# Comparative Study of Spinal Anesthesia by Bupivacaine Heavy (0.5%), Bupivacaine Heavy (0.5%) with Ketamin or Midzolam in Paediatric Patients

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**ABSTRACT:**

**Background:** *Various anatomical and physiological differences make neural blockade in paediatric surgery different from that in adults .Recent availability of preservative free midazolam and ketamine used as adjuvants, prompted us to take up this study to explore the advantages to be gained by the use of these adjuvant drugs in spinal anaesthesia. The aim of this study was to evaluate spinal anaesthesia in children by using 0.5% bupivacaine which and either preservative free ketamine of preservative free midazolam adjuvants to 0.5% bupivacaine.*

**Materials and Methods:** *In 60 patients of 7-12 age group years posted for routine surgeries below the level of umbilicus were included after fitness according to ASA grading I and II. Group I received spinal anaesthesia using bupivacaine heavy 0.5%, Group II received spinal anaesthesia using bupivacaine heavy 0.5% with preservative free ketamine, Group III received spinal anaesthesia using bupivacaine heavy 0.5% with preservative free midazolam.*

**Observation:** *There was statistically no significant ($p>0.05$) difference between mean values of onset of sensory blockade (min) and height of sensory blockade in the three groups. While statistically highly significant ($p<0.01$) difference of mean duration of motor blockade, time of two segment regression and duration of post operative analgesia was found. The commonest adverse effects were shivering, nausea and vomiting. Only in group I, 4 cases require supplementation of general anaesthesia as surgical procedures outlasted the duration of sensory blockade of bupivacaine.*

**Conclusions:** *The time of onset of sensory block of bupivacaine was not significantly affected by the addition of adjuvants namely ketamine and midazolam. The duration of postoperative analgesia was significantly prolonged by addition of ketamine and midazolam. The addition of ketamine and midazolam to bupivacaine did not produce significant complications attributable to them.*

**Key words:** *Spinal anaesthesia, Bupivacaine, Ketamine, Midazolam.*

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## INTRODUCTION

Various anatomical and physiological differences make neural blockade in paediatric surgery very different from that in adults. Embryological development is incomplete at birth and many organs and their functions are not fully mature[(1)]. Myelin is a lipid layer; the degree of myelination of nerve fibres influences considerably the pharmacodynamic effects of local anaesthetics. Complete myelination is not achieved until the end of 12 years of age. This lack of myelination in young patients favors the action of local anaesthetics by better penetration into the nerve fibres[(1,2)].

High lipid solubility makes bupivacaine a potent local anaesthetic agent with increased lipophilicity. After subarachnoid administration of bupivacaine, absorption is attributed to spread of bupivacaine away from the site of injection, uptake by the nerve tissue and vascular absorption.[(1,3)]availability of better, safer local anaesthetic agents, better understanding of their pharmacological effects in children and lesser haemodynamic effects in children have led to a renewed interest in paediatric spinal anaesthesia.

Studies have proved that spinal anaesthesia in children is a safe and very useful technique in normal as well as high risk children and is a definite alternative to general anaesthesia.[(4)]Recent availability of preservative free midazolam and ketamine used as adjuvants, have further enhanced the safety and efficacy of paediatric spinal anaesthesia, which prompted us to take up this study to explore the advantages to be gained by the use of these adjuvant drugs in spinal anaesthesia. Midazolam is a newer benzodiazepine, which has a shorter duration of action and high potency. Midazolam is the only benzodiazepine approved for use in neonates.

The changes in arterial blood pressure are minimal with spinal anaesthesia in patients up to 8 years of age[(5)]. Found there was a significant inverse linear correlation between time to recovery and age.

Accordingly, they concluded that only those surgeries requiring one hour or so can be done under spinal anaesthesia in children.

To prolong the duration of spinal anaesthesia and to give substantial postoperative analgesia, various drugs were tried as adjuvants to local anaesthetics. Combined with Bupivacaine in caudal block for post operative analgesia morphine[6], clonidine[7], Ketamin[8], midzolam[9] found to produced post operative analgesia of 20 hours. The aim of this study was to evaluate spinal anaesthesia in children aged 7-12 years posted for below umbilical surgeries by using 0.5% bupivacaine which acted as a control group and using either preservative free ketamine of preservative free midazolam as adjuvants to 0.5% bupivacaine. Evaluation of duration of postoperative analgesia, requirement of supplementation of anaesthesia in case of failure or inadequacy of effects and complications if any was noted.

## MATERIALS AND METHODS

In our study, after obtaining the approval of the ethical committee, 60 patients, in the age group of 7-12 years posted for routine surgeries below the level of umbilicus were selected. Care was taken to exclude the patients who were found to have spinal deformity and congenital anomalies, local infection or sepsis at the injection site, any decompensated systemic disorder and bleeding disorders including anticoagulation therapy. Parental refusal was also included in exclusion criteria.

All children were examined and assessed pre-operatively for anaesthetic fitness with respect to ASA grading I and II. Routine investigations were done. Nature of anaesthesia to be given was explained to the patients and parents and valid, written consent was obtained from the parents. Children were not allowed solid food for 6 hours before surgery but clear fluids were allowed up to 2 hours before commencement of anaesthesia. Intravenous line was established with 22G intravenous cannula.

**Premedication:** All the patients were given injection midazolam 0.03 – 0.05 mg/kg body weight intravenously for sedation and restraining during lumbar puncture. The patients were randomly allocated into 3 groups consisting of 20 patients each.

