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Research Article

Post-Operative Analgesic Effect of Caudal Neostigmine added to Bupivacaine as Compared with Caudal Bupivacaine alone for Pediatric Elective Infra Umbilical Surgery. A Prospective Cohort Study

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Keywords

- Caudal block
- Bupivacaine
- Neostigmine
- Analgesic effect
- Infra umbilical surgery

Abstract

Background: Caudal epidural block is one of the most commonly used, popular, safe and easy regional anesthetic techniques to be performed in children undergoing infra-umbilical surgeries. The main disadvantage of single-shot caudal anesthesia is the short duration of action. Neostigmine is one of adjuvant with local anesthetic agents to improve the efficiency and quality to prolong the duration of analgesia after surgery. This study aimed to assess the effect of adding neostigmine to bupivacaine on post-operative analgesia in pediatric patient during infra umbilical surgery

Methods: Hospital based Prospective cohort study was conducted among 68 children's, whose aged is between 1-12 years, American Association of Anesthesiologists I & II undergoing elective infra umbilical surgery received caudal bupivacaine alone or bupivacaine with neostigmine. A systemic random sampling technique was used to select study participants. Postoperative severity of pain, time to request and total analgesic consumption was evaluated up to 24 hours after the operation. Based on the normality assumption, the analysis was done by independent sample t- test, a chi-square test and Mann–Whitney U-test. A p-value <0.05 was considered as statistically significant.

Results: In this study the median duration of postoperative analgesia in neostigmine group was 644 min while it was 322.5 min in bupivacaine alone group with statistically significant difference. With a p-value <0.0001. Median postoperative pain severity was being statistically significant difference at 4th, 8th, 12th and 24th hour with p-value of <0.05 but it was statistically insignificant at arrival, 1st and 2nd hour. Median post-operative analgesic consumption in mg within 24 h neostigmine group was 250 and bupivacaine alone group was 750 statistically significant with p-value of <0.0001.

Conclusion: Caudal neostigmine with bupivacaine provides effective post-operative analgesia in pediatrics undergoing infra-umbilical surgeries.

ABBREVIATIONS

ASA: American Society of Anesthesiologist; BAG:Bupivacaine Alone Group; BNG: Bupivacaine Neostigmine Group; CB: Caudal Block; FLACC: Face Legs Activity Cray Consolable; NRS: Numerical Rating Scale; OPS: Objective Pain Scale; PONV: Postoperative Nausea and Vomiting; POP: Postoperative Pain; SPSS: Statistical Package for Social Science; TASH: Tikur Anbesa Specialized Hospital

INTRODUCTION

Based on an international association study pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage [1].

The caudal block was first described in 1933 by Campbell and today it has become one of the most popular regional analgesic techniques [2].

Caudal block is useful for infra-umbilical surgery interventions in children for providing pain relief intra and post-operatively and also to reduce intraoperative inhalational or opioid agent consumption [3,4]. The main disadvantage of caudal administration of bupivacaine alone has a short duration of action (120 -150 min). There is a concern regarding the use

of caudal catheters to administer repeated doses or infusions of local anesthetic due to the risk of infection [5,6]. Caudal opioids have some adverse effects like nausea, vomiting, pruritus, urinary retention, and respiratory depression [7].

According to a WHO report, 80% of people worldwide do not receive adequate treatment for pain based on that only one in four patients had adequate relief from POP [8-13]. In Ethiopia, intra and postoperative analgesia is commonly achieved by the use of suppository paracetamol (PCM).

Neostigmine acts by inhibiting the breakdown of acetylcholine in endogenous neurotransmitters by producing analgesia when given in a central neuraxial route [10].

Therefore, this study was conducted to evaluate the effect of adding neostigmine to bupivacaine for the prevention of postoperative pain in pediatric patients undergoing infra-umbilical surgeries.

