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The Effect of Adding Midazolam in Caudal Block for Prolongation of Post-Operative Analgesia in Children Underwent Hypospadias Repair, in Soba University Hospital; "Parallel Randomized Trial"

Abstract

Introduction: Single shot plain bupivacaine is the most popular local anesthetic being used worldwide for caudal anesthesia. There are many agents used as adjunct such as ketamine, clonidine, morphine, adrenaline and midazolam.

Objective: This study aimed to assess the effect of adding midazolam to bupivacaine caudally for prolongation of post-operative analgesia.

Methods: A double blind controlled trial was conducted in Soba University Hospital from October 2014 to May 2015 among children who underwent surgical repair of hypospadias. 50 children were assigned randomly in two groups the study group (A) n=25 received midazolam 50µg/kg plus bupivacaine 0.5 ml/kg of 0.25%, while the control group (B) n=25 received bupivacaine alone 0.5 ml/kg of 0.25%. The study used FLACC pain scale. The vital signs and pain score were recorded hourly for the first three hours and then every 3 hours for the rest of 24 hours.

Results: Two groups were comparable concerning the age, weight, and ASA classification. All patients in the two groups did not feel pain post-operatively throughout the first four hours. Two patients (8%) in group B started to feel pain after four hours, while one patient (4%) in group A felt pain after five hours post-operatively. 11 patients (44%) in group A felt pain while 14 patients (56%) did not feel pain during the first 24 hours post-operatively, however 8 patients (32%) in group B felt pain, while 17 patients (68%) did not feel pain throughout the first 24 hours. Among those who experienced pain in the two groups the majority of group A felt pain after 10 hours (n= 3 &12%), while most of group B felt pain after 6 hours (n=4 & 16%). In both groups rescue analgesia was given according to the severity of pain, as for mild pain the patients were received oral paracetamol/Ibuprofen and those with moderate pain received diclofenac injections. Among those who felt pain in the two groups the mean duration of post operative analgesia was significantly longer in group A than in group B (10.72± 4.07 & 6.31± 1.98) hours respectively) with P-value (0.007). There were no side effects recorded in the study group. However two patients developed nausea and vomiting in the study group.

Conclusion: Addition of midazolam 50 µg/kg to caudal bupivacaine 0.5ml/kg of 0.25% significantly resulted in prolongation of post operative analgesia duration.

Keywords: Caudal block; Midazolam; Hypospadias

Research Article

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Elwaleed Ibrahim S[1]*, Zeinab Musa M[2] and Aziza Mustafa[3]

[1]*Department of Anesthesia, Alneelain University, Sudan*
[2]*Department of Anesthesia, University of Khartoum, Sudan*
[3]*Department of Surgery, Alahfad University, Sudan*

***Corresponding author:** Elwaleed Seddig Ibrahim, Department of anesthesia, Faculty of medicine, Alneelain University, alshuda and soba locality, gabra / alshariga, block 13/129, Khartoum state, Khartoum, Sudan, Tel: +249122983223; Email: abumohamed97@yahoo.com

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Introduction

Caudal anesthesia (CA) is one of the most commonly used regional techniques in pediatric patients. It may also be used in ano-rectal surgery in adults. Caudal anesthesia involves needle and/or catheter penetration of the sacro-coccygeal ligament covering the sacral hiatus that is created by the unfused S4 and S5 laminae. It is commonly used for orthopedic and surgical procedures below the umbilicus, including urogenital, rectal, inguinal, and lower extremity surgery. Pediatric caudal blocks are most commonly performed after the induction of general anesthesia [1].

Single shot of plain bupivacaine is the most popular local anesthetic being used worldwide for caudal anesthesia, in order to extend the duration of analgesia there are many agents which were used as adjunct such as ketamine, clonidine, diamorphine, morphine, fentanyl, pethidine neostigmine, sodium bicarbonate, adrenaline and midazolam [2].

Magnitude of the problem

There is extensive use of opioids such as meperidine to relieve post-operative pain in children underwent surgery. On the other hand the patients usually transfer to the ward immediately after recovery where there is no monitors and few nurses that they could not catch all post-operative patients, so it is a big challenge is this country.

Justification

To reduce the utilization of opioids in the post-operative period among children underwent surgery. Also by doing such procedure, the study will improve the skills among anesthesia providers and make them familiar with caudal anesthesia.The aims of this study is to prolong the post-operative analgesia among children undergoing surgical repair of hypospadias in Soba University Hospital by adding midazolam 50 µg/kg plus bupivacaine 0.5 ml/kg of 0.25% and at the same time to reduce the utilization of opioids post-operatively.

