ORIGINAL ARTICLE

The Effect of Addition of Clonidine to Bupivacaine in Caudal Block On the Duration of Analgesia in Children Undergoing Herniotomy

Samuel C **OJIAKOR**[1,2]
Nosa P **EDOMNWONYI**[3,4]
Beatrice U **UMEH**[1,2]

[1]*Department of Anaesthesiology Nnamdi Azikiwe University, Awka Anambra State, NIGERIA*

[2]*Department of Anaesthesiology Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, NIGERIA*

[3]*Department of Anaesthesiology University of Benin, Benin City Edo State, NIGERIA*

[4]*Department of Anaesthesiology University of Benin Teaching Hospital Benin City, Edo State, NIGERIA*

Author for Correspondence
Dr Samuel C **OJIAKOR**
Department of Anaesthesiology Nnamdi Azikiwe University/ Nnamdi Azikiwe University Teaching Hospital Nnewi, Anambra State.

Phone: +234 803 740 8192
Email: drojiakorsc@yahoo.com

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ABSTRACT

Background: Caudal epidural analgesia is a frequently performed regional block in childhood analgesia. However, its effects are limited by short duration of action using local anaesthetics alone.
Objective: To evaluate the efficacy of caudal block in children using bupivacaine augmented with clonidine for elective inguinal herniotomy
Methodology: This was a cross sectional study of children aged 2–6 years scheduled for elective inguinal herniotomy. Fifty-two children in American Society of Anesthesiologists (ASA) physical status I or II were randomly divided into two groups I(BS) and II(BC) of 26 each. Group I received plain bupivacaine with saline while group II received plain bupivacaine combined with clonidine. The outcome measure assessed was post-operative pain scores using Objective Pain Scale (OPS) and the results were analyzed using SPSS (Statistical Package for Social Sciences version 17 Chicago, Illinois) and presented as mean, frequencies and counts. Parametric data were compared using student's t- test. A p value of < 0.05 was considered significant.
Results: The groups were comparable in terms of age, weight and height. The mean duration of analgesia in clonidine group (8.16 ± 1.70 hours) was significantly longer than saline group (4.00 ± 1.41 hours, p=0.001). Pain scores were lower in the clonidine group. There are no significant changes in the haemodynamic variables in both groups.
Conclusion: This study demonstrated that the addition of clonidine to plain bupivacaine in a single shot caudal block prolonged the duration of postoperative analgesia without increasing the incidence of side effects.

Key words: *Caudal Epidural, Bupivacaine, Clonidine, Analgesia, Herniotomy, Children.*

INTRODUCTION

Caudal epidural blockade in children continues to grow in popularity with increasing applications for surgical procedures below the umbilicus because it is relatively easy to perform and combines a high success rate with low risk of complication.[1,2] Caudal anaesthesia is commonly performed in combination with general anaesthesia as a means of providing postoperative analgesia or as a technique to reduce the requirements of general anaesthetic agents thus improving the postoperative recovery profile.[2,3] In addition, caudal epidural blockade has also found increasing role in the management of acute and chronic pain outside the peri-operative period.[3]

The major drawback to single shot caudal block is the relative short duration of postoperative analgesia ranging between 2 to 6 hours, even with the use of long acting local anaesthetic agents such as bupivacaine leading to the need for additional analgesia in the late postoperative period.[3,4,5,8]

Various methods and additives have been employed in an attempt to prolong the duration of caudal analgesia. For example, increasing the dose or concentration of local anaesthetic prolongs the duration of analgesia but with a corresponding increased risk of toxicity.[4,6,10] Also the placement of a caudal catheter for continuous administration of caudal solutions to extend the analgesia beyond the limit of single shot injection has become unpopular due to the potential risk of infection associated with the technique as a result of the proximity of site of injection to the anal orifice.[7]

Additives like opioids, ketamine, clonidine, dexmedetomidine, midazolam and dexamethasone have been studied and reported to have varying degree of success.[11,14,17,18,19,20]

Clonidine, an alpha-2 agonist was initially used as an antihypertensive but has now been discovered to possess significant analgesic property which were demonstrated in several studies when combined with local anaesthetics for caudal analgesia.[14,15,16,27,28] Several mechanisms have been suggested on how clonidine induced prolongation of caudal analgesia with local anaesthetics.[16] It crosses the blood brain barrier causing a direct suppression of spinal neurons and interacting with alpha-2 adrenoceptors at spinal and supraspinal sites thereby inhibiting neurotransmission in the peripheral sensory Að and C fibers through a slow retrograde axonal transport along the nerves.[21] Again, clonidine induces vasoconstriction through interaction with alpha-2 adrenoceptors located at peripheral vascular smooth muscles, thereby delaying the absorption and elimination of local anaesthetics.[26]

This study seeks to determine if the caudal administration of 1.5 µg/kg clonidine mixed with 0.75 ml/kg bupivacaine (0.25%) will achieve adequate and prolonged duration of analgesia among children aged 2- 6 years undergoing elective herniotomy.

