Original

Comparison of Pre-emptive Analgesic Effect of Rectal Ketamine and Caudal Bupivacaine in Pediatric Lower Abdominal Surgery

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Abstract

Introduction: Ketamine is a medication that suppresses the central nervous system and can be used as an analgesic. The aim of this study is to compare the post-operative pain reduction of rectal ketamine and caudal bupivacaine in pediatric lower abdominal surgery.

Materials and Methods: This double-blind clinical trial was performed on 68 children aged 1-7 years whom were allocated into two groups of 34 patients. The first Group received rectal ketamine (2mg/kg), and the second received 0.75mg/kg caudal bupivacaine (0.125%). Mean pain intensity and hemodynamic variables were recorded 2,6,12 and 24 hours following lower abdominal surgery in children. Pain was assessed using FLACC (Face, Legs, Activity, Cry, Consolability) Scale.

Results: There were no significant difference in terms of pain intensity between admission and discharge from recovery ($p>0.05$). Patients who received ketamine endured less pain than bupivacaine 2, 6, and 12 hours following surgery ($p<0.05$). Mean extubation time and duration of recovery stay was significantly shorter in the ketamine group.

Conclusion: Rectal ketamine was associated with more effective pain control and shorter recovery stay, when compared to caudal bupivacaine in lower abdominal pediatric surgery.

Keywords

- Postoperative pain
- Rectal Ketamine
- Caudal Bupivacaine
- Pain Management
- Lower abdominal surgery

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Introduction

Pain management after painful surgeries in children is very important and the lack of proper control of pain leads to increase in mortality .Injecting a drug in the epidural space is one of the most common regional anesthetic methods. In this method, one or more drugs are injected in a single dose or continuous infusion via a catheter adjusted in epidural space.[1, 2]

The severity of postoperative pain can increase usage of analgesics and the duration of patient's admission and, on the other hand, affect his ordinary activities. Therefore, good management of postoperative pain can improve patient's quality of life[3] and increase the satisfaction of patients and their parents, as well as improve and facilitate post-operative care.[4, 5]

Pain relief methods vary according to the type of surgery, patient characteristics and the drugs used. Reduction of pain intensity in abdominal surgeries can be done via local or systemic routes.[6, 7]

Several types of drugs can be used to reduce postoperative pain, including narcotics, NSAIDs and Phencyclidine derivatives like Ketamine.[6] Use of narcotic drugs accompanied by some side effects including depression of the respiratory system, itching, nausea and vomiting after surgery.

One of the side effects of non steroidal anti-inflammatory drugs is the increased risk of bleeding, [5, 7] they also have mild analgesic effects. On the other hand ketamine is a chemical derivative of Phencyclidine. It has sedative effects and is mainly used for starting and maintaining anesthesia. Its major mechanism is blockage of the NMDAR (N-Methyl-D-Aspartate Receptor) in the spinal cord; also it binds to the opioid receptor (μ). Ketamine is a medication that suppresses the central nervous system. Compared with some other anesthetic drugs, ketamine is less harmful because it does not disturbbreathing, blood circulation and gag reflex. Common side effects of ketamine hydrochloride include: double vision, dream-like feeling, hallucination, and jerky muscle movements.[4]

Methods of ketamine administering in medicine is intra rectal, intravenous or intramuscular injection. Bupivacaine is generally used to induce local, regional or epidural anesthesia in the lumbar or sacrum. It is also used to make obstruction through infiltration in subarachnoid space or to create nerve blockage in dentistry. Systemic absorption of bupivacaine is complete and attaches to plasma proteins. Its metabolism is mostly hepatic and excreted via the kidney. The half-life of the drug in adults is 3.5 hours, onset of drug effect is slowly and the duration of effect is long.

The use of intra-rectal administration of some drugs, such as narcotics, acetaminophen and midazolam, is recommended for premedication or postoperative pain control (preventive analgesia).

In spite of the proper effect of administering bupivacaine in epidural space and intra rectal ketamine in controlling postoperative pain, data regarding rectal administration of Ketamine as a postoperative analgesic is scarce. The aim of this study was comparing the effect of intra-rectal ketamine with the effect of bupivacaine in the lower epidural space by caudal method in pain control after pediatric lower abdominal surgery.

