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A Comparative Study of Caudal Epidural Injection of Morphine-Bupivacaine and Ketamine-Morphine-Bupivacaine Combination for Post-Operative Pain Management in Children

Authors
Dr Sukham Thoibahenba Singh[1], Dr Keisham Upendra Singh[2]
[1,2]Associate Professor, Dept. of Anaesthesiology, JNIMS, Imphal
Corresponding Author
Dr Keisham Upendra Singh
Associate Professor, Dept. of Anaesthesiology, JNIMS, Imphal, India

Abstract
Background: *It is an accepted fact that children and infants do feel pain and should be treated adequately. The importance and benefit of regional technique to ameliorate postoperative pain is well-known. Various drugs and combinations have been tried to find a best solution. This study is done to assess if Ketamine when added to Morphine and Bupivacaine in Epidural block improves the quality and duration of pain relief.*
Methods: *40 children were allocated to two groups- Group A was given 50 µg/Kg with 0.25% bupivacaine and Group B received ketamine 0.5 mg/Kg in addition. The degree of pain relief was compared between the two groups.*
Results: *It was observed that in Group A 20% of the children were pain free and majority of the patients (40%) required supplementary analgesia. 50% of the patients in Group B required no supplementary analgesia and the rest required mostly only 1 dose of supplementary analgesia in the next 72hours of post operative period.*
Conclusion: *It may be concluded that addition of ketamine 0.5 mg/Kg to morphine 50 µg/Kg and 0.25% bupivacaine administered through Epidural route provides better quality and the longer duration of analgesia in the post operative period.*
Keywords: *Postoperative Pain, Morphine, Bupivacaine, Ketamine, Caudal Epidural.*

Introduction

Management of pain in children for surgical procedures is often a problem as they are given proportionately less analgesics than adults. Commonly available modalities for children are oral preparations, IV narcotics and regional blocks[1,2]. Oral drugs like NSAIDS e.g. aspirin, acetaminophen, diclofenac, tramadol have their own side effects. The mainstay of treatment of postoperative pain is parenteral opiods. Morphine and pethidine are commonly used opiods but they are underdosed for fear of respiratory depression. Morphine is usually given at the dose of 50µg/kg intravenously at 2-4 hours interval. Newer synthetic opiods like fentanyl, sufentanyl and alfentanyl with lesser side effects and duration of action are also used. With the introduction of newer techniques like continuous intravenous infusion of opiods, patient controlled analgesia (PCA), caudal and epidural administration of continuous or intermittent opiods and anaesthetic preparation like bupivacaine, lignocaine, ketamine, clonidine etc.,pain management have invariably improved. Use of regional block for postoperative pain has been well established[1,3]. Still it is yet to find an ideal drug or combinations which will be easy to administer without any discomfort to last the entire postoperative period and without any undesirable side effects. Central neuroaxial block for postoperative pain is generally given with epidural injection of bupivacaine, opiods or combination of both or other drug combinations. Epidural morphine diffuses through the dura into the CSF and its action is due to agonistic activity on the opiod receptors in the spinal cord and by its rostral spread in the CSF resulting to interaction with central opiod receptors. Epidural bupivacaine acts on the dorsal nerve routes. Ketamine selectively reduces responses of central neurons to N-Methyl D-Aspartate. Epidural administration of bupivacaine or ketamine-bupivacaine or ketamine alone have been used for pain relief in children[4]. Attempts have been made to minimize the side effects of morphine by addition of other drugs. Thus, this double blind randomized control trial was planned to determine whether ketamine which is seemingly having a different mechanism of action is complimentary to the combined effects of morphine-bupivacaine when given through caudal route in paediatric age group and produce better quality of analgesia.

Material and Methods

40 children aged more than or equal to 1 year, of ASA I or II presenting for routine surgery other than head and neck surgery were selected after obtaining parental informed consent. Exclusion criteria were: patients with abnormal sacral hiatus, infected sacral area, allergy to study analgesics or anaesthetics. The patients were randomly allocated to any of the groups.

