Comparison of bupivacaine alone and in a combination with lidocaine for caudal block in patients undergoing circumcision: A historical cohort study

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ABSTRACT

Objective: Optimal analgesia following ambulatory surgery is an important matter in patient satisfaction, and it reduces unnecessary hospital admissions. This study investigated whether a caudal block with bupivacaine alone or in a combination with lidocaine can alter postoperative pain scores, complications, and perioperative and postoperative analgesic consumption.

Material and methods: This is a retrospective study that included children who underwent elective circumcision surgery under general anesthesia and caudal analgesia between January and June 2018. Among the 103 children, 17 cases were not analyzed due to an unsuccessful caudal block and procedures simultaneously underwent another operation unrelated to circumcision. We divided the study participants into two groups according to the type of local anesthetic applied: 0.5 mL/kg 0.25% bupivacaine (Group B) and 0.5 mL/kg 0.25% bupivacaine + 3 mg/kg 1% lidocaine (Group BL) caudally.

Results: Pain scores were similar between these groups and remained in the mild-to-moderate range throughout the hospitalization ($p>0.05$). There were significant differences regarding the rescue analgesic use, first micturition, and mobilization times ($p<0.001$). In addition, we applied the multivariable logistic regression for fentanyl consumption adjusted for first mobilization and micturition time, unlike mobilization, a significantly increased risk for postoperative delayed micturition (OR, 1.06; 95% CI, 1.0–1.12; $p=0.038$) was found with intra-operative intravenous fentanyl use.

Conclusion: Our results suggest that the caudal block with a lidocaine+bupivacaine combination decreases rescue analgesic consumption at day–case surgery. In circumcision procedures, the caudal block is an effective and safe analgesic method for intraoperative and postoperative pain control with no side effects. This trial was registered at Clinicaltrials.gov, NCT03911648.

Keywords: Bupivacaine; caudal block; circumcision; lidocaine.

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Introduction

Optimal analgesia following ambulatory surgery is an important aspect of patient satisfaction, and it reduces unnecessary hospital re-admissions. Circumcision, which is performed on an outpatient basis, is commonly a short operation in boys. Various methods are used to manage the postoperative pain in this procedure, such as the caudal block, penile block, topical analgesia, or intravenous analgesics. The caudal block is applicable widely in pediatric day–case surgery, providing excellent postoperative analgesia and attenuation of the stress response in children.^[1]

It has been shown that regional anesthetic techniques are safe, effective, and reliable, and as a result, they are widely recommended for sub-umbilical procedures in pediatric patients.^[2–4]

Since 1947, lidocaine has been used safely and effectively in almost every possible type of procedure requiring a local anesthetic (LA). Lidocaine has a limited duration of action, which is sometimes desired in LA, but for many procedures, it is less than ideal. Bupivacaine has a much longer duration of action; however, due to its slow onset, it is not an ideal sole agent for procedural analgesia in most sit-

uations. Combining these two amides LA agents in one syringe offers to the clinician and the patient the best effects of both the drugs: the very rapid onset of lidocaine and the prolonged duration of bupivacaine.^[5] Recent studies suggest that lidocaine and bupivacaine can be used in a combination or as a sole agent when applying regional anesthesia in children.^[5,6] But it remains unknown whether these combinations are useful or simply reflect underlying status. To the best of our knowledge, we are the first to investigate the potential effect of bupivacaine alone and in a combination with lidocaine when applying caudal epidural block in children. We tested the primary hypothesis that combining the two different LAs has a synergistic analgesic effect and decreases the need for additional analgesic doses. Second, providing intra-operative and postoperative analgesia reduces the risk of hemodynamic deteriorations, the length of hospital stay (LOS), first micturition and mobilization times, and surgical and anesthetic complications.