General objective

To compare the post-operative analgesia of caudal midazolam-bupivacaine with bupivacaine for children undergoing hypospadias repair in Soba University Hospital.

Specific objectives

(i) To estimate the duration of post-operative analgesia after uses of caudal midazolam-bupivacaine.

(ii) To estimate the duration of post-operative analgesia after uses of caudal bupivacaine alone.

(iii) To evaluate the side effects of using caudal midazolam-bupivacaine and bupivacaine alone.

Pain scale

FLACC: The FLACC assessment tool was developed in an attempt to provide a simple consistent method of pain assessment in non verbal or preverbal children. This tool incorporates 5 categories of behavior that have been used in other behavioral scales. The acronym FLACC (Face, Legs, Activity, Cry and Consolability) facilitates recall of the categories, each of which is scored from 0-2 with total scores ranging 0-10 similar to other clinical assessment tools. Inter-rater reliability of the FLACC among 2 observers was established in 30 children in the PACU (r=0.94). Validity was established by demonstrating an appropriate decrease in FLACC scores after analgesic administration. Also, a high degree of agreement was found between FLACC scores, the PACU nurses global rating of pain, and with OPS scores. The reliability and validity of this tool has been established in diverse settings and in different patient populations [3-13] (Table 1).

Table 1: The criteria for the FLACC behavioral pain scale.

Behaviour	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting, back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams, sobs, frequent complaints
Consolability	Content, relaxed	Reassured by touching, hugging or being talked to, distractible	Difficult to console or comfort

0 = Relaxed and comfortable; 1-3 = Mild discomfort; 4-6 = Moderate pain; 7-10 = Severe discomfort/pain

Material and Methods

Double blind randomized controlled trial was conducted in Soba university hospital in the period from October 2014 – March 2015. The target population was all children of age between 1-12 years old who planned to undergo hypospadias repair. The total number of patients waiting for surgical repair was 70 patients; thirteen of them were excluded, while 57 patients met the inclusion criteria and their parents agreed to participate in this study. The 57 patients were assigned randomly via computer software program to be sample size, which done by a third party. 29 patients out of 57 were assigned randomly as treatment group. Neither the participants nor the observers know the participants' treatment assignment. The primary outcome measure was the duration of post-operative analgesia, while the secondary outcome measures were the requirement of rescue analgesia post-operatively and the complications of the intervention.

Inclusion criteria

a. Patients ASA class I and II.

b. Age 1-12 years.

c. Patients planned for hypospadias repair under general anesthesia.

Exclusion criteria

a. Parent refusal.

b. Patient ASA class III or IV.

c. Age below 1 year or more than 12 years.

d. Infection at the site of injection.

e. Patient with coagulopathy.

f. Patient with neurological deficit.

After fulfilling the inclusion criteria, fifty children were assigned randomly into two groups using software program. Group A the study group (n = 25) received caudal midazolam 50µg/kg plus bupivacaine 0.5 ml/kg of 0.25%, while group B the control group (n = 25) received caudal bupivacaine alone 0.5 ml/kg of 0.25%.

$$n = \frac{Nz^2pq}{(N-1)\mathrm{xd}^2+z^2pq}$$

n = sample size

N = the total number of patient per year from the waiting list

p = the prevalence of hypospadias (50%)

q = (1- p)

d = maximum allowable error (5%)

$$n = \frac{57x1.96^2x0.5x0.5}{(56-1)x(0.05)^2+1.96^2x0.5x0.5} = 50$$

Procedure

After admission of the patient to the operating room, an Intravenous line was secured and the monitor was attached. Then Induction of general anesthesia (GA) was performed to all patients either with endotracheal tube or laryngeal mask airway. After induction of GA and secured the airway the patient turned to the left side, the lower part of back was scrubbed and draped. Then the sacral hiatus was identified using the anatomical landmarks. Using a needle 21G – 23G with a 45 degree to the skin could inserted, penetrating the sacro-ccosygeal ligament, then withdraw the needle few millimeters, reduced the angle of the needle to 10-15 degree and advance it more caudad. After that gentle aspiration was done to exclude inadvertent intravascular or intrathecal needle, then a calculated dose and volume according to the patient weight was injected in the caudal space. Then the patient put back into supine position. After emergence all patient admitted to post operative care unit (PACU), where the observation of post operative analgesia started. The heart rate, respiratory rate, blood pressure, pain score (FLACC) were recorded hourly in the first four hours and then every three hours for the rest of the 24 hours. Also the requirement for supplemental analgesia was recorded in the first 24 hours after surgery. The study observed the side effects which have appeared in both groups.

