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ORIGINAL ARTICLE

Ketamine as an Adjuvant to Bupivacaine in Caudal Block for Pediatric Patients Undergoing Lower Abdominal Surgeries

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ABSTRACT

Background: Caudal anesthesia is a generally used regional anesthetic technique that can be useful in providing peri and postoperative analgesia. This study aimed to compare between the analgesic effect of adding ketamine to bupivacaine in caudal epidural block (CEB) for pediatric patients undergoing lower abdominal surgeries versus bupivacaine alone.

Methods: A total of 30 pediatric patients aged 1 - 3 years ASA I-II equally divided into two groups: Group C received general anesthesia GA and CEB using 0.25% bupivacaine 1ml/kg only. Group K received GA and CEB using 0.25% bupivacaine 1 ml/kg plus 0.5 mg/kg ketamine. Baseline HR and MAP were recorded then every 20 min till end of operation and at 1, 4, 8, 12hr. postoperatively Pain scores were evaluated by FLACC pain scale. Time of 1st analgesic rescue and its total doses were recorded.

Results: The results showed that there was a highly significant difference between studied groups regarding intraoperative MAP and HR at 10min and 30 min after induction. There were highly significant differences between the studied groups regarding first time for rescue analgesia was longer in group K and total dose intra and postoperatively was lower in group K. As regards pain assessment, a significant increase in FLACC scale of group C compared with group K.

Conclusions: The addition of 0.5 mg/kg ketamine as adjuvant to 1 ml/kg of 0.25% bupivacaine caudally safely prolongs the duration of postoperative analgesia.

Keywords: Ketamine, Bupivacaine, Caudal Block, Lower Abdominal Surgeries**.**

INTRODUCTION

Caudal anesthesia is a generally used regional anesthetic technique that can be useful in providing peri and postoperative analgesia. It can serve as the sole anesthetic or can be an adjuvant to general anesthesia. The advantage of caudal anesthesia occurs mainly in pediatrics for infraumbilical surgeries [1].

Postoperative pain management is a complementary part of the practice of pediatric anesthesiologists. Different methods and medications that have been tried to provide postoperative pain relief in pediatric population are not free from significant side effects. However, the limited duration of analgesia following a single injection of local

anesthetics mandates, the seeking for an adjuvant that may prolong it safely. The use of an indwelling catheter for prolonging the duration of action of local anesthetics is usually not practiced due to concerns about proximity to the gluteal region area giving rise to infection and toxicity risks in the young population [2].

In recent years, the addition of adjuvants such as opioids, ketamine, and alpha-agonists to local anesthetics has resulted in prolonging the duration of block, improved pain control, parental satisfaction, and faster recovery. Ketamine is a selective antagonist of N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. It joins specifically to dizocilpine (MK-801) of NMDA receptor, near the channel pore, and is an uncompetitive antagonist [3].

Post-operative pain management had constantly been a major concern of parents as well as pediatric anesthetists. Opposed to the ancient nation that children don't feel pain, many studies have focused on the importance of good pain management in children [4]. Therefore, pediatric surgeons, anesthetists and pharmacologists had been in a constant search to find a safe and effective analgesic for children. There is increasing interest in combining regional and general anesthesia (GA) to relieve intraoperative and postoperative pain[5]**.** The conclusion of the study was the addition of 0.5 mg/kg ketamine as adjuvant to 1 ml/kg of 0.25% bupivacaine caudally increasingthe duration of postoperative analgesia.

METHODS

This Comparative Prospective randomized double blind controlled clinical studywas carried outin Zagazig University Hospitals, during the period (from September 2018 to September 2022) after approval by institutional review board committee at Faculty of Medicine Zagazig University. In accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. A written informed consent was taken from all parents. The study including a total of 30 pediatric patients scheduled for lower abdominal surgerieswere randomly allocated to one of two groups by a computer-generated table of random numbers and equally divided into two groups:

- Group (C): 15 patients received general anesthesia (GA) and caudal epidural block (CEB) using 0.25% bupivacaine 1ml/kg only.
- Group (K): 15 patients received GA and CEB using 0.25% bupivacaine 1 ml/kg plus 0.5 mg/kg ketamine.

Inclusion criteria:1. Parents accept the procedure by written consent, 2.Age: 1 - 3 years, 3.Sex: both boys and girls, 4. Physical state: American Society of Anesthesiologists (ASA) class I or II, 5. Type of operation: lower abdominal surgeries and 6. Duration of surgery: about an hour and half.

