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Prospective, randomized, double-blinded comparison of the effects of caudally administered levobupivacaine 0.25% and bupivacaine 0.25% on pain and motor block in children undergoing circumcision surgery

Z. KAYA, M. SÜREN, S. ARICI, S. KARAMAN, H. TAPAR[1], F. ERDEMIR[2]

Department of Anesthesiology and Reanimation, Gaziosmanpasa University School of Medicine Tokat, Turkey
[1]Anesthesiology and Reanimation Department, Sorgun State Hospital, Yozgat, Turkey
[2]Urology Department, Gaziosmanpasa University, Medical Faculty, Tokat, Turkey

Abstract. – BACKGROUND: Caudal anesthesia is widely used as intraoperative and postoperative analgesia in children's subumbilical surgeries such as on the urogenital system, lower extremities and lower abdomen to reduce the stress response to surgery and to facilitate the general anesthesia.

AIM: The purpose of this study was to compare the effects of caudally administered bupivacaine and levobupivacaine of equal volume and concentration on motor block and postoperative pain in children undergoing circumcision surgery.

PATIENTS AND METHODS: The prospective, randomized, double-blind study included 60 patients with ages ranging from 1-10 years and ASA (American Society of Anesthesiologists) physical status of I-II who underwent elective circumcision surgery. The patients were divided into two groups: group B received 0.5 ml/kg of bupivacaine 0.25% caudally and group L received 0.5 ml/kg of levobupivacaine 0.25% caudally. Postoperative pain was assessed by children's and infant's postoperative pain scale and motor block was assessed by the Bromage scale.

RESULTS: The mean children's and infant's postoperative pain scale of group B was significantly lower than that of group L ($p < 0.001$). Three patients in group B and seven patients in group L needed additional analgesia after the incision. There was no significant difference between groups in terms of Bromage scores and in both groups the residual motor block was found to be zero at the 150th minutes.

CONCLUSION: According to these findings, bupivacaine has an adequate quality of analgesia than levobupivacaine. We suggest that bupivacaine for caudal block at the concentration of 0.25% (0.5 ml/kg) provides an adequate level of analgesia for outpatient circumcision surgery.

Key Words:
Analgesia, Anesthesia, Caudal, Bupivacaine, Levobupivacaine, Circumcision.

Introduction

The number of outpatient minor surgeries due to various indications is increasing. In parallel to this increase, the most common outpatient surgeries in children are minor surgeries such as inguinal hernia and circumcision[1]. In these types of surgeries, application of regional anesthesia in infants and children is done together with sedation or general anesthesia[2]. Caudal anesthesia following inhalation or intravenous anesthesia induction is widely used as intraoperative and postoperative analgesia in children's subumbilical surgeries such as on the urogenital system, lower extremities and lower abdomen to reduce the stress response to surgery and to facilitate the general anesthesia[3-6]. Postoperative pain management in children is a necessity for both medical and ethical reasons. Circumcision in children is followed by severe pain, especially during the first 2 hours of postoperative period. Pain control after surgery increases patient satisfaction and shortens hospital stay[7]. Although extremely rare in infants and children, local anesthesia toxicity has been reported to cause transient neurological symptoms, seizures, dysrhythmias and cardiac collapses. This observation has been connected to higher amounts of local anesthetic used in children than in adults[2]. Bupivacaine and levobupivacaine are long-acting agents most commonly used for caudal anaesthesia in children[7]. An evidence-based clinical update, Dobereiner et al[8] found that in many studies, 1 ml/kg of bupivacaine 0.2-0.25% and 1 ml/kg of levobupivacaine 0.2-0.25% were commonly used, only one study with Locatelli et al[6] used 0.5 ml/kg of bupiva-

Corresponding Author: Ziya Kaya, MD; e-mail: zkayaahz@gmail.com.

caine 0.25% and 0.5 ml/kg of levobupivacaine 0.25%. In this study, 0.5 ml/kg of bupivacaine 0.25% and 0.5 ml/kg of levobupivacaine 0.25% were administered at low doses like Locatelli et al[6] to avoid side effects and toxicity. Many studies have demonstrated that although racemic bupivacaine is the most commonly used local anesthetic drug for caudal analgesia in pediatric patients, levobupivacaine, which is the enantiomer of the pure racemic bupivacaine S (-), is less toxic, provides similar analgesic effect as bupivacaine has a wider safety margin and forms less motor block[2,5,6,9]. 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[10].

