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Effectiveness of Caudal Epidural Block using Bupivacaine with Neostgmine for Pediatric Lower Extremity Orthopedic Surgery in Cure Ethiopia Children's Hospital

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Abstract

Background: This study was conducted to assess analgesia and side effects of neostgmine administered with caudal bupivacaine for pediatric lower extremity orthopedic surgeries in routine clinical practice.

Methods: In this blinded effectiveness trial, we studied 86 children aged 1-12 years undergoing lower extremity orthopedic surgeries. After induction of general anesthesia, 43 children in Group-B received 1 ml/kg of 0.25% bupivacaine and the other 43 in Group-BN received 1 ml/kg of 0.25% bupivacaine with 2.5 mic/kg neostgmine caudally. Demographic data, hemodynamic data before and after caudal, ASA status, duration of general anesthesia, duration of surgery, episode of post-operative nausea and vomiting (PONV), frequency of rescue analgesics per 24 hour, pain score and sedation score were recorded. Analgesic duration was defined as time from caudal injection to first rescue analgesic administration. Mann-Whitney test to compare median values and chi-square test for nominal data were used. A value "P<0.05" was considered as statistically significant.

Result: The median analgesic duration in Group-B was 5.8 ± 2.3 hr and 8.7 ± 5.3 hrs in Group-BN (p=0.003). Number of patients who required rescue analgesic drug doses within 24 hr twice, four times and more than four times were significantly different among the groups (p<0.05). There was no difference among the groups regarding pain and sedation scores. The PONV incidence was observed in Group-B (4.6%) and Group-BN (13.9%) which is not statistically significant (p>0.05) across the groups.

Conclusion: In routine clinical practice, addition of neostgmine to caudally administered bupivacaine prolongs analgesic duration without significant difference in PONV. It also decreases rescue analgesic consumption within 24 hours.

Keywords: Caudal epidural block; Analgesia; Bupivacaine; Neostgmine

Introduction

Procedural pain being the acute type has probability of progressing to chronic pain unless intervened properly [1]. Pediatric orthopedic surgery, which is one of painful procedures, needs proper pain therapy perioperatively. Caudal Epidural Block (CEB), which is technically easier in pediatrics than adults, can be used as a modality of treating pain due to lower limb orthopedic surgeries [2,3]. Among local anesthetics, bupivacaine is widely used for caudal epidural analgesia in children because of beneficial ratio of sensory to motor block beside longest duration of action [4,5]. Different additives are used to prolong the analgesic effect of local anesthetics administered caudally as a single shot [6-11]. Neostgmine is one of the additives known for significant analgesic prolongation. However, postoperative nausea and vomiting (PONV) incidence associated with caudal neostgmine is as high as 33.3% when co-administered with bupivacaine [12].

The aim of this study was to assess analgesia and side effects of neostgmine administered with caudal bupivacaine for lower extremity pediatric orthopedic surgeries in routine clinical practice.

Methods and Materials

After approval from institutional review board (IRB), we studied 86 consecutive ASA I-II children, aged 1-12 years, undergoing elective lower extremity orthopedic surgeries in Cure Ethiopia children's hospital. Prospective effectiveness trial study design was employed. Patients with no parental consent, contraindication for caudal block, use of other additives, failed or partial block, simultaneous operation on other site, and postoperative sedation were excluded. All subjects were elective patients scheduled for surgical correction of congenital orthopedic abnormalities. Caudal 1 ml/kg of 0.25% bupivacaine for Group-B and 1 ml/kg bupivacaine plus 2.5 mic/kg of neostgmine for Group-BN were used as needed. The maximum volume of solution used was 20 ml. The study was blinded in that patients or their attendants and physicians or nurses giving postoperative care were not aware of study solution used. The blocks were done 15-30 minutes before skin incision following aseptic technique using 21-23G needle. One Msc anesthesia student and two nurses collected the data. All patients were premedicated with glycopyrolate and 1 mic/kg fentanyl to facilitate insertion of LMA or ETT without muscle relaxants, induced with propofol or halothane and maintained with either isoflurane or sevoflurane using standard monitoring. A senior anesthesiologist supervised perioperative care team. During surgery adequate analgesia

