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Efficacy of Caudal Ketamine with Different Concentrations of Levobupivacaine for Postoperative Analgesia in Paediatric Subumblical Surgeries

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Abstract

Background: Caudal anaesthesia is the most popular regional anaesthetic technique used in the paediatric age group. Ketamine has been shown to have a synergistic effect with caudal local anaesthetics. Levobupivacaine is generally a well-tolerated anesthetic and analgesic with a wide range of clinical effectiveness and can be used as an alternative to bupivacaine.

Methods: After approval from the hospital ethics committee and obtaining a parental informed written consent, fifty children with ASA score I and age ranges from 2-6 years randomized into 2 groups. Group I (n=25) received 0.75 ml/kg levobupivacaine 0.175% and preservative free s(+)-ketamine 0.5 mg/kg. Group II (n=25) received 0.75 ml/kg levobupivacaine 0.25% and preservative free s(+)-ketamine 0.5 mg/kg. Postoperative pain, duration of analgesia and time to first spontaneous leg movement between the two groups were compared.

Results: There were no statistically significant differences between the two groups as regarding the mean duration of analgesia and pain score assessed by using the FLACC scale; P value of >0.05. Mean duration of motor block determined by the mean time to first spontaneous leg movement was significantly longer in group II when Compared to group I; P value of 0.000.

Conclusion: The addition of ketamine decreased the required concentration of caudal levobupivacaine with a comparable duration of postoperative analgesia and significantly less residual motor blockade as compared to higher concentration.

Keywords: Caudal; Ketamine; Levobupivacaine

Introduction

Postoperative pain relief has become an important aspect of anaesthetic care including paediatric anaesthesia patient. It can be provided by using various analgesics or opioids in patients receiving general anaesthesia and also through various techniques of regional anaesthesia. The advantages of regional anaesthesia include a decreased requirement of general anaesthesia allowing early extubation and providing long lasting analgesia extending well into the postoperative period [1,2].

Caudal anaesthesia is the most popular regional anaesthetic technique used in the paediatric age group [3]. It is recommended for most surgical procedures of the lower part of the body, mainly below the umbilicus, including inguinal hernia repair, urinary and digestive tract surgery and orthopaedic procedures on the pelvic girdle and lower extremities [4].

However, the single-shot "kiddie caudal" may have only a short duration of action [5]. Ketamine local anaesthetics combinations have been demonstrated to speed the onset of analgesia, prolong the duration of caudal analgesia, and reduce the incidence of ineffective analgesia [6,7]. Ketamine has been shown to have a synergistic effect with caudal local anaesthetics [8]. Epidural ketamine has allowed lower concentrations of bupivacaine and ropivacaine to be used and as a result, the incidence of postoperative motor block has been lower [9]. When administered via the caudal route, ketamine produce its effects solely by blocking NMDA receptors in the spinal cord [10]. Levobupivacaine, which is the enantiomer of the pure racemic bupivacaine S (-), is generally a well-tolerated anesthetic and analgesic with a wide range of clinical effectiveness and can be used as an alternative to bupivacaine [11,12].This study aim to compare the effect of addition of ketamine to two different concentrations of levobupivacaine.

Material and Methods

After approval from the hospital ethics committee, a parental informed written consent was obtained for 50 children undergoing elective subumblical surgery with ASA score I. The age of the children ranges from 2-6 yrs classified randomly into 2 groups using computer generated random numbers. Group I (n=25) received 0.75 ml/kg levobupivacaine 0.175% and preservative free s(+)-ketamine 0.5 mg/kg and group II (n=25) received 0.75 ml/kg levobupivacaine 0.25% and preservative free s(+)-ketamine 0.5 mg/kg.

Children with a history of allergy to local anesthetics, pre-existing neurological or neuromuscular disorders, abnormal haemostasis, abnormalities of sacrum, vertebral column or spinal cord and back sepsis were excluded from the study.