The aim of this prospective randomized and double-blind study was to compare the effects of a single-dose administration of isobaric bupivacaine 0.25% and isobaric levobupivacaine 0.25% on postoperative pain and motor block in circumcision surgery in children.

Patients and Methods

The study included 60 patients between the ages of 1-10 years and ASA (American Society of Anesthesiologist) physical status of I-II scheduled for circumcision surgery predicted to last less than 90 min. The approval of the local Ethics Committee (Cumhuriyet University, School of Medicine, Sivas Clinical Resarch Ethical Committee; Number, 2009-12/13; Date, 06/01/2010) and written consent from parents was obtained. Patients with known allergic reaction to amide-type local anesthetics, a history of seizures, bleeding diatheses, known systemic diseases (kidney, liver, respiratory, cardiac), infection or anatomic malformation at the region where the caudal anesthesia was planned to be applied were excluded from the study.

Patients were randomly divided into two groups. After patients fasted for 6 hours, premedication with 0.5 mg/kg oral midazolam was administered 30 min prior to surgery to avoid stress during the induction of anesthesia. After the premedication, patients were taken to the operation room. Parameters such as heart rate (HR), oxygen saturation (SpO_2), end tidal carbon dioxide (CO_2) and mean blood pressure (MBP) were monitored. The induction of anesthesia was done by a mixture of 8% minimum alveolar concentration (MAC) sevoflurane + 60% nitrogen protoxide + 40% oxygen. When anesthesia reached an adequate depth, a peripheral venous line was secured in the forearm with the 22 gauge needle, 5 ml/kg infusion with Lactated Ringer's solution was started and patients' ventilation was maintained by a laryngeal mask without using neuromuscular blockers. After the laryngeal mask was placed, sevoflurane MAC was lowered to 1% and spontaneous breathing was preserved. Following these procedures, patients were randomized, using the sealed-envelope technique (based on computer-generated random numbers), to receive a caudal block with either bupivacaine 0.25% or levobupivacaine 0.25%; total volume 1 ml/kg and the drug was prepared for caudal administration by a doctor that did not participate in the study. All blocks and subsequent follow-ups were done by another doctor who did not know which drug was administered. After sterile draping the patient was placed in the left lateral decubitus position, the caudal area was entered with an Epican caudal needle (B. Braun, Melsungen, Germany). After negative aspiration (avoiding the blood and cerebrospinal fluid), 0.5 ml/kg bupivacaine 0.25% diluted in 0.9% saline (group B) or 0.5 ml/kg levobupivacaine 0.25% diluted in 0.9% saline (group L) was administered within approximately two minutes (min). Heart rate, SpO_2, end tidal CO_2 and MBP were recorded after the caudal blockade approach and at every 5 min. Before the surgical incision, the onset of analgesia was assessed by sending mechanical stimuli to circumcision skin using an Allis clamp (provides pain stimulus to a wider area than pinprick stimulus)[11] approximately 10 min after the caudal administration. The absence of gross movements (extension or flexion of the arms and legs, chest extension, flexion of the head, abdominal contraction) or absence of significant difference (± 15%) in MBP and HR showed that analgesia was adequate. In the cases where movements or changes were present, the analgesia was considered inadequate and an additional fentanyl 1 mcg/kg intravenous (IV) was given. After approximately five min, the same mechanical stimuli was given and the condition of analgesia was re-assessed. The analgesic onset time of the patients were recorded. In the event of the same responses, the block was considered to be unsuccessful and the patient was excluded from the study. After surgery, patients were transferred to the recovery room and their postoperative pain, MBP, HR, nausea and vomiting, the need for additional analgesia and motor block follow-ups