Materials and Methods

This was a double-blind clinical trial study done in Imam Hossein Hospital in Isfahan, Iran between 2016 and 2017. The targets of our study were children undergoing lower abdominal surgery.

Among them patients who had: ASA scores of I& IIs, an age range of 1 to 7 years, patients with no history of seizure or attention deficit hyperactive disorder, no history of increased intracranial pressure, No use of steroidal and non-steroidal pain medication, no history of coagulation disorders, no caudal infection and parental consent to participate were included in the study. Patients with drug withdrawal from the anus and/orreceive any drug outside the prescribed protocol were excluded.

The sample size was estimated to be 34 in each group which was calculated using the sample size formula, with a 95% confidence interval, 80% probability, 1.17standard deviation of pain intensity. All data were analyzed by SPSS software version 22 and T-test, Chi-square and ANOVA(Analysis of variance)with repeated observations.

After obtaining the approval of the ethics committee of our university and gathering signed consent forms, 68 children were distributed in two groups of 34 patients by a random allocation method. The first group, 2 mg/kg of ketamine (from TRITTAU - Germany) was prepared in the syringe (10 mg/ml), and administered Intra-rectally (in the lateral position). In the second group, 0.75 ml/kg of Bupivacaine 0.125% (from AstraZeneca–Sweden) was injected through sacro–coccygeal hiatus by a 23–gauge syringe under sterile conditions. Intervention was done at the end of the surgery just before restoration of consciousness in both groups. Drugs were prepared by a staff anesthetist not otherwise involved in study.

As premedication, all patients received 0.1 mg/kg intravenous midazolam in the waiting room. After induction of general anesthesia with 5 mg/kg Sodium thiopental and 0.5 mg/kg Atracurium and tracheal intubation, anesthesia was continued with 1% Isoflurane and Entonox (mixture 50% nitrous oxide: 50% oxygen).

The hemodynamic parameters of patients were controlled during the course of the operation.

Pain intensity was measured and recorded for the two groups, using FLACC [8] (Face, Legs, Activity, Cry, Consolability) scoring system first on admission to the recovery, when discharged from the recovery and after 2, 6, 12 and 24 hours after surgery.

Table 1: FLACC scoring

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

The FLACC scale is an appropriate tool for evaluating the severity of pain in children. This tool has 5 parts that examine the pain level from facial reactions, palpation, mobility, crying and relaxation. More details are provided in **Table 1**. Each of these sections will receive a score of zero to two, which is ultimately added together and based on the overall score: A score of 0 means lack of pain and a score of 10 means the most severe pain. The overall score is divided into three classes: 0 to 3 (mild pain), 4 to 7 (moderate pain), and grades 8 to 10 mean severe pain[9]. During the study, if the FLACC score was equal to or greater than 5, 0.5 mg / kg of intravenous pethidine was used and the amount and time of receiving the first dose of pethidine were recorded in the questionnaire.

The success of caudal block in children in the bupivacaine group was confirmed by determining the level of sensory block and reduction in anal sphincter tone.

The duration of anesthesia was assessed and recorded in minutes from the time of anesthesia induction until the extubation. The duration of extubation (in minutes) was from the time when the anesthetic inhaler was stopped until the endotracheal tube was retracted. The recovery duration was determined based on the Modified

Aldrete's Scoring[10]. This rating system is a commonly used scale to determine the patient's safe discharging time from PACU.

The incidence of nausea and vomiting, disorientation and need for urinary catheterization were also recorded in the two groups. At the end of the study, parents' satisfaction with child painlessness was assessed based on Likert's criteria[11] with 5 levels (very low, low, moderate, high, and very high) **Table 2**.

Table 2: Likert Scoring

Very high	High	Moderate	Low	Very low	level
5	4	3	2	1	Score

Results

In this study, 68 children underwent abdominal surgery in two groups of 34 patients. During the study, no patient was excluded due to unwanted side effects. The distribution of the demographic variables has been shown in **Table 3**. According to the table, the mean age, weight and frequency of sex in the two groups did not have a significant difference.