Pre-medication was done with oral diazepam 0.1mg/Kg 2 hours before surgery. Induction was done with O_2, N_2O and sevoflurane by face mask or intravenous thiopentone. Intubation was done with Succinylcholine 2mg/Kg or one of the non-depolarizing muscle relaxants vecuronium 0.1 mg/Kg or atracurium 0.5 mg/Kg. Anaesthesia was maintained by O_2, N_2O, sevoflurane and one of the non-depolarizing agents plus caudal block.

The study drugs administered were according to randomly assigned groups and were as follows:

Group A-Morphine 50 µg/Kg and 0.25% bupivacaine

Group B-Morphine 50 µg/Kg with 0.25 bupivacaine+ ketamine 0.5 mg/Kg

The volume of bupivacaine were as follows

Above T_{10}-1.25ml/Kg

Below T_{10}-1ml/Kg

Below L_1-0.5ml/Kg

The drugs were prepared by one of the supervisors and the principal investigator who was not aware of the drug, gave the caudal block and followed up. Rescue analgesic of IV morphine 50 µg/Kg was given if two or more of the following parameters namely sweating, increase in heart rate by 20% and lacrimation were noticed. Reversal was done with neostigmine 0.05 mg/Kg with atropine 0.02 mg/Kg at the end of the surgery.

Heart rate, SpO_2, ECG, NIBP and details of rescue analgesia were monitored and recorded at 15 minutes interval. Follow up was done at half-hourly interval for the first 3 hours and 6 hourly upto 72 hours. Postoperative analgesia was provided with pethidine 0.5 mg/Kg IV when VAS or modified VAS score >4 or in children less than 5 years when AIIMS score>4. HR, NIBP, rate of respiration, degree of pain relief, total dose and frequency of analgesic requested were recorded. Pain relief was assessed by VAS and AIIMS pain discomfort scale. Side effects like nausea, vomiting, urinary retention, pruritus and respiratory depression were recorded.

Observations and results are analyzed with the help of the Biostatics Dept. using suitable methods. All the patients data were fed into a microcomputer using Microsoft Excel software and data were analyzed using statistical package of excel supplemented with Microsoft package. Age and weight of the subjects were analyzed by Kruskal-Wallis test, sex determination was analyzed by Chi square analysis. As the children ranges from 1 yr. to 12 yr. and since basal physiological parameters (HR, BP, RR) varies with age, these parameters are subjected to statistical test using Chi square analysis by working out the proportion of the subjects whose parameters are more or less than 90th percentile for the particular age and sex. Intraoperative and postoperative physiological parameters were subjected to Descriptive Statistics and analyzed by working out the ranges of the individual subjects for all the measurement at different times and calculating the medians of the ranges. The median values of the range of change in HR, BP, RR, SPO_2, $EtCO_2$ were analyzed by Kruskal-Wallis test. Postoperative pain scores were compared by Chi square analysis by working out the proportion of those patients whose pain score readings were more than 4 as it is clinically relevant. Analgesia requirement in the two groups was compared with Chi square test by working out the proportion of subjects who required analgesia. Fisher exact test was incorporated wherever the proportion of these variables between two groups were compared. A p value of less than 0.05 was taken as statistically significant.

Results

The demographic profile of the two groups as shown in Table 1 were comparable and there was no statistically significant difference. The mean age and the standard deviation in years are 4.83 ± 3.69, and 5.25± 3.19 respectively (p=0.53). The mean weight and standard deviation are 14.85 ± 7.60 and 14.88 ± 5.05. M:F ratio are 14:6 and 13:7 respectively.

