ORIGINAL ARTICLE

Caudal block using Ketamine with Bupivacaine and Bupivacaine alone for post-operative analgesia in Paediatric inguino-scrotal surgeries

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Abstract

Background: Caudal block is a common technique for pediatric analgesia, but with the disadvantage of short duration of action of bupivacaine after single injection. Caudal ketamine could offer significant analgesic benefits. We compared the analgesic effects and side effects of ketamine added to bupivacaine in pediatric patients under-going inguino-scrotal surgeries.

Materials and Methods: 80-patients (3 to 10 years) were randomly assigned into 2-groups by lottery method. After sevoflurane in oxygen general anaesthesia induction, each patient received either a single caudal dose of bupivacaine 0.25% (1 mL/kg) with normal saline or bupivacaine 0.25% with ketamine 0.5 mg/kg. Haemodynamic variables, MOPS score, analgesia duration, use of analgesics and side effects were assessed during the first 12 h.

Results: Addition of ketamine to caudal bupivacaine significantly prolonged the duration of analgesia than the use of bupivacaine alone. There was statistically significant difference between bupivacaine alone and in combination with ketamine with regards to the analgesia time ($p < 0.05$). No significant difference was observed in incidence of side-effects.

Conclusion: Addition of ketamine to caudal bupivacaine significantly prolonged analgesia in children undergoinginguinoscrotalsurgeries.

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Introduction:

Pain is difficult to assess in pediatric population that is the reason post-operative pain is usually undertreated in this age group. Due to the strong emotional component of pain in children pain relief is necessary.[1] Caudal block is one of the most commonly used regional anaesthetic technique for providing intra and post-operative analgesia in children for surgeries below the level of umbilicus.[2] It reduces general anaesthetic requirement, attenuates the stress response to surgery, facilitates smooth rapid recovery and effective pain relief with less cost for care.[3] Local anaesthetic agent bupivacaine due to its long duration is mostly used for providing analgesia through the caudal route but has the disadvantage of limited duration with single shot caudal injection.[4] Caudal analgesia duration can be prolonged using a caudal catheter so the drug doses can be repeated or by the addition of various agents such as opioids, clonidine, dexmedetomidine, epinephrine and ketamine.[5] The use of caudal, catheter carries the risk of infection so this method failed to gain popularity.[6,7] Among the adjuvants opioids like morphine, pethidine provided prolonged pain relief but at the cost of side effects like pruritus, nausea, vomiting and respiratory depression.[8]

Studies have shown that supplementation of bupivacaine with ketamine prolonged analgesia duration thus avoiding the side effects of opioids.[9] Ketamine a phencylidine derivative primarily blocks N- methyl- D -aspartate receptors leading to a decrease in activation of dorsal horn neurons. These receptors are wide spread in the central nervous system and substantia-gelatinosa of spinal cord playing an important

role in central processing of pain. Moreover antinociceptive actions of ketamine also involves blockage of nor epinephrine and serotinine receptors.[10] Therefore we investigated the addition of ketamine to bupivacaine on the duration of post-operative analgesia.

Materials and Methods:

Objective: Study was conducted to compare the mean pain score with bupivacaine versus ketamine plus bupivacaine in children undergoing inguino scrotal surgeries.

Study design: This is single blinded, randomized control trial

Study duration: this study was carried over period of 1-year i.e. January 2018 to January 2019

Study setting: Department of Anesthesia, Khyber Teaching Hospital, Peshawer.

Sample size: 80-patients were enrolled

Sampling technique:Non probability consecutive sampling technique was used.

Inclusion criteria: Patients aged 3 to 10 years. Patients of both gender. Patients undergoing inguino-scrotal surgeries i.e. inguinal hernia, femoral hernia and hypospadias, urethroplasty. Children with American Society of Anesthesiologists (ASA) class-I and ASA-II, were included in the present study.

Exclusion criteria: The children having allergy or sensitivity to bupivacaine and ketamine. Patients having any contraindication to caudal injection, i.e., infection at the site, bleeding disorder, and caudal vertebral anomalies, etc., were excluded from the study.

