Original Article

A comparative study of dexmedetomidine and fentanyl as adjuvants to levobupivacaine for caudal analgesia in children undergoing lower limb orthopedic surgery

ABSTRACT

Background: Levobupivacaine is an effective local anesthetic agent with less systemic toxicity than racemic bupivacaine, but it has short postoperative analgesic duration. Dexmedetomidine and fentanyl are promising adjuncts to provide excellent and prolonged postoperative caudal analgesia. This study compared the effects of caudal levobupivacaine plus dexmedetomidine and levobupivacaine plus fentanyl for postoperative analgesia and sedation in children undergoing lower limb orthopedic surgery.

Patients and Methods: Ninety children, whose age ranged from 1 to 7 years, American Society of Anesthesiologists I-II, undergoing orthopedic lower limb surgery under general anesthesia received caudal block for postoperative analgesia. The children were randomly allocated into three groups: Group L (control) received 0.75 ml/kg levobupivacaine 0.25% diluted in saline; Group LD received 0.75 ml/kg levobupivacaine 0.25% with dexmedetomidine 1 μg/kg; and Group LF received 0.75 ml/kg levobupivacaine 0.25% with fentanyl 1 μg/kg. Following the administration of the drugs; hemodynamic variables, the total anesthesia time, sedation score, Face, Legs, Activity, Cry, Consolability score, duration of analgesia, and side effects were recorded.

Results: Demographically, all the groups were comparable, both the baseline and the intraoperative hemodynamic profile were similar in all groups. The mean duration of analgesia and the mean sedation score in the Group LD were significantly greater as compared to both the other groups.

Conclusion: Dexmedetomidine may be a better additive to levobupivacaine than fentanyl for caudal postoperative analgesia, arousable sedation with comparable hemodynamic and side effect profile in children.

Key words: Caudal block; children; dexmedetomidine; fentanyl, hemodynamic; levobupivacaine; postoperative analgesia; sedation

Introduction

Postoperative pain is an annoying subjective sensation for both children and their parents. Various methods have evolved for providing postoperative pain relief in pediatric patients aiming to a better quality of sleep and a prolonged duration of sedation.

The regional anesthetic techniques significantly decrease the postoperative pain and systemic analgesic requirements. Caudal route is one of the simplest and safest techniques in pediatric surgery, with a high success rate.[1]

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Elfawal SM, Abdelaal WA, Hosny MR

Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Address for correspondence: Dr. Wail Ahmed Abdelaal, Department of Anesthesiology, Intensive Care and Pain Management, Faculty of Medicine, Ain Shams University, Cairo, Egypt. E-mail: wailabdelaal64@yahoo.com

In recent years, the reduced cardiotoxicity and central nervous system toxicity associated with the use of levobupivacaine, the pure (S−) enantiomer of bupivacaine, rather than bupivacaine, have been demonstrated in preclinical studies,[2,3] and many researchers have determined its potential benefits for clinical use. One of the major disadvantages of caudal analgesia is the limited duration of analgesia following single injection. To decrease postoperative analgesic requirements after single shot caudal epidural blockade, various additives, such as morphine, fentanyl, ketamine, clonidine, and dexmedetomidine, with local anesthetics have been investigated.[4]

Fentanyl, a lipophilic opioid, is added frequently to local anesthetics in children, but its beneficial effects are debated. Side effects, such as nausea, vomiting, or respiratory depression, are not uncommon.[5]

Dexmedetomidine is a potent and highly selective α2 adrenergic agonist that has been described as a safe and effective additive in many anesthetic applications and analgesic techniques.[6] In contrast to other agents, it has sympatholytic, analgesic and sedative effects, and is remarkably free from side effects except for manageable hypotension and bradycardia.[7] This study was designed to compare the analgesic properties of caudal dexmedetomidine versus fentanyl added to levobupivacaine in pediatric patients subjected to lower limb orthopedic surgery.

Patients and Methods

The study was conducted after obtaining approval of the Ethical Committee of Ain Shams University. Written informed consent was obtained from all parents before surgery. Ninety patients with the American Society of Anesthesiologists (ASA) physical status I-II, aged 1-7 years of both sex scheduled for lower limb surgeries (lower extremity lengthening, correction of lower extremity deformities) were included in this study. Clinical examination and routine investigation were done to all the patients.

Patients with known allergy to the study drugs, ASA grading 3 or above, suspected coagulopathy, infection at the site of caudal block, history of developmental delay, neurological diseases, and those whose parents did not approve inclusion in the study were excluded from the study.

