Comparision of Caudal Bupivacaine with Additives Fantanyl or Ketamine for Post-Operative Pain Relief in Children: A Randomized Controlled, Double Blinded Study

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ABSTRACT

Background and Aims:*Ensuring adequate analgesia in the post-operative period is an indispensable part of a balanced anesthesia technique with increasing scope of day care surgery and emphasis on early discharge. In children undergoing infra-umbilical and lower limb surgeries, caudal block is a reliable and safe technique that can be used with general anesthesia for intra and post-operative analgesia. The present study was designed to compare the analgesic efficacy of ketamine and fentanyl as additives to bupivacaine given caudally in children undergoing lower abdominal and lower limb surgery.*

Materials and Methods:*A total of 60 children aged 1-5 years undergoing lower abdominal and lower limb surgery were included in this randomized, controlled, double-blind study. Three groups of 20 each were assigned to receive caudal block with bupivacaine 0.25% 0.5 ml/kg alone (group A) or along with 1 ml/kg fentanyl (group B) or 0.5 mg/kg ketamine (group C). Assessment of post-operative pain was done using the Objective Pain Scale. Requirement of rescue analgesia and side effects were also noted.*

Results:*Children who received ketamine with bupivacaine caudally (group C) had the longest duration of post-operative analgesia [Group A vs. Group C: 150 min (p=0.32) vs. 180 min (p=0.00)] and requirement of first dose of analgesia in groups A, B and C ranged from 183±16.5 min, 350±2.5 min and 594±148.12 min respectively. The mean number of doses of rescue analgesia that patients received in 24 hours in group A, B and C were 6.0, 1.63 and 1.40 respectively.*

Conclusion:*Caudally administered Ketamine in the dose of 0.5 mg/kg with bupivacaine provides prolonged post-operative analgesia in comparison to fenatnyl 1 µg/kg with bupivacaine with minimal side effects.*

Keywords: *Ketamine, fentanyl, bupivacaine, children*

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INTRODUCTION

Ensuring adequate analgesia in the post-operative period is an indispensable part of a balancedanesthesia technique with increasing scope of day care surgery and emphasis on early discharge.Patients can experience pain after discharge when suitable medical help is unavailable. Inchildren undergoing infra-umbilical and lower limb surgeries, caudal block is a reliable and safetechnique that can be used with general anesthesia for intra and post-operative analgesia[(2)]. It isthe one of most commonly used regional technique for post-operative analgesia in children[(3)]. Post-operative pain relief is commonly provided by parenteral or oral drugs including opioids andnon-steroidal anti-inflammatory drugs (NSAIDs). Inability toensure adequate pain relief dueto variability and individual sensitivity is a considerable drawback ofthis approach. Some of thesedrugs such as oral NSAIDs have been reported to have side effects like gastrointestinalhemorrhage and renal papillary necrosis.[(4)] Therapeutic doses of opioids are not administered dueto concerns of respiratory depression, nausea, vomiting, and distressing pruritus.[(5)] Manyanesthetic agents have been used for caudal analgesia in pediatric patients. Bupivacaine and Levobupivacaine have proven clinical effectiveness and safety.[(6-8)] A number of adjuvants such asfentanyl, clonidine, Ketamine and, midazolam have been added to local anesthetic solutions to prolongcaudal analgesia as a single bolus[(9-14)]A combination of ketamine and bupivacaine increasesthe potency and duration of analgesia[(15-16)]. Caudal fentanyl in a dose of 1 mcg lkg in addition to bupivacaine has been associated with decreased heart rate due to the systemic effect of fentanyl[(17)].The present study aims to compare the hemodynamic and analgesic effects of caudal bupivacaine along with fentanyl and ketamine as adjuvants in children aged 1 to *5* yearsundergoing lower limb or genitourinary surgery.

MATERIALS AND METHODS

This prospective double-blinded study was conducted in the department of anesthesiology and

critical care of Geetanjali Medical College, Udaipur, Rajasthan which is a tertiary care hospital.After approval of the research protocol by the institutional ethics committee and informed consentfrom the legal guardians of 60 ASA status I children between *1-5* years of age undergoing lower limbor genitourinary surgery were randomly divided into three groups of 20 each:

Group A received *0.25%* bupivacaine as *0.5* ml/kg. Group B received *0.25%* bupivacaine as *0.5*Ml/kg with fentanyl 1 mcg/kg. Group C received *0.25%* bupivacaine as *0.5* ml/kg with ketamine *0.5* mg/kg. Normal saline was added to make equal volumes of the mixtures.

The following children were excluded from the study:

a. Bleeding/coagulation disorder
b. Hepato-renal disease
c. Cardiovascular disease
d. Local deformity/infection in sacral region
e. Neurosurgical spinal disorder
f. Known allergy to local anesthetics
g. Body weight *>25* kg

All the children were examined a day prior to surgery. Pre-operatively hemoglobinestimation and urine examination for albumin and sugar were performed. All children werescheduled to receive general anesthesia combined with caudal block. In the pre-operativehold area, peripheral intravenous access was secured and all children were administered inj.ketamine 2mg/kg and inj. glycopyrollate 0.02 mg/kg. To facilitate endotracheal intubationinj. Succinyicholine*1.5* mg/kg was used. For maintenance of anesthesia, mixture of oxygen, nitrous oxide, sevoflurane and intermittent doses of inj. atracurium were used. Intraoperatively, the children received *5%* dextrose in 0.33% normal saline at 4 ml/kg/hour.