Table 1: Demographic Data

	Group A	Group B
Age in yr.(mean±S.D)	4.83 ± 3.69	5.25 ± 3.19
Weight in Kg(mean±S.D)	14.85 ± 7.60	14.88 ± 5.05
Male:Female	14:6	13:7

The type of surgery are grouped as thoracic and mediastinal, hepatobiliary, intestinal, renal and ureteric, urinary bladder and genital as listed in Table 2. There is no statistical significant difference (p=0.82).

Table 2: Type of Surgery

Type of surgery	Gr. A(no. of children)	Gr. B(no. of children)
Thoracic and mediastinal	1	2
Hepatobiliary	1	2
Intestinal	6	4
Renal and ureteric	9	9
Urinary bladder	2	2
Perineal and Genital	1	1
Total	20	20

The distribution of children according to the site of surgery in the two groups were also comparable and there was no statistically significant difference (p=0.68) as shown in Table 3.

Table 3: Site of Incision in Different Groups

	Gr. A(no. of children)	Gr. B(no. of children)
Upper abdominal & thoracic (>T_{10})	2	4
Abdominal (<T_{10})	17	15
Lower abdominal &perineal (<L_1)	1	1

The basal pulse rates, blood pressure and respiratory rates are shown and analyzed in Table 4. The no. of children having basal reading more than 90th percentile of specific age and sex were worked out. The parameters are comparable without any significance.

The change in intraoperative pulse rate and systolic blood pressure along with the basal values are compared in Table 5&6. The median of the ranges of intraoperative pulse rates in Groups A&B are 27.5 and 20 respectively. The median of the ranges of systolic of the two groups are 20&10. The values are comparable with no statistical significance.

Table 4: Basal PR, BP & RR

	Gr. A	Gr. B
PR(No of cases having >90th percentile)	6	7
BP(No of cases having >90th percentile)	5	5
RR(No of cases having >90th percentile)	2	0

Table 5: Descriptive Statistics of Ranges of Intraoperative Pulse Rates

	Gr. A	Gr. B
Mean	28.8	18.1
Median	27.5	20
Standard deviation	14.39	7.11
Range	53	25
Minimum	7	5
Maximum	60	30
Confidence level(95.0%)	6.74	3.33

Table 6: Descriptive Statistics of Ranges of Intraoperative BP

	Gr. A	Gr. B
Mean	23	13.95
Median	20	10
Standard Deviation	10.44	9.26
Range	35	40
Minimum	5	0
Maximum	40	40
Confidence level(95%)	4.89	4.33

The changes in the postoperative pulse rates, systolic BP and respiratory rates at various time intervals were also compared. The mean ± standard deviations of the ranges of postoperative pulse rates are 35.2 ± 12.16, and 29.4 ± 7.51 and the medians are 36&30 respectively (Table 7). The mean ± standard deviation of the ranges of postoperative systolic BP are 17.45 ± 7.24 and 13± 4.52 with 18,10 being the medians of the ranges (Table 8). The mean ± standard deviation of the ranges of postoperative respiratory rates are 11.95 ± 3.47 and 11 ± 2.2 with medians of the ranges being 12&11 respectively (Table 9). No statistically significant difference was found.

Table 7: Descriptive Statistics of Ranges of Postoperative Pulse

	Gr. A	Gr. B
Mean	35.2	29.4
Median	36	30
Mode	20	36
Standard Deviation	12.16	7.51
Range	42	30
Minimum	20	10
Maximum	62	40
Confidence level(95.0%)	5.69	3.52

Table 8: Descriptive Statistics of Ranges of Postoperative Systplic BP

	Gr. A	Gr. B
Mean	17.45	13
Median	18	10
Standard Deviation	7.24	4.52
Range	22	14
Minimum	10	6
Maximum	32	20
Confidence level(95.0%)	3.39	2.11

Table 9: Descriptive Statistics of Ranges of Postoperative RR

	Gr. A	Gr. B
Mean	11.95	11
Median	12	11
Standard Deviation	3.47	2.20
Range	14	8
Minimum	8	6
Maximum	22	14
Confidence level(95%)	1.62	1.03

Pain scores were recorded initially at half-hourly interval upto the first 3 hours and then at 6 hourly intervals postoperatively. The no. of subjects with pain score >4 were directly compared. Upto 36 hours Group B had less no. of children with pain score >4. The finding is statistically significant at 6 hr & 12 hr but at 18 hr onwards the difference was not significant. (Table 10). None of the children required rescue analgesia.