Table 3: Distribution of demographic variables in two groups

P	Group		Variable	
		Bupivacaine	Ketamine	
0.4	3.1±5.5	3.1±2.5	Mean age (year)	
0.3	15.4±57.13	14.3±57.78	Mean weight (Kg)	
0.14	24 (70.6)	29 (85.3)	Male	Number(percent) of Sex
	10 (29.4)	5 (14.7)	Female	

There was no significant difference between the severity of pain in both groups at the time of admission and discharging from the recovery, but patients in ketamine group had less pain intensity at 2, 6 and 12 hours after the operation. According to the ANOVA with repetition of observations, the severity of pain was considerably different in the two groups ($p = 0.007$) and the ketamine group had less pain intensity after the operation **Table 4** and **Figure 1**.

Table 4: Mean and standard deviation of pain intensity of the two groups during the period of stay in recovery and ward

P	Group		Time
	Bupivacaine	Ketamine	
0.3	4.12±0.54	4.0±29.84	Recovery admission time
0.11	3.0±71.46	3.0±47.71	Recovery discharging time
0.002	3.0±29.68	2.0±74.75	2h after OR
<0.001	2.0±82.58	2.0±21.77	6h after OR
0.009	2.0±29.68	1.0±76.92	12h after OR
0.07	1.0±85.61	1.0±53.83	24h after OR

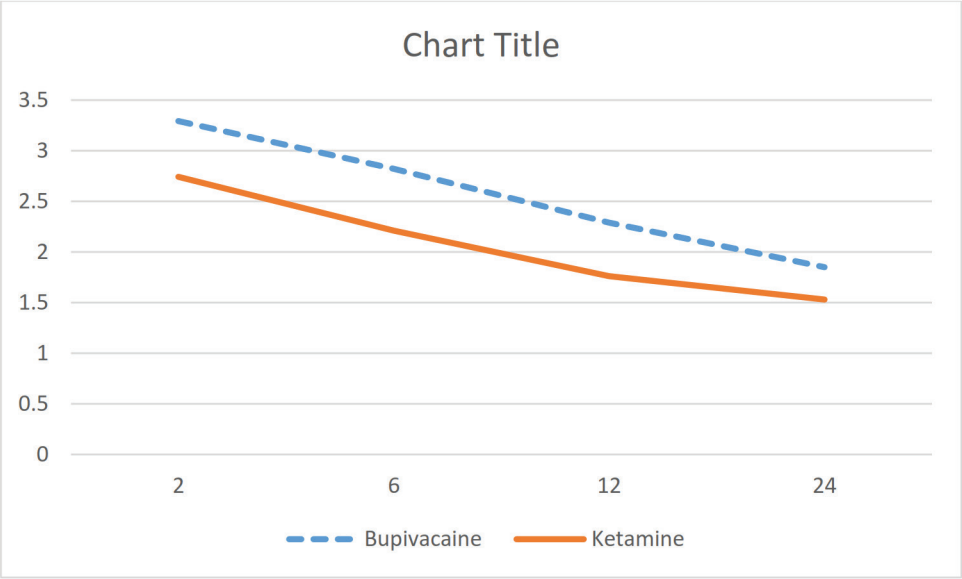

Figure 1: Mean Pain intensity during hospitalization in two groups

Any serious he modynamic disorder requiring medical intervention was not observed in any of the patients. The mean duration of extubation was 6.35 ± 1. 54 and 8.23 ± 1.85 minutes in ketamine and bupivacaine recipients, respectively. The extubation time was considerably lower in the ketamine group (p <0.001). The mean duration of recovery was 44 ± 13.6 and 52.5 ± 5.94 minutes in the two groups, respectively. The ketamine group had a lower recovery period (P <0.001). The number of patients requesting additional analgesics in the two groups of ketamine and bupivacaine was 15 and 21, respectively, (44.1% vs. 61.8%) which was not statistically meaningful. Mean duration of time until receiving additional analgesic in the two groups was 18.67±15.18 and 40.71±36.1 minutes, respectively, and this time in the ketamine group was significantly lower (P = 0.033).Two patients in

the ketamine group and 5 patients in the bupivacaine group had nausea and vomiting (5.9% vs. 14.7%) whilst in the recovery. Moreover, 3 (8.8%) of the bupivacaine group suffered from urinary retention (p = 0.24).