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was defined as less than 20% or no increment of blood pressure, heart rate or respiratory rate in response to surgical manipulation. Duration of analgesia was defined as time interval in hours between caudal injections to first rescue analgesic administration. Modified Objective Pain Score (MOPS) consisting of five criteria: crying, movement, agitation, posture and localization of pain was used to assess pain along with patients' self-report of pain. Each criterion scores 0 to 2 to give a total score of 0 to 10. Morphine 0.1 mg/kg and ketorolac 0.5 mg/kg were used as rescue analgesics for MOPS ≥ 4 or patients' self-report of pain regardless of pain score. Morphine was used as first line and ketorolac as second line drugs. Objective sedation score based on eye opening was used to assess sedation as follows: 0-spontaneous eye opening, 1-eye opening on speech, 2-eye opening on physical stimuli and 3-unarousable. Postoperative pain and sedation scores were recorded in 30th min, 1st hr, 2nd hr, 4th hr, 6th hr, 12th hr and 24th hr. Episode of emesis and frequency of rescue analgesic requirement within 24 hr were recorded along with pain and sedation. Intravenous 0.15 mg/kg ondansetron and 0.15 mg/kg metoclopramide were used to treat PONV.

Sample size was determined from previous study [13] based on difference in proportion of patients who required 3 doses of rescue analgesics within 24 hour using 80% power of detecting the difference at 5% level of significance. Except pain score in median (range) form, data were expressed as Median ± SD.

Mann Whitney and chi-square tests were used for analysis and a p-value<0.05 was considered significant.

Results

Total of 97 patients were selected to join either group during preoperative visit, yet 11 patients were excluded from the study and only 86 patients were enrolled. Out of 11 excluded patients, 8 had failed CEB due to technical difficulty to inject solution to caudal epidural space; and 3 had caudals with other additives than used for this study (2 with epinephrine and 1 with morphine). 25 male and 18 female patients in Group-B and 27 male and 16 female patients in Group-BN were employed. The age of patients in Median ± SD was 9.0 ± 3.0 years in Group-B and 7.0 ± 2.8 years in Group-BN. The median weight of patients in both groups was 21.0 ± 7.4 kg in Group-B and 20.0 ± 6.0 kg in Group-BN. The groups were similar in sample size, demographic variables, ASA status, duration of general anesthesia and preoperative blood pressure distributions. However, the preoperative heart rate and duration of surgery showed significant variation among the groups (p<0.05) (Table 1). Types of procedures the eighty six patients had undergone were as follows in both groups: nine hip surgeries (open reduction), six femoral and hamstring surgeries (hamstring lengthening, distal femoral osteotomy and medial distal femoral epiphysis), two knee surgeries (knee arthrodesis), thirty four tibio-fibular surgeries (proximal tibial ostiotomy) and thirty five uncle and foot surgeries (triple arthrodesis and tendon release) (Figure 1). Intraoperative hypotension, bradycardia and hypoxia did not occur in study subjects. During emergence from anesthesia, two patients from group-B had pain due to prolonged surgical time and laryngospasm was observed in two patients from group-BN.

Statics	Group-B	Group-BN
Sex of patients (M:F)	25:18	27:16
Age of patients (Median ± SD)	9.0 ± 3.0 years	7.0 ± 2.8 years
Weight of the patients (Median ± SD)	21.0 ± 7.4 kg	20.0 ± 6.0 kg
ASA status (ASA I: ASA II)	41:2	40:3
Duration of surgery (Median ± SD)	60.0 ± 48.2 min	84.2 ± 50.9 min*
Duration of anesthesia (Median ± SD)	120.0 ± 62.4 min	137.9 ± 62.3 min
Preop systolic BP(Median ± SD)	89 ± 16 mmHg	120.0 ± 62.3 mmHg
Preop diastolic BP(Median ± SD)	49 ± 16.0 mmHg	42 ± 16 mmHg
Preoperative heart rate(Median ± SD)	101.0 ± 19.6 beats/min	127.1± 21.4 beats/min*

*P<0.05

Table 1: Demographic and perioperative data of the patients.

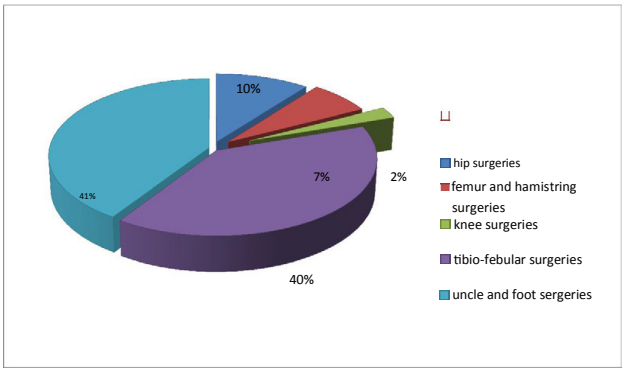

Figure 1: Types of surgery.

