RESEARCH

A PROSPECTIVE, RANDOMISED COMPARATIVE STUDY ON THE EFFECT OF PRESERVATIVE-FREE KETAMINE WITH LEVOBUPIVACAINE VS LEVOBUPIVACAINE FOR CAUDAL BLOCK IN LOWER ABDOMINAL SURGERIES IN CHILDREN

Saravanan S[1], Karthikeyan C[2]

[1]Assistant Professor, Department of Anaesthesiology, Kilpauk Medical College, Kilpauk, Chennai.
[2]Assistant Professor, Department of Anaesthesiology, Kilpauk Medical College, Kilpauk, Chennai.

Received : 05/08/2022
Received in revised form : 19/09/2022
Accepted : 28/09/2022

Keywords:
Analgesia, Postoperative, Caudal, Levobupivacaine, Ketamine.

Corresponding Author:
Dr. Karthikeyan C,
Email: karthickdoc27@gmail.com
ORCID: 0000-0002-4958-7776

DOI: 10.47009/jamp.2022.4.4.131

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2022; 4 (4); 664-668

Abstract

Background: In the paediatric population, caudal anaesthesia has developed as a dependable and successful anaesthetic method. However, one of the biggest barriers to fully utilising caudal block as an efficient analgesic approach is the local anaesthetic medications' with limited duration of action. The aim is to compare the efficacy of producing postoperative pain relief and the safety of using a caudal epidural. **Materials and Methods:** A randomised controlled study was conducted at the Institute of child health, anaesthesiology department, between September 2012 and October 2012. Sixty children between the age group 6 months to 8 years scheduled for elective lower abdominal surgeries, were randomly divided into two groups for study. Group L Received a caudal epidural block with 1ml/kg of 0.25% levobupivacaine with 0.5mg/kg of preservative-free ketamine. Group K Received a caudal epidural block with 1ml/kg of 0.25% levobupivacaine alone. **Result:** Most children (95%) are males, with females accounting for only 5%. Half of the surgeries (51.7%) were for Congenital Hydrocoele and another half for Inguinal Hernia Repair (48.3%). There were no postoperative problems in 81.7%of the patients, urine retention in 10%, and nausea and vomiting in the remaining 8.3%. **Conclusion:** Preservative-free ketamine combined with levobupivacaine in the caudal epidural block prolongs postoperative anasthesia without significantly affecting hemodynamics compared to levobupivacaine alone.

INTRODUCTION

Various approaches for pain management following juvenile lower abdomen surgery have been employed in the past, including administering opioid and non-opioid medicines and peripheral nerve blocks and performing central.[1] Caudal is a perioperative joint neuraxial surgery for pain relief in children after lower abdominal surgeries such as orchidopexy and hernia repair. In these circumstances, the primary medication is frequently local anaesthetics, which are not usually enough to cause lasting analgesia if provided alone in caudal.[2]
Regional anaesthetic methods have been encouraged for pain management in paediatric surgery because they reduce the need for parenteral opioids and improve postoperative pain control efficiency and patient-parent satisfaction.[3]
Caudal block is unique for its ease of application, safety, and efficacy. Caudal block techniques have grown in popularity in recent years, with local anaesthetics combined with adjuvants such as fentanyl, dexamethasone, neostigmine, morphine, ketamine,magnesium sulphate, clonidine, and dexmedetomidine being used. Using these adjuvants will prolong analgesia, resulting in a more extended period of initial analgesic desire and less opioid administration.[4]
Caudal epidural anaesthesia is widely used worldwide and is an attractive technique for providing adequate and gratifying analgesia for paediatric perioperative pain management. The most often employed local anaesthetic has been bupivacaine. However, systemic toxicity has been recorded despite dose recommendations.[5] Moreover, ropivacaine, a local anaesthetic that allows for epidural analgesia in adults, has been employed in children since it has been related to less neurotoxicity and cardiac depression than bupivacaine and induces a shorter duration of motor blockage. On the other hand, the average length of analgesia delivered by a single-shot approach is restricted.[6] Various medications have been added to local anaesthetics to increase the duration and quality of epidural analgesia. Clonidine appears to be one of the most appealing and safe adjuvants,

while ketamine has been shown to significantly extend postoperative analgesia in its racemic form. S-ketamine without preservatives has just been accessible for usage.[7]

