A COMPARISON OF TWO DIFFERENT DOSES OF BUPIVACAINE IN CAUDAL ANESTHESIA FOR NEONATAL CIRCUMCISION: A RANDOMIZED CLINICAL TRIAL

Original Article

NEONATAL SÜNNET İÇİN UYGULANAN İKİ FARKLI BUPİVAKAİN DOZUNUN KARŞILAŞTIRILMASI: RANDOMİZE KLİNİK ÇALIŞMA

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ABSTRACT

Objective: We aimed to compare the analgesia quality of caudal block of low volume, high concentration bupivacaine to the conventionally used volumes and concentrations of the drug in neonates undergoing circumcision with sole caudal anesthesia.

Material and Methods: Fifty neonates, undergoing circumcision were randomly assigned to low volume high concentration (group LVHC, n=25) and control groups (group C, n=25). In group LVHC 0.5 ml/kg bupivacaine 0.375% (1.875 mg/kg) and group C 1 ml/kg bupivacaine 0.25% (2.5 mg/kg) was used. Hemodynamic parameters, block onset and analgesia periods were compared. Pain scores were evaluated hourly for 3 hours postoperatively with NIPS (neonatal infant pain score). Student's *t*-test for continuous variables, X^2 and Mann–Whitney U-tests were used for nominal and/or categorical variables.

Results: Demographic, hemodynamic data, block onset time (group LVHC and C values were 4.9±1 vs 5.2±2 mins, respectively; p=0.53) was similar and postoperative median NIPS were identical among the groups (median value of (0); p=0.7, p=0.9, p=1). None of the neonates required additional analgesic postoperatively.

Conclusions: Low volume high concentration caudal bupivacaine provided a similar perioperative analgesia quality, time and safety profile compared to conventional doses in awake neonates undergoing circumcision. LVHC

bupivacaine may be used to reduce the risk of local anesthetic toxicity in neonates.

Key words: *Neonatal caudal anesthesia; bupivacaine; circumcision.*

ÖZET

Amaç: Bu çalışmadaki amacımız neonatal sünnet prosedüründe kaudal blokta kullanılan düşük volüm, yüksek konsantrasyonlu bupivakain ile konvansiyonel olarak kullanılan doz ve konsantrasyonun analjezi kalitesinin karşılaştırılmasıdır.

Materyal ve Metod:Sünnet planlanan elli neonat, randomize olarak düşük volüm, yüksek konsantrasyon (grup DVYK, n=25) ve kontrol gruplarına (grup K, n=25) ayrıldı. DVYK grubu neonatlara 0.5 ml/kg, %0.375 bupivakain (1.875 mg/kg), grup K'daki neonatlara ise 1 ml/kg, %0.25 bupivakain (2.5 mg/kg) ile kaudal blok uygulandı. Hemodinami, blok başlama ve analjezi süreleri karşılaştırıldı. NIPS (neonatal infant pain score) ile değerlendirilen ağrı, postoperatif 3 saat boyunca saatlik olarak kaydedildi. İstatistik değerlendirme, parametrik değerler için Student's t-testi, nominal, kategorik değişkenler içinse, X2 ve Mann–Whitney U-testi ile yapılmıştır.

Bulgular: Demografik, hemodinamik veriler, blok başlama süreleri (grup DVYK ve K değerleri sırasıyla 4.9±1 vs 5.2±2 dakikadır; p=0.53) ve postoperatif median NIPS skoru (postoperatif 1, 2, 3 saatlerde median değer (0); p=0.7, p=0.9, p=1) gruplar arasında benzerdi. Hiçbir neonatın cerrahiyi izleyen 24 saat içinde ilave analjezik ihtiyacı olmadı.

Sonuç:DVYK kaudal bupivakain uygulaması, konvansiyonel bupivakain ile karşılaştırıldığında, benzer perioperative analjezi kalitesi, süresi ve güvenlik profili sağlamıştır. DVYK bupivakain, neonatal kaudal blok uygulamasında lokal anestezik toksisitesini azaltmak amacıyla da tercih edilebilir görüşündeyiz.