Data collection

The observation form was in English language, which its validity was checked by the supervisor. The data was collected by registrars of anesthesia, they were blind. The registrars were trained about the procedure and technique of data collection. The observation of the study was started for all participants immediately after finishing the operation at the recovery room. In the first four hours the observation was taken hourly, and then every 3 hours for the rest of 24 hours. The filled forms were checked to assure the quality of data.

Data analysis

The data was edited, coded then entered to the software SPSS. Box plot was used to test the normality of data. Descriptive statistics which included frequency, minimum, maximum mean, standard deviation, and percentages were used. Independent t-test was used for association whenever a variable has a P-value < 0.05, it was considered significant.

Ethical consideration

The ethical clearance has been approved by the ethical committee of the SMSB and the hospital, and then informed consent was obtained from the parents of the children. The parents had the right to participate or withdraw from this study. Confidentiality and privacy of the participants were assured. All observation forms were kept in a locked cabinet and they would be destroyed after data entry, analysis.

Results and Discussion (Flow diagram)

Fifty patients were enrolled in this study; they were assigned randomly into two groups. Group A the study group (n = 25) received caudal midazolam 50µg/kg plus bupivacaine 0.5 ml/kg of 0.25%, while group B the control group (n = 25) received caudal bupivacaine alone 0.5 ml/kg of 0.25%.

Demographic characteristics of the patients (Table 2-4) (Figures 1-6)

Discussion

The study used combination of caudal midazolam and bupivacaine in comparison with bupivacaine alone. Group A the study group (n = 25) received caudal midazolam 50µg/kg plus bupivacaine 0.5 ml/kg of 0.25%, while group B the control group (n = 25) received caudal bupivacaine alone 0.5 ml/kg of 0.25%. The result showed significant prolongation of post-operative analgesia among the study group with p-value (0.007). Among those who felt pain in the two groups the mean duration of post operative analgesia was significantly longer in group A than in group B (10.72± 4.07 & 6.31± 1.98 hours respectively) with P-value (0.007). In comparison to others studies this study showed that adding midazolam to bupivacaine prolonged the duration of post-operative analgesia greater than adding morphine, so the side effects of morphine such as delayed respiratory depression, nausea, vomiting, and pruritus can be avoided. There were no significant side effects or complications reported among the treatment group.

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Flow diagram of the progress through the phases of a parallel randomized trial of 2 groups (that is, enrollment, intervention allocation, follow-up, and data analysis).