Ethical approval was taken from hospital ethical committee. Written informed consent was taken from parents/guardians of all children. Demographic data including name, gender, preoperative assessment and ASA class was noted. All children were kept nil per oral for 4-6 hours and no pre-medication was used. Patients were randomized to two groups by lottery method. Patients were divided in group-A and group-B. Patients were induced with inhalational anesthetic agent sevoflurane in oxygen and 22 gauge intravenous cannula passed on the dorsum of hand. An appropriate sized endotracheal tube was passed after using injection atracurium 0.5mg/kg body weight. Infusion Ringer's lactate was given. No intra-operative opioids or benzodiazepines were used. Monitoring was done with SPO2 with pulse oximeter, blood pressure and respiratory rate intra-operatively at 5-minutes interval and post-operatively ½-hourly for first 6-hours and then 2-hourly thereafter. After induction of general anaesthesia the patient was placed in left lateral recumbent position, caudal space identified, cleaned with antiseptic solution and drapped. A 25-guage spinal needle was inserted through skin, subcutaneous tissue and ligaments into epidural space. After negative aspiration for blood and CSF, drugs were injected into the caudal epidural space. Children in group-A receivedcaudal bupivacaine 0.25% in a dose of 1ml/kg and ketamine preservative free 0.5mg/kg. Children in group-B received caudal bupivacaine 0.25% in a dose of 1ml/kg. After completion of the block children were turned to supine position and surgical incision made. Effectiveness of the block was assessed by haemodynamic stability and decreased need for inhalational anaesthetics. Block was considered adequate when there was no increase in heart rate, blood pressure and respiratory rate by 15% of the baseline intra-operatively. At the end of surgery the kids were recovered giving injection neostigmine 0.05mg/kg and atropine 0.02mg/kg and extubated. Patients were shifted to recovery room and followed up for pain till 12 hours. Pain was assessed by Modified Objective Pain score (MOPS). MOPS is an observational pain scoring system which has been validated for use by parents. Score describes five points: crying, agitation, movement, posture, localization of pain. Each observation scores from 0-2 to get a total of 0-10. Duration of analgesia was defined as the time between caudal injection of the drug and first administration of post-operative analgesia. End of adequate analgesia means that pain score was 4 or > 4. Analgesia was given to

Table 1: *Changes in Intraoperative Variables from Baseline*

Group	Group-A (n=40)	Group-B (n=40)	P- Value
Mean Heart Rate/ min (Baseline)	94.29 ± 8.00	90.17 ± 7.71	0.145
Mean Heart Rate/min (Intra-operative)	89.70 ± 8.56	84.47 ± 6.29	0.234
Mean Arterial Pressure (Baseline) (mm Hg)	70.70 ± 4.70	68.47 ± 4.07	0.111
Mean Arterial pressure (Intra-operative) (mm Hg)	69.11 ± 6.30	66.11 ± 3.95	0.134
Mean Respiratory Rate/min (Baseline)	14.82 ± 1.33	15.23 ± 1.85	0.136
Mean Respiratory Rate/min (Intra-operative)	14.64 ± 1.16	14.17 ± 1.28	0.141

Table 2: *Total Duration of Analgesia (Hours)*

Group	Group A (n=40)	Group B (n=40)
Mean	5.7	9.3
SD	0.81	1.65

P-value= 0.02 significant

Table 3: *Comparison of pain in both groups*

Group	N	Pain Score Mean	Std. Deviation	Std. Error Mean
Group-A (Bupivacaine)	40	3.6500	.83359	.13180
Group-B (Bupivacaine plus ketamine)	40	1.5250	.96044	.15186

p-value = 0.000 (significant)

Table 4: *Data stratification for age in both groups*

Group	Age of subjects	N	Pain Score Mean	Std. Error Mean
Group-A (Bupivacaine)	3 - 7 years	18	3.9444	.15065
	7- 10 years	22	3.4091	.19361
	Total	40	3.6500	.13180
Group-B (Bupivacaine plus ketamine)	3 - 7 years	18	1.5000	.14575
	7 - 10 years	22	1.5455	.25250
	Total	40	1.5250	.15186
Total	3 - 7 years	36	2.7222	.23098
	7 - 10 years	44	2.4773	.21193
	Total	80	2.5875	.15579

p-value= 0.000 (Significant)