Anahtar Kelimeler:*Yenidoğan kaudal anestezi;bupivakain;sünnet.*

INTRODUCTION

Caudal epidural anesthesia is one of the most commonly performed regional block for postoperative analgesia in pediatric surgery .(1) and is often used to provide perioperative analgesia in neonates and infants.(2) Sole caudal block may be a safe alternative to general anesthesia in this population.(3) However, there are only a few studies and case reports considering caudal anesthesia alone in neonates.(3,7)

Local anesthetics used for pediatric caudal anesthesia are bound to serum proteins, mainly to alpha-1 acid glycoprotein (AAG). As the plasma concentration of AAG is decreased, the risk of local anesthetic toxicity would be higher in infants.(8) The commonly used bupivacaine dose for caudal anesthesia in small infants for infra-umblical surgery is 2.5 mg/kg. However, it was reported that following caudal administration of a single dose of L-bupivacaine (2.5 mg/kg), the highest Cmax level in children younger than 3 years was found to be close to the toxic threshold of adult patients.(9) Therefore, in neonates and infants, the dose of the local anesthetic during regional anesthesia should be reduced for safety reasons.

In this study we hypothesized that, low volume, high concentration (0.5 mL/kg, 0.375%) caudal regional block with bupivacaine (1.8 mg/kg) provides as effective and prolonged analgesia as the conventionally used volumes and concentrations (1 mL/kg; 0.25%; 2.5 mg/kg) in neonates undergoing circumcision with sole caudal anesthesia.

METHODS

This was a single-centre, balanced randomised (1:1), double-blinded, parallel-group study conducted at Yeditepe University Hospital (Istanbul, Turkey) between March and November 2011. After obtaining Ethical Committee approval (01.02.2011/N^{o} 073; chair-person Professor Recep Serdar Alpan, MD) and parental consent, 50 full-term neonates undergoing elective circumcision were enrolled in this study. Exclusion criteria were coagulopathy, sepsis, infection at the puncture site, anatomic abnormality in the caudal region, parental refusal.

Patients did not receive a sedative or an analgesic drug before caudal block. Preoperative laboratory tests included protrombin time, partial thromboplastin time and complete blood count. All the neonates were born at our hospital and routinely received vitamin K. Neonates were randomly assigned to low volume high concentration group (group LVHC, n=25) and to control group (group C, n=25) using a computer generated randomization table by a pediatric surgeon who did not participate to the conduct of the study. Patients were fasted for 4 hrs before caudal anesthesia.

Intravenous access was obtained prior to caudal block. Children received 5% dextrose in 0.45% saline at a rate of 4 ml/kg/h until feeding was restarted. Heart rate (HR), noninvasive blood pressure (NIBP), measured on the upper limbs, and oxygen saturation by pulse oximetry (SpO_2) were monitored and recorded during the procedure at 5 minutes intervals.

All neonates were placed in the left lateral position and caudal block was performed using an aseptic technique and a 25 G caudal needle (Epican; BBraun Melsungen, Germany). Aspiration test was used to detect blood or cerebrospinal fluid. Patients in group LVHC received a caudal injection of 0.5 ml/kg bupivacaine 0.375% (1.875 mg/kg), while the patients in group C received a caudal injection of 1 ml/kg bupivacaine 0.25% (2.5 mg/kg). All the caudal blocks were performed by two anesthesiologists experienced in the neonatal caudal block at least for 4 years. The patients were positioned for surgery after the procedure. Adequacy of the block was assessed with the absence of hemodynamic response, facial grimace and aversive response to a manual pinprick test. Caudal block level was evaluated by the absence of facial grimace or crying to a pinch test. Circumcisions were performed using a standardized technique. An intraoperative successful blockade was defined as no hemodynamic reaction (heart rate or mean arterial pressure >20% compared with the baseline) and absence of crying in response to surgical stimulus. All the neonates were awake during the procedure.

Postoperative pain was assessed with neonatal infant pain scale (NIPS) (10) every hour for 3 hours postoperatively. When the score was > 3, 15 mg/kg rectal paracetamol was considered as a rescue

analgesic. Side- effects encountered during the study period were also recorded. Block onset time, block level, the time required for the first analgesic drug administration and postoperative total paracetamol dose were recorded and compared among the groups. Caudal block failure rate was also recorded. No attempt was made to assess the degree of motor block because of its subjectivity in neonates. Postoperative evaluation was done by pediatric nurses who were blinded to the groups.

All the neonates were discharged from the hospital on the same day of the surgery. Home discharge was decided according to absence of the surgical bleeding and adequate breast feeding. Rectal paracetamol suppository (15 mg/kg) was prescribed for postoperative pain. Parents were educated and asked to evaluate the same pain scale to give rectal paracetamol if the neonates have pain. The parents were called by an anesthesiologist who was blinded to the groups for postoperative pain evaluation and the need for paracetamol twenty-four hours after the surgery.

STATISTICAL ANALYSIS

The data obtained are presented as the mean (±SD) and median, where appropriate.

We determined the number of the patients participated in our study according to the previous studies performed on the topic.(11,12) Statistical analyses were performed with Student's *t*-test for continuous variables. X^2 and Mann–Whitney U-tests were used for nominal and/or categorical variables. We considered a p value less than 0.05 for statistical significance.