Ketamine has been shown to have analgesic effects via caudal, epidural, and spinal pathways via several mechanisms, including cholinergic, N-methyl-d-aspartate (NMDA), adrenergic, and 5-hydroxytryptamine (or 5-HT) receptors, and also adrenergic and noradrenergic receptors. Because there is evidence that ketamine preservatives promote neurotoxicity, preservative-free ketamine formulations are suggested for neuraxial administration.[8]

Levobupivacaine outperforms racemic bupivacaine in terms of safety and postoperative motor block while providing the same analgesic effectiveness. Levobupivacaine has a lower affinity and severity of depressive effects on the heart and the central nervous system's important centres.[9]

AIM

This study examines the effectiveness and safety of caudal epidural injection of 1ml/kg of 0.25 percent levobupivacaine with 0.5mg/kg preservative-free ketamine with levobupivacaine alone in 60 children aged six months to eight years who had lower abdomen surgery.

MATERIALS AND METHODS

A randomised controlled study was conducted at the Institute of child health, anaesthesiology department, between September 2012 and October 2012. Sixty children between the age group 6 months to 8 years scheduled for elective lower abdominal surgeries, were randomly divided into two groups for study. The study started after the ethical committee's approval and written informed consent of parents or guardians.

Inclusion Criteria

Age between 6 Months to 8 Years, ASA-1 & 2, Surgery: Elective lower abdominal surgery, Duration: Less than 120 minutes.

Exclusion Criteria

Patient with suspected coagulopathy, uncontrolled systemic disorders, infection at the site of caudal block, known allergic to study drugs, patient with skeletal deformities, H/O developmental delay & neurological disease. Group L received a caudal epidural block with 1ml/kg of 0.25% levobupivacaine with 0.5mg/kg of preservative-free ketamine. Group K received a caudal epidural block with 1ml/kg of 0.25% levobupivacaine alone.

The primary outcome of the study was measured during the post-operative analgesic duration, whereas, the secondary outcome included pain, sedation, pulse rate, blood pressure, SPO2, and problems such as nausea and vomiting, respiratory depression, urine retention, and so on were evaluated at 0,1/2,1,2,3,4,5,6,8,10,12 hours postoperatively. The assessment was conducted by the staff nurse without the knowledge of group allocation, to maintain the randomisation of the study. The FLACC pain scale was used to measure pain, and rescue analgesia of syrup paracetamol 15mg/kg was administered if the pain score was four or above.

Statistical analysis was done using the SPSS software [version 16]. The quantitative data are expressed as mean (standard deviation) and median, and the qualitative data as frequency. For quantitative data like age, weight, intra-operative and postoperative blood pressure, pulse rate, and duration of rescue analgesia, used Independent Sample T Test (Unpaired Student T Test). The Mann-Whitney U Test is employed for ordinal data such as the postoperative FLACC pain score and the postoperative Ramsay Sedation Scale. Where applicable, qualitative data such as operation type and postoperative complications were analysed using chi-square and Fisher's exact tests.

RESULTS

Table 1: Distribution of Age, Gender, Surgery, and Complication of the studied population.

Variable		Frequency	Percentage
Age distribution	<2	9	15.0
	2-4	22	36.7
	4-6	12	20.0
	>6	17	28.3
Gender	Females	3	5.0
	Males	57	95.0
Surgery	Hydrocele	31	51.7
	Inguinal Hernia	29	48.3
Complications	None	49	81.7
	Urinary retention	6	10.0
	Both vomiting and nausea	5	8.3

(36.7%) of the children are between 2 and 4, while nearly half (48.3%) are older than 4. Most children (95%) are males, with females accounting for only 5%. Half of the surgeries (51.7 percent) were for Congenital Hydrocoele and the other half were for Inguinal Hernia Repair (48.3 percent). There were no postoperative

ISSN (O): 2687-5365; ISSN (P): 2753-6556

problems in 81.7 percent of the patients, urine retention in 10%, and nausea and vomiting in the remaining 8.3 percent. Figure 1 denotes the post-operative complication seen in the patients.