Material and methods

Design and settings

The study was approved by the ethics committee of the Istanbul University, Faculty of Medicine (2019/366), and we obtained written informed consent from all study subjects as a routine practice. The study was performed in a State Hospital from January through June 2018. We retrospectively compared the efficacy of bupivacaine alone and in combination with lidocaine at performing caudal block on analgesia in pediatric patients who underwent circumcision by assessing the required analgesic doses, pain scores, hemodynamic deteriorations, LOS, first micturition, and mobilization times. All children underwent elective circumcision under general anesthesia with caudal analgesia, and the American Society of Anesthesiologists (ASA) Class 1 cases were included. Patients with an unsuccessful caudal block and who simultaneously underwent another operation unrelated to circumcision were excluded. After meeting our inclusion criteria, the remaining 86 patient charts were analyzed.

The patients were divided into two groups with respect to the type of LA used:

Group B: Patients received 0.5 mL/kg bupivacaine 0.25% caudally, and the maximum given volume was 20 mL (n=42).

Group BL: Patients had 0.5 mL/kg bupivacaine 0.25% with the addition of 3 mg/kg lidocaine 1% caudally, the maximum given volume was 20 mL (n=44).

Anesthetic and analgesic management

Anesthesia and analgesia were managed according to the routine practice for pediatric patients by a single anesthetist at our institution. Premedication was performed using 0.5 mg/kg midazolam per-orally (p.o.) once diluted by juice 20 minutes prior to the procedure. In the operating room, routine monitorization included the heart rate (HR), pulse oximetry (SpO₂), temperature, and the mean arterial pressure (MAP). After insertion of an intravenous access, children received 5% dextrose in 0.33 normal saline, given at a rate of 5 mL/kg/hr. Anesthesia was delivered with an intravenous bolus of ketamine 2 mg/kg and propofol 2 mg/kg. The patients were provided an O₂ mask by 2 L/min. If respiratory depression occurred, patients were provided by assisted ventilation with 100% O₂ by respiratory mask. After the induction of anesthesia, patients were positioned laterally, with their hips flexed to 90°, the caudal block was performed under aseptic conditions by a 20–22-gauge caudal needle (Epican Paed caudal B-Braun Melsungen AG). The needle was passed through the sacrococcygeal ligament into the caudal space with a 40°–60°-degree angle. A distinct “pop” can be felt when the caudal block space is entered. Immediately after the anesthetic was injected, the children were turned to a supine position. In the case of the needle touching the bony tissue, blood aspiration, or bulging into the subcutaneous tissue, the block was considered unsuccessful. All operations were allowed to begin 10 minutes after the caudal block.

Data collection

Clinical data were recorded from the anesthesia-monitoring forms including patient characteristics, duration of anesthesia, surgery, time to perform caudal block, post anesthetic care unit (PACU) stay, medications, hemodynamic, and respiratory follow-ups and LOS. The Ramsay scale (RS) was used for the consciousness assessment at 5-min intervals during surgery, and the RSs were kept at 5–6.^[7] If RS<5, the administration of a propofol 1 mg/kg was applied 1 or 2 times. Intra-operative and post-operative anesthesia complications such as hypotension, bradycardia, respiratory depression, cardiac arrest, seizure, leg weakness, and post-operative nausea-vomiting (PONV) were recorded from nurse observation forms. The motor weakness was assessed as:

0=ability to stand or strong leg movement,

1=ability to move legs but unable to stand,

2=no leg movement.^[8]

The need for and timing of rescue medication were also part of the evaluation of clinical parameters for block efficacy, and we

Main Points:

- The application of caudal block before the surgery leads to a reduced stress response and thus provides profound analgesia.
- * The reduced use of intra-operative fentanyl during surgery favors the micturition of the children.
- * Our study showed a significant reduction of intraoperative opioid consumption in the mixed group.