RESULTS

One child in group LVHC was excluded from the study due to caudal block failure. Therefore, another child was added to the group. During the follow up period one patient in the same group was given paracetamol suppository due to postoperative fever. This patient was also replaced by another neonate. A total of fifty children participated and completed this study. Flow chart of the study is shown in **Figure 1**.

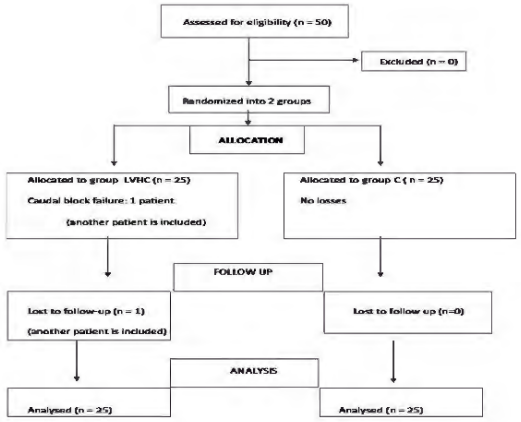

Fig 1. *Flow chart of the study.*

Demographic and surgical data are given in **Table 1**.

	Group LVHC (n=25)	Group C (n=25)	p value
Age (days)	19 ± 7	19 ± 8	0.9
Weight (gr)	3766 ± 492	3684 ± 643	0.6
Height (cm)	51 ± 1	51 ± 2	0.8
Block onset time (mins)	4.9 ± 1	5.2 ± 2	0.5
Duration of surgery (mins)	13.2±2	13.3±3	0.8
Discharge time (mins)	230±23	231±25	0.9

Table 1. *Demographic and surgical data, caudal block onset and discharge time.*

Abbreviations: Group LVHC; low volume high concentration local anesthetic group
Group C; control group.

There were no differences among the groups.

Heart rate and the mean arterial blood pressure values recorded during the anesthesia period were similar between the groups (**Figures 2 and 3**).

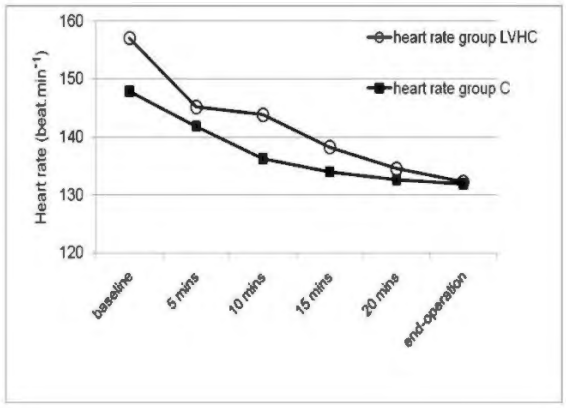

Figure. 2 *Variations in the heart rate values throughout the study period. None of the comparisons reached statistical significance between the groups (p>0.05). Abbreviations; bpm, beat per minute, group LVHC, low volume high concentration group; group C, control group.*

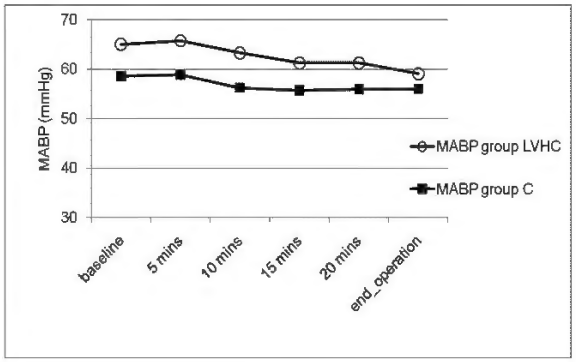

Figure. 3 *Variations in the mean arterial blood pressure values throughout the study period. Abbreviations; MABP, mean arterial blood pressure, group LVHC, low volume high concentration group; group C, control group.*

Caudal block onset time was not statistically different among the groups. (LVHC and Control group values were 4.9 ± 1 vs 5.2 ± 2 mins: 95% CI (-1.17-0.6), respectively; p=0.53, Table 1). None of the neonates in both groups required additional analgesic for the first twenty four hours following the surgery; therefore postoperative analgesic requirement was similar (p>0.1).

Sensorial block level after caudal block in group C was T 4-6, and L 1 - T 12 in group LVHC.

None of the neonates had a NIPS score of > 3 throughout the study period. Postoperative median NIPS (a median value of 0 at postoperative 1, 2, and 3. hours) were identical among the groups (p=0.7, p=0.9, p=1) (**Figure 4**).