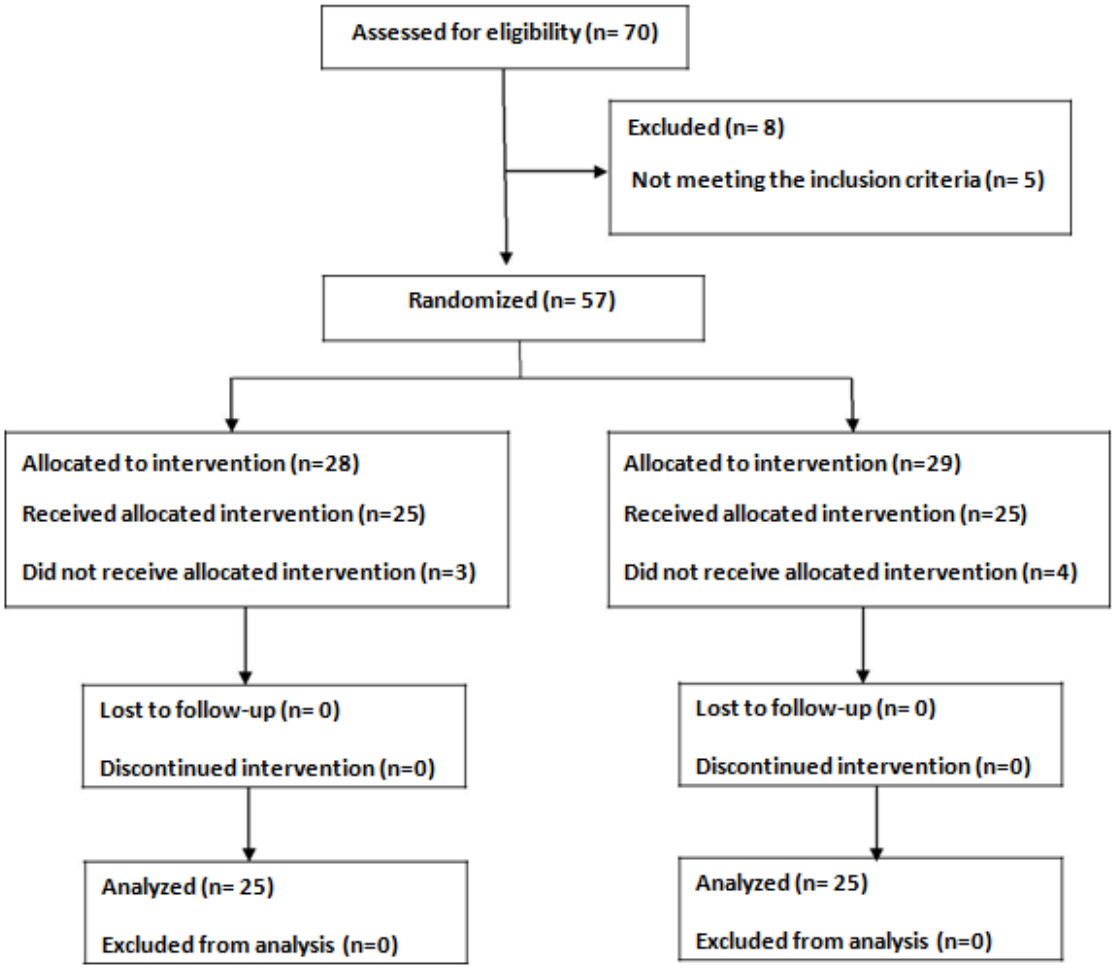

Table 2: Demographic characteristics among the two groups.

	A (n=25)				B (n=25)			
	min	max	mean	SD	min	max	mean	SD
Age	1	12	6.94	3.07	1.5	10	5.4	2.44
weight	10	34	20.11	6.93	9	42	17.92	7.29

Table 3: The severity of pain and rescue analgesia given among the two groups.

Pain			A			B
	N	%	Rescue analgesia	N	%	Rescue analgesia
Mild	8	72.7	Paracetamol/Ibuprofen	7	87.5	Paracetamol/Ibuprofen
Moderate	3	27.3	Diclofenac injection	1	12.5	Diclofenac injection
Total	11	100		8	100	

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Table 4: The side effects among the two groups.

	A		B	
	Yes	NO	Yes	NO
Nausea and vomiting	0	25 (100%)	2 (8%)	23 (92%)
Pruritus	0	25(100%)	0	25 (100%)
Respiratory depression	0	25(100%)	0	25 (100%)
Others	0	25(100%)	1 (4%)	24 (96%)