All the children were fasted, unpremedicated and intravenous canula 22 gauge was inserted in the word after application of EMLA cream for 30 min. Anaesthesia was induced by propofol 3 mg/kg in a mixture of 50% nitrous oxide-oxygen. Then laryngeal mask airway inserted and checked by manual ventilation for audible leak and/or the ability to inflate the lungs. Anesthesia was maintained by sevoflurane at 1 MAC (age adjusted) in 50% oxygen–nitrous oxide through spontaneous ventilation. Non-invasive blood pressure (BP), heart rate (HR), respiratory rate (RR), oxygen saturation (SpO_2) and end-tidal CO_2, were monitored continuously intra-operatively.

The child was carefully placed in the lateral decubitus, with the upper thigh at 90° and the lower thigh at 45° flexion. After all aseptic precautions, ultrasonography (LOGIQe, GE Healthcare, Wauwatosa, WI, USA) with its linear probe (8-13 MHz) was used using a short axis view at the level of the lower sacral vertebra, the hyperechoic sacral cornua appear as two inverted U- shaped structures on both sides of the sacral hiatus. A needle is advanced percutaneously using an out-of-plane technique, then the probe is rotated 90° to obtaine an in-plane view of the needle as it pierces the posterior sacrococcygeal ligament. The ligament appears as a hyperechoic band between the cornua. The dorsal surface of the sacrum appears as a deeper hyperechoic line, and the space between the two bands is the sacral hiatus. Spread of local anesthetic within the epidural space noticed by expansion of hypoechogenicity or dural movement with narrowing of the dural space confirms correct needle position. Then the punctured site was covered with dry gauze. After that the child was repositioned supine. No other analgesics were given.

A mechanical stimulus was applied after 15 min of caudal injection at the surgical dermatome or at the immediate superior dermatome with a modified Allis clamp. Any movement due to the stimulus or significant change in the HR, BP or RR, discontinues the stimulus. Significant change in HR, BP, or RR on application of the clamp is defined as more than 20% change of baseline data. In this situation, children were treated with an i.v. bolus of fentanyl 2 mcg/kg and this block considered unsuccessful and this patient was excluded from the study.

After extubation, patients were taken to recovery room; the postoperative pain was evaluated by FLACC Scale [13] for pain assessment in children (Face, Legs, Activity, Crying and Consolability), each given a score of 0-2 and the total score is from 0 to 10 at 0 h, 4 h, 8 h and 24 h postoperative. Also duration of analgesia and time to first spontaneous leg movement in both groups were monitored. Duration of analgesia is defined as the time from caudal injection to the time of first dose analgesia. In recovery or ward, rectal paracetamole 20 mg/kg was administered for pain score with a range from 4 to 7 and intravenous meperidine 1 mg/kg for pain score of >7.

Behaviour	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	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
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams, sobs, frequent complaints
Consolability	Content, relaxed	Reassured by touching, hugging or being talked to, distractible	Difficult to console or comfort

Table 1: The FLACC scale for pain assessment in children.

Each of the five categories is scored from 0-2, resulting in total range of 0-10, FLACC=Face, Leg, Activity, Cry, Consolability

- 0=No pain
- 1-3=Mild pain
- 4-7=Moderate pain
- 8-10=Severe pain

Sample size

The sample size was calculated using Epi-Info software statistical package created by World Health organization and center for Disease Control and Prevention, Atlanta, Georgia, USA version 2002. The sample size was calculated at N=20.

The criteria used for sample size calculation were as follows:

1. 95% confidence limit

2. 80% power

3. The ratio between experimental and control groups is 1:1

4. Expected outcome in in treatment group is double times better than control groups (40-80% of optimal required).

Statistical analyses

The data were tabulated and statistically analyzed to explore any significant results. Quantitative data are presented using mean and standard deviations and qualitative data were described using frequency and percentages. Comparisons of continuous variables were done using the unpaired Students t-test and the pain score in the two groups calculated using the FLACC scale were compared using Pearson Chi-square test. $P<0.05$ was considered statistically significant.

Results

In the two groups, no patient was excluded due to failed caudal block. There were no statistical differences as regarding age, weight or duration of surgery as shown in Table 2.