On arrival to the operating theater, the standard monitors including noninvasive blood pressure, five lead electrocardiography and pulse oximetry, temperature monitor, and peripheral nerve stimulator (Infinity Kappa, Dräger, Lübeck, Germany) were attached to the patient, and 22-24-gauge cannula was inserted into an available peripheral vein. Patients were placed in a supine position, then general anesthesia was induced using sevoflurane in oxygen/air (FiO_2 50%). Cis-atracurium 0.1 mg/kg was given intravenous (IV) and intubation was done with appropriate-sized endotracheal tube and they underwent controlled mechanical ventilation.

Patients were placed in lateral decubitus position with hips flexed to 90°, and under all aseptic precautions, a single dose caudal block was performed with 23-gauge needle using the standard loss of resistance technique. Proper position of the needle was confirmed by the pop sensed during penetration of the sacro-coccygeal ligament, which was followed by the whoosh test[8] done using 1-3 ml of air, after needle insertion and negative aspiration of blood or cerebrospinal fluid. Patients were randomized into three groups (30 patients each) using the sealed envelope technique (based on computer-generated random numbers) to receive a caudal block. Group L (control) received 0.75 ml/kg levobupivacaine 0.25% diluted in normal saline 0.9%. Group LD received 0.75 ml/kg levobupivacaine 0.25% with dexmedetomidine 1 μg/kg and Group LF received 0.75 ml/kg levobupivacaine 0.25% with fentanyl 1 μg/kg. Note that the doctor who did not participate in the study was aware of the children's age and weight while preparing for the drugs for the three groups.

After performing caudal block, the patient was turned to the supine position, surgical procedure started after 15 min from the caudal block, if there was an increase in heart rate (HR) or mean arterial blood pressure of more than 20% of the baseline value after skin incision, then it was considered as block failure and these patients were excluded from the study. Anesthesia was maintained using 1.5% sevoflurane in an oxygen–air mixture (1:1 ratio), muscle relaxation was maintained by 0.02 mg/kg cis-atracurium when the first twitch in the train-of-four (T1) is recovered to 25% of its baseline height, and IV fluid volume was maintained using lactated ringer solution 4 ml/kg/h. No other narcotic, analgesic, sedative, or antiemetic was used intraoperatively. The mean arterial pressure (MAP), HR, and peripheral oxygen saturation (SpO_2), as well as end tidal CO_2, were recorded every 5 min all through the surgery. By the end of the surgery, reversal of muscle relaxation was done by atropine 0.02 mg/kg and neostigmine 0.05 mg/kg IV. On return of spontaneous ventilation, sevoflurane was discontinued and the endotracheal tube was removed, and the patient was shifted to the postanesthesia care unit. Duration of surgery and wake up time were recorded. All physicians, anesthetists, and surgeons, as well as patients' parents, were blinded to the caudal medication administered. Postoperatively, the HR, MAP,

SpO_2, and respiratory rate were assessed, postoperative pain was assessed by Face, Legs, Activity, Cry, Consolability (FLACC) score [Table 1], requirement of rescue analgesia (ibuprofen 40 mg/kg/day in four divided doses in 24 h) was noted, and duration of analgesia (time from caudal block to time at which FLACC score was 4 or more) was recorded. FLACC score was recorded at 15 min following extubation and then every 30 min for the first 4 h and hourly thereafter till the score was 4 or more, which was considered the end point of the study, and at this point, systemic analgesics were given for analgesia.

The categories for scoring Such as zero, one, or two points are assigned to each of the five categories shown in the table: FLACC. Total points assigned may be from 0 to 10.

Sedation was assessed by Ramsay sedation scale. In addition, postoperative side effects such as nausea and vomiting, respiratory depression (decrease in SpO_2 of <90% requiring supplementary oxygen), and urinary retention were noted.

Statistical analysis

Sample size was calculated on the basis of previous studies[9-11] that the addition of caudal dexmedetomidine had prolonged the duration of analgesia than the caudal local anesthetic alone or in combination with caudal fentanyl. Using PASS 11 for sample size calculation, in away ANOVA study, sample sizes of 27, 27, and 27 the total sample of 81 subjects are obtained from three groups whose means are to be compared. The total sample of 81 subjects achieves 80% power to detect differences among the mean duration analgesia of 300 min using an *F*-test with a 0.05 significance level. Thirty patients per group were included to replace any missed data.

Data were analyzed using SPSS version 17.0. Numerical variables were presented as mean and standard deviation and categorical variables were presented as frequency (%). Student's unpaired *t*-test was used for comparisons of numerical variables between groups. $P \leq 0.05$ was considered statistically significant.