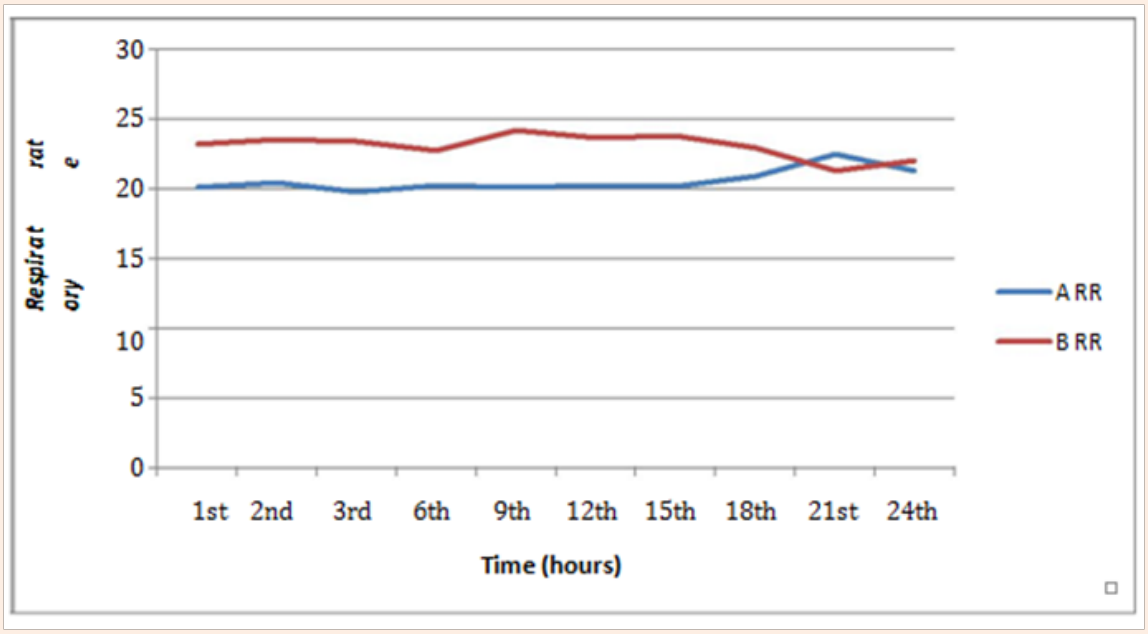

Figure 1: Post-operative respiratory rate among the two groups.

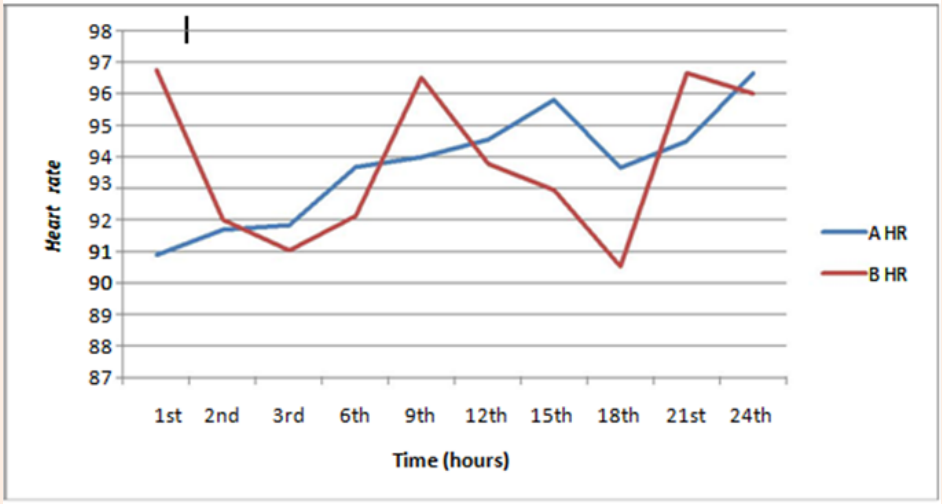

Figure 2: Post-operative heart rate among the two groups (mean).

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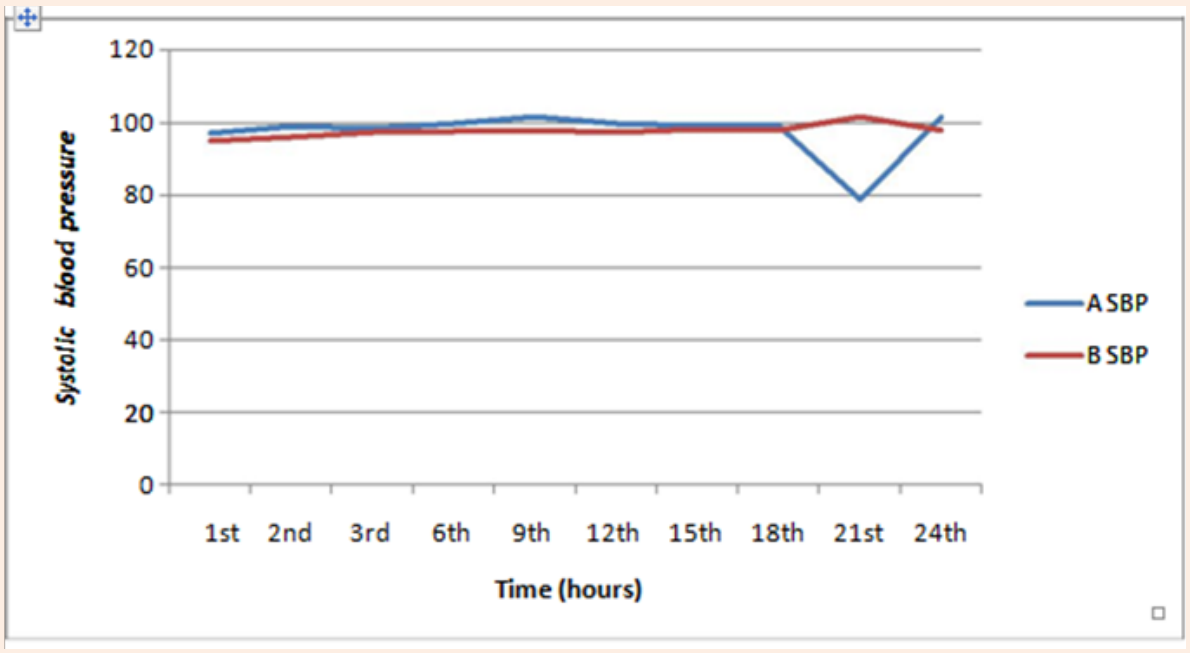