Parental satisfaction with painlessness between the 2 groups is shown in **Table 5**. There was no significant difference between the two groups (p = 0.8).

Table 5: Distribution of variables in two groups

P	Group		Variable	
		Bupivacaine	Ketamine	
<0.001	8.1±32.85	6.1±35.54	Mean Extubation time (min)	
0.3	52.5±5.94	6±44.13	Mean Recovery time (min)	
0.15	21 (61.8)	15 (44.1)	Number (percent) of analgesic recipient	
0.033	40.36±71.1	18.15±67.18	First time (min) receiving additional analgesic	
0.23	5 (14.7)	2 (5.9)	Number (percent) of vomiting in recovery	
0.24	3 (8.8)	0 (0)	Number (percent) of urinary retention	
0.8	22 (64.7)	21 (61.8)	Completely satisfied	Number (percent) of satisfaction
	12 (35.3)	13 (38.2)	Moderately satisfied	

Discussion

There severity of pain was no considerably different between the two groups in the recovery, but the pain intensity was lower during 24 hours after the operation, at 2, 6 and 12 hours after the use of rectal ketamine.

In a study by Moshiri et al., results showed that the consumption of analgesics, pain intensity, hemodynamic symptoms, maternal drowsiness and Apgar score after cesarean section were similar in Ketamine and control groups, and no difference was observed between them. The mean time of first application of analgesic after the operation in the ketamine and control groups was 99.75 ± 68.88 minutes and 96.1 ± 52.59 minutes, respectively; indicating that rectal ketamine administration had no significant effect on post-cesarean pain reduction.[12] But in the present study, 2 mg/kg of rectal ketamine has a positive effect on children's pain control.

In a study by Arbabi et al., the efficacy of administering bupivacaine, bupivacaine-midazolam and bupivacaine-ketamine for caudal postoperative analgesia in children aged 1 to 3 years has been examined.

The results showed that the median postoperative painlessness period in midazolam + bupivacaine was higher in comparison to other groups. [13]

Although in our study caudal bupivacaine has been less successful compared with rectal ketamine in controlling the pain.

Sayin et al. in 2006 showed that use of ketamine for premedication and sedation before general anesthesia for herniorrhaphy and circumcision in children, has a sufficient and adequate sedative effect. The results revealed that children who received 10 mg/kg intra-rectal ketamine (5%) were more sedentary than those with lower concentrations [14, 15] which is consistent with our study.

A study by Tyler et al., showed that the use of rectal ketamine provides a better sedation than rectal midazolam in minor children's surgery. [16]

In the study of Hosseini et al., The use of rectal acetaminophen versus bupivacaine in the inguinal hernia repair was investigated. Based on FLACC, patients who received rectal acetaminophen had lower pain than the bupivacaine recipient group.[3]

In another study by Heidari et al., 70 children undergoing tonsillectomy were evaluated for postoperative pain control. In this study, a group of children received rectal ketamine 2 mg/kg. Another group received 20 mg/kg intra-rectal acetaminophen. In both groups, vital signs, severity of pain, sedation score and the side effects of drugs taken within 24 hours, was compared. It was noted that intra-rectal ketamine compared with acetaminophen suppository in tonsillectomy was associated with more reduction in pain which also confirm our results .[17]

Conclusion

Our aim was to determine the effect of rectal ketamine on postoperative pain control in children's lower abdominal surgery and compare it with caudal bupivacaine. The children who received rectal ketamine had less pain intensity after surgery, although there was no significant difference between the average pain between the two groups at the time of entry and exit from the recovery. Also, hemodynamic parameters were controlled in both groups of ketamine and bupivacaine over a specified period of time, and there wasn't any impairment of these parameters which required medical intervention in both groups.

Overall, our results indicate that the use of rectal Ketamine might be a good option for pain relief after surgery. But for further confirmation, an expanded study is recommended with more surgeries.

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Ethics Approval

The present article is the result of a doctoral dissertation which was approved by Isfahan University of Medical Sciences ethic committee at No. 395101 with ethical code number of ir.mui.rec.1395.3.1.1.

Conflict of Interest

There is no conflict of interest.

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