were evaluated. Mean arterial pressure and HR were recorded at postoperative 10th, 20th, 30th, 45th, 60th and 90th min. The post-operative pain was monitored by using children's and infant's postoperative pain scale (CHIPPS) that contains five parameters[12] (Table I), and CHIPPS scores of the patients were recorded at postoperative 15th, 30th, 60th, 90th, 120th, 180th and 240th min. If the CHIPPS score was 10 or below, there was no need for additional analgesia. If the score was above 10, it was accepted that there was a need for additional analgesia and 20 mg/kg rectal paracetamol was administered as a treatment. Before all patients were discharged, their parents were instructed to give 20 mg/kg paracetamol orally if their children experienced pain at home. The Bromage scores of the patients were recorded at postoperative 30th, 60th, 90th, 120th and 150th min and used in evaluating motor block was administered as follows: 0: full motor strength (flexion of knees and feet), 1: flexion of knees, 2: little movement of feet only, 3: little movement of knees or feet[13]. After surgery, patients were transferred to the recovery room, Aldrete score were recorded every five min until the score reached to eight[14]. Thereafter patients were transferred to the inpatient clinic. Four hours after patients arrived at the inpatient clinic, patients were re-evaluated by a surgeon and an anesthesiologist. Patients were discharged if the Bromage score was zero and CHIPPS score was below seven. Assuming an incidence of effective block during operation of 0.95, a two-sided type I error of 0.05, a power of 0.80 and an effect size of 0.30; 27 patients in each group were required to find a significant difference in the incidence of effective block during operation.

Statistical Analysis

All variables were examined for outliers and non-normal distributions. Quantitative datas are presented as means and standart deviation and qualitative datas as frequency and percentage. Additional analgesic requirement and nausea and vomitting were compared by Pearson chi-square test. Continuous variables such as age, weight, anesthesia and surgery duration were compared by Student's *t*-test and analgesic onset time was compared by Mann-Whitney U test. A repeated measures analysis of variance (RMANOVA) was used to determine between group effects (Bupivacaine and Levobupivacaine), within-subject effects, and interactions between groups and time. Sphericity assumption was checked with the Mauchly's test and Gerainhause-Geisser p values were used. Analyses were completed by using MedCalc version 10.2.0.0. (MedCalc Software, Inc, Mariakerke, Belgium) and SPSS version 18 (SPSS Inc., Chicago, IL, USA). Statistical significance for all analysis was set at $p < 0.05$.

Results

Caudal block was successfully applied to all patients and none of the patients had complications during the blocking procedure. The mean age of patients in group B was 6 ± 2.1 years, while in group L it was 6.5 ± 2.6 years. There was no significant difference in demographic values such as age, weight, anesthesia and surgery duration and ASA scores between two groups (Table II).

Three patients from group B and seven patients from group L needed additional analgesics after the incision. Adequate analgesia in these patients was provided by fentanyl 1 mcg/kg IV (Table II). None of the patients experienced nausea or vomiting.

There was no significant difference in analgesic onset time between two groups ($p > 0.05$). The mean onset time was 10.5 min in the bupivacaine group, 11.1 min in the levobupivacaine group.

Group B had a significantly lower mean CHIPPS scores at 15th ($p = 0.005$, F = 8.630, df = 1), 30th ($p < 0.01$, F = 16.804, df = 1) and 90th ($p = 0.018$, F = 5.882, df = 1) min than group L

Table I. Children and Infants Postoperative Pain Scale (CHIPPS)[8].

Item	Structure	Points
Crying	None	1
	Moaning	2
	Screaming	3
Facial expression	Relaxed/smiling	1
	Wry mouth	2
	Grimace (mouth and eyes)	3
Posture of the trunk	Neutral	1
	Variable	2
	Rear up	3
Posture of the legs	Neutral, released	1
	Kicking about	2
	Tightened legs	3
Motor restlessness	None	1
	Moderate	2
	Restless	3

Table II. The clinical and demographic characteristics of the participants according to assigned groups.

		Bupivacaine (n = 30) n (%)/mean ± SD	Levobupivacaine (n = 30) n (%)/mean ± SD	p
Age		6.0 ± 2.1	6.5 ± 2.6	0.48
Weight		21.6 ± 5.3	23.2 ± 7.4	0.36
Anesthesia duration		33.5 ± 7.6	31.1 ± 7.2	0.21
Surgery duration		25.7 ± 6.7	24.9 ± 6.5	0.67
ASA		I	I	
Additional analgesics	No	27 (90.0)	23 (76.7)	0.17
	Yes	3 (10.0)	7 (23.3)	
Nausea and vomiting	No	30 (100.0)	30 (100.0)	–

ASA, American Society of Anesthesiology.