METHODS AND MATERIALS

Study design and sampling technique prospective cohort study design was conducted from October 30, 2019, G.C to January 30, 2020, at Tikur Anbesa specialized hospital which is located in Addis Ababa, Ethiopia. A total of sixty-eight pediatric patients were analyzed whether they received caudal block with the additive of neostigmine or bupivacaine alone group after induction of anesthesia over these three months.

The study was registered at http://www.researchregistry.com with the UIN: research registry 7478. This work is reported in line with STROCSS criteria from http://www.strocssguideline.com.

Data collection tool and procedure

After ethical approval was obtained from Addis Ababa University ethical committee and informed consent was taken from parents 68 patients belonging to ASA physical status I and II in the age range of 1- 12 years of either sex, for infra-umbilical surgeries were recruited.

The sample size was divided into two groups BAG and BNG, having 34 patients in each group receiving caudal bupivacaine 0.25% 1ml/kg and BNG received caudal bupivacaine 0.25% 1ml/kg plus neostigmine 2μg/kg. Failed caudal block, day case surgery, additive drugs used during caudal analgesia other than neostigmine, and dose other than 1ml/kg bupivacaine and 2 μg / kg neostigmine were excluded from the study.

Induction of anesthesia was selected by an anesthesiology resident student, MSc anesthesia student, and MSc anesthetists done with Propofol, thiopental, ketamine, and maintenance with halothane or Isoflurane. The caudal block was done left lateral decubitus position. Patient monitoring attached ECG, noninvasive blood pressure, pulse oximeter, precordial stethoscope, and time to start induction was documented. The postoperative time patients were transferred to PACU and to the ward when they recover from anesthesia. The patient was observed by trained nurses and pain was managed based on patient complaints. Either FLACC/ NRS pain score was assessed & measured at arrival, 1st, 2nd, 4th, 8th, 12thand 24thhour after the end of the surgery, time to first analgesic request, and total analgesic consumption in 24 hrs. In addition, adverse effects such as postoperative nausea and vomiting, motor block, urinary retention, and sedation were documented when it is reported within 24 hours

Variability of the study

The dependent variable this study was Pediatrics who received caudal neostigmine or bupivacaine, ASA status I and II, and Pediatric patients aged from 1-12years. The independent variable of this study was Failed caudal block, Additive drugs used during caudal analgesia other than neostigmine, and Dose other than 1ml/kg bupivacaine and 2 μg /kg neostigmine.

Data Analysis Procedure

Statistical analysis was performed using the statistical package for the social sciences, version 26 (SPSS). Descriptive statistics were used to summarize data, tables, and figures to display the result. Shapiro Wilk test was used to test normality while homogeneity of variance was assessed by using Levene's test for equality of variance, chi-square test was used to analyze categorical variables. Mann-Whitney U-test was used to analyze ordinal and non-normally distributed variables, with a power of 95% confidence level. In this study, a p-value <0.05 was considered statistically significant.

RESULTS

A total of sixty eight pediatric patients (34 patients in each group) were analyzed whether they received caudal block with additive of neostigmine or bupivacaine alone group after induction of anesthesia.

Socio demographic and preoperative patient characteristic The Socio demographic patient characteristics were comparable for all patients in the two groups. But there is no statistically significant difference between the two groups p- value >0.05 (Table 1).

Hemodynamic response before and after caudal anesthesia between two groups

There was no statistically significant difference in baseline vital sign, before, after skin incision, immediately at arrival and 60 minutes in hemodynamic response (PR and MAP) between two groups with P-value >0.05 (Table 2).

Comparison of postoperative pain severity by FLACC/ NRS pain rating scale between two groups.

The median FLACC/NRS score were comparable immediately at PACU, 1st and 2nd hour post operatively between bupivacaine alone and neostigmine with bupivacaine groups with statistically

Table 1: Socio demographic and preoperative patient characteristic between BN & BA groups in pediatric elective infra-umbilical surgery.

