pediatrics. The ease of performing a successful block resulting in reliable analgesia in the immediate postoperative period has made it a popular, safe, most accepted, and most used technique.[3] However, the duration of analgesia provided by a caudal block is limited by the duration of action of the local anesthetic. Various adjuvants to local anesthetics have been investigated to circumvent this issue. The use of these additives has been with the aim of improving the quality of block and...
duration of analgesia. Many of these adjuvants – fentanyl, clonidine, dexmedetomidine, neostigmine, ketamine, midazolam – have side effects specific to the type and dose of adjuvant used.\textsuperscript{[4,5]} The alpha-2 agonists, clonidine, and dexmedetomidine are associated with bradycardia and prolonged sedation.\textsuperscript{[6-14]} Opioids are associated with risk of respiratory depression and the neurotoxicity of midazolam is still a controversy. The ideal adjuvant is still a matter of contention and the quest for a drug that provides maximal analgesia with minimal side effects for caudal block in children continues till date.

Dexamethasone is a long-acting corticosteroid with antiinflammatory action. When administered in combination with local anesthetics in the epidural space, it has been shown to reduce postoperative rescue analgesic consumption following abdominal and orthopedic surgeries.\textsuperscript{[15,16]} The inherent intense antiinflammatory effects of dexamethasone promote the analgesic effectiveness. The added advantage of minimal side effects when compared to other adjuvants makes this drug an attractive choice for further evaluation. This study was conducted with the aim of assessing the analgesic efficacy of dexamethasone administered in the dose of 0.1 mg/kg with 0.125% bupivacaine for caudal block in children undergoing elective subumbilical surgeries.

**Material and Methods**

The study was done as a prospective randomized controlled, double-blinded clinical trial after getting Institutional Ethical Committee approval and informed consent from parents. Children in the age group of 6 months to 6 years of age, of American Society of Anesthesiologist (ASA) physical status I and II scheduled for elective subumbilical surgeries were enrolled into the study after getting parental informed consent. Exclusion criteria included infection at the site of caudal block, sacral bone abnormalities, bleeding diathesis, and allergy to any of the study drugs. Preanesthetic evaluation was done on the day prior to surgery. Randomization was done using sealed envelope technique. All the children were premedicated with oral midazolam 0.5 mg/kg, 30 min prior to induction of anesthesia in the preoperative holding area. After shifting into the operating room, preinduction monitors were instituted, which included pulse oximetry, electrocardiogram, and noninvasive blood pressure monitoring. The baseline values were recorded and documented. Inhalation induction of anesthesia was done using oxygen 100% and sevoflurane 8% and an intravenous line was secured. Fentanyl 2 mcg/kg was administered intravenously. Airway management was with the use of face mask, laryngeal mask airway, or endotracheal tube and was left to the discretion of the attending anesthesiologist. Maintenance of anesthesia was with 33% O\textsubscript{2}:67% N\textsubscript{2}O mixture and sevoflurane 2%.

The child was then turned to the lateral position for administration of the caudal block. With a sterile technique, the caudal space was identified using standard landmarks and a 22 G short beveled needle was inserted into the caudal epidural space.

Children in group C received 1 ml/kg of 0.125% bupivacaine with 0.25 ml/kg saline in the caudal epidural space, while children in Group D received 1 ml/kg of 0.125% bupivacaine with 0.1 mg/kg dexamethasone in the caudal epidural space. The drugs for administration in the caudal space were prepared by an anesthesiologist not participating in the study. The caudal block was performed in the lateral position by another anesthesiologist who was blinded to the drug that was injected. The surgical incision was made 5 min after caudal placement of the study drugs. The patients were observed for any limb movement, increase in heart rate or mean arterial pressure by 15% more than the baseline values, and presence of any of these parameters was considered a failed caudal block. These children were excluded from the study and managed with additional doses of fentanyl intraoperatively.

Intraoperative monitoring included heart rate, noninvasive blood pressure measurement, pulse oximetry, and end-tidal capnography. The recorded parameters were documented every 5 min intraoperatively till awakening. After extubation the pain score was assessed using Face, Legs, Activity, Cry, Consolability (FLACC) scale at intervals of 0, 15, 30, 60, 90, 120, 150, 180 min. Patients were shifted to the ward after observation in the postanesthesia care unit for 3 h. The pain scores were assessed and documented in the ward every hour for the first 6 h and second-hourly for 24 h.