(Figure 1). There was a statistically significant decrease in the mean CHIPPS scores with time starting from the first measurement within groups ($p < 0.001$). However, in both groups there was no need for additional analgesia until discharge. Six patients from group B and eight patients from group L required oral paracetamol within the first 24 hours after discharge.

There was no significant difference in Bromage scores between two groups but there was a statistically significant decrease in the mean Bromage scores from the baseline measurements with time starting at 60 min within groups ($p < 0.001$). 21 patients from group B had a Bromage score of zero, three patients had a score of one and six patients had a score of two. 22 patients from group L had a Bromage score of zero, seven patients had a score of one and one patient had a score of two. Nine patients in group B and eight patients in group L had a Bromage score of zero at the 150th min. Bromage scores of all patients are presented in Figure 2.

There was no significant difference in terms of mean heart rates between the two groups ($p > 0.05$). However, when the comparison was done within the groups, there was a significant decrease observed within the first 30 min ($p < 0.05$, Figure 3).

No significant difference was observed between the two groups in terms of mean blood pressure ($p > 0.05$). However, when the comparison was done within the groups, there was a significant increase compared by the first measurement of MBP at 45th min, 60th min and 90 ^{h} min within the Bupivacaine group ($p < 0.001$, Figure 4).

Discussion

Same dose of either isobaric bupivacaine 0.25S% or isobaric levobupivacaine 0.25% was applied as a single dose caudal block under general anesthesia in patients undergoing circumcision surgery. The prospective, randomized, double-blind comparison showed that bupivacaine provides longer duration of analgesia than levobupivacaine. Although there is no significant difference between Bromage scores of the groups ($p > 0.05$), there is a tendency of decrease in levobupivacaine group.

Table III. Bromage scores of the groups within minutes.

		Bromage 0. min n (%)	Bromage 30. min n (%)	Bromage 60. min n (%)	Bromage 90. min n (%)	Bromage 120. min n (%)	Bromage 150. min n (%)
Group B	0	21 (70%)	21 (70%)	22 (73.3%)	26 (86.7%)	29 (96.7%)	30 (100%)
	1	3 (10%)	3 (10%)	8 (26.7%)	4 (13.3%)	1 (3.3%)	–
	2	6 (20%)	6 (20%)	–	–	–	–
Group L	0	22 (73.3%)	22 (73,3%)	25 (83.3%)	29 (96.7%)	30 (100%)	–
	1	7 (23.3%)	8 (26.7%)	5 (16.7%)	1 (3.3%)	–	–
	2	1 (3.3%)	–	–	–	–	–

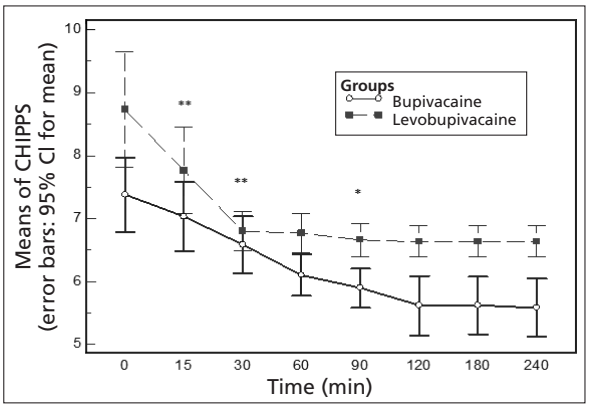

Figure 1. The mean CHIPPS. Mean CHIPPS scores were significantly different between the Bupivacaine and Levobupivacaine groups (Between-Subjects Effects, $p < 0.001$). There was no statistically significant interaction between treatment group and time ($p = 0.128$). (*$p < 0.05$, **$p < 0.01$).