Variables	Bupivacaine alone group (n=34)	Bupivacaine with neostigmine group (n=34)	P-value
Sex			
Male n(%)	21(61.8 %)	27(79.4 %)	0.11
Female n (%)	13(38.2 %)	7(20.6 %)	
Age(years)*	4 (2-5.25)	3(2-6)	0.941
Weight(kg)*	14(10-19.25)	4.5(10-20)	0.711
ASA Status			
ASAI n (%)	26(76.5 %)	27(79.4 %)	0.77
ASAII n (%)	8(23.5 %)	7 (20.6 %)	
Type of surgery			
Urogenital n (%)	12 (35.5 %)	19 (55.9 %)	
GI/Lower abdominal n (%)	22 (64.7 %)	13 (38.2 %)	
Calf venous malformation n (%)	0 (0%)	2 (5.9 %)	
Duration of surgery (min)*	135 (90-176.25)	120(87.5-162.5)	0.449
Duration of anesthesia (min)*	152.5 (103.75-188.75)	130 (100-176.25)	0.332
Induction agent			
Thiopental	13(38.2%)	14(42.2%)	0.722
Propofol	8(23. 5%)	10(29.4)	
Ketamine	13(38.2%)	10(29.4%)	

Table 2: Hemodynamic response before and after caudal analgesia between BN & BA groups in pediatrics elective infra-umbilical.

Variables	Bupivacaine alone group (n=34)	Bupivacaine with neostigmine group(n=34)	P- value
Base line pulse rate**	124.91±15.927	121.91±22.28	0.525
Base line MAP *	69 (63-82)	72.5 (64.75-80)	0.956
Vital sign before skin incision			
Pulse rate**	126.18±17.02	122.82±21.67	0.481
Mean arterial pressure*	71(63-82)	70 (64-79)	0.703
Vital sign after skin incision			
Pulse rate*	124 (109.75-133.5)	124(115.5-130)	0.636
Mean arterial pressure*	67.5 (60-80)	64 (60-72)	0.141
Vital sign immediately at arrival (PACU)			
Pulse rate**	115.97±9.22	112.88±10.06	0.192
Mean arterial pressure *	66(60.75 -72)	65.5(60-67.5)	0.619
Vital sign within 60 min			
Pulse rate **	114.65±8.339	115.65±9.764	0.532
Mean arterial pressure *	73(66.5-80.5)	70(66-78.5)	0.507

NB: BN=bupivacaine with neostigmine added, BA= bupivacaine alone,**= mean ±SD, *= =median(Inter-quartile range), PR= Pulse rate in beat per minute, MAP = mean arterial blood pressure in mmhg, Independent sample t-test for normal distributed data and Mann -Whitney U test for non-parametric test was used, p-value < 0.05 is significant.

insignificant difference (p- value of >0.05).But the median FLACC/NRS were lower in neostigmine with bupivacaine group at 4th, 8th, 12th and 24th hour post operatively with statistically significant (p-value of <0.05) (Table 3 & Figure 1).

Comparison of time to first analgesia request, total dose of analgesic consumption in mg 24 h, Proportion of pt. need analgesia in 24h n (%) & number of analgesic request in 24h between two groups.

The result for time to first analgesia request found that neostigmine with bupivacaine group prolongs the analgesia duration than in bupivacaine alone group with statistically significant (p- value <0.05 (Table 4 & Figure 2).

Total dose of analgesic consumption paracetamol in mg within the first 24 h in neostigmine with bupivacaine group median were less used than bupivacaine alone group which is statistically significant (p-value <0.05).

The number of analgesic request in 24 h median compared in neostigmine with bupivacaine group were less number request than bupivacaine alone group with statistically significant (p-value <0.05).

Incidence of post-operative complication between two groups

The incidence of post-operative nausea and vomiting over 24 hours is 2.9% in both groups. But statistically insignificant difference between two groups with and also the other complication like **motor**/leg weakness, sedation and urinary retention statistically insignificant difference between the two groups with (p-value >0.05) (Figure 3).

Table 3: Comparison of postoperative pain severity by FLACC/NRS pain rating scale between BN & BA groups in pediatrics elective infra-umbilical surgery.