METHODOLOGY

Study Design

This was a prospective, randomized, comparative, double-blind study conducted at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Anambra State.

The study population was drawn from paediatric surgical patients scheduled for elective unilateral herniotomy.

Inclusion / Exclusion Criteria

Children in American Society of Anesthesiologists (ASA) physical status I or II, aged 2-6 years, scheduled for unilateral herniotomy and whose parents/ guardians consented were included. Excluded were children with known allergy to the study drug, bilateral inguinoscrotal hernia, patients with sacral abnormalities, pre-existing neurological diseases, infection at the site of caudal administration, haemoglobinopathies and those whose parents/ guardians refused consent.

Sample Size Estimation

Using data from a previous study in a similar setting.[15] the sample size was calculated using the formula:[25]

$$N = (p_1 \times (1- p_1) + p_2 \times (1- p_2)) \times z^2 / h^2$$

Value substitution evaluated to a sample size of 23 patients for each group. Allowing 10% loss to protocol violation approximated to 52 patients, 26 patients in each group were recruited.

Statistical Analysis

Data were analyzed with SPSS (Statistical Package for Social Sciences) version 17. Continuous data were summarized as mean and standard deviation (SD), dichotomous data as counts and frequencies. Parametric data was compared using student's t-test, categorical data were analysed using Fisher's exact test. A p value < 0.05 was considered significant.

Ethical Issues

Study approval was obtained from NAUTH Ethics & Research Committee and National Agency for Food, Drug, Administration and Control (NAFDAC). Written informed consent were obtained from eligible subjects' parents/guardians including information on their right to withdraw from the study if they wish without undue consequences or alteration of standard.

Randomization

The children were randomized into one of the two groups through blind balloting of papers on which group I or group II was written and were kept in a large opaque envelope. Each consenting parent was made to pick one piece of paper after thoroughly shaking the envelope. Group I received a mixture of 0.75ml/kg of plain bupivacaine (0.25%) and saline while group II received a combination of 1.5µg/kg clonidine and 0.75ml/kg of plain bupivacaine (0.25%) both of equal volumes in one syringe. Anaesthesia was induced with a stepwise increase of halothane 1-3% in 100% oxygen using a tight fitting face mask and Jackson-Rees breathing circuit. Following loss of consciousness, intravenous access was secured with size 24G cannula and normal saline was commenced at a rate of 10 ml/kg in the first 1 hour.

Thereafter, patient was positioned in the left lateral decubitus position with the knees drawn up to the chest. Under strict aseptic conditions, sacral hiatus was identified by running up the thumb from the coccyx towards the sacrum. 'The sacral hiatus is the third point of the equilateral triangle formed with two posterior superior iliac spines (dimples on the skin). After sacral hiatus was identified, a size 22-gauge short bevel hypodermic needle was inserted into the sacral hiatus at angle 60^0 to the skin. The needle was

then slightly advanced cranially while readjusting the angle until a characteristic "give" was felt which indicated the penetration of the sacro-coccygeal membrane, subsequently a sudden loss of resistance as the needle was advanced further about 2 mm cephalad indicated entrance of the needle into the caudal epidural space. Subcutaneous needle placement was ruled out by absence of subcutaneous emphysema using a 2ml air in fluid syringe while dural puncture and intravascular puncture was ruled out by negative aspiration test for cerebrospinal fluid and blood respectively. All the caudal blocks were performed by the investigator.

Thereafter syringes of study solution of either 0.75 ml/kg of bupivacaine (0.25%) plus saline (0.1ml/kg) or 0.75 ml/kg of bupivacaine (0.25%) plus 1.5 µg/kg (0.1 ml/kg) clonidine prepared by another anaesthesiologists was administered by the investigator who was blinded to the drug composition. Dressing was applied to the skin puncture site and the patient was returned to supine position and surgery commenced. Anaesthesia was maintained with 0.5-1% halothane in 100% oxygen with the patient breathing spontaneously via face mask connected to Jackson Rees circuit at a flow rate of 2.5 to 3-minute volume. Changes in heart rate, blood pressure and lacrimation were used to assess the depth of analgesia.