Exclusion criteria:1. Parent refusal, 2. Local infection and anatomical abnormalities at the site of caudal block and contraindication for regional anesthesia, 3. History of allergy to local anesthetics and other drugs used, 4.

Coagulation disorders, 5. Pre-existing neurological or spinal diseases, 6. Patient with coexisting medical diseases, 7. History of developmental delay or mental retardation, which could make observational pain intensity assessment difficult, 8. Raised intracranial pressure and 9. Emergency surgery.

Data collected during the study were:i) Patient characteristics: Age, weight, sex, ii) HR and MAP: Were recorded before and after induction of anesthesia then every 20 min till the end of operation and at 1, 4, 8, 12hr postoperatively, iii)Total doses of rescue (fentanyl) analgesia intraoperative, iv)Time of first analgesic request (paracetamol) postoperative and 12hpostoperatively were recorded and v)Assessment of pain using FLACC pain scale at 1, 4, 8, 12h postoperatively.

FLACC pain scale **[6]**Assessment of Behavioral Score:

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

If the recorded pain score ≥ 4, IV paracetamol 15 mg/kg was given for control of postoperative pain.

Anesthetic approach

1. Preoperative

During preoperative visit, patient's age, weight, baseline vital parameters were recorded. Detailed history, physical examination was done. Routine laboratory investigations such as complete blood count (CBC), bleeding time, Prothrombine Time (PT), Partial Thromboplastine Time (PTT) and clotting time were carried out. All patients kept fasting as per institutional protocol 2 hr for clear liquid and 6 hr for semisolid and solid food, premedication was done by atropine IM 0.01-0.02 mg/kg.

2. Intraoperative

On arrival to the operating room, all patients were connected to the monitor including (ECG), non-invasive blood pressure (NIBP), pulse oximetry for measuring the peripheral oxygen saturation (SpO_2) and capnogram to maintain End tidal carbon dioxide ($Etco_2$). Then general anesthesia was induced using inhalation of 0.8 MAC sevoflurane in 100% oxygen with spontaneous ventilation. Intravenous line was inserted (22 or 24 G cannula): and secured then ringer lactate and glucose 5% 1:1 was infused at a rate of 4 ml/kg/h for 1st 10kg and 2 ml/kg/h for 2nd 10kg during and after the operation till oral fluid and feeding is started. Tracheal intubation by appropriate size of endotracheal tube (ETT) was facilitated by intravenous atracurium 0.5 mg/kg. Anesthesia was maintained by sevoflurane mean alveolar concentration MAC 0.8 with oxygen and maintenance of muscle relaxation by atracurium when needed. Controlled mechanical ventilation was used to keep $EtCO_2$ between 30-35mmHg.

Patients were positioned in a lateral decubitus position. The sacral region was properly sterilized with betadine and the sacral hiatus between the sacral conru was palpated. Then, a 23 G short needle was used to puncture the sacral surface at a 45-degree angle. When the sacro-coccygeal ligament seemed to be

punctured, the needle was tilted more toward the skin surface and the needle was inserted 2-3 mm deeper. Then 1 mg /kg bupivacaine was injected alone or with 0.5 mg /kg ketamine. The proper placement of the needle was confirmed by 'swoosh' test in which a stethoscope was placed over the lower lumbar spine, corresponding to an area immediately above the end of the cannula. If the injection heard, this was recorded as a positive result that indicate proper placement of the needle. If the injection was inaudible or equivocal, it was recorded as a negative test that indicates improper placement of the needle **[7].**

Inadvertent Dural puncture or intravascular placement was excluded by negative aspiration, both initially and after 2 ml of injection of the anesthetic drug. In addition, the volume of local anesthetic was injected slowly with continuous ECG monitoring. Adequate intraoperative anesthesia defined by hemodynamic stability, as evidenced by the absence of an increase in the heart rate (HR) or a mean arterial pressure (MAP) greater than 20% compared to the baseline values that were obtained before anesthesia. If the readings increased >20%, the child received a rescue opioid in the form of fentanyl 1-2 µg/kg because analgesia was considered inadequate, and the total amount of intraoperative fentanyl given recorded.

Statistical analysis:

Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0). According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD.Comparisons between the 2 groups of categorical variables was done using Chi square test (X2).P value was set at <0.05 for significant results &<0.001 for high significant result.

RESULTS

The patient characteristics including age, weight and gender did not show any statistically significant differences between the two groups**(Table1)**.