Variable * pain FLACC/NRS Score	Bupivacaine alone group (n=34)	Bupivacaine with neostigmine group(n=34)	P-value
Immediately postoperatively	1(0-1)	1(0-1.25)	0.747
1st h post Postoperatively	1(0-1)	0(0-1)	0.209
2nd h post-operatively	1(0-2)	0(0-1)	0.159
4th h post-operatively	3(2-3)	2(1-2.25)	0.001*
8th h post-operatively	3(2-4.25)	2(1-3)	<0.0001*
12th h post –operatively	4(4-5)	3(2-3)	<0.0001*
24th h post-operatively	5(3.75-5)	3(2-3)	<0.0001*

NB: BN=bupivacaine with neostigmine, BA= bupivacaine alone, * = M =median; (Inter-quartile range),*= statistically significant, Mann -Whitney U test was used, p-value < 0.05 is significant.

Table 4: Comparison of time to first analgesia request, total dose of analgesicConsumption in mg 24 h & number of analgesic request in 24h between BN &BA groups in pediatrics elective infra-umbilical surgery .

Variables *	Bupivacaine alone group (n=34)	Bupivacaine within neostigmine (n=34)	p-value
Time to first analgesic request minutes	322.5(242.5-375)	644(450-1440)	<0.0001*
Total dose of analgesia Paracetamol consumption in mg 24 h	750(500-750)	250(0-500)	<0.0001*
Number of analgesic request in 24h	3(3-4)	1.5(0-2)	<0.0001*
Proportion of pt. need analgesia in 24h n (%)	34(100%)	23(67.6%)	<0.0001*

NB: *= statistically significant, * =median or inter-quartile range, chi-square (x2) test and Mann -Whitney U test was used, p-value < 0.05 is significant.

Table 5: Incidence of post-operative nausea & vomiting over 24 hour complication between two groups BN & BA groups in pediatrics elective infra-umbilical surgery.

Post-operative complication Within 24 h (n= %)	Bupivacaine alone group(n=34)	Bupivacaine with neostigmine group (n=34)	P-value
Nausea and vomiting (n %)	1(1.45%)	1 (1.45%)	1.00
Motor/leg weakness (n %)	0	0	
Sedation (n %)	0	0	
Urinary retention (n %)	0	0	

NB: (n= %) = number (proportion), Bupivacaine alone group (BA), Bupivacaine with neostigmine group (BN), chi-square (x2)–test was used with p-value <0.05 is significant.