Assessment of pain using Objective Pain Scale[24] (see Table 1) was carried out every 15 minutes in the first 1 hour in Post Anaesthesia Care Unit (PACU), then hourly for the next 5 hours, at 8 hours, 12 and 24 hours in the ward.

OPS Scores exceeding 4 points in PACU were treated with Intravenous Paracetamol 15 mg/kg while oral paracetamol 15mg/kg was used in the ward. Haemodynamic parameter changes were documented.

Table 1. Objective Pain Scale (OPS)

Parameter	Finding	Points
Blood pressure	<20% of Preoperative	0
	20-30% of Preoperative	1
	>30% of Preoperative	2
Crying	Not crying	0
	Responds to age appropriate nurturing (tender loving care)	1
	Does not respond to nurturing	2
Movements	Relaxed	0
	Moving about Constantly	2
	Thrashing [moving wildly]	2
	Rigid	2
Agitation	Asleep or calm	0
	Mild agitation	1
	Hysterical (cannot be comforted)	2
Pain Complaints	Asleep	0
	States no pain	0
	Cannot localize	1
	Localize pain	2

Key: OPS Score: 0-4 = No pain – mild Pain 5-7 = Moderate Pain 8-10 = Severe Pain

Incidences of nausea, vomiting, time to first ambulation and spontaneous voiding were noted.

At the end of surgery, oropharynx was suctioned and halothane discontinued but 100% oxygen was continued for about 15 to 20 minutes till full recovery. The patients were positioned laterally and transported to post-anaesthesia care unit. The vital signs and pain were assessed for a minimum of 60 minutes before they were transported to the ward. Follow up of Patients was done through the paediatric surgical outpatient clinic; phone calls were also made to the parents whose children did not present to the clinic.

Measurement of Outcomes

Proportion of patients scoring less than or 4 points in the postoperative period using the Objective Pain Scale and time from caudal administration of study drug to first analgesia requirement were our primary outcomes. The secondary outcomes include incidence of side effects such as nausea and vomiting, time to first ambulation as well as parents'/guardians' satisfaction which was assessed using a 3 level objective Likert item as satisfied, dissatisfied and neither satisfied nor dissatisfied.

RESULTS

A total of 52 children aged 2–6 years in ASA physical status I or II were enrolled into this study, with 26 patients in each group. None was lost to protocol violation. There was no significant difference with regards to the demographic characteristics between the study groups as shown in table 2.

Table 2. Patients demographic characteristics (Mean ±SD)

Parameters	Group I N=26	Group II N=26	*P* value	Level of significance
Age (years)	3.38 ± 1.55	3.81± 1.36	0.307	NS
Weight (kg)	14.44 ± 3.89	15.06 ± 2-67	0.507	NS
Height (cm)	90.27± 9.45	90.35± 7.83	0.975	NS

N S -Not significant

In the first 1 hour after surgery, the proportion of patients with Objective Pain Scale (OPS) scores less than or equal to 4 were the same in both groups; but from 3 hours, the proportion of patients with OPS scores ≤ 4 became significantly fewer in group I. Fifteen (57.7%) of patients in group I while 100% (26) of patients in group II were pain free having pain scores ≤ 4. (p = 0.003) At 6 hours postoperatively, all the patients in group I had received supplementary analgesia but 76.9% (20) of patient in group II still maintained OPS score ≤ 4. This difference was significant as shown in table 3 (p= 0.001)

The duration of analgesia defined as the time to first analgesia requirement was 4.00 ± 1.41 hours in group I and 8.16 ± 1.70 hours in group II and this difference was significant as shown in Table 4 and Figure 1 (p= 0.001)

Table 4 also revealed that the differences in mean total analgesic (oral Paracetamol) consumption during the 24 hours' observation period between the two groups were significant.