Table 10: Number of Patients Whose Pain Score >4

	6 hr	12 hr	18 hr	24 hr	30 hr	36 hr	54 hr
Gr. A	*3	**7	4	10	4	2	1
Gr. B	0	0	1	6	1	0	0

*Statistically significant p=0.04
**Statistically significant p=0.006

The narcotic analgesic requirement during intraoperative and postoperative period at various time intervals were noted in terms of no. of subjects requiring the same and total no. of doses required. 13 subjects in Group A & 5 in Group B required narcotic analgesia during intraoperative period (Table 11). The difference was found to be significant (p=0.019).

Table 11: Number of Subjects Requiring Intraoperative Narcotic

	No. of subjects	No. of doses	Mean dose
Gr. A	*13	16	0.8
Gr. B	5	8	0.4

*Statistically significant p=0.019

The no. of children who received various doses of narcotics are shown in Table 12. 4 children in Gr. A and 12 children in Gr. B did not require any postoperative narcotic. 3 children in Gr. A required 3 doses and 1 child required 4 doses while none in Gr. B required more than 2 doses of narcotics. The difference in the two groups is strongly significant (p=0.0005).

Table 12: No. of Subjects Receiving Postoperative Doses of Narcotic

	0 dose	1 dose	2 doses	3 doses	4 doses
Gr. A	*4	**4	***8	****3	1
Gr. B	12	7	1	0	0

*Statistically significant p=0.035
**Statistically significant p=0.0316
***Statistically significant p=0.0006
****Statistically significant p=0.0425

Complications like nausea & vomiting, pruritus and respiratory depression were monitored. There were 4 cases of nausea & vomiting in both the groups, 1 case of pruritus in both the groups was reported. There were no serious side effects like respiratory depression and no statistical significant difference seen.

Table 13: Number of Subjects with Complications

	Vomiting	Pruritus	Respiratory depression
Gr. A	4	1	0
Gr. B	4	1	0

Discussion

Children and infants do also feel pain and untreated or undertreated pain can cause psychological and physiological harm[2,5]. The benefit of regional techniques for pain management is undoubted[3]. Use of local anaesthetic alone is limited by the shorter duration of action and lack of postoperative sedation[6]. Combination of bupivacaine with morphine have shown to improve and prolong analgesia. Combination of bupivacaine with drugs like ketamine[7-10] have been used with improvement in the quality and duration of analgesia. Studies on pain management using single bolus[11] have been carried out for minor lower abdominal operations where the degree and duration of pain is mild to moderate. But for major operations pain relief is necessary to prevent postoperative respiratory complications. So in this study all different operations were included and follow up period was extended upto 72 hrs.

Morphine, when used in the caudal route, had been administered in different doses ranging from 30-100 µg/Kg[12,13.] In this study only 50 µg/Kg was administered in both the groups. Ketamine 0.5 mg/Kg in children undergoing lower abdominal procedure was found to produce good analgesia[14,15].

Duration of analgesia with caudal morphine 50 µg/Kg has been shown to be 20.5 ± 3.6 hr. by Jensen et al[13] & 19.5 ± 1.6 hr by Dalens et al[15.] In our study we observe that children receiving morphine-bupivacaine had a median duration of action of 6-12 hrs. In morphine- bupivacaine-ketamine group 50% of the patients did not require any supplementary analgesic in the entire postoperative follow up period of 72 hrs. Rest of the patients except one who received 2 doses, required only 1 supplemental dose of analgesia at the median time interval of 18-24 hrs.