Regarding MAP the mean and standard deviation values of intra-operative MAP (mmHg) before induction, 50 min and 70 min after induction there were no significant differences between the groups. While there was highly significant difference between them which was found to be significantly higher in group C compared to group K at 10 and 30 min after induction **(Table 2).**

Regarding HR the mean and standard deviation values of intra-operative HR (beat/minute) before induction, 30 min, 50 min and 70 min after induction there were no significant differences between the groups inintra-operative HR. While there was a highly significant difference between them, which was found to be significantly higher in group C compared to group K at 10 and 30 min after induction **(Table 3)**.

Regarding postoperative MAP (mmHg) at 1st, 8th and 12thhour there were no significant differences between the groups in post-operative MAP. While there wassignificantly higher in group C compared to group K at 4th hour postoperative**(Table 4).**

Regarding post-operative HR (beat/minute) at 1st, 8th and 12thhour there were no significant differences between the groups inpost-operative HR. While there was significantly

higher in group C compared to group K at 4th hour postoperative**(Table 5).**

Regarding FLACC scale there was a significant difference between the studied groups at 1st, 4th and 8th hours. There was a significant increase in FLACC scale of group C compared with that of group K.While there was a no significant difference at 12thhr regarding FLACC**(Table 6).**

Regarding the total intra operative fentanyl consumption (µg/kg) was found to be significantly higher in group C compared to group K. Also, there were highly significant differences between the studied groups regarding first time for rescue analgesia and the amount of post-operative (IV) paracetamol consumption (mg/kg). It was found that the first time for rescue analgesia was significantly longer in group K.Also, the total amount of paracetamol needed postoperatively was significantly lower in group K compared to group C **(Table 7)**.

Table 1: Demographic data and clinical characters of the studied groups.

	Group C	Group K	t	P
Age (months)	23.9±7.5	23.8±5.2	0.04244	0.9665
Weight (kg)	12.1±1.32	11.96±1.17		
Gender N (%) Boy Girl	 7 (46.7%) 8 (53.3%)	 6 (40%) 9 (60%)	 0.0005 chi square	 0.982

Mean ± SD: mean and standard deviation; N: Number; ASA: American Sociaty of Anesthesia; group C: control group; group K: Ketamine group.
p> 0.05 was considered non-significant.

Table 2: Intra-operative MAP (mmHg) distribution among studied groups

Intraoperative MAP (mmHg)	**Group C**	**Group K**	**T**	**P**
Before induction MAP	84.26±2.12	82.93±1.66	1.9131	0.06602
10 min after induction	102.06±1.9	84.93±1.66	26.2956	0.001
30 min	90.26±1.98	84.98±1.66	7.9145	0.0000
50 min	85.55±2.75	84.93±1.66	0.7475	0.461
70 min	85.03±2.33	84.97±2.71	0.0650	0.9486

Mean ± SD: mean and standard deviation; group C: control group; group K: Ketamine group; Min: minute; MAP: mean arterial pressure.
p> 0.05 was considered non-significant.

Table 3: Intra-operative HR (beat/minute) distribution among studied groups

Intra operative HR (b/m)	Group C	Group K	T	P
Before induction HR	110.2±8.79	107.46±8.4	.8728	0.3902
10 min after induction	133.2±8.79	109.33±7.6	7.956	0.001
30 min	110.22±8.79	107.46±8.45	0.8767	0.3881
50 min	112.53±7.54	111.33±7.41	0.4396	0.6636
70 min	112.46±9.12	108.90±7.11	1.1923	0.2431

Mean ± SD: mean and standard deviation; group C: control group; group K: Ketamine group; Min: minute; HR: heart rate.
p> 0.05 was considered non-significant.

Table 4: Post-operative MAP (mmHg) distribution among studied groups

Post operative MAP (mmHg)	Group C	Group K	T	P
1h	85.57±3.25	84.87±2.88	0.6243	0.5375
4h	96.16±2.88	84.97±1.86	12.641	0.001
8h	85.55±2.75	84.98±1.88	0.6627	0.5129
12h	84.56±2.99	84.15±3.94	0.321	0.7506

Mean ± SD: mean and standard deviation; group C: control group; group K: Ketamine group; h: hour; MAP: mean arterial pressure.
p> 0.05 was considered non-significant.