Table 3. Proportion of patients with OPS score ≤ 4 and corresponding mean pain scores at various time intervals. (Mean ±SD)

Time (mins/hrs)	Group I			Group II			P	Level of significance
	N	%	Pain score	N	%	Pain score		
0	26/0	100	0.0	26/0	100	0.0	-	-
15mins	26/0	100	0.0	26/0	100	0.0	-	-
30mins	26/0	100	0.0	26/0	100	0.0	-	-
45mins	26/0	100	0.8±0.3	26/0	100	0-0	-	-
1 hr	26/0	100	1.1±1.2	26/0	100	0.6±0.9	0.412	NS
2 hrs	23/3	88.5	2.0±1.7	26/0	100	1.0±1.0	0.235	NS
3 hrs	15/11	57.7	3.5±2.0	26/0	100	2.3±1.1	0.0003	S
4 hrs	7/19	26.9	4.7±1.7	24/2	92.3	2.4±1.1	0.0000	S
5 hrs	3/23	11.5	5.6±1.5	22/4	84.6	2.7±1.2	0.0000	S
6 hrs	0/26	-	-	20/6	76.9	3.3±1.6	0.0000	S
8 hrs	0/26	-	-	15/11	58.0	4.0±1.7	-	-
12 hrs	0/26	-	-	1/25	3.9	5.9±1.9	-	-
24 hrs	0/26	-	-	0/26		-	-	-

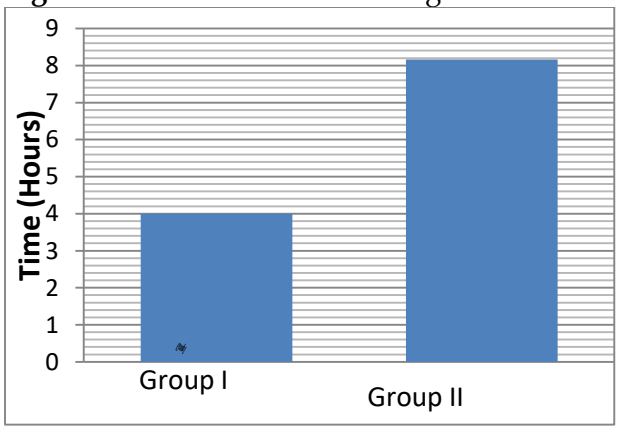
NS- Not significant S - Significant

Table 4. Time to first analgesic requirement and total analgesic consumed (Mean ± SD)

Parameter	Group I N=26	Group II N=26	P value	Level of significance
First analgesic time (hours)	4.00± 1.41	8.16 ± 1.70	0.001	S
Total analgesic (mg)	369.81± 128	243.60± 85	0.001	S

S -significant.

Figure 1. Mean duration of analgesia



Group I – Bupivacaine – Saline
Group II- Bupivacaine – Clonidine

The mean total analgesic consumption was 369.81 ± 12 mg and 243.60 ± 85 mg for groups I and II, respectively (p= 0.001). There are no significant changes in the haemodynamic variables between the two groups and no episode of nausea or vomiting was recorded.

Table 5 shows the mean vital signs at baseline and at the end of surgery. There were no significant changes.

Table 6 shows that mean time to first spontaneous voiding and ambulation was similar in the two groups.

Table 5. Baseline vital signs (Mean ± SD)

Parameter	**Group I N = 26**	**Group II N = 26**	***P* value**	**Level of significance**
Baseline HR/min	120.31±14.84	122.39±14.33	0.452	NS
EOS HR/min	106.50±11.70	104.52±10.58	0.443	NS
Baseline RR /min	26.62± 3.43	25.31± 2.52	0.742	NS
EOS RR /min	20.41± 2.66	20.00± 1.52	0.708	NS
Beeline MAP	59.27± 7.10	61.08± 6.50	0.310	NS
EOS MAP	61.10±6.80	58.52±6.40	0.254	NS

NS - Not Significant EOS- End of Surgery

Table 6. Time to First Ambulation and Voiding (Mean ±SD)

Parameter	Group I N = 26	Group II N = 26	*P* Value	Level of significance
Ambulation (hours)	2.38±0.9	2.54±1.2	0.605	NS
First Void (hours)	1.88±0.4	1.96±1.2	0.597	NS

NS - Not Significant

Twenty-four (96%) and 25 (96.2%) parents or guardians of children in groups I and II respectively expressed satisfaction with the quality of analgesia, but 2 (4%) and 1(3.8) parents or guardians of children in groups I and II respectively were neither satisfied nor dissatisfied.

DISCUSSION

Caudal block has a great advantage especially in children for prolonging the duration of post-operative analgesia and reducing the frequency of parenteral opioids and other analgesic administration.