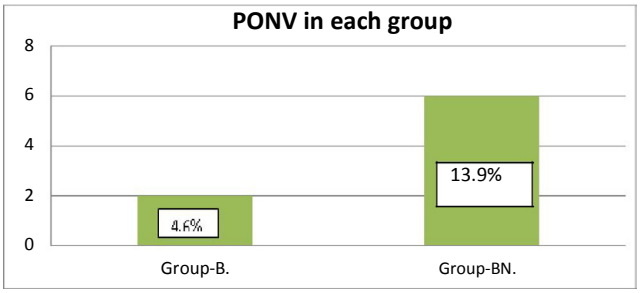

Figure 2: Prevalence of PONV.

Postoperatively, two (4.6%) patients in group-B and six (13.9%) patients in group-BN had nausea and vomiting (p>0.05) (Figure 2).

Within twenty-four hours, difference in number of patients who required rescue analgesic doses twice, four times and more than four times were significant (p<0.05) across groups. More number of patients from Group-B required analgesics four times and more than four times per 24 hours (Figure 3).

Duration of analgesia (Median ± SD) was 5.8 ± 2.3 hours in Group-B and 8.7 ± 5.3 hours in group-BN (p=0.003) (Figure 3).

Median pain score at each interval was zero in both groups. There was no variation in pain score at 30thminute, 1st hour, 2nd hour, 4th hour, 6th hour, 12th hour and 24th hour (p>0.05) (Figure 4 and Table 2).

Discussion

In this study, we confirmed that addition of 2.5 mic/kg of neostgmine to caudally administered 1ml/kg of 0.25% bupivacaine increases analgesic effectiveness of caudal epidural block. Neostgmine, the additive we used, has no reported side effects associated with its preservative when administered caudally [14,15]. Besides, the availability of neostgmine as a reversal of non-depolarizing muscle relaxant in every setup makes it more accessible than other additives. Although exact analgesic mechanism not known, the main effect of

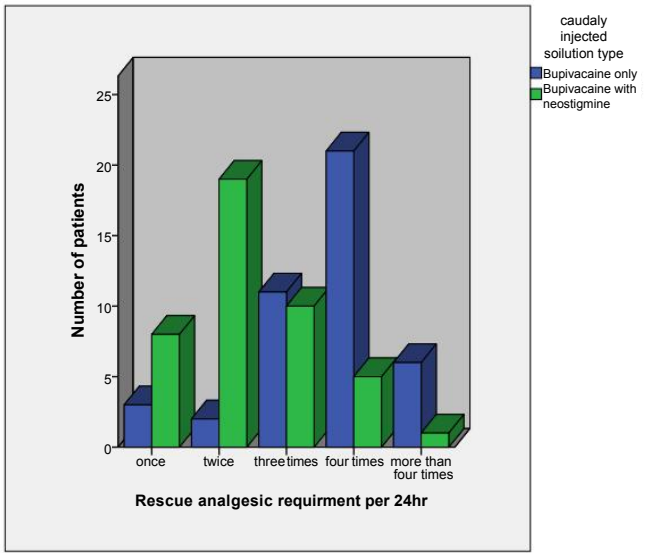

Figure 3: Frequency of rescue analgesic within 24 hour.

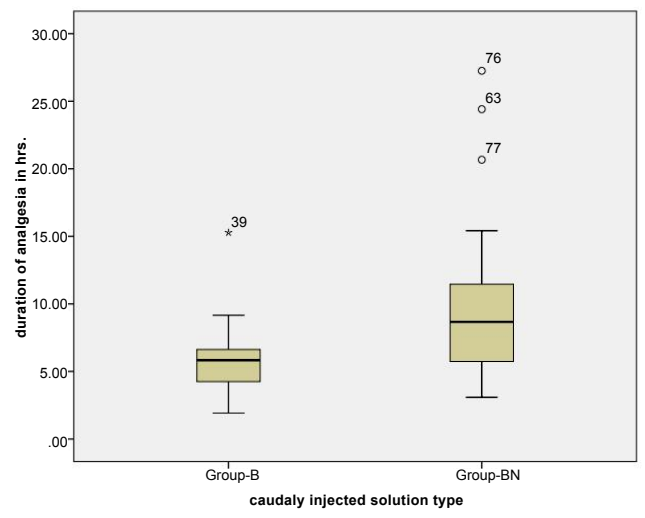

Figure 4: Analgesic duration.