Results

None of the caudal blocks were considered as failed block and all the 90 enrolled participants were included in the study. Demographically, all groups were comparable. In addition, there was no statistical difference between the duration of anesthesia between the groups [Table 1].

The HR changes among the studied groups were comparable at all-time groups (LH, LFH, and LDH) [Figure 1] and also the means of mean arterial blood pressure changes among the studied groups were comparable at all-time groups (L, LF, and LD) [Figure 1].

The mean FLACC score was significantly lower in Group LD as compared to Group LF and Group L [Table 2], however the mean sedation score was significantly greater in group receiving dexmedetomidine as compared to group receiving fentanyl and control group [Table 2].

The mean duration of analgesia in the Group LD was significantly longer as compared with Group LF and Group L [Table 2], also the number of patients need analgesia in the first 6 h postoperative was significantly increased in control group and LF Group [Table 2].

Postoperative vomiting, itching, and respiratory depression were significantly occurred in the LF Group compared to other groups. The other adverse effects were comparable among studied groups [Table 3].

Discussion

The present study compared the effect of dexmedetomidine and fentanyl when added to 0.25% levobupivacaine for caudal block in patients undergoing lower limb surgeries.

Table 1: Demographic data for the study groups

Patient characteristics	Mean ± SD			*P*
	Group L (*n* = 30)	Group RF (*n* = 30)	Group RD (*n* = 30)	
Age (years)	6.5±2.1	6.1±2.7	6.2±2.3	0.64
Weight (kg)	21.2±5.7	20.5±4.54	21.6±4.32	0.35
Sex (male/female)	18/12	17/13	20/10	0.426
Duration of anesthesia (min)	69.4±10.5	68.4±17.6	71.3±17.8	0.53

All values are expressed as mean ± SD with $P < 0.05$ as significant. SD: Standard deviation

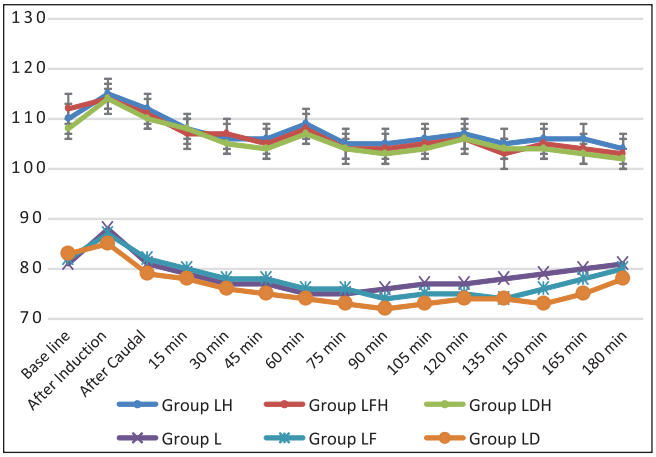

Figure 1: Mean arterial blood pressure and heart rate changes at various interval in all the study groups

Table 2: Mean Face, Legs, Activity, Cry, Consolability score, sedation score, 1st time of analgesia, and number of patients requiring analgesia in first 6 h

Patient characteristics	Mean ± SD			*P*
	Group L (control) (*n* = 30)	Group LF (fentanyl) (*n* = 30)	Group LD (dexmedetomidine) (*n* = 30)	
FLACC score (15 min after extubation)	1.943±0.700	1.33±0.606	0.800±0.761	0.004
Sedation score (15 min after extubation)	1.61±0.413	2.00±0.525	2.53±0.681	0.0012
Time of analgesia (min)	321.8±10.2	330.4±14.7	490.4±13.6	<0.001*
Patient requiring analgesia (%)	23 (79.3)	15 (50)	9 (32.1)	<0.001*

All values are expressed as mean ± SD with all values are expressed as mean+SD with $P < 0.05$ as significant. FLACC: Face, Legs, Activity, Cry, Consolability

Table 3: Incidence of adverse effects in the study groups

Patient characteristics	Control (%)	Fentanyl (%)	Dexmedetomidine (%)	*P*
Hypotension	1 (3.4)	2 (6.8)	2 (6.8)	0.512
Bradycardia	0 (0)	2 (6.8)	3 (10.2)	0.13
Respiratory depression	0 (0)	8 (26.2)	2 (6.8)	<0.0001*
Itching	0 (0)	7 (23.8)	0 (0)	<0.0001*
Vomiting	1 (3.4)	6 (20.4)	2 (6.8)	0.041*

*Statistical significance ($P < 0.05$)