We observed that patients who received 1.5 µg/kg of clonidine combined with reduced volume of 0.75ml/kg of 0.25% bupivacaine maintained OPS score ≤ 4 for a longer period compared with those who received 0.75ml/kg of bupivacaine and saline with a statistical significant difference (p = 0.001)

This finding were similar to those of Lee and colleague and Parameswari *et al.* that reported that 82.6% maintained OPS score of < 4 for 8 hours and 66% maintained < 4 (FLACCS; Face, Legs, Activity, Cry, Consolability Scale) for 6 hours respectively among patients who received the combination of bupivacaine and clonidine.[14,15]

Adequate analgesia in the postoperative period has been known to maintain normal cardio respiratory parameters, facilitate better wound healing and early mobilization. The mean duration of post-operative analgesia defined by the time to first analgesia requirement in this study was significantly prolonged in the group II (8.16± 1.70 hours) compared with group I (4.00± 1.41 hours), p= 0.001

Upadhay and co-workers also agreed with the result in this study when they evaluated the efficacy of clonidine as an adjuvant to bupivacaine for caudal analgesia in children using 0.75 ml/kg of plain bupivacaine (0.25%) with 1 µg/kg of clonidine.[28] The quality of analgesia was better in the clonidine group

with the mean duration of postoperative analgesia of 10.33± 0.84hours and 5.59± 0.64hours for the clonidine and bupivacaine alone groups, respectively (p<0.05).

Sharpe *et al.* on the other hand revealed that a small volume of local anaesthetic could affect the quality of analgesia provided by clonidine.[29] They used a low volume of 0.5 ml/kg of plain bupivacaine (0.25%) added to 1 µg/kg of clonidine and observed that the duration of analgesia was not significantly prolonged because the volume of bupivacaine used was inadequate to deliver clonidine up to the site of action hence justifying the choice of 0.75 ml/kg of bupivacaine used in this present study.

The total analgesic consumed in twenty four hours observed in this study was significantly less in the bupivacaine–clonidine group (II) - 243.60±85mg compared with bupivacaine-saline group (I) - 369.81±128mg (p = 0.001) This findings were similar to those of Lee and Rubin who demonstrated that the total analgesic requirement in 24 hours were significantly less in the clonidine group receiving 16 and 29 administrations of morphine and paracetamol respectively compared to 26 and 40 administrations of morphine and paracetamol respectively in the group that received bupivacaine only(p= 0.001).[14]

There was no statistically significant decrease in the haemodynamic parameters in the bupivacaine–clonidine group (II) compared with bupivacaine–saline group (I) and none of the patient required therapeutic intervention due to decrease in heart rate and blood pressure. This implies that 1.5 µg/kg of caudal clonidine used in this present study did not produce excessive haemodynamic changes from baseline. Meghani and co-workers in their study also confirmed that lower dose of caudal clonidine did not significantly decrease the heart rate and blood pressure perioperatively.[27] This study did not observe any statistical difference in the mean time to first ambulation and voiding in the group that received clonidine (II) compared with the bupivacaine with saline (I).

Postoperative nausea and vomiting are common symptoms that can make anaesthetic technique unpopular and even delay the discharge of patient despite with effective analgesic profile. This study did not observe any incidence of vomiting in any of the groups.

The evaluation of parents or guardians level of satisfaction with the quality of analgesia achieved revealed that majority of parents or guardians of children in both groups expressed satisfaction with the quality of analgesia,96% (24) for group I and 96.2% (25) for group II. This result was because parents were happy with the anaesthetic technique that made their children awake quickly with an additional benefit of absence of pain and vomiting.

This advantage favours the introduction of caudal block using clonidine as a routine technique for day case anaesthesia and is in agreement with the study done by Adudu and Adudu who evaluated mother's attitude to caudal block for analgesia compared with the use of intramuscular pentazocine.[30] They found that majority of the mothers (83.3%) expressed satisfaction and acceptance for the quality of analgesia achieved with caudal block when successfully placed compared to 55.5% who were satisfied with injection pentazocine.

Children were followed up through the paediatric outpatient clinic two weeks after discharge from the hospital. There was no report of any untoward events while the clinical examination including the inspection of the back did not show any abnormality.

CONCLUSION

This study showed that 1.5 µg/ kg of clonidine combined with 0.75 ml/kg bupivacaine (0.25%) compared with 0.75 ml/kg of bupivacaine (0.25%) alone, provided superior quality of analgesia without increasing the incidence of side effects.

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