ANALGESIC EFFECTIVENESS OF DEXAMETHASONE-LEVOBUPIVACAINE COMBINATION FOR CAUDAL ANALGESIA IN PEDIATRIC PATIENTS UNDERGOING INFRAUMBILICAL SURGERY: A RANDOMIZED CONTROLLED DOUBLE-BLIND STUDY

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Abstract

Background: The aim of this study was to evaluate the postoperative analgesic role of dexamethasone as an adjuvant to levobupivacaine in a single shot caudal block in children undergoing lower abdominal or urological procedures.

Methods: The study involved 50 children between 1 and 7 years of age scheduled for elective lower abdominal or urological procedures. The children were randomly allocated into one of two treatment groups according to injected solution of caudal block: Group L or Group DL. Group L (n = 25) received levobupivacaine 0.8 ml/kg and Group DL (n = 25) received levobupivacaine 0.8 ml/Kg mixed with dexamethasone 0.1 mg/kg. The primary outcome measure was the quality and duration of analgesia. Secondary outcome measures included the degree of sedation, residual motor block and any side-effects. The postoperative pain was evaluated using a objective pain scale (OPS).

Results: Up to two hours postoperatively, all children had no pain in both groups. From 3 hours up to 12 hours, OPS scores were significantly lower in Group DL. Duration of analgesia was significantly longer in Group DL ($p = 0.009$). Children in Group DL required significantly smaller doses of paracetamol during the 24 hours ($p < 0.001$). Sedation score was 1 during the first 24 postoperative hours except in few children. Few children developed nausea and vomiting or fever.

Conclusion: Mixing dexamethasone 0.1 mg/kg with levobupivacaine provided significantly better and longer duration of postoperative analgesia after caudal block in pediatric patients.

Keywords: Caudal anesthesia, pediatric analgesia, dexamethasone, NSAIDs, infraumbilical surgery.

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Introduction

Postoperative pain following common surgeries in children is frequently managed by a regional analgesic modality combined with a general anesthetic. These modalities include inguinal and iliohypogastric nerve block (INB), local infiltration (INF), and caudal analgesia (CA)[1]. In general, regional anesthetics can reduce intra-operative anesthetic requirement, allow rapid recovery, control postoperative pain and eludes opioids use[2]. Therefore, the risk of side effects of intravenous (IV) opioids such as over-sedation, respiratory depression, vomiting, and ileus can be avoided[3].

Currently, caudal epidural block is the most commonly used regional analgesic technique in pediatric patients, being the easiest to perform and to teach, with extensive safety record in children[4]. It is successfully used as an effective postoperative analgesic modality after subumbilical and genitourinary operations[5]. The principal disadvantage of single-shot caudal block is the short duration of analgesia[6]. Even long-acting local anesthetics as bupivacaine provide only up to 4 to 8 hours of analgesia[7].

Continuous caudal block with catheter placement did not gain wide acceptance owing to the risk of infection and delayed mobility[8]. Alternatively, various drugs have been tried as an adjuvant to the local anesthetic solutions to prolong the duration of a single injection caudal anesthesia. These include opioids, clonidine, ketamine sufentanil, and α2-agonists[9-13].

Dexamethasone, a corticosteroid hormone with powerful anti-inflammatory and analgesic properties is commonly used for the management of postoperative pain, nausea, and vomiting[14,15]. Epidural administration of dexamethasone has been shown to reduce the incidence and severity of postoperative pain in adults[16] and to control nausea, vomiting, fever and delayed oral intake, in children[17].

The aim of this study is to evaluate the role of dexamethasone as an adjuvant to levobupivacaine in a single shot caudal block for providing adequate postoperative analgesia in children undergoing lower abdominal or urological procedures.

Patients and Methods

The study involved 50 children between 1 and 7 years of age with ASA class I or II scheduled for elective lower abdominal or urological procedures of anticipated duration <120 minutes. The study was conducted during the period from June 2017 to September 2017 after obtaining approval from Institutional Review Board of the Kasr-El-Ainy University hospitals.

Exclusion criteria included known or suspected coagulopathy, allergy to any local anesthetic, congenital anomaly of the spine, intake of aspirin or any analgesic drugs in the preceding week and local skin infections. After approval of the local ethical committee each child's guardian provided a written informed consent to participate in the study.

Using a computer-generated random table, children were randomly allocated into one of two treatment groups: Group L or Group DL. Group L (n = 25) received a caudal injection of levobupivacaine 0.25% 2 mg/kg (0.8 ml/kg). Group DL (n = 25) received a caudal injection of levobupivacaine 0.25% at a dose of 2 mg/kg (0.8 ml/Kg) mixed with dexamethasone 0.1 mg/kg. The maximum volume was 20 ml in both groups.