Table 2: Patient characterisation Age, Weight, and Duration of surgery.

Variable	Group	Mean and Std deviation	p-value
Age	Levobupivacaine	3.200 ± 1.8551	0.009
	Ketamine	4.650 ± 2.2558	
Weight	Levobupivacaine	11.90 ± 3.69856	0.019
	Ketamine	14.0667 ± 3.25823	
Duration of surgery	Levobupivacaine	29.83 ± 9.603	0.076
	Ketamine	35.00 ± 12.387	

The mean (S.D) of the age is 3.2 ± 1.8551, which is statistically significant between the levobupivacaine and ketamine groups. The mean (S.D) weight is 4.650 ± 2.258, which is also statistically significant between the levobupivacaine and ketamine groups. The mean (S.D.) surgical duration for the levobupivacaine and ketamine groups is (29.83 9.603) and (35.00 12.387), respectively. The difference in operation duration between the two groups is minor.

We have seen a significant difference in the mean arterial pressure (MAP) in the 1st hour (p = 0.038) and 2nd hour (p = 0.029) in the postoperative period. The use of ketamine anaesthesia had higher levels of MAP when compared with the levobupivacaine group. [Figure 2] denotes the overall measured MAP.

Figure 1: Observe post-operative complications in patients of Group L and Group K

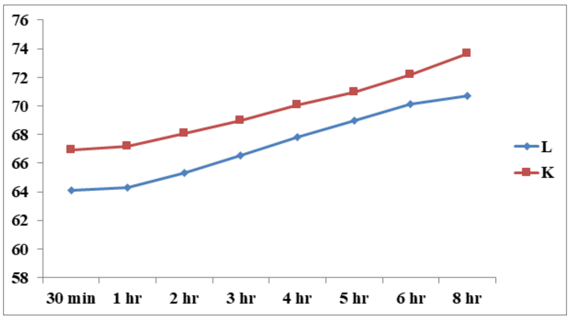

Figure 2: Measured levels of MAP during the post-operative period (L – denotes the group which was administered with levobupivacaine and K- denotes the MAP for group administered with ketamine)

In addition, we also assessed the pulse rate as one of the secondary outcomes in both groups, where we have seen that the group administered with ketamine had a lower pulse rate when compared with the other group. [Figure 3] portrays the significant difference in pulse rate measured during the post-operative period from 30 min to the 8th hour.