Oral paracetamol 15 mg/kg was given as a rescue analgesic if the pain score was more than 3 and the number of rescue doses received in 24 h was recorded. Respiratory depression was defined as an oxygen saturation of <93% on the pulse oximeter or respiratory rate <10 per minute requiring oxygen supplementation and assisted ventilation. Bradycardia was defined as heart rate <60 per minute or 20% below the baseline value, whichever was lower and was treated with atropine 20 mcg/kg intravenously. Hypotension was defined as systolic blood pressure 20% less than the baseline value that was treated with injection ephedrine in fractionated doses.

**Statistical analysis**

The sample size was calculated as 60 subjects per group, to detect a difference in the duration of analgesia with an alpha error of 0.05 and beta error of 0.09. Allowing exclusion due
to failed caudal, 130 children in the age group of 6 months to 6 years coming for infraumbilical surgeries were enrolled in the study. Analysis was done using the Statistical Package for the Social Sciences (SPSS) version 15.0 software. The observed variables are expressed as mean and standard deviation or numbers and percentage. Continuous covariates were compared using analysis of variance. The comparison was studied using the Chi-square test or Fisher’s exact test or independent t-test as appropriate, with the $P$ value reported at the 95% confidence interval. $P < 0.05$ was considered statistically significant.

**Results**

Demographic data are given in Table 1. There was no statistically significant difference between the two groups in terms of age, gender, and weight of children and the duration of surgery. The type of surgery is given in Table 2.

Duration of analgesia was defined as the time taken from the caudal placement of drug till the first recording of FLACC score more than 3. The mean duration of analgesia in Group C was 433.85 (±144.72) min, while in Group D, it was 1044.92 (±392.29) min [Figure 1]. In Group C, the minimum duration of analgesia was 240 min and the maximum duration of analgesia observed was 960 min, while in Group D, the minimum duration of analgesia was 300 min and maximum was 24 h, beyond which monitoring was not done.

Children in Group D who received caudal dexamethasone along with bupivacaine had a statistically significant increase in the duration of analgesia, with a $P$ value of 0.005.

The mean number of rescue analgesics required by patients in Group D was 0.88 (±0.85), while in Group C, the mean number of rescue analgesics required by the patients was 1.769 (±0.523), which was statistically significant ($P < 0.05$).

The mean pain scores were similar in both the groups for the first 4 h, after which time it was significantly lower in group D at 5th, 6th, 16th, 20th, and 24th hour compared to group C [Figure 2]. Twenty-seven (41.5%) children in group D did not receive any rescue analgesics whereas all the patients in group C received at least one rescue analgesic dose. Sixty-two (94%) children in group C received two or more number of rescue analgesics, which was statistically significant ($P < 0.05$). No adverse events were reported in both the groups. There was no statistically significant difference in the hemodynamic parameters between the two groups.

**Discussion**

Caudal analgesia is the traditional technique of provision of intra and postoperative analgesia in children for surgeries of the abdomen, pelvis, and the lower limb. The effectiveness of the caudal block is only limited by the duration of action of the local anesthetic, when administered as a single-shot injection. This has led to the use of several adjuvants to prolong the duration of action of the local anesthetic. In recent years, the perioperative use of dexamethasone has increased, including its use in central and peripheral nerve block and

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**Table 1: Demographic data of patients in both the groups**

| Parameter                      | Group C          | Group D          |
|--------------------------------|------------------|------------------|
| Age (years)                    | 2.49 (±1.54)     | 2.94 (±1.70)     |
| No of males/females            | 61/4             | 62/3             |
| Weight (kg)                    | 12.0 (±2.91)     | 12.7 (±3.74)     |
| Duration of surgery (min)      | 33.46 (±14.38)   | 37.92 (±11.52)   |

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

| Type of surgery     | Group C (N=65) | Group D (N=65) |
|---------------------|----------------|----------------|
| Herniotomy          | 10             | 7              |
| Circumcision        | 20             | 32             |
| PV sac ligation     | 7              | 9              |
| Cystoscopy/dilation | 10             | 3              |
| Orchiopexy          | 6              | 5              |
| Hypospadias         | 10             | 8              |
| Lower limb procedures | 2             | 1              |