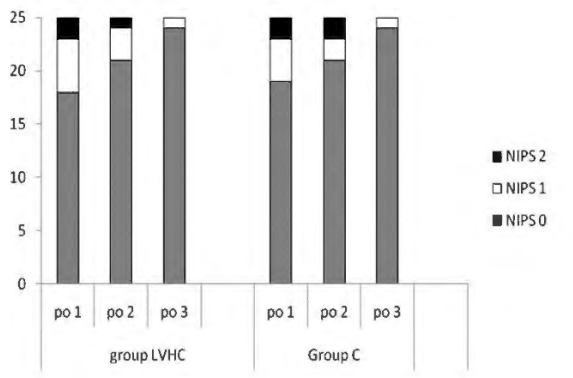

Figure. 4 *NIPS pain scores for the groups. Comparison of LVHC group versus control group did not reach statistical significance (p>0.05). Values are given as the number of the patients. Abbreviations; group LVHC, low volume high concentration group; group C, control group; po 1, 2, 3; postoperative hours 1, 2, 3.*

There was no difference among the groups regarding the hospital discharge times (group LVHC 231±23 mins vs group C 231±25 mins; p=0.9), 95% CI (-14-13).

No complications or drug-related side effects were observed during the study. None of the neonates developed acute urinary retention in the postoperative period.

DISCUSSION

Hoelzle et al demonstrated that the caudal anesthesia is feasible in patients ≤5 kg and technically easier and less dependent on immobility in awake infants compared to the spinal anesthesia.(13) Caudal epidural anesthesia alone has been recommended for neonates to reduce the risk of postoperative complications,(14) as it obviates the necessity for general anesthesia and endotracheal intubation. As a result, we performed sole caudal anesthesia to neonates undergoing circumcision in order to avoid risks of general anesthesia.

Uguralp et al demonstrated that caudal anesthesia is a safe, effective, inexpensive anesthetic technique and superior alternative to general anesthesia in premature infants and neonates when performed by experienced anesthesiologists. The authors did not observe any complications in their study(15). Findings of our study are parallel with the aforementioned paper. All the caudal blocks were performed by two experienced anesthesiologists in our study.

The quality and level of the caudal block is dependent on the dose, volume and concentration of the local anesthetic drug.[1] The analgesia duration has been shown to depend on the level of cranial spread of local anesthetic drug injected to caudal epidural space in children.[16] There are some attempts to reduce the dose, prolong the analgesia time and decrease the risk of motor block during the procedure by using high volume (1.8 mL/kg) and low local anesthetic concentrations(1) When high volumes of local anesthetic agents are used for neonatal caudal anesthesia, cranial spread of ≥ T12 (up to T3) is likely(17) However, a block level limited to the sacral dermatomes is enough for the circumcision procedure and transient motor block is not a major concern in neonates. Therefore, we used high local anesthetic concentrations (0.375%) along with a reduced volume providing a decreased local anesthetic dose (1.875 mg/kg). Caudal anesthesia with 0.375% bupivacaine was shown to be safe in neonates.18 The reason for the similar postoperative analgesia time among the groups despite using different volume and concentrations, is probably due to the blockade of the A alpha nerve fibers more satisfactorily when increased concentration of the local anesthetic agent is used.(19) This theory may also explain the prolonged postoperative analgesia obtained in LVHC group neonates considering the low block levels (L1-Th12). Furthermore, a recent ultrasonographic study on pediatric patients evaluating the different local anesthetic volumes (0.7, 1, 1.3 mL/kg) has shown that, high volumes injected via caudal route resulted in similar spread characteristics compared with low volumes.(20) Another study by Schrock CR et al. has shown that, increased local anesthetic volume did not increase the

duration of postoperative analgesia when the aforementioned caudal local anesthetic volumes were compared (0.7 vs 1.3 mL/kg).(21) Therefore, volume alone may not explain the prolonged analgesic effect as is the case in our study.

We did not observe any complications related to the caudal block, a finding correlated with a previous study[22], probably due to the appropriate management of the neonates by experienced anesthesiologists with maximal precaution.

Study limitations: Lack of the assessment of the local anesthetic plasma levels is a limitation of our study. However most of the families did not permit us to do extra punctures for blood sampling.
In conclusion, low volume, high concentration bupivacaine solution used during caudal anesthesia provides a similar perioperative analgesia quality, postoperative analgesia time and safety profile compared to the conventionally used doses in neonates undergoing circumcision procedure awake. Therefore, we recommend using low volume, high concentration bupivacaine in outpatient neonates to reduce the risk of local anesthetic toxicity.

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