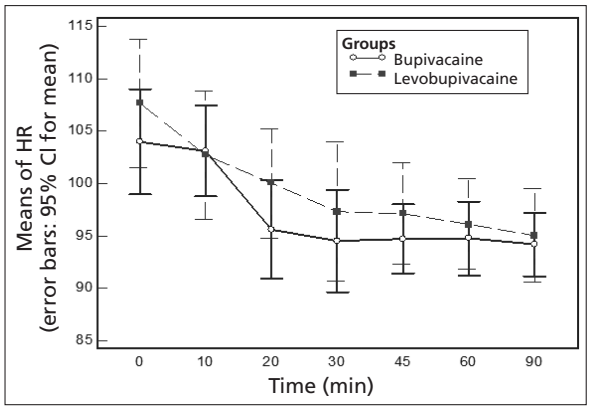

Figure 3. The mean heart rate. The mean heart rates were not statistically significantly different between the Bupivacaine and Levobupivacaine groups (Between-Subjects Effects $p = 0.376$). There was no statistically significant interaction between treatment group and time ($p = 0.857$).

As with all invasive procedures, pain management is also important in minor surgeries. Caudally administered single dose of local anesthetic during intraoperative and postoperative period has been reported to provide an adequate level of analgesia. Many studies put forward that the effect of analgesic might vary depending on the type of the surgery, patient's age, type and amount of the local anesthetic agent[4,6,13,15-23]. In a prospective, randomized, double-blind study, Locatelli B et al[6] compared bupivacaine 0.25%, levobupivacaine 0.25% and ropivacaine 0.25% and used a total dose of 1 ml/kg for orchidopexy or inguinal hernia repair, and of 0.5 ml/kg for phimosis or incision level lower than L3. They reported that Bupivacaine had a longer analgesic effect than levobupivacaine and ropivacaine. In our study, we used 0.5 ml/kg of Bupivacaine 0.25% and Levobupivacaine 0.25% in circumcision surgery as in Locatelli et al[6] The results obtained from our study are similar in longer lasting analgesic effect of Bupivacaine compared with Levobupivacaine.

Despite the results of Locatelli et al[6], Breschan et al[13] compared analgesic effects of same dose and concentration of 1 ml/kg of bupivacaine 0.2%, levobupivacaine 0.2%, ropivacaine 0.2%, where Ivani et al compared 1 ml/kg of ropivacaine 0.2% and bupivacaine 0.2%. Both studies showed that there was no difference in

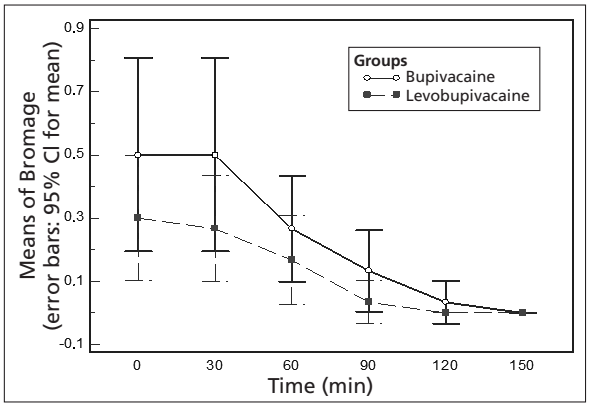

Figure 2. The mean Bromage scores. Mean Bromage scores were not statistically significantly different between the Bupivacaine and Levobupivacaine groups (Between-Subjects Effects, $p = 0.193$). There was no statistically significant interaction between treatment group and time ($p = 0.336$).

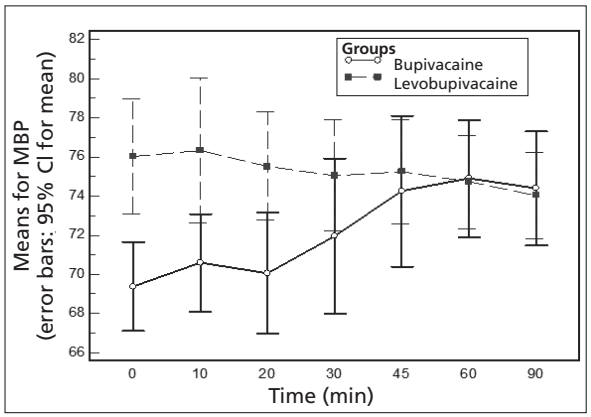

Figure 4. The mean blood pressure. The mean blood pressures were not statistically significantly different between the Bupivacaine and Levobupivacaine groups (Between-subjects effects $p = 0.376$).