Time intervals	Group-B	Group-BN
Pain score at 30th minute	0 (0-4)	0 (0-4)
Pain score at 1st hour	0 (0-4)	0 (0-4)
Pain score at 2nd hour	0 (0-4)	0 (0-4)
Pain score at 4th hour	0 (0-3)	0 (0-4)
Pain score at 6th hour	0 (0-4)	0 (0-2)
Pain score at 12th hour	0 (0-4)	0 (0-4)
Pain score at 24th hour	0 (0-4)	0 (0-6)

Pain score expressed in median (range) form.

Table 2: Pain score in postoperative period.

neostgmine is inhibition of acetylcholinestrase which degrades the acetylcholine. Thus, neostgmine increases the prevalence of Ach around the nerve endings. Spinal M1 and supra spinal M1 and M2 muscarnic receptors, that are also binding site of opioids, are responsible for antipain effect of Ach [16-18]. In addition, neostgmine may increase the release of acetylcholine from presynaptic nerve terminals, block neural potassium channels, and have a direct agonistic effect [19].

The analgesic duration (Median ± SD) was 8.7 ± 5.3 hrs in Group-BN and 5.8 ± 2.3 hrs in Group-B (p=0.003). Although highly significant prolongation of analgesia time, the duration in combination group was slightly shorter than the one reported in a previous study with 2 mic/kg dose of neostgmine [20]. Deference in study design and descriptive statics used may explain this discrepancy. Despite external validity, effectiveness studies exhibit low or fair results that often overestimated by efficacy studies with high internal validity. Mean duration was higher than the median one but the latter was used as non-parametric test employed for data analysis.

Longer duration of pain-free condition may implies less number of doses required within certain period of time. Similar to previous report, we observed difference in number of rescue analgesic doses required within 24 hr among the groups. Sunanda et al. [19] in a comparative study of 50 patients, using nearly equal caudal dose of bupivacaine with 2 mic/kg of neostgmine, reported significant change (p=0.001) in number of patients (4/25 vs. 12/25) requiring three doses of rescue analgesics within 24 hr [13]. In this study, although the difference in number of patients requiring three doses was not significant, the differences in number of patients requiring four doses (21/43 vs. 5/43) and more than four doses (6/43 vs. 1/43) were significant (p<0.05). The pain scores at 30th min, 1st hr, 2nd hr, 4th hr, 6th hr, 12th hr & 24th hr was comparable among the groups unlike previous reports. This might be due to pain score recorded at a time either the block was working or after the rescue analgesics had been given coincidentally. The two groups were comparable in terms of Sedation score which is in line with a previous report [21].

The most common side effect of neostgmine when combined with caudally administered bupivacaine is PONV with the incidence of 0-33.3% [12,21]. In this study, the incidence of PONV in group-BN was 13.9% which is within the range of previous studies. Besides, PONV was also observed in 2 patients (4.6%) in Group-B of our study. The PONV was not so severe that well managed by intravenous ondansetrone and metochlopramide. Pramod et al. reported zero incidence of PONV using the 0.5 ml/kg dose which is lower than the dose used in this study with similar concentration (0.25%) of bupivacaine for CEB [21] but Abdulatif et al. [20] in RCT of 60 patients using similar concentration and dose of bupivacaine to ours and reported 10% PONV incidence rate [13]. Therefore, the incidence of PONV in each group of this study (4.6% vs. 13.9%) was within the reported range in previous studies (0-10% vs. 16.7-33.3%). However, the difference in the emesis between groups of this study was not statistically significant (p>0.05) which is consistent with some previous reports [11,13,22].

Conclusion

Based on the result, we conclude that adding neostgmine to caudally administered bupivacaine significantly increases the pain relief time in routine clinical practice. Besides, using neostgmine with bupivacaine decreases the number of doses of rescue analgesic required in the first postoperative day without significant complications. Thus, it minimizes consumption of analgesic drugs and probably avoids side effects associated with repeated use of analgesics particularly opioids.

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