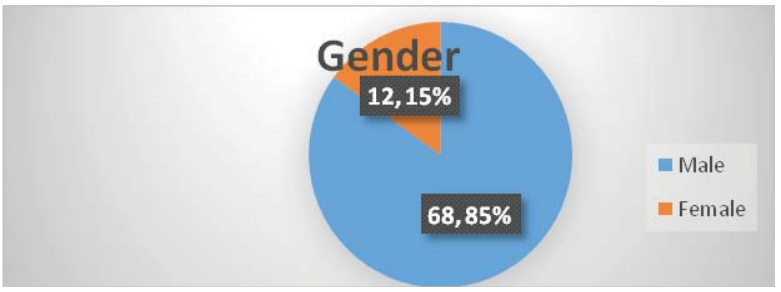


Figure 1: Frequency of gender in sampled population

children when their MOPS reached 4 or more. Post-operative analgesia was given with oral ibuprofen 10 mg/kg/dose maximum four doses in 24-hours. All data was entered in specially designed proforma. Confidentiality of data was maintained.

Data analysis: SPSS version 21 was used to enter and analyses the data. Quantitative variable like age and post-operative pain were represented by mean ± SD. Qualitative variable like gender and complications were presented by calculating frequency and percentage. Both groups were compared for post-operative pain by using independent sample t-test. P-value ≤0.05 was considered as significant. Data was stratified for age, gender and ASA class. Post-stratification, both groups were compared for post-operative pain by using independent sample t-test for each strata. P-value≤0.05 was considered as significant.

Results:

The mean age of patient in group-A was 5.5 ± 1.1 years. In group-B mean age was 5.3 ± 1.5 years. Age was comparable for both groups.

There were 68-male and 12-female making 85% and 15% of sampled population. Male female distribution was almost equal.

Duration of analgesia was calculated for both groups in hours. Longer analgesia was achieved using combination of ketamine and bupivacaine as compared to bupivacaine alone. P value was also significant.

Both groups were compared for post-operative pain and t-test was applied to calculate p-value of mean pain score. P value less than 0.05 was taken as significant. The mean pain score after 12 hour of surgery was 3.6 ± 0.8 in group-A and 1.5 ± 0.9 in group-B. p value was significant.

Data stratification for age group and mean pain score was significant. Data stratification for pain mean score against gender and ASA class was not significant.

There were no significant complications noted in any group. Most common complication was

Table 5: *Data stratification gender in both groups*

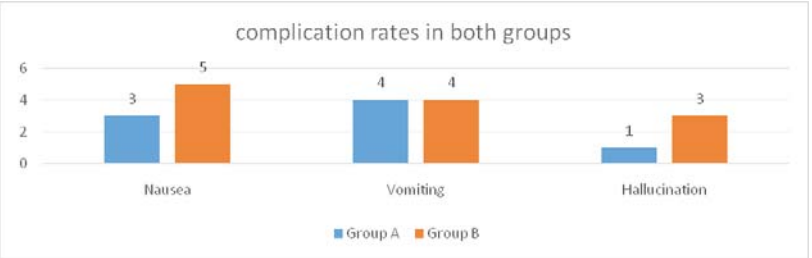
Group	Gender of subjects	N	Pain Score	Std. Error Mean
Group-A (Bupivacaine)	Male	33	3.6000	.18353
	Female	7	3.7000	.19331
	Total	40	3.6500	.13180
Group-B (Bupivacaine plus ketamine)	Male	35	1.0556	.05556
	Female	22	1.9091	.24538
	Total	5	1.5250	.15186
Total	Male	68	2.3947	.23108
	Female	12	2.7619	.20956
	Total	80	2.5875	.15579

P-value= 0.458 (not significant)

Table 6: *Data stratification for asa class in both groups*

Group	ASA class	N	Mean	Std. Deviation
Group-A (Bupivacaine)	ASA 1	13	3.4615	.96742
	ASA 2	27	3.7407	.76423
	Total	40	3.6500	.83359
Group-B (Bupivacaine plus Ketamine)	ASA 1	18	1.4444	.61570
	ASA 2	22	1.5909	1.18157
	Total	40	1.5250	.96044
Total	ASA 1	31	2.2903	1.27000
	ASA 2	49	2.7755	1.44720
	Total	80	2.5875	1.39342

p-value= 0.130 (not significant)



nausea followed by vomiting and hallucination in both groups but they were insignificant in both groups.