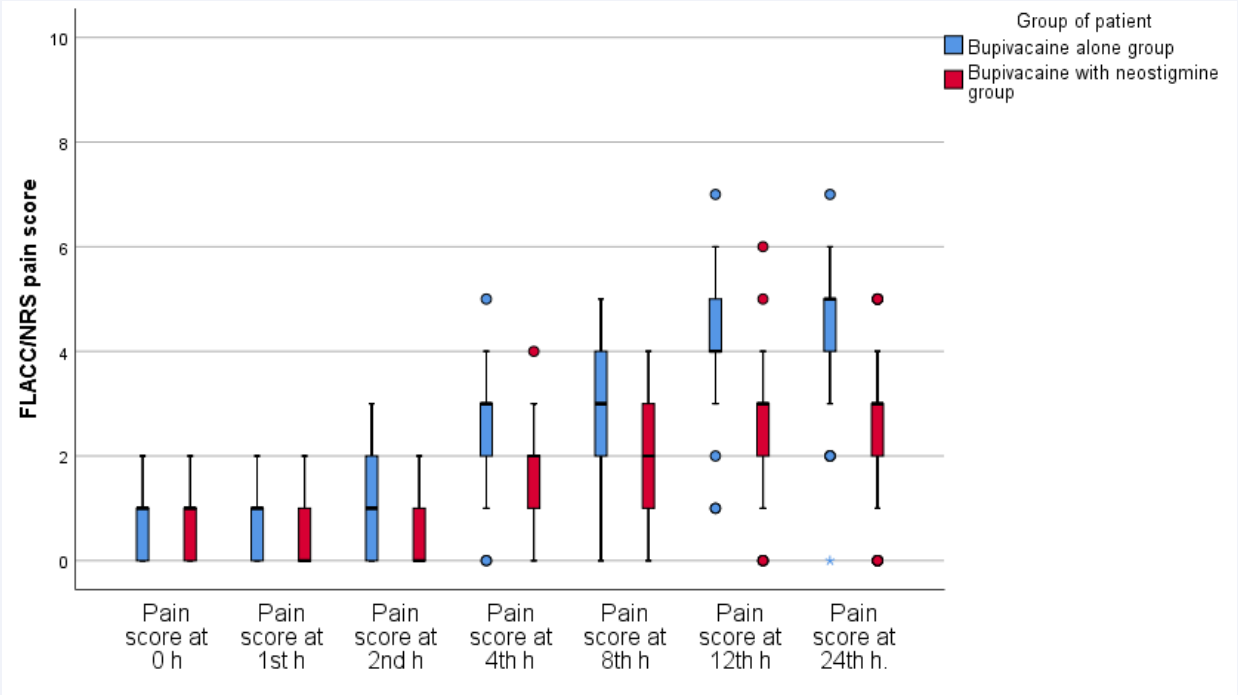

Figure 1 Comparison of postoperative pain severity using 11 points FLACC/NRS (0-10) score between BN & BA groups in pediatrics elective infra-umbilical surgery.

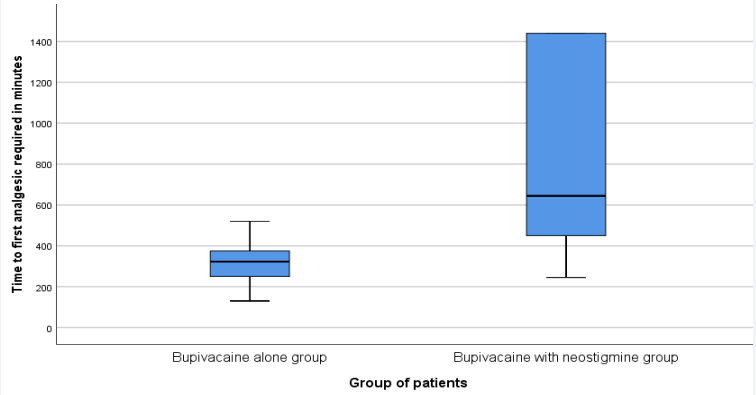

Figure 2 Comparison of time to first analgesia request between BN and BA groups within 24 hours in minutes groups in pediatrics elective infra-umbilical surgery.

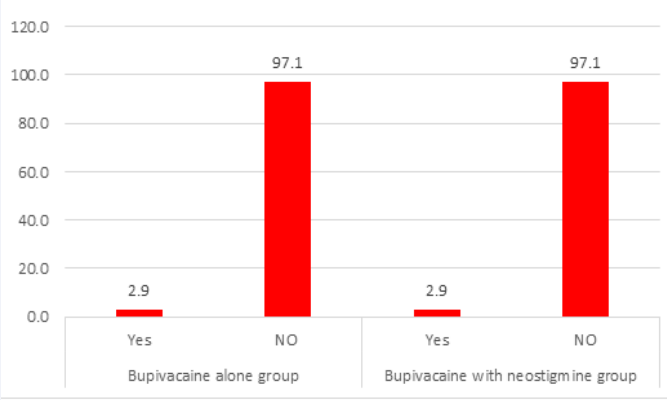

Figure 3 Incidence of post-operative nausea & vomiting over 24 hour complication between two groups BN & BA groups in pediatrics elective infra-umbilical surgery.