However, addition of ketamine to morphine-bupivacaine has increased the duration of action and intensity of pain relief in our study as 50% of the patients did not require any additional analgesic. Complications like nausea, vomiting, pruritus &urinary retention were seen with caudal administration of drugs notably with opiods Atia et al[12] & Wolf et al[16] reported 39% & 40% incidence of nausea & vomiting with 50 µg/Kg caudal morphine respectively. In this study, there were 10% incidence of pruritus in Gr.A&B and incidence of nausea & vomiting are similar. This suggest that with addition of ketamine to morphine- bupivacaine, morphine dose could be reduced with similar analgesic effect and probably less of side effects. This could be probably be due to potentiation of action of morphine by ketamine. The different sides of analgesic action of the two drugs makes them complimentary in producing complete analgesia.

Conclusion

It may be concluded that addition of ketamine 0.5 mg/Kg to morphine 50 µg/Kg and bupivacaine 0.25% administered through epidural route for postoperative pain relief in children undergoing major surgical procedures provides better quality and duration of analgesia in the post operative period.

References

1. Haberkern CM, Donald CT, Krane EJ. Post operative pain management in children. Mount Sinai Journal of Medicine 1991;58: 247-256.
2. VenKeuren K and Eland JA. Postoperative pain management in children. Nursing Clinic of North America 1997;32: 31-44
3. Howard R. preoperative and postoperative pain control. Archives of Disease in Childhood 1993;69: 699-703
4. Naguib M, Sharif AMY, Seraj M, Gammal ME and Dawlatly AA. Ketamine for caudal analgesia in children comparison with caudal bupivacaine. British Journal of Anaesthesia1991;67: 559-564
5. Chugani HT, Phelps ME. Maturation changes in cerebral functions in infants determined by FDG positron emission tomography. Science 1986;231: 840-843
6. Wolf AR and Hughes D. Pain relief for infants undergoing abdominal surgery: comparison of infusion of I.V. morphine and extradural bupivacaine. British Journal of Anaesthesia 1993;70: 10-16
7. Findlow D, Aldridge LM and Doyle E. Comparison of caudal block using bupivacaine and ketamine with ilioing-uinal nerve block for orchidopexy in children. Anaesthesia1997;70: 10-16
8. Nalini V, Erika S, et al. Role of ketamine for analgesia in adults and children. Journal of Anaesthesiology Clinical Pharmacology 2016;32(3): 298-306.
9. Mendonça FT, Almeida MFC, Guimarães CCR et al., Comparative study between epidural ketamine and morphine in patients submitted to mastectomy. Rev Dor. São Paulo, 2013;14(3):169-73
10. Sethi M, Sethi N, Jain P, Sood J. Role of epidural ketamine for postoperative analgesia after upper abdominal surgery. Indian J Anaesth 2011;55:141-5.
11. William MS, Juan B, Lydia K. Regional anaesthesia for hernia repair in children: local vs. caudal anaesthesia. Canadian Journal of Anaesthesia 1995;42: 197-200
12. Atia J, Ecoffey C, Sandouk P, Gross JB and Samil K. Epidural morphine in children pharmacokinetics and CO_2 sensitivity. Anesthesiology 1986;65: 590-594.

13. Jensen BH, Caudal block for postoperative pain relief in children: a comparison between bupivacaine and morphine. Acta Anaesthesiologica Scandinavica 1981;25: 373-375.
14. Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia by bupivacaine in child. British Journal of Anaesthesia1995;75: 698-701.
15. Dalens B, Tanguy A, Haberer JP. Lumbar epidural anaesthesia for operative and postoperative pain relief in infants and young children. Anesthesia and Analgesia1986;65: 1069-1073.
16. Wolf AR, Hughes D, Wade A, Mather SJ and Prys-Roberts C. Postoperative analgesia after paediatricorchidopexy evaluation of a bupivacaine-morphine mixture. British Journal of Anaesthesia 1990;64: 430-435.