Figure 3: Post-operative systolic blood pressure among the two groups.

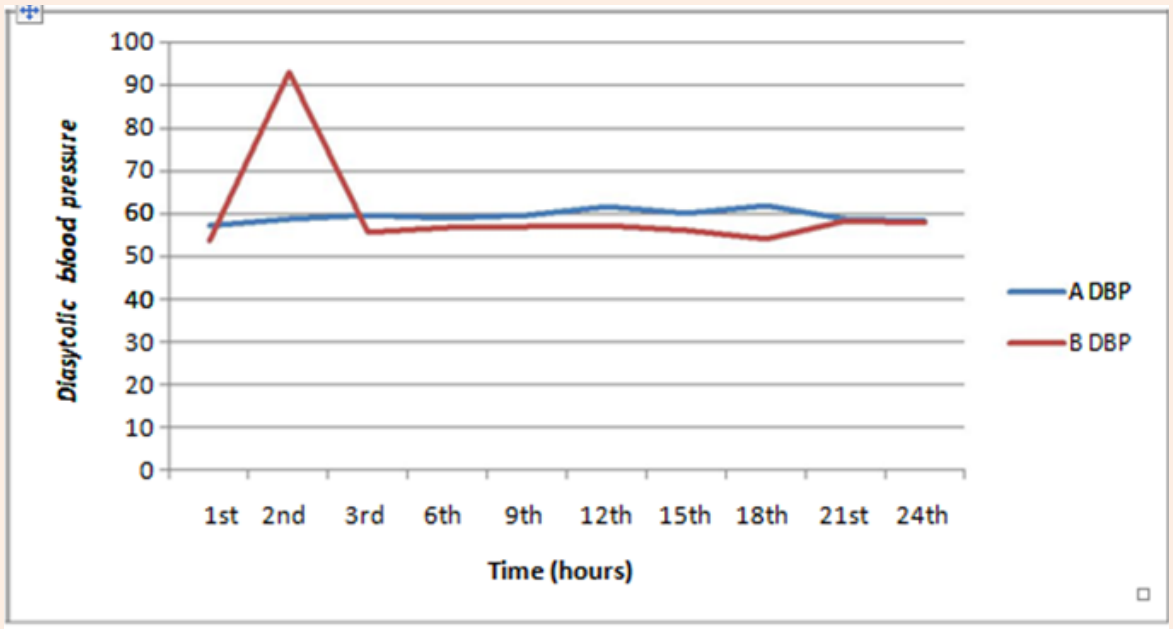

Figure 4: Post-operative diastolic blood pressure among the two groups.

The respiratory rate was significantly lower among those who receive midazolam during the first fifteen hours; this is may be due to the sedative effect of midazolam, the study suggested include sedation score in the observation form in further studies since it was not included here.

Limitations and strengths

Availability of the bupivacaine in governmental hospital was a challenge and shortage of the observers (registrars of anesthesia) was another limitation. On the other hand feasibility of the midazolam and applicability of the procedure were the strengths of the study.