DISCUSSION

In our study, the Socio-demographic characteristic of age, Wight, gender, ASA status, duration of surgery, and duration of anesthesia were comparable in both groups, and hemodynamic parameters vital signs like baseline, before and after skin incision by mean or median (blood pressure & heart rate). There were no statistically significant differences between the two groups (p-value>0.05) which is similar to the study conducted in Turkey by Dilek Memis and in India by Dr. Tahira Akhter et al [14,15]

In this study, the result with a median duration of postoperative analgesia was 322.5 minutes vs 644 minutes in the bupivacaine alone group and neostigmine with bupivacaine group postoperative. Respectively (P-value<0.05). This finding is similar to the study done in Pakistan by Mohsin Riaz et al., showed that the mean duration of postoperative pain relief in BNG was 11.97 ± 3.80 h and BAG was 6.70 ± 2.12 h statistically significant difference with a p-value <0. 001 [16].

Our study also shows a comparable result with a study done by S Fyneface -Ogan etal in Nigeria 2014 on the comparison of caudal bupivacaine and neostigmine to relieve postoperative pain in children showing that the mean postoperative duration of analgesia was 4.77 ± 0.8 vs 7.7 ± 1 h in bupivacaine alone group and neostigmine with bupivacaine group respectively [17].

In contrast to this study, research done in Turkey by Dilek Memis et al., showed that the mean duration of postoperative pain relief did not differ bupivacaine alone group was 15.40 ± 10.97 h and neostigmine with bupivacaine group was 15.45 ± 10.99 with (P-value > 0.05) [18].

In this study, the median postoperative pain severity was assessed by FLACC/NRS scale between two groups at the 4th, 8th, 12th, and 24th hours after surgery with a p-value of <0.05. But it is statistically insignificant at arrival (PACU), 1st and 2nd h. is finding were similar to the result done by Dr. Emil Batarseh 2015 in Arab West Asia which showed that postoperative pain severity is statistically significant at 4 th,8th,12th, and 24th hour with the p-value of <0.05 while it was insignificant at arrival, 1st and 2nd hour [19].

Another study conducted in India by Bhardwaj N et al showed that there was no mean duration of postoperative pain severity between the two groups which is incomparable with our study finding [20].

In this study, the median postoperative analgesia consumption in mg within 24 h in neostigmine group was 250 and bupivacaine alone group was 750 statistically significant with a p-value of <0.0001.

In another study conducted in Arab West Asia by Dr. Emil Batarseh [21], and in Egypt by El-Miseery et al. [22], post-operative total analgesia consumption is lower in the neostigmine with bupivacaine group than bupivacaine alone group in 24 hours with p-value <0.05.

According to the result of this study, postoperative nausea and vomiting were too low in bupivacaine alone and neostigmine with bupivacaine groups respectively, which is statistically insignificant between the two groups (p-value>0.05).

In contrast with our study, research conducted by Batra YK et al. [12], and Kaushal D [13] in India found that postoperative nausea and vomiting were statistically significant. The possible reason may be due to they had used a higher dose of neostigmine.

CONCLUSION

Caudal analgesia using neostigmine added with bupivacaine (2μg/kg) is increased the duration of postoperative analgesia for pediatric elective infra umbilical surgical procedures without any significant side effects.

Recommendation

We recommended the use of additive neostigmine with bupivacaine for caudal analgesia undergoing infra-umbilical pediatrics surgeries to prolong postoperative analgesic effectiveness.

We also recommended additional randomized controlled study

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We would like also than Addis Ababa University library to cite the preprint version of this study.

Data Availability

All data analyzed during this study are included within the article.

Ethical Approval: Ethical clearance was obtained from the department ethical clearance committee college of health science department of anesthesia Addis Ababa University before the start of the study. Get permission from TASH clinical director's office after submission of an official letter

CONSENT

The importance of the study was explained and written informed consent was obtained from each participant relative by the data collector. Participant's involvement in the study was on voluntary bases, participants who were not willing to participate in the study & those who wish to quit their participation at any stage were informed to do so without any restriction.

Disclosure

The publisher to recommend that the preprint version of the previous study was cited (1).

This work is reported at line with STROCSS criteria at www.strossguideline.ccom.

AUTHORS' CONTRIBUTIONS

All authors should have made substantial contributions to all of the following: the conception and design of the study, or acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be submitted.

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