Caudal anesthesia was administered in the lateral position with a 22G hypodermic needle andone of the three study drugs solution were administered as for random allocation of the groups while the other authors whogave caudal block were blinded to the study groups.Twoauthors were involved in preparing the above mentioned mixtures. Heart rate, systolic bloodpressure (SBP), sp02, awareness (sweating, tears) was recorded intraoperatively. Theparameters recorded post-operatively were pulse rate, blood pressure, sp02. The ObjectivePain Scale developed by Hannallah and colleagues[18] was used for the assessment of pain.

At the end of surgery, neuromuscular blockade was reversed using inj. neostigmine 0.05mg/kg and inj. atropine 0.02 mg/kg followed by extubation. The children were monitored forvomiting, pruritus and respiratory depression and discharged from the recovery room whenan Aldrete score of 10 was achieved[18]. The time of first requirement of rescue analgesicwas recorded. Pain scores were assessed at 15 minutes, 1 hour, 4 hours and 8 hours 12 hours. Aftersurgery. When the patient had a pain score of >6, oral acetaminophen 15-20 mg/kg wasadministered. Vomiting and time of the first micturition were noted along with the totalnumber of acetaminophen doses of rescue analgesia in 24 hours.

STATISTICAL ANALYSES

The data was analysed applying the student'st-test Chi square test and Analysis of variance (ANOVA) where applicable data was expressed as mean + standarddeviration and $P<0.05$ was considered to be significant.

RESULTS

The patients in all three groups were comparable with respect to age and body weight (Table1). The surgical procedures that the children underwent were repair of hypospadias, inguinal Herniotomy, orchidopexy, circumcision and correction of congenital dislocation of the hip. Oncomparison, there was no statistical difference between the groups with respect to the typeand duration of surgery and the volume of the study drugs.

Intraoperative Hemodynamic Parameters: There was no significant change in heart rate immediately after surgical incision and Intraoperatively in group A and group C. Group B had a significant decrease in heart rateAfter incision that persisted till 10, 15 and 20 minutes (p value 0. 12', 0.001 and 0.00Respectively). After 20 minutes, there was no significant difference in heart rate in all threeGroups. No significant change was observed in any of the groups with respect to systolic anddiastolic blood pressure, and oxygen saturation. All three groups were comparable in pain scores in the first 3 hours after surgery (Table 2).Group A had significantly higher pain scores as compared to group B at 150 and180 minutes.Patients in group B had significantly higher pain score in comparison to Group C at 310 and360 minutes. The mean pain score in group C remained low up to 24 hours.

Rescue ana1gesia: The duration of post-operative analgesia was significantly higher in group C in comparisonto group A and group C. The mean number of doses of rescue analgesia that patients receivedin 24 hours in group A, B and C were 6.0, 1.63 and 1.40 respectively.

Side effects: One patient in group B had an episode of vomiting in the recovery room 20 minutes aftersurgery which was treated with intravenous metoclopramide. Two patients in group C had'vacant stares' up to one hour which was not apparently distressing to the parents and resolvedSpontaneously in about 2 hours.

Table 1: Demographic Table

	Age in year (Mean+SD)	Weight in kg (Mean+SD)
Group A	3.25+1.20	13.35+ 2.05
Group B	2.97+1.40	12.95+3.98
Group C	3.45+1.27	14.28+3.43
F Value	0.692	0.869
P Value	0.505	0.425

Table 2: Post Operative Objective Pain Score(Hanallah)

Time		15min.	1 hrs.	4hrs.	8hrs	12hrs	24hr.
Group A	**Mean**	1.15	1.05	5.50	6.00	7.00	7.00
	SD	.933	.826	1.150	.000	.000	.00
	Median	1.00	1.00	6.00	6.00	6.5	6.5
Group B	**Mean**	.90	1.30	2.25	2.25	6.00	6.00
	SD	.308	.470	.639	.605	.00	.00
	Median	1.00	1.00	2.00	2.00	6.00	6.00
Group C	**Mean**	1.30	1.35	2.10	2.10	2.55	4.62
	SD	.470	.489	.852	.632	.51	1.68
	Median	1.00	1.00	2.00	2.00	3.00	6.00

P Value: Group A vs. B: 0.00 (150 minute), 0.001 (180 minute)
Group A vs. C: 0.32 (150 minute), 0.00 (180 minute)
Group B vs. C: 0.00 (310 minute), 0.00 (360 minute)

Table 3: Objective Pain Scale (OPS) of Hanallah et al for Post-Operative pain Assesment