Table 5: Post-operative HR (beat/minute) distribution among studied groups

Post operative MAP (mmHg)	Group C	Group K	T	P
1h	85.57±3.25	84.87±2.88	0.6243	0.5375
4h	96.16±2.88	84.97±1.86	12.641	0.001
8h	85.55±2.75	84.98±1.88	0.6627	0.5129
12h	84.56±2.99	84.15±3.94	0.321	0.7506

Mean ± SD: mean and standard deviation; group C: control group; group K: Ketamine group; h: hour; HR: heart rate.
p> 0.05 was considered non-significant.

Table 6: FLACC distribution among studied groups

FLACC	Group C	Group K
	Median (IQR)	Median (IQR)
FLACC_1h	1 (2-1)	0 (1-0)
FLACC_4h	5 (5-4)	0 (1-0)
FLACC_8h	3 (4-3)	2 (2-1)
FLACC_12h	3 (3-2)	4 (4-3)

Group C: control group; group K: Ketamine group; FLACC: face, leg, activity, cry, console ability; min: minutes;h: hour; IQR: inter quartile range.
p> 0.05 was considered non-significant.

Table 7: Total intra operative fentanyl consumption(µg/kg) and total postoperative (IV) paracetamol consumption (mg/kg).

	Group C Mean ± SD	Group K Mean ± SD	T	P
Total intra operative fentanyl consumption (µg/kg)	7.86 ± 5.79	1.4 ± 3.73	3.6326	0.0011
1st Time for post operative analgesia (h)	5.73±1.03	10.66±1.32	-11.404	0.0000
Post-operative (IV) paracetamol consumption (mg/kg)	17.0±3.16	8.66±2.55	7.9547	0.0000

Mean ± SD: mean and standard deviation; group C: control group; group K: Ketamine group.
p< 0.001 was considered highly significant.

DISCUSSION

Ketamine is a popular drug, used for different purposes. It can be administered by almost any route and combined with various sedative and analgesic agents. The dose used to enhance the effect of LAs when performing caudal blocks in children (0.5-1.0mg/kg) [8].

Therefore, epidurally administered ketamine exerts profound analgesic actions at spinal cord level without exerting any systemic side effects. Hence, addition of ketamine (preservative free drug which is safe for epidural administrations) to caudal bupivacaine has been shown to prolong the duration of postoperative analgesia in children undergoing orchidopexy and inguinal herniotomy [9].

Regarding MAP and HR, the result of the current study is there was no significant difference between the studied groups as regarding different MAP, HR readings during the operation at before induction, after induction 50 min and 70 min. While there was highly significant difference between them as regarding intra-operative MAP and HR which was found to be significantly higher among group C compared to K at 10 and 30min after induction.

Regarding MAP and HR, the result of the current study is there was no significant difference between the studied groups as regarding different MAP, HR readings postoperative at 1st, 8th and 12th hr. While there wasa highly significant difference between them as regarding postoperative MAP and HR which was found to be significantly higher among group C compared to K group at 4th hour postoperative.On the other hand**Shirmohammadie et al [10]** reported that intraoperative heart rate and blood pressure was not significantly different in the following groups (group B 1 ml/kg of 0.25% caudal bupivacaine, group BN 1 ml/kg of 0.25% caudal bupivacaine mixed with 2 µg/kg neostigmine, group BK 1 ml/kg of 0.25% caudal bupivacaine mixed with 0.5 mg/kg ketamine andgroup BM 1 ml/kg of 0.25% caudal bupivacaine mixed with 50 mcg/kg midazolam.However, our study was in an agreement with **Kumar et al [11]** found no differences in heart rate or mean arterial blood pressure between 0.25% bupivacaine

(1ml/ kg) alone or bupivacaine 0.25% with ketamine 0.5mg/kg.

In this work there were highly significant differences between the studied groups regarding first time for rescue analgesia and the amount of fentanyl andparacetamol needed postoperatively. It was found that the first time for rescue analgesia was significantly longer among group K compared to group C.

Also, the total amount of paracetamol needed postoperatively was significantly lower ingroup K compared to group C. This is in agreement with **Shirmohammadie et al [10]** reported that post-operativedose of supplementary analgesic in 24 h in group B was also higher than that in groups BK, BM and BN respectively.