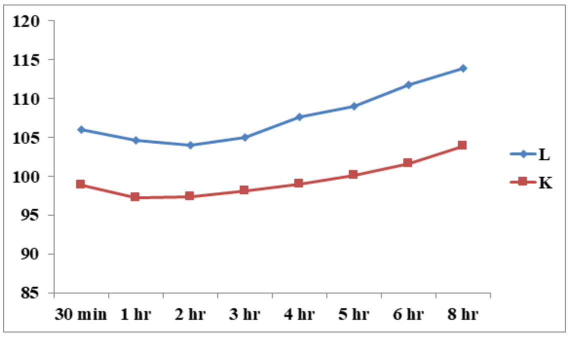

Figure 3: Post-operative assessment of pulse rate in both the groups

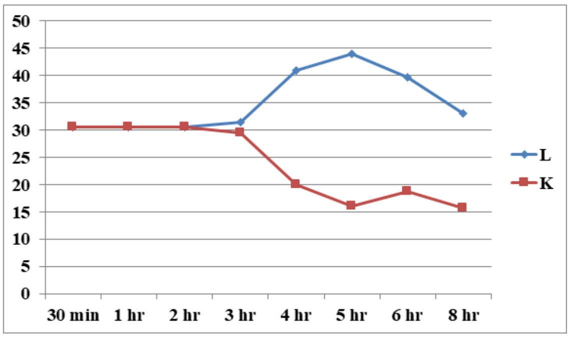

Figure 3: Postoperative FLACC pain score in both groups

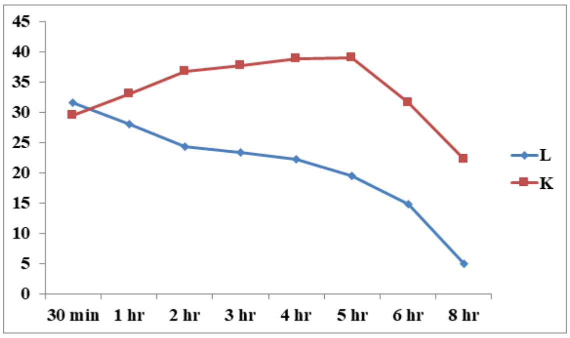

Figure 4: Post operative Ramsay Sedation Scale

Further to this, the assessment of the FLACC pain score and Ramsey Sedation Scale have revealed significant details about both groups. When we compared FLACC pain data for both the groups, it has seen that ketamine administration has shown a lower FLACC pain score than levobupivacaine after a 2-hour post-administration period. In addition, the ketamine group has also revealed a significant difference in the Ramsay Sedation Scale when compared with the other group. [Figure 3 and Figure 4] denote the overall significant difference in both groups with the scale assessment.

DISCUSSION

In children, caudal epidural anaesthesia is an efficient method of giving postoperative analgesia. In this study, we discovered that combining 0.5 mg/kg ketamine with 0.25 percent levobupivacaine 1ml/kg enhances the duration of postoperative analgesia. Unfortunately, due to infection concerns, caudal catheters are not commonly used for repeated doses or infusion of local anaesthetic solution. On the other hand, the inclusion of different adjuvants has resulted in the prolonging of caudal analgesia utilising a single-shot approach. Furthermore, caudal epidural anaesthesia gives adequate postoperative analgesia. As a result, it lowers the need for general anaesthetic while providing pain-free waking.

It reduces the danger associated with deeper planes of anaesthesia. In some circumstances, it may be possible to avoid using airway instrumentation. Furthermore, it allows for faster and more comfortable wake-up periods in the operating room, as well as speedier discharge and hence faster turnaround time in the post-anaesthesia care unit. Finally, it offers appropriate postoperative analgesia as part of a multimodal pain management strategy, including paracetamol, non-pharmacological support, and occasionally opioids.

The primary disadvantage of caudal anaesthesia is that it only lasts a short time after a single injection of local anaesthetic solution. Even long-acting local anaesthetics like bupivacaine only offer 4 to 8 hours of analgesia. Additionally, even a single dose of opioids can produce vomiting and respiratory depression and should be avoided to the greatest extent feasible. Regional blocks can therefore lessen the frequency of vomiting. Furthermore, it lowers unwanted reflexes linked with the anal sphincter and testis, which might result in laryngospasm.

To reduce systemic adverse effects, we employed ketamine at a lower dosage of 0.5 mg/kg in addition to levobupivacaine for the caudal epidural block in this trial. As a result, the ketamine intravenous analgesic dosage is greater than the caudal dose. Furthermore, it has a shorter duration of action and greater adverse effects.

Locatelli BG et al. reported a caudal block with levobupivacaine, and ketamine provides more excellent lasting analgesia than levobupivacaine alone.[10]

It is recommended in addition to local anaesthesia since it requires a larger dose to work as a solitary anaesthetic. However, if used solely, the risk of systemic toxicity increases due to increased systemic absorption. In addition, it is only used as a single shot bolus since continuous infusion through an epidural catheter is not recommended because it causes neural tissue damage.

Yentur EA et al. reported that benzethonium chloride and chlorobutanol are used in ketamine to produce neurotoxicity as preservatives. As a result, wherever feasible, utilise preservative-free ketamine.[11]

We observed that the duration of postoperative analgesia was extended in the ketamine group. The average duration of postoperative analgesia in the 'k' group was 10.40 minutes, while it was 5.93 minutes in the 'L' group. Therefore, 0.05 is the 'P' value.