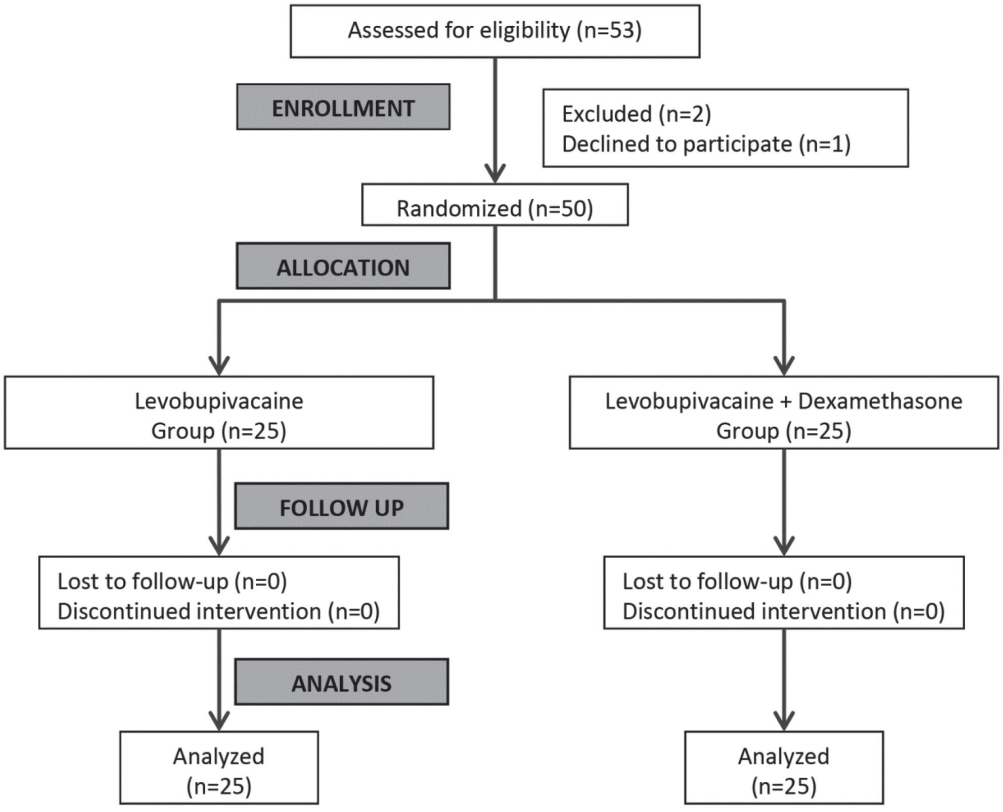
Patients were kept fasting for 6 hours before the procedure and clear fluids were allowed up to 3 hours before the surgery. No preoperative medications were administered. Anesthesia was induced with sevoflurane 8% in 100% oxygen and maintained by sevoflurane 2-2.5% in 50% oxygen-air mixture. Upon Loss of eyelash reflex, ventilation was assisted manually to maintain end tidal CO_2 (P_ECO_2) at 32-36 mmHg. Intravenous (IV) line was inserted for fluid replacement that consisted of 0.45% NaCl in 5% dextrose solution given at a rate of 3-5 ml/kg/h. Systolic and diastolic blood pressure (SBP and DBP) were measured automatically. Heart rate (HR) from ECG and P_ECO_2 and SPO_2 were monitored before induction and intraoperatively at 3 minutes intervals. Laryngeal mask airway was inserted then the patient was placed in the left lateral decubitus. Under sterile conditions caudal block was performed by a consultant anesthetist using 22-gauge needle which was advanced 0.5-1 cm for study drugs administration then a small

sterile dressing was placed over the injection site in all patients. Children received the study drug according to the random allocation. The volume of caudal solution given to each child was diluted with normal saline (0.9%) to a maximum of 20 ml. Preservative-free drugs were used and prepared by an anesthetist not involved in the trial. Caudal block efficacy during surgery was defined as absence of purposeful or non-purposeful movements or significant (>20%) increase in blood pressure, HR or RR associated with surgical incision which was made 15-20 min after caudal block. In case of inadequate level of analgesia, fentanyl 1 μg/kg was given and those patients were excluded from the study. After operation, the duration of surgery was noted and the patients were transferred to the recovery room. The SBP, DBP, HR, SPO_2 and RR were monitored in recovery room.