Variables	Group I	Group II	P value
Age(yrs)	3.57 ± 1.16	4.18 ± 1.25	0.079
Weight(kg)	14.7 ± 3.22	15.5 ± 2.87	0.335
Duration of surgery(min)	28.6 ± 10.9	26.6 ± 11.1	0.523
ASA	I	I	
Intraoperative iv analgesia	none	none	
Type of surgery	13	15	
Inguinal hernia	6	5	
Orchidopexy	1	1	
Hypospadius	5	4	
Hydrocele			

Table 2: Patients data.

Values presented as mean ± SD; ASA, American Society of Anesthesiology.

Pain score at 0 h	**0-3 (no or mild pain) n (%)**	**4-10 (moderate to severe pain) n (%)**
Group I	25 (100)	0 (0)
Group II	25 (100)	0 (0)
Pain score at 4 h	**0-3 (no or mild pain) n (%)**	**4-10 (moderate to severe pain) n (%)**
Group I	25 (100)	0 (0)
Group II	24 (96)	1 (4)
Pain score at 8 h	**0-3 (no or mild pain) n (%)**	**4-10 (moderate to severe pain) n (%)**
Group I	24 (96)	1 (4)
Group II	23 (92)	2 (8)
Pain score at 24 h	**0-3 (no or mild pain) n (%)**	**4-10 (moderate to severe pain) n (%)**
Group I	4 (16%)	21 (84%)
Group II	6 (24%)	19 (76%)

Table 3: Pain scores calculated using the FLACC scale in the two groups.

From Table 3, it was found that there was no significant difference between the two groups as regarding the pain score using the FLACC pain scale from 0 h to 24 h post-operatively with a P value >0.05. All the children in the two groups had no or only mild pain after transfer of patients to PACU (at 0 h). By the end of the first 4 h, children in group I only practice mild or no pain (pain score 0-3) but in group II there is only 1 patient (4%) had moderate pain (pain score=5) and there was no significant statistical difference; P value of 0.312. At 8 h, 1 child in group I (4%) and 2 children in group II (8%) had moderate to severe pain (pain score 4-10) and there was no significant statistical difference; P value of 0.552. 24 h post-operatively, 21 patients (84%) in Group I had moderate-to-severe-pain (pain score 4-0) and 19 patients (76%) in Group II had moderate-to-severe pain (pain score 4-10) with no significant statistical difference; P value of 0.480.

Variable	Group I	Group II	P value
Duration of analgesia (h)	12.1 ± 5.7	14.4 ± 6.14	0.188
time to first spontaneous leg movement (min)	42.3 ± 12.7	67.5 ± 15.9	0.000*

Table 4: Duration of analgesia and time to first spontaneous leg movement in the two groups.

As shown in Table 4, there was no significant difference as regarding mean duration of analgesia between group I (12.1 ± 5.7) and group II (14.4 ± 6.14); P value of 0.188, while it was found that the mean time to first leg movement as representing the mean time of residual motor blockade in group II (67.5 ± 15.9) was significantly longer than that in group I (42.3 ± 12.7); P value of 0.000.

Discussion

Caudal anaesthesia is the most commonly performed regional anaesthetic technique in infants and children undergoing inguinal, anorectal and lower extremity surgical procedures [14]. It is established to be safe in children, because the procedure is technically simple to perform, the success rate is high and complications are rare [4].

S-enantiomer levobupivacaine is thought to have a superior safety profile with reduced local anaesthetic toxicity so that may explain the recent increase in its use in the UK [15]. 41.7% of UK paediatric anaesthesiologists now using levobupivacaine for caudal analgesia with decrease in the use of racemic bupivacaine from 94% in 2002 to 43.4% in 2009 [16,17].

Caudal Bupivacaine alone can provide excellent analgesia in early postoperative period but rescue analgesics are required as block wears off when Bupivacaine is used alone in caudal epidurals [18].