Cook B et al. found that adding ketamine 0.5mg/kg to bupivacaine 0.25 percent (1ml/kg) results in a longer mean duration of postoperative analgesia following orchidopexy (12.5 hours) than clonidine 2mg/kg (5.8 hrs) or epinephrine 5mg /ml (3.2 hrs).[12]

In children having herniotomy, Naguib M et al. investigated the analgesic efficacy of bupivacaine 0.25 percent (1ml/kg) with and without ketamine 0.5 mg/kg.[13] Moreover, there was no significant difference in analgesia quality; only 7% of patients who got the ketamine and bupivacaine combination required any additional analgesia in the first 24 hours following surgery, compared to 20% and 50% of children who received ketamine and bupivacaine alone.

CONCLUSION

Our findings show that combining preservative-free ketamine with levobupivacaine in the caudal epidural block prolongs postoperative analgesia without significantly affecting hemodynamics compared to levobupivacaine alone. Thus, preservative-free ketamine in low doses can be used as an addition to local anaesthetics in caudal epidural anaesthesia to extend the analgesic effect.

REFERENCES

1. Boric K, Dosenovic S, Jelicic Kadic A, Batinic M, Cavar M, Urlic M, et al. Interventions for postoperative pain in children: An overview of systematic reviews. Paediatr Anaesth. 2017;27(9):893-904. doi: 10.1111/pan.13203.
2. Malik KM, Imani F, Beckerly R, Chovatiya R. Risk of Opioid Use Disorder from Exposure to Opioids in the Perioperative Period: A Systematic Review. Anesth Pain Med. 2020;10(1):e101339. doi: 10.5812/aapm.101339.
3. Suksompong S, von Bormann S, von Bormann B. Regional Catheters for Postoperative Pain Control: Review and Observational Data. Anesth Pain Med. 2020;10(1):e99745. doi: 10.5812/aapm.99745.
4. Abukawa Y, Hiroki K, Morioka N, Iwakiri H, Fukada T, Higuchi H, et al. Ultrasound versus anatomical landmarks for caudal epidural anesthesia in pediatric patients. BMC Anesthesiol. 2015;15:102. doi: 10.1186/s12871-015-0082-0.
5. De Negri P, Ivani G, Visconti C, De Vivo P. How to prolong postoperative analgesia after caudal anaesthesia with ropivacaine in children: S- ketamine versus clonidine. Pediatr Anesth. 2001;11(6):679-83.
6. Keyser CY. Caudal blockade for children undergoing infra-abdominal surgery. AORN J. 2014;100(3):306-22. doi: 10.1016/j.aorn.2013.10.027.

7. Beyaz SG, Tokgöz O, Tüfek A. Caudal epidural block in children and infants: retrospective analysis of 2088 cases. Ann Saudi Med. 2011;31(5):494-7. doi: 10.4103/0256-4947.84627.
8. Lundblad M, Lönnqvist PA. Adjunct analgesic drugs to local anaesthetics for neuroaxial blocks in children. Curr Opin Anaesthesiol. 2016;29(5):626-31. doi: 10.1097/ACO.0000000000000372.
9. Das A, Majumdar S, Kundu R, Mitra T, Mukherjee A, Hajra BK, et al. Pain relief in day care arthroscopic knee surgery: A comparison between intra-articular ropivacaine and levobupivacaine: A prospective, double-blinded, randomized controlled study. Saudi J Anaesth. 2014;8(3):368-73. doi: 10.4103/1658-354X.136435.
10. Locatelli BG, Frawley G, Spotti A, Ingelmo P, Kaplanian S, Rossi B, et al. Analgesic effectiveness of caudal levobupivacaine and ketamine. Br J Anaesth. 2008;100(5):701-6. doi: 10.1093/bja/aen048.
11. Yentur EA, Mirzai IT, Mirzai H, Ates U, Baka M, Yurtseven M. Repeated epidural injections of ketamine with preservative benzethonium chloride produce evidence for neurotoxicity in rabbits. Pain Clin. 2003;15(3):299-307.
12. Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia produced by bupivacaine in children. Br J Anaesth. 1995;75(6):698-701. doi: 10.1093/bja/75.6.698.
13. Naguib M, Sharif AM, Seraj M, el Gammal M, Dawlatly AA. Ketamine for caudal analgesia in children: comparison with caudal bupivacaine. Br J Anaesth. 1991;67(5):559-64. doi: 10.1093/bja/67.5.559.