Kaur and Anand, [12] reported thatcaudal bupivacaine and ketamine combined prolonged postoperative analgesia by 5–6 h and significantly reduced the need for subsequent postoperative analgesia by more than 50% compared with caudal bupivacaine alone.**Fahim and Menshawi[13]** reported that the total dose of postoperative paracetamol consumption was signifcantly lower in group BD (1 ml/kg bupivacaine 0.25% mixed with dexmedetomidine 1 μg/kg) and group BK (1 ml/kg bupivacaine 0.25% mixed with ketamine 0.5 mg/kg) when compared with group B(1 ml/kg bupivacaine 0.25%). The time to 1st postoperative analgesic demand was significantly longer in group BD and group BK when compared with group B.

regarding pain assessment, this study assessed the pain by FLACC scale which was significantly increased within the same group at different measurement times in the two groups. There was a significant increase in FLACC scale of group C compared with that of group K at 1, 4 and 8 hr. While there was a non- significant difference at 12hr regarding FLACC. **Fahim and Menshawi[13]** reported that Postoperative FLACC scores were significantly lower in group BK and BD compared with group B at 4–8 h and at 4–12 h respectively.

CONCLUSION

The results of this study made us to conclude that the addition of 0.5 mg/kg ketamine as an adjuvant to 1 ml/kg of 0.25% caudal bupivacaine could lengthen the duration of postoperative analgesia in children undergoing lower abdominal surgeries without increasing the incidence of side effects.

Conflict of interest: None.

Financial Disclosures: None.

REFERENCES

1- **Dalens B and Hasnaoui A.** Caudal anesthesia in pediatric surgery: success rate and adverse effects in 750 consecutive patients. AnesthAnalg. 1989;68(2):83-9

2- **Trifa M, Tumin D, Tobias J.** Dexmedetomidine as an adjunct for caudal anesthesia and analgesia in children. Minerva Anestesiol. 2018; 84(7):836–47

3- **Pinault D.** N-methyl d-aspartate receptor antagonists ketamine and MK-801 induce wake-related aberrant gamma oscillations in the rat neocortex. Biol Psychiatry **(2008).**63(8):730–5

4- **Groenewald B, Agri O, Hetz S, Chown S and Terblanche J.** Respiratory dynamics of discontinuous gas exchange in the tracheal system of the desert locust, Schistocercagregaria. J. Exp. Biol. **2012;** 215(13):2301-7.

5- **Akbas M, Titiz T, Ertugrul F, Akbas H and**

Melikoglu M. Comparison of the effect of ketamine added to bupivacaine and ropivacaine, on stress hormone levels and the duration of caudal analgesia. ActaAnaesthesiol.Scand. 2005; 49(10): 1520—1526.

6- **Merkel S, Voepel-Lewis T, Shayevitz J and Malviya S**. The FLACC: A behavioural scale for scoring postoperative pain in young children. Pediatric nursing; 1997. 23 (3):293-797.

7- **Sawan Z, Balata A, ElhossienyKh and Ahmed E.** Ultrasound-guided ilioinuginal/ iliohypogastric block versus caudal block for pediatric inuginalherniotomy. ZUMJ **2019;** 1907-1305 (R1). 267- 278.

8- **Sih K, Campbell S, Tallon J, Magee K, Zed P.** Ketamine in adult emergency medicine: controversies and recent advances. Ann Pharmacother.2011; 45(12):1525-34.

9- **Findlow D, Aldridge LM, Doyle E.** Comparison of caudal block using bupivacaine and ketamine with ilioinguinal nerve block for orchidopexy in children. Anaesthesia 1997;52(11):1110–1113.

10- **Shirmohammadie M, Soltani A, Arbabi S and Nasseri K.** A randomized-controlled, double-blind study to evaluate the efficacy of caudal midazolam, ketamine and neostigmine as adjuvants to bupivacaine on postoperative analgesic in children undergoing lower abdominal surgery. Acta Biomed 2018; 89(4): 513-518.

11- **Kumar P, Rudra A, Pan A and Acharya A.** Caudal additives in pediatrics: A comparison among midazolam, ketamine and neostigmine co administered with bupivacaine. AnesthAnalg 2005; 101(1):69–73

12- **Kaur D and Anand S.** Comparison between caudal bupivacaine and bupivacaine with ketamine for postoperative analgesia in children: A prospective randomized clinical study 2016;10 (3):488-492

13- **Fahim H and Menshawi M**. Efect of caudal dexmedetomidine versus ketamine in prevention of emergence delirium in pediatric patients undergoing congenital inguinal hernia repair under sevofurane anesthesia Ain-Shams Journal of Anesthesiology 2022;14(45):1-10.

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