noted both from the medical records. During the operation, BP, HR, SpO₂, and temperature were monitored continuously and recorded every 5 minutes. An intraoperative increase in HR by >20% was defined as insufficient analgesia and was treated with fentanyl 0.5 mg/kg. After surgery, patients were transferred to the PACU. Pain scores and hemodynamic and respiratory follow-ups were obtained every half an hour at PACU. Tramadol was given at a 0.5 mg/kg dose intravenously if the pain score was ≥ 4 at PACU. At our institution, pain scores were typically recorded on a scale from 0 to 10 by the FLACC (face, legs, activity, cry, consolability) score, which is based on objective behavioral variables, every half an hour at PACU.^[9] Respiratory depression was defined as a decrease in SpO₂ to <92%. If the pain score was ≥ 4 , paracetamol 15 mg/kg was prescribed orally every 6 hours at the post-surgery ward. All patients were discharged on the same day after being comfortable, mobile, tolerating oral fluids, and passing urine.

Statistical analysis

Baseline characteristics are presented as the mean $\pm$ standard deviation or median (minimum–maximum) for quantitative variables, and as number (percentage) for qualitative variables. Normality was tested using the Kolmogorov–Smirnov test. Non-normally distributed interval and ordinal data were analyzed using the Mann–Whitney U test. Parametric data with three or more occasions or conditions were analyzed by repeated-measures one-way analysis of variance, and nonparametric data with three or more occasions or conditions were analyzed using the Friedman test. Quantitative variables were compared using an unpaired Student's *t*-test. Categorical data were compared using χ^2 test with Yates' correction or Fisher's exact test, depending on the sample size. The variables "fentanyl," "tramadol," and "paracetamol" were analyzed according to their presence or absence. Multivariate analysis was conducted using logistic stepwise regression. Data included in the logistic equation with a *p*-value <0.05 were considered to be independent risk factors. A data analysis was performed using the Statistical Package for the Social Sciences (IBM SPSS Corp.; Armonk, NY, USA) 21 software. A *p*-value <0.05 was considered significant in the outcome analysis.

Results

Among the 103 children who underwent elective circumcision during the 6-month study period, 4 children were not analyzed due to an unsuccessful caudal block, and 13 children simultaneously underwent another operation unrelated to circumcision, leaving 86 patients enrolled in the study, 42 in Group B and 44 in Group BL, who were divided considering the LA type used in the caudal block.

Table 1 lists the patient characteristics, intraoperative fentanyl consumption, and the durations of application in the study population. There were no significant differences between the two groups with respect to age, weight, and duration of the caudal block, anesthesia,

and surgery (*p*>0.05). However, there is a significantly reduced intravenous fentanyl consumption in Group BL (*p*<0.001).

Regarding the caudal block outcomes, the first micturition (Group B 96 $\pm$ 26, Group BL 65.7 $\pm$ 15), and first mobilization (Group B 92 $\pm$ 28, Group BL 57.3 $\pm$ 14) times were significantly earlier in patients with the caudal block using the lidocaine+bupivacaine combination (*p*<0.001) (Table 2).

The baseline MAP and HR were similar in two groups. Compared with the baseline values, a greater reduction in MAP and HR was observed in Group BL (Figure 1) (*p* <0.001).

Average pain scores at PACU were not significantly different in the two groups (*p*=0.12; *p*=0.81) (Figure 2).

Table 3 presents the results of the logistic regression analysis. In the multivariable logistic regression model for fentanyl consumption adjusted for first mobilization and micturition time, unlike mobilization, a significantly increased risk of postopera-

Table 1. Demographic, clinical, and intraoperative characteristics of 86 patients in the study group

Variable	Group B (n=42)	Group BL (n=44)	p
Age (yr)	5.6 $\pm$ 2.1	5.9 $\pm$ 1.4	0.54
Weight (kg)	21 $\pm$ 5.8	21 $\pm$ 4.4	0.78
Intra-operative monitoring data			
Time to perform caudal block (min)	3.6 $\pm$ 1	3.5 $\pm$ 0.9	0.83
Duration of anesthesia (min)	35 $\pm$ 4.5	34.4 $\pm$ 4.8	0.92
Duration of surgery (min)	21.9 $\pm$ 4.5	22 $\pm$ 4.5	0.74
Patients receiving fentanyl (number)	12 (28%)	0	<0.001