the quality of postoperative analgesia and that all three drugs provide effective, adequate and similar analgesia in the perioperative and postoperative periods[3,13]. Frawley et al[19] 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[19]. In one other study, three different local anesthetic drugs were compared in orchidopexy and inguinal hernia surgeries, caudal block was found to be more effective in the bupivacaine and levobupivacaine groups compared to the ropivacaine group. However, there was no difference in the requirement for analgesia after wake up and need for the first analgesia after caudal application[18]. Unlike the studies mentioned above[3,13,17-19], in our study the quality of postoperative analgesia were determined to be significantly higher in the bupivacaine group. We suggest that this difference may be due to the fact that we used a low dose local anesthetic agent. In an evidence-based clinical update conducted by Dobereiner et al showed that in many studies, no difference detected with high dose of local anesthetic agents on the quality of postoperative analgesia[3,8,13].

Different studies have shown that postoperative motor block intensity varies and has a short duration[6,13,16-19]. In connection with this, Breschan C et al compared the effects of 1 ml/kg of levobupivacaine 0.2%, ropivacaine 0.2% and bupivacaine 0.2% on motor block and reported that the ropivacaine and levobupivacaine groups have a significantly lower motor block degree than bupivacaine group in the first two hours, but this significant difference was lost after two hours. They suggested that due to the weaker motor block in the levobupivacaine group it might be a preferred anesthetic in outpatient surgeries[13]. Similarly, Locatelli et al[6] and Ivani et al[16] investigated the effects of 1 ml/kg of bupivacaine 0.25% and levobupivacaine 0.25% on motor block, the bupivacaine group had a longer effect that was significantly different than the levobupivacaine group, but this effect had diminished in the following hours[6,15]. Similar results were also found in many other studies[8,16]. On the contrary, Ingelmo et al[18] compared the effects of 1 ml/kg of ropivacaine 0.2%, bupivacaine 0.2% and levobupivacaine 0.2% on motor block, similar results were obtained for all groups in terms of both waking up and close follow-up after waking up. Frawley GP et al[19] reported that there was no significant difference between groups in terms of motor block in their study where they compared higher concentrations of 1 ml/kg of bupivacaine 0.25% and levobupivacaine 0.25%. In addition, after the 150th min there was no residual motor block left in any of the patients. Results of this current study are in parallel with those of Frawley et al[19] and Ingelmo et al. The results from Ivani et al. where they compared the effect of 1 ml/kg of ropivacaine 0.2% and levobupivacaine 0.2% on motor block also show similarity with Frawley et al[19] and Ingelmo et al[21]. There are studies[16,21] that showed that motor block is proportional to the dose of the local anesthetic used. It was reported that motor block cannot be compared when low doses of local anesthetic is used, however when high dose local anesthetic is used, the comparison can be made and the residual motor block goes in parallel with the increasing drug concentration (> 0.175%). Similar to these studies, the fact that we did not see any difference in motor block in our patients might be because we used low doses of local_anesthetics and this finding overlaps with our observations of low degree of motor block and early return of motor function.

There are many parameters used to evaluate the effectiveness of caudal anesthesia which applied for postoperative analgesia, two of those parameters are MBP and HR. Generally, at the beginning of a surgical procedure, a 15-20% or more increase of these two parameters compared to baseline is considered to be an insufficient block[17,18]. Many studies related to this topic have reported that effects of local anesthetics on MBP and HR values are similar and no significant difference was found[3,6,13,15-18]. In our study, we did not detect any significant difference between groups in either of these parameters when evaluated separately. However, comparison of MBP within groups at first 30 min has a significant increase and HR at first measurements has a significant decrease. In addition, we concluded that this statistical analysis does not have a clinical significance because the difference in MBP and HR were lower than 10%.

Conclusions

Although both local anesthetics have less motor blockade, caudally administered 0.5 ml/kg of bupivacaine 0.25% provided a better analgesic quality during circumcision surgery.

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