The primary outcome measure of the study was the quality and duration of analgesia. Secondary outcome measures included degree of sedation, residual motor block and any side-effects. The postoperative pain was evaluated using a 0-to-10 points objective pain scale (OPS), based on blood pressure, agitation, crying, movement and verbalization of pain. Pain was assessed at 1, 2, 3, 4, 6, 12 and 24 hours following recovery from anesthesia. Duration of analgesia was defined as the time from caudal block to first analgesic requirement. A pain score <4 was considered adequate analgesia. Whenever the child has OPS score ≥4, paracetamol syrup 15 mg/kg was administered with minimum 4 hours intervals between successive doses of paracetamol. Rescue analgesia with IV pethidine 0.5 mg/kg was used if the score was still ≥4 within this time interval. The total dose of supplementary analgesics required by each child in 24-h period was recorded.

Sedation was assessed with three-point scale (Score 1 = calm, cheerful; score 2 = restless; score 3 = tense and tearful). The incidence of residual motor block was evaluated using modified Bromage scale (score 0 = no motor block; score 1 = inability to stand unassisted; score 2 = ability to flex ankle but not the knee; score 3 = complete motor block in fully awake child). Motor block of score ≥1 after awakening and

Fig. 1
CONSORT Flow Diagram



180 minutes after caudal block was considered to be a significant residual motor blockade. The observations were made by an experienced anesthesiologist blinded to the study groups for 24 hours. Any side-effects such as emesis, motor weakness and pruritus were recorded.

Sample Size Estimation

According to the results of a previous study[18], based on the primary outcome measure (pain score), 25 patients per group are required to have a 80% chance of detecting, as significant at the 5% level, a lower pain score in the experimental group of 1.3 ± 1.0 compared to 2.1 ± 1.1 hours in the control group. The sample size was estimated using the online power calculator for continuous outcome superiority trial under Sealed Envelope Ltd. 2012. Available from: https://www.sealedenvelope.com/power/continuous-superiority/

Statistical Analysis

Statistical analysis was done using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA). Numerical data was summarized using mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Comparisons between quantitative variables were done using t-test or Mann-Whitney test. For comparing categorical data, Chi square test or Fisher's exact test was used. All tests were two-tailed. A p value <0.05 was considered significant.

Results

Table 1 shows that the two studied groups were comparable regarding age, sex, weight BMI and duration of the procedure. Type of surgery is shown in Table 1.

Up to two hours postoperatively, all children had no pain with OPS of zero. The median pain score of the two groups is shown in Table 2. From 3 hours up to 12 hours, OPS scores were significantly lower in Group DL (Table 2). Duration of analgesia was significantly longer in Group DL (p = 0.009). Children in Group DL required significantly smaller doses of paracetamol during the 24 hours (p <0.001).

The majority of children in the two groups were calm and cheerful with a sedation sedation score of 1 during the first 24 postoperative hours. Few children scored 2 (Table 3). Few children developed nausea and vomiting or fever (Table 3). All children were hemodynamically stable throughout the postoperative period. None of the children had residual motor block, pruritus or respiratory depression.

Table 1
Baseline characteristics of the two groups

	Group L (n = 25)	**Group DL (n = 25)**	**p-value**
Age (years)	4.3 ± 1.4	4.7 ± 1.7	0.419
Sex (M/F)	19/6	18/7	0.747
Weight (kg)	17.3 ± 2.7	18.1 ± 3.3	0.357
Duration procedure (min)	47.6 ± 24.4	47.4 ± 23.5	0.977
Type of surgery			1.000
Inguinal hernia	15 (60%)	15 (60%)	
Orchiopexy	5 (20%)	6 (24%)	
Hypospadius	5 (20%)	4 (16%)	

Data are presented as mean ± SD or number (%)

Table 2
Quality of analgesia during the postoperative period in the two groups

	Group L (n = 25)	Group DL (n = 25)	p-value
Objective Pain Scale score			
After 3 hours	2 (0-6)	0 (0-2)	<0.001
After 4 hours	4 (2-6)	2 (0-4)	0.001
After 6 hours	4 (2-6)	2 (2-6)	0.005
After 12 hours	4 (2-6)	4 (2-6)	0.039
After 24 hours	4 (2-6)	4 (2-6)	0.550
Duration of Analgesia (min)	238.8 ± 16.2	416.0 ± 10.4	0.009
Total Paracetamol received (mg)	530.4 ± 163.3	399.6 ± 176.4	<0.001

Data are presented as median (range) or mean ± SD

Discussion

The results of this study demonstrated that adding dexamethasone as an adjuvant to single-shot levobupivacaine-based caudal block provides superior analgesic quality in children undergoing infra-umbilical surgical procedures. Addition of dexamethasone was associated with significantly lower pain intensity and longer duration of analgesia with reduced further analgesic requirements in the first 24 postoperative hours.