Data are presented as the mean $\pm$ SD. Data are presented as the number of patients (%). PACU: post-anesthesia care unit; RS: Ramsey scale

Table 2. Post-operative data of 86 patients

Variable	Group B (n=42)	Group BL (n=44)	p
Patients receiving Paracetamol (nbr)	16 (38%)	3 (6.8%)	<0.001
First mobilization (min)	92 $\pm$ 28	57.3 $\pm$ 14	<0.001
First micturition (min)	96 $\pm$ 26	65.7 $\pm$ 15	<0.001
Length of hospital stay (hr)	7.1 $\pm$ 1.2	7 $\pm$ 0.9	0.69

Table 3. Analysis of risk factors for anesthetic outcomes in 86 patients

Variable	Wald	p	OR	95% CI
Mobilization (min)	0.075	0.78	0.993	0.94–1.04
Micturition (min)	4.28	0.038	1.06	1.0–1.12

Figure 1. Mean arterial pressure and heart rate values in the two groups

Figure 2. Pain scores at PACU in two groups

tive delayed micturition [odds ratio (OR), 1.06; 95% confidence interval (CI), 1.0–1.12; $p=0.038$] was found with intra-operative intravenous fentanyl use.

No complications such as bradycardia, hypotension, or PONV occurred between the groups. Respiratory depression was not seen in any child. One child was reported to have early transient motor weakness in group BL. The modified Bromage score for this patient was equal to 1 (partial flexion to knees). The symptom resolved after 3 hours post-operatively, and the child progressively started to walk at the ward.

Discussion

Based on the perception that recovery was more consistent with this protocol, we compared outcomes for this population with a historical cohort of patients managed with caudal epidural analgesia. To the best of our knowledge, this is the first study comparing the effects of a lidocaine-bupivacaine mixture with bupivacaine alone on the intensity and effectiveness of the caudal block in children. The pain scores were similar between these groups and remained in the mild range throughout the hospital-

ization. However, we found that patients managed with caudal analgesia with the bupivacaine+lidocaine combination at appropriate doses required less intravenous/p.o. analgesics intra-operatively and post-operatively. On another hand, the caudal block success was determined as 96.1% in our institution. More importantly, the time to first micturition and mobilization was shorter in the lidocaine+bupivacaine group when compared with bupivacaine alone.

Pain is difficult to assess in pediatrics, and compared with adults, lower concentrations of LAs are sufficient in children. LAs have a greater volume of distribution, a lower clearance, and a higher free non-protein-bound fraction in children.^[10] Bupivacaine and lidocaine are the two most commonly used LAs in children, but to the best of our knowledge, there is no study that addressed the benefit of a lidocaine-bupivacaine mixture at performing caudal block. Our results showed a significant reduction of intraoperative fentanyl and postoperative paracetamol consumption in the mixed group. This can be explained by a better analgesic management with this combination. Accordingly, during the period of surgery, we found no significant deterioration in the HR and MAP.

As we know, different anesthesia techniques can be applied during circumcision. In fact, without sedation or general anesthesia, regional blocks would be impossible in pediatric patients. Thus, general anesthesia prior to performing central blocks is the standard practice of most pediatric anesthesiologists. Recent studies have suggested that, due to neurotoxic effects of inhalation anesthetics and hypnotics in the immature developing brain, the popularity of regional anesthesia is rising worldwide.^[11] A recent recommendation from the European and American Societies for Regional Anesthesia states that the performance of regional anesthesia in children under general anesthesia or deep sedation is associated with acceptable safety and should be viewed as the standard of care.^[12] In our institution, we performed all general anesthesia procedure without using inhaler anesthetics combined with regional anesthesia without any adverse event.