Breschan et al. suggested that levobupivacaine is the preferred local anesthetic for caudal blockade in outpatient surgeries due to its lower motor blockade than bupivacaine and rapid onset of analgesia than ropivacaine and bupivacaine. They studied 182 children to compare the

efficacy of caudal extradural 1 ml/kg of levobupivacaine 0.2%, ropivacaine 0.2% and bupivacaine 0.2%. They noted that the onset of analgesia was significantly later in ropivacaine and bupivacaine than in levobupivacaine but no statistical difference between the groups as regarding postoperative pain scale. We think that is because they used high dose of local anesthetic agents. They also concluded that motor blockade was significantly less after levobupivacaine and ropivacaine than after bupivacaine during the first 2 h postoperatively [19].

Kaya et al. studied 60 pediatric patients to compare the effect of caudally administered 0.5 ml/kg levobupivacaine 0.25% and bupivacaine 0.25% on pain and motor blockade. They concluded that bupivacaine has better quality of analgesia than levobupivacaine but no difference between the two groups when comparing the motor blockade. They explained that as they used low doses of local anesthetics [20].

Ivani et al. had studied three different concentration of caudal levobupivacaine 1 ml/kg (0.125%, 0.2%, and 0.25%) without additives in children and they found that 0.125% concentration was associated with significantly less motor blockade than that with other concentration but also had significantly shorter duration of postoperative analgesia than that with levobupivacaine 0.2% or 0.25% [21] so if levobupivacaine is used without additives, it should be used in high concentration to ensure good quality of postoperative analgesia.

Several adjuvants have been used to prolong the duration of analgesia with bupivacaine for caudal analgesia in children. Opioids, ketamine and midazolam are some of the commonly used drugs. The use of opioids is associated with an increased incidence of pruritus and post-operative nausea and vomiting [21-24]. The advantage of ketamine is that it prolongs the duration of analgesia without an increase in the incidence of respiratory depression, pruritus and urinary retention which are commonly seen with opioids.

Panjabi et al. had proved that ketamine 0.5 mg/kg is the optimum dose added to caudal bupivacaine 0.25%, 0.75 ml/kg with significantly longer duration of postoperative analgesia than that with ketamine 0.25 mg/kg. Also they found that ketamine 0.5 mg/kg is the optimum dose added to caudal bupivacaine 0.25%, 0.75 ml/kg with significantly lower incidence of behavioural side effects than that with ketamine 1 mg/kg [25]. So in our study we used ketamine at dose of 0.5 mg/kg to be combined with levobupivacaine.

Our results are going with that of Locatelli et al., found that caudal levobupivacaine 0.175% combined with preservative free S(+)-ketamine had significantly longer duration of postoperative analgesia than that with levobupivacaine 0.2% alone without additives levobupivacaine and also 0.15% combined with preservative free S(+)-ketamine. Also they found that duration of postoperative analgesia due to caudal levobupivacaine 0.15% combined with preservative free S(+)-ketamine was comparable with that caused by levobupivacaine 0.2% alone without additives. So according to Locatelli et al. ketamine improve postoperative analgesia when added to levobupivacaine and help to decrease the required concentration of levobupivaciane for caudal block in pediatric patients [26]. Nasr et al. added ketamine 50 mg to 2-2.5 ml of 0.5% bupivacaine intrathecally and this leads to a rapid sensory block and a longer duration of analgesia [27].

On the other hand, Davies et al. 2012, suggested that the addition of preservative free S(+)-ketamine 0.5 mg/kg or clonidine 1.8 mcg/kg or both to levobupivacaine 0.25% did not improve postoperative analgesia and appear to offer no benefit [28]. We think that they reached these results as they used single high concentration of levobupivacaine (0.25%) with ketamine, clonidine or both. But in our study, we used two different concentrations of levobupivacaine combined with same dose of ketamine (0.5 mg/kg) which enable us to determine the effect of ketamine when combined with caudal levobupivacaine. Our opinion is supported by Dobereiner et al., as they showed in their studies that if the local anesthetic agents are used in high doses, there will be no difference in postoperative analgesic efficacy [29].

In conclusion, the addition of preservative free S(+)-ketamine to levobupivacaine improve duration of postoperative analgesia and decrease the required concentration of levobupivacaine so decrease incidence of residual motor blockade in children undergoing subumblical surgeries.

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