Discussion:

Caudal block is a simple, safe and popular regional block performed in pediatric anaesthesia Bupivacaine is the most common local anesthetic used for caudal analgesia with duration of only 4-6 hours.[11] We investigated the addition of ketamine to bupivacaine on the duration of peri-operative analgesia. In our study we found that the mean duration of analgesia was 5.7 ± 0.81 hours and 9.3 ± 1.65 hours with bupivaciane alone & bupivacaine plus ketamine respectively. Supporting our study Thendralarasu and colleagues observed pain free duration of 4.6 ± 0.88 hours with bupivacaine while the addition of ketamine increased the mean analgesia duration to 10.3±1.71 hours.[12] Similarly Martindol and Stoddart found that the median time to first analgesia administration was 10-hours after caudal block using bupivacaine along with ketamine in contrast to 4.75-hours in the bupivacaine only group.[13] Findlow and Aldridge made comparison of caudal block using bupivacaine and preservative- free ketamine with illio-ingninal nerve block for orchidopexy in children. Using modified pain score for the assessment of post-operative pain supplemental analgesia was required after 10 hours of the caudal block.[14] The findings of many other authors also support our study. Cook and associates studied sixty children with three different adjuncts clonidine adrenaline and ketamine along with 0.25% bupivacaine. They observed that ketamine 0.5mg/kg lead to a longer mean duration of post-operative analgesia after orchidopexy (12.5 hours) than either clonidine 2μg/kg (5.8 hours, p <0.05) or epinephrine 5μg / ml (3.2 hours, P <0.01).[15]

In contrast to the present study Masoum used three different doses of ketamine i.e 0.25 mg/kg, 0.5 mg/kg & 0.75 mg/kg along with 0.75 mg/kg of 0.25% bupivacaine. Their result demonstrated that the most effective and safest dose of ketamine for pain control was 0.5 mg/kg after pediatric surgery in the inguinal region.[16] Simple and associates worked on the optimal dose of ketamine and concluded that 0.25-0.5mg/kg is safe and without any adverse effects supporting our findings.[17] Ketamine is a unique analgesic that does not cause respiratory depression associated with opioids but causes hallucinations and emergence delirium.[18] These side effects have been reported with higher doses of 1mg/kg.[19] Naguib and fellows compared the analgesic effects of bupivacaine 0.25% (1mg/kg with and without ketamine 0.5mg/kg in children

undergoing inguinal herniotomy. Although there was no significant difference in the quality of analgesic between the groups only 7% of patients who received the ketamine bupivacaine combination required any further analgesia in the first 24-hours after surgery compared with 20% & 50% respectively of children in the ketamine only and bupivacaine only groups.[20] Ketamine used in our study was racemic i.e. mixture of both enantionmers (S (+) and R (-)) as it is easily available & less expensive than the S (+) - ketamine. Although the anesthetic potency of S(+) - ketamine is twice that of racemic mixture due to high affinity for the NMDA receptors the incidence of psychological side effects do not differ at equal plasma concentration.[21] No significant complications were noted in both groups making the combination therapy a safe option for perioperative pain control in pediatric population.

Conclusion:
Combination therapy of ketamine with bupivacaine is better option for post-operative pain control in children undergoing inguino scrotal surgery. It will reduce the fear of surgery subjectively and prevent the post-operative complications of surgery as well.

Conflict of interest: None

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Role and contribution of authors:
Dr Umbrin Naz, collected the data, references and did the initial writeup.

Dr Muhammad Ilyas, collected the data and helped in introduction writing.

Dr Ambareen Sifatullah, collected the data and helped in interpretation of data.

Dr Sayed Shah Hassanain, collected the refereecnes and helped in discussion writing.

Dr Robina Bangash, helped in collected the data.

Dr Zaid Javaid, collected the data and helpd in result writing.

Dr Parhaizgar Khan, critically review the article and made the final changes.

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