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**Figure 1:** Mean duration of analgesia in the two groups

**Figure 2:** Mean pain scores in the two groups
intravenously during surgery. Several studies have shown a definite improvement in the duration of analgesia when dexamethasone is used along with local anesthetics.\textsuperscript{17-21}

Dexamethasone as an adjuvant to local anesthetic for peripheral nerve or neuraxial block has various mechanisms of actions such as direct membrane action in unmyelinated fibers, vasoconstriction, action on potassium channels, and suppression of other inflammatory mediators. Though the exact mechanism of action has not been definitely elucidated, one or more of the above mechanisms alone or in combination could play a role in its use as an analgesic adjuvant.\textsuperscript{22}

The dose of caudal dexamethasone (0.1 mg/kg) in our study was selected based on a previous study regarding the analgesic effect of epidural dexamethasone in adults, which showed that effective analgesia was provided by 5 mg of epidural dexamethasone but not 5 mg of intravenous dexamethasone in patients undergoing laparoscopic cholesystectomy, which implied that epidural dexamethasone has greater analgesic efficacy than intravenous dexamethasone at the same dose.

The analgesic effects of caudal dexamethasone are predominantly due to local effects in the spinal cord as evident from the fact that the intravenous dose that potentiates analgesia was found to be much higher at a dose of 0.5 mg/kg as reported by Hong et al.\textsuperscript{23} The transcription nuclear factor-kappa B (NF-κB), which is responsible for the development of pathological pain, is regulated by dexamethasone, which could be responsible for the prevention of central sensitization after surgery and improved analgesia following a caudal block.

In our study the addition of dexamethasone at 0.1 mg/kg with 0.125% bupivacaine increased the duration of analgesia effectively, which are consistent with the findings by Kim et al.\textsuperscript{24} Girgis\textsuperscript{25} in their study used a dose of 0.2 mg/kg of dexamethasone with 0.25% bupivacaine and the time to first analgesic requirement was 11.2 h. Although we used a lower dose of dexamethasone (0.1 mg/kg) with 0.25% bupivacaine, the mean duration of analgesia in our study in the dexamethasone group was 17.4 h.

The pain scores were not different between the groups in the first 4 h probably due to the fact that the analgesic effects of bupivacaine would have persisted in both the groups during this time period. The difference between the pain scores in the two groups was observed after this period, with the mean pain scores lower in the dexamethasone group.

The pain scores were also not uniformly statistically significant at different time intervals after 5 h in the two groups. This can be explained by the rescue analgesics given when the pain score was more than 3 in the group where plain bupivacaine was administered. This would have contributed to the reduction in pain score in this group. In addition, the overall reduction in the number of rescue doses in the dexamethasone group substantiates the above explanation. The benefits of adding dexamethasone is also highlighted by the statistically significant increase in the mean duration of analgesia, when compared to the group without dexamethasone.

There are some limitations to this study. The inclusion of children in the age group of 6 months to 6 years of age with varying thresholds for pain and ability to communicate pain could have led to variability in the pain scores. In addition, patients coming for a wide variety of subumbilical surgeries were chosen for the study. The varying degree of invasiveness of the different procedures could have contributed to varying degrees of pain. However, the different types of surgeries were equally distributed between the two groups. Another limitation was the fact that we could not determine the maximum duration of action of dexamethasone beyond 24 h, as the study was completed at that point of time, as per the protocol.

Studies using caudal dexamethasone have also demonstrated its effect in preventing nausea and vomiting. The dual advantage of analgesia with no side effects would make this drug a standard adjuvant in caudal analgesia. In our study we did not evaluate the adverse effects of dexamethasone such as hyperglycemia and adrenal suppression as these are uncommon following a single dose. It also adds to the cost and leads to unwanted needle pricks in the child for repeated blood sampling. To conclude, the addition of 0.1 mg/kg of dexamethasone to 0.125% concentration of bupivacaine effectively improves the analgesic efficacy in single-shot caudal anesthesia, without significant side effects. Further research is needed to define the exact dose required and the maximum duration of action of the administered dose.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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