A previous study compared propofol vs. propofol+ketamine for small procedural anesthesia in children, which resulted in reduced additional propofol and fentanyl doses in the mixed group and is associated with a better hemodynamic stability than propofol alone, without delaying recovery.^[13] Another study had evaluated and compared the preemptive efficacy of intravenous ketamine with placebo and caudal ropivacaine in pediatric patients showed that caudal LA has a superior preemptive effect compared with intravenous ketamine administration.^[14] Our results showed that we did not need to use extra propofol during surgery. Besides, we consumed a significantly reduced amount of intravenous fentanyl in the mixed group. We thought that our method of ketamine administration and applying of the caudal block before the surgery may have a benefit compared to preemptive analgesia that could affect our pain management success.

The application of caudal block before the surgery leads to a reduced stress response and thus provides profound analgesia with minimal hemodynamic alteration. This may also be associated with the combination of propofol and ketamine used during induction, which have opposing hemodynamic effects on the cardiovascular and respiratory systems. In compliance with our present findings, hemodynamic parameters remained in normal ranges, and no clinically significant cardiovascular deterioration was observed in the study population.

One of the secondary aims, time to first mobilization and micturition after surgery, may play a more significant role in cost efficiency because it likely contributes to recovery. A previous review exploring the postoperative urinary retention showed its incidence after general anesthesia and systemic analgesia were significantly higher than with regional anesthesia and epidural analgesia.^[15] The ability to void has always been considered as one of the criteria to discharge outpatients.^[15] The studies in rats^[16] have shown that the sedating-hypnotic agents and volatile anesthetics suppress the micturition reflex. The urodynamic effects caused by sedative-hypnotic agents appear to be a result of the inhibition of the pontine micturition center and the voluntary control of the cortex on the bladder. Since we applied a multivariable logistic regression analysis within the groups with/without fentanyl consumption adjusted for first the mobilization and micturition time, our results supported the findings above. Therefore, we thought the reduced use of intra-operative fentanyl during surgery may favor the micturition of the children. Hence, it is an imperative to evaluate the true reason of delayed micturition in large prospective clinical trials.

The absolute risk of permanent neurological injury after epidural anesthesia in children is unknown, but earlier studies suggested a low rate of serious complications associated with the caudal block in children.^[17-19] In an investigation describing complications after 10,556 central nerve blocks in children, the incidence

of complications was 0.29% (CI 95% 0.21–0.43).^[20] A subsequent prospective survey among pediatric regional anesthesia network reports none of the complications resulted in long-term sequela for children, which lead to an estimated incidence of complications with the sequela of 0.005%, by receiving >2 mg/kg bupivacaine.^[21] Compared to this, the incidence of short-term complications in our study might have been considered relatively low. In our investigation, one child was reported to have early transient motor weakness in Group BL (Bromage Score 1). We consider that the complication was a reflection of the age significance. It is once again noteworthy that the lower concentrations of LAs are sufficient in children. Any other neurological complications (such as, hematoma, epilepsy, or ischemic injuries to the spinal cord) or surgical complications were not observed at all.

This study contributed additional data in support of the LA type used during the caudal block in patients undergoing circumcision. We are aware of certain limitations in our study, and one of them is the risk of bias in the dataset. Because of the retrospective nature of the design, there may often be missing data related to the outcomes, such as documenting the pain scores and post-operative outcomes. The number of patients in this study was not sufficient to speculate about the incidence of possible complications in children. Because all cases were day-care surgery, we were not able to investigate long-term surgical outcomes.

However, one and the same person simultaneously applied anesthesia in observations. This may have impacted the strength of the association between simultaneous recordings of the data.

In conclusion, our results suggest that the caudal block with a lidocaine+bupivacaine combination decreases rescue analgesic consumption in children and accelerates mobilization and micturition at day-care surgery. In circumcision, the caudal block is an effective and safe analgesic method for intra-operative and postoperative pain control with no side effects.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of the Istanbul University, İstanbul School of Medicine (2019/366).

Informed Consent: Written informed consent was obtained from all participant's parents who participated in this study.

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