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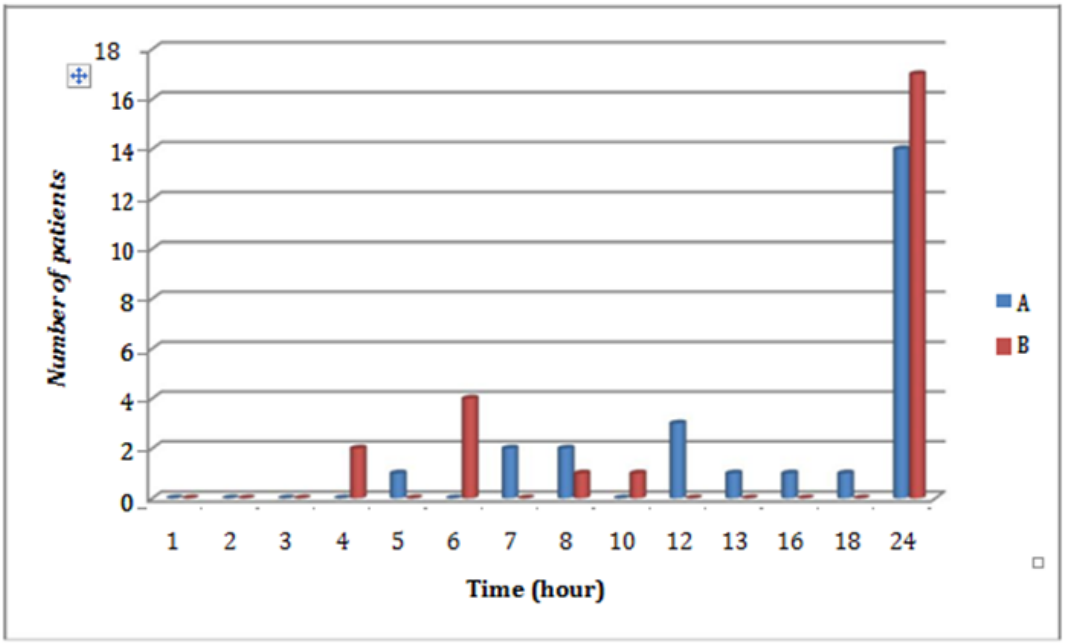

Figure 5: The onset of pain post-operatively among the two groups.

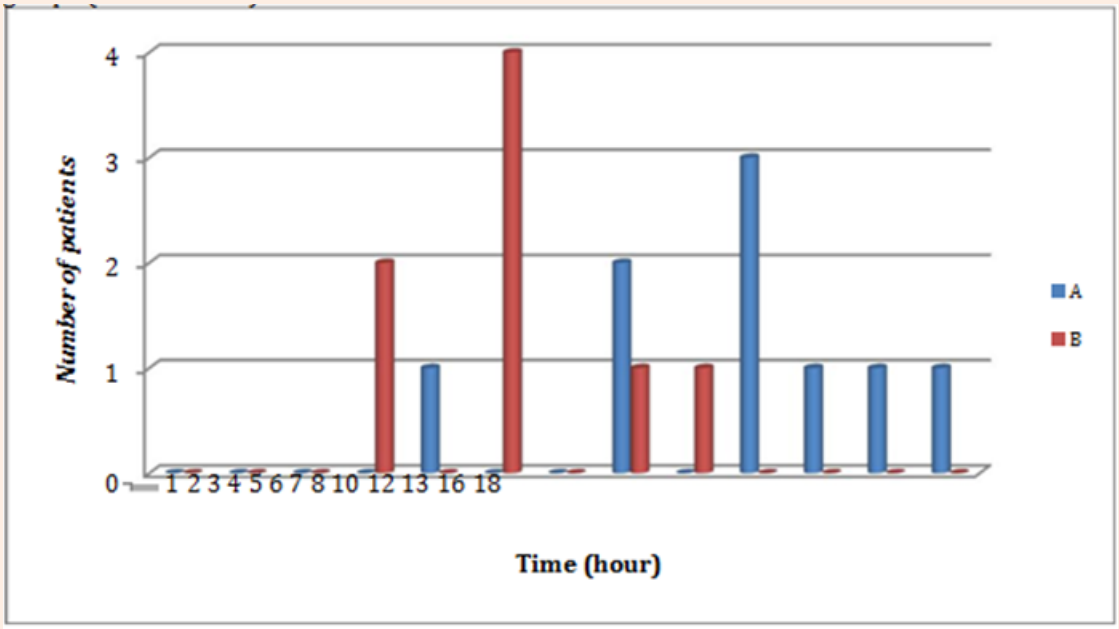

Figure 6: The duration of post-operative analgesia in those who experience pain among the two groups (P-value 0.007).

Conclusion

In conclusion this study demonstrated that the addition of midazolam 50 µg/kg to caudal bupivacaine 0.5ml/kg of 0.25% significantly resulted in prolongation of post- operative analgesia duration from 6.31± 1.98 hours to 10.72± 4.07 hours.

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