Levobupivacaine, the pure S (−)-enantiomer of bupivacaine, has strongly emerged as a safer alternative for regional anesthesia than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile.[2,3] Frawley *et al*. compared 1 ml/kg of levobupivacaine 0.25% and bupivacaine 0.25% on 310 patients undergoing subumbilical surgery and the analgesic effects of the drugs were found to be similar during both the intraoperative and postoperative periods.[8] Levobupivacaine could replace bupivacaine in children for postoperative analgesia because of various studies suggests that it is less cardiotoxic than racemic bupivacaine.[8,12-14]

Fentanyl is the most common additive to local anesthetics to caudal block, but it has undesirable side effects.[15] Dexmedetomidine is a highly selective α2 adrenergic receptor agonist which prolongs the duration of analgesia when added to caudal levobupivacaine. In a study conducted in adult population by Bajwa *et al*., they have concluded that dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset, establishment of sensory anesthesia, prolonged postoperative analgesia, lower consumption of postoperative local anesthetic for epidural analgesia, and much better sedation levels.[16] In the absence of sufficient amount of data for caudal dexmedetomidine in children, this study was designed by using a low dose of dexmedetomidine (1 μg/kg). The selected caudal dose of dexmedetomidine was based on previous reports in children.

However, Anand *et al*. have concluded that caudal dexmedetomidine (2 μg/kg) with 0.25% ropivacaine (1 ml/kg) for pediatric lower abdominal surgeries achieved significant postoperative pain relief that resulted in a better quality of sleep and a prolonged duration of arousable sedation and produced less incidence of emergence agitation following sevoflurane anesthesia.[17]

In the present study, the results of demographic data were comparable between the studied groups.

As regards postoperative FLACC score, duration of analgesia, and number of patients required analgesia in the first 6 h, there was a significant decrease in FLACC score and number of patients required analgesia in first 6 h in dexmedetomidine group in comparison with the other two groups. Furthermore, the 1st time to rescue analgesia was significantly prolonged in LD Group compared to control and fentanyl groups.

Our study supported by the results of El Shamaa and Ibrahim suggested that the use of dexmedetomidine, during single dose injection, as an additive to the local anesthetic bupivacaine in caudal epidural analgesia prolongs the duration of postoperative analgesia following lower abdominal as well as perineal surgery.[18]

Two studies were done by Dutt *et al*. and Nasr and Abdelhamid who compared caudal fentanyl or dexmedetomidine on lower abdominal and limb surgeries and cardiac surgery in pediatrics, respectively, and concluded that in dexmedetomidine group, the pain score was decreased and the duration of postoperative analgesia was prolonged.[19,20] The hemodynamic variables (MAP and HR) were comparable in between the studied groups. These results were supported by Dutt *et al*. who compared the addition of fentanyl or dexmedetomidine to caudal ropivacaine in pediatrics who underwent lower abdominal and lower limb surgeries and concluded that hemodynamics was comparable between the two studied groups.[19]

In addition, a study done by Manohar and Yachendra, 2015, found that addition of dexmedetomidine to

bupivacaine produced longer duration of analgesia compared to dexmedetomidine with ropivacaine in pediatric patients received caudal block for infra umbilical surgeries.[21]

Furthermore, the study done by Mahendru *et al*. who compared the intrathecal administration of fentanyl, clonidine, and dexmedetomidine in the lower limb surgeries and concluded that the mean values of MAP and HR were comparable between the studied groups throughout the intra- and post-operative periods.[10]

Nasr and Abdelhamid compared the efficacy of the caudal dexmedetomidine or caudal fentanyl on the stress response and postoperative analgesia and concluded that the HR and MAP were significantly decreased in the dexmedetomidine group.[20]

This difference may due to the high volume used in caudal block (1.6 ml/kg), and the type of operation (open heart).

As regards the postoperative adverse effects (respiratory depression, vomiting, and itching), they were increased significantly in the fentanyl group. Similar observation was supported by Bajwa *et al*. who evaluated the addition of either fentanyl or dexmedetomidine to epidural analgesia in lower limb surgeries and revealed that the incidence of postoperative nausea and vomiting was significantly occurred in the fentanyl group.[16]

In addition, Constant *et al*. compared caudal clonidine and caudal fentanyl and concluded that the adverse effects, especially vomiting occurred mainly in the fentanyl group.[22]

Conclusion

Dexmedetomidine can be considered a suitable additive to levobupivacaine for caudal block providing long-lasting postoperative analgesia, arousable sedation along with stable hemodynamics, and minimal side effects.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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