Table 3
Quality of sedation and adverse effects during the postoperative period in the two groups

	Group L (n = 25)	Group DL (n = 25)
Number of Children with sedation score 2 (restless)		
After 2 hours	2	0
After 3 hours	4	2
After 4 hours	2	1
After 6 hours	2	2
After 12 hours	1	1
After 24 hours	1	0
Adverse Effects, n (%)		
Nausea & vomiting	2 (8%)	1 (4%)
Fever	1 (4%)	1 (4%)

Being reliable, safe and easy-to-perform, caudal block is one of the most popular and commonly used regional blocks with general anesthesia in pediatric practice. A recent systematic review showed that CB is superior compared to INF, INB, or their combination in terms of reduced need for rescue analgesic[19].

Despite its popularity, the short duration of single-shot technique is a challenging disadvantage. Long-acting local anesthetics, continuous block with catheter placement and additive drugs are suggested solutions. In the current study, levobupivacaine was used to take the advantage of its long duration of action. Levobupivacaine is the S(-)-isomer of the racemate bupivacaine. Compared to bupivacaine, it is less toxic to the CNS and is less likely to cause myocardial depression and fatal arrhythmias[20]. It has been used safely and effectively in caudal block of children undergoing lower abdominal surgery[21,22]. The optimum dose of local anesthetic is not yet known, but it has been suggested that only high volumes of 0.7-1.0 ml/kg can achieve an analgesic effect to the level T10[23]. In the current study, a dose of 0.8 ml/kg was used. A recent study compared three volumes of levobupivacaine: 0.6 ml/kg, 0.8 ml/kg and 1.0 ml/kg for caudal block in children, 1-7 years undergoing orchidopexy and inguinal hernia repair. They found that the three volumes provide the same quality of

postoperative analgesia[24].

Epidural opioids are commonly used in pediatric practice. Nevertheless, caudal opioids carry the risk of nausea, vomiting, pruritus, urinary retention, and respiratory depression[25]. Likewise, α2-agonists may produce hypotension, bradycardia, and excessive sedation when administered epidurally[26,27]. This can hinder the use of caudal block for day-care anesthesia.

Dexamethasone as an anti-inflammatory corticosteroid is commonly used perioperatively to manage postoperative nausea, and vomiting and reduce postoperative pain scores and opioid consumption[15,28]. Recently, there has been renewed interest regarding the role of inflammation in the development of postoperative pain[29]. Few studies reported beneficial analgesic effect of dexamethasone addition to local anesthetics in caudal block in children.

Hong et al. 30 found that the addition of dexamethasone to ropivacaine in a dose of 0.5 mg/kg enhanced postoperative analgesia of caudal block after pediatric orchiopexy. However, this dose is markedly higher than commonly used doses of 0.1 to 0.2 mg/kg. A smaller dose of 0.1 mg/kg significantly prolonged the duration of analgesia after ropivacaine-based caudal block 18. The latter study was the basis on which the dose of caudal dexamethasone was selected. Other randomized-controlled trial reported that dexamethasone prolonged the duration of postoperative analgesia and decreases the incidence of PONV after caudal block using bupivacaine 31,321.

Compared to clonidine, caudal dexamethasone provided longer duration of analgesia with lesser sedation scores and more stable hemodynamics[33]. A more recent study compared dexamethasone with dexmedetomidine, and magnesium as adjuvant to ropivacaine caudal anesthesia in 128 pediatric patients (3-12-year olds) undergoing infraumbilical surgeries. The three drugs provided comparable and significant prolongation of duration of analgesia[34].

The exact mechanism of analgesic effect of epidural dexamethasone is not fully understood. It might have a direct local anesthetic action on nerves[35]. Dexamethasone could prevent central sensitization through inhibition of the transcription factor nuclear factor-k B (NF-kB)[36]. NF-kB is expressed in the nervous system and has an important role in the development of pathological pain[37].

In conclusion, the addition of dexamethasone in a dose of 0.1 mg/kg to levobupivacaine provided significant prolongation of the duration of postoperative analgesia after caudal block in pediatric patients. It reduced pain intensity and analgesic requirements throughout the postoperative period with hemodynamic stability. The addition of dexamethasone was associated with few trivial adverse effects including nausea and vomiting and fever in a limited number of patients.

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