Parameter	Finding	Points
Systolic blood pressure	Increase<20% of preoperative blood pressure	0
	Increase<20-30% of preoperative blood pressure	1
	Increase>30% of preoperative blood pressure	2
Crying	Not crying	0
	Respond to age appropriate nurturing (tender loving care)	1
	Does not respond to nurturing	2
Movements	No movements relaxed	0
	Restless moving about in bed constantly	1
	Thrashing (moving wildly)	2
	Rigid (stiff)	2
Agitation	Asleep or clam	0
	Can be comforted to lessen the agitation (mild)	1
	Can not be comforted (hysterical)	2
Complains of pain	Asleep	0
	States no pain	0
	Can not localize	1
	Localizes pain	2

Table4: Oral analgesia

	Time of First analgesia (hrs.)	No. of doses in 24 hrs.
Group A	183+16.5	6.00+ 00
Group B	350+20.5	1.63+.597
Group C	594+148.12	1.40+.502

Table5: Modified Alderte Recovery Scoring System

Parameter	Finding	Points
Activity: able to move, voluntarily or command	Four extremities	2
	Two extremities	1
	No extremities	0
Respiration	Able to breathe deeply and cough freely	2
	Dyspnoea, shallow or limited breathing	1
	Apnoea	0
Circulation	Blood Pressure within 20 mm Hg of preoperative level	2
	Blood Pressure within 20-50 mm Hg of preoperative level	1
	Blood Pressure + 50 mm Hg of preoperative level	**0**
Consciousness	Fully awake	**2**
	Arousable on calling	**1**
	Unresponsive	**0**
Oxygen Saturation	Saturation >92%	**2**
	Needs oxygen to maintain saturation >90%	**1**
	Saturation <90% with oxygen	**0**

Nine or more points are required for recovery to be confirmed

DISCUSSION

Lower abdominal and lower limb surgeries in children are associated with considerable postoperative Pain. In this study, the authors evaluated the efficacy of fentanyl and ketamine asadjuvants to bupivacaine in caudal analgesia in comparison to that of bupivacaine alone inChildren undergoing genitourinary and lower limb surgeries.Many previous researchers[19-21] have observed that caudal block with local anesthetics alone Provides adequate intra-operative analgesia in only *57-84%* of children, whereas 93-100% ofChildren had adequate analgesia when caudal block with fentanyl 1 mcg/kg was used. Theefficacy of caudal block for intra-operative analgesia can be affected by a number of factors.Such as the volume and concentration of local anesthetic used, the surgical procedure, criteriaused to define adequate analgesia and the depth of general anesthesia[22]. Locatelli et al[7] and Breschan et al[8] concluded from their study that bupivacaine and levobupivacaine are equally Potent and had longer analgesic effect. Hence, 0.25% bupivacaine was chosen for the presentstudy. In contrast to the definition of adequate analgesia adopted in the present study, Constant et a1[19] and Martindale and co-workers[23]used an increase by 15% in thehemodynamic parameters as criteria for adequate caudal block. Constant and colleagues[19] Maintained anesthesia with 0.6 MAC of isoflurane, whereas in the present study anesthesiawas maintained using 1% sevoflurane and 67% nitrous oxide at the time of surgicalincision. The deeper plane of anesthesia in our study may have offered stable hemodynamicParameters.

No statistical differences were observed in all the groups with regard to intra-operative. Hemodynamic changes except for a significant decrease on heart rate in group B whichReceived fentanyl. The decrease in heart rate was not associated with hypotension and did notrequire any intervention. (Which may be attributed to the systemic effects of fentanyl).

In the present study, the mean duration of post-operative analgesia from the time of extubation to the first administration of rescue analgesic in group A was 183±16.57 minutes.This was in contrast to a study which observed *5* hours of post-operative analgesia using 1ml/kg of bupivacaine for caudal block.[24] The mean duration of post-operative analgesia ingroup B (350±20.5 minutes) was consistent with previous studies.[24-25] By reducing the doseof Ketamine from 1 mg/kg to *0.5* mg/kg the incidence of side effect were reduced[24] by *5%* but theduration of analgesia obtained in group C was significantly longer than that in groups A and B. Our findings are consistent with those of Cook and colleagues[24] who demonstrated that The addition of Ketamine 0.5 mg/kg to bupivacaine 0.25%, 1 ml/kg provided longer durationof analgesia than bupivacaine alone and behavioral side effects attributable to ketamine werenot observed. We chose to monitor patients for a period of 24 hours post-operatively. This isin contrast to a few other studies[26,27] where there was only a six-hour period of observation. Post-operatively and the rest of the assessment was done by parents which could introducesome inconsistencies, as parents differ in the way they perceive their children to be in painand the threshold for administering rescue medications varies between parents.[28]

CONCLUSION

Addition of fentanyl 1 mcg/kg or ketamine *0.5* mg/kg to caudal bupivacaine prolongs postoperativeanalgesia in children undergoing genitourinary and lower limb surgery. Caudalfentanyl with bupivacaine does not increase the incidence of post-operative respiratorydepression. Post-operative pain relief is prolonged significantly with ketamine as compared to fentanyl.

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