**Group I:** Received spinal anaesthesia using bupivacaine heavy 0.5% in the dose of 0.06 ml/kg body weight, **Group II:** Received spinal anaesthesia using bupivacaine heavy 0.5%-0.06ml/kg + preservative free ketamine 0.5 mg/kg body weight, **Group III:** Received spinal anaesthesia using bupivacaine heavy 0.5%-0.06ml/kg + preservative free midazolam 0.02 mg/kg body weight.

**Technique:** Before starting the procedure pulse rate, blood pressure, respiratory rate and oxygen saturation were recorded. All the children were placed in the left lateral position. Painting and draping was done with aseptic precautions.

Lumbar puncture was done in the L4-5 interspace with 25 G spinal needle with stylette and the direction of the bevel was kept parallel to longitudinal fibres of dura with spinal anesthesia as per respective groups. Close monitoring of pulse rate and blood pressure was done throughout the procedure. Time of onset of sensory block was assessed by pin prink and response noticed by face grimace or pain acknowledgement to pinprink. Onset of motor block was judged by observing the progress of paralysis in the legs and anterior or lateral abdominal muscles as the child cried or coughed. The paralyzed muscles bulged outward while the non paralyzed muscles contracted inwards during expiration.

The duration of anaesthesia was considered as the time interval between injection of drug and the time of reappearance of the movements of the feet.Spinal anaesthesia was considered satisfactory if the child was free of pain during surgery and no supplementary agents other than midazolam intravenously were necessary for sedation. We considered fall in systolic blood pressure more than 30% of baseline as a hypotension. Similarly fall in heart rate more than 30% of baseline was considered as bradycardia.

Postoperatively pulse, blood pressure and respiratory monitoring was continued for half an hour in post anaesthesia care unit and thereafter in the wards. Duration of post operative analgesia was noted. Patients was visited daily till their discharge from hospital to find out development of any complication of the technique.

## STATISTICAL ANALYSIS

Qualantitative data was presented in tabular form as mean, standard deviation and range (minimum to maximum). Qualitative data was compared using Chi square test. Analysis of Variance (ANOVA) with post-Hoc statistical test was used to compare pairwise difference of means in between the three groups.

## OBSERVATION

Maximum numbers of patients in all three groups were in the age group of 7-10 years. By applying $\chi^2$ test there is no significant difference in the distribution of age in all three groups. Mean age in Group I was 9.4 years, in Group II was 9.2 years and in Group III was 9.6 years. Statistical significance level (p value) of 0.05 was decided to state statistical difference in between the groups.

As shown in Table 1, there is statistically no significant ($p>0.05$) difference between mean values of onset of sensory blockade (min) and height of sensory blockade in the three groups. While statistically highly significant ($p<0.01$) difference of mean duration of

motor blockade, time of two segment regression and duration of post operative analgesia was found.

Pairwise comparison cancelled a highly significant ($p<0.01$) difference of mean motor blockade duration in either of the three groups.

Group I vs Group II, $t = 15.31$, $p < 0.01$, Group I vs Group III, $t = 12.48$, $p < 0.01$ and Group II vs Group III, $t = 6.23$, $p < 0.01$.

There was a highly significant ($p < 0.01$) mean difference of two segment regression time when compared in the three groups.

Group I vs Group II, $t = 9.21$, $p < 0.01$, Group I vs Group III, $t = 2.87$, $p < 0.05$ and Group II vs Group III, $t = 6.49$, $p < 0.01$.

Also a highly significant ($p<0.01$) difference of post operative analgesia was noted in three groups.

Group I vs Group II, $t = 16.75$, $p < 0.01$, Group I vs Group III, $t = 8.31$, $p < 0.05$ and Group II vs Group III, $t = 4.92$, $p < 0.01$, highly significant.

As shown in Table 2, there was a highly significant($p < 0.01$) difference between mean values of preoperative and maximum intraoperative fall in systolic blood pressure in between group I and group III while there is no significant difference in group II ($p > 0.05$). Highly significant difference between mean values of preoperative and maximum intraoperative fall in heart rate (beats/ min) in group I and group III ($p < 0.01$) while there is no significant difference in group II ($p > 0.05$).

The commonest adverse effects were shivering, nausea and vomiting. High or complete spinal blockade was not noted in any case. Only in group I, 4 cases requires supplementation of general anaesthesia where surgical procedures outlasted the duration of sensory blockade of bupivacaine.(Table 3)

**Table 1: Time of Onset of sensory blockade:**

| Variables | | Group I | Group II | Group III | P value |
|---|---|---|---|---|---|
| **Time of Onset(min)** | Mean ± SD | 5.14±1.2 | 4.98±1.01 | 5.06±1.31 | >0.05 |
| | Range | (4-6) | (3-6) | (4-6) | |
| **Height of sensory blockade (thoracic segment)** | Mean ± SD | 5.4±1.02 | 5.8±1.11 | 5.02±1.15 | >0.05 |
| | Range | (T4-T10) | (T5-T10) | (T4-T10) | |
| **Duration of motor blockade(min)** | Mean ± SD | 83.2±8.2 | 120.1±7.01 | 103.9±9.31 | <0.01 |
| | Range | (75-100) | (110-130) | (100-115) | |
| **Time to two segment regression (min)** | Mean ± SD | 84.2 ± 8.2 | 106.6 ± 7.01 | 100.1 ± 7.31 | <0.01 |
| | Range | (75-100) | (100-120) | (90-110) | |
| **Duration of post operative analgesia (hours)** | Mean ± SD | 1.34±0.52 | 6.2±1.2 | 2.9±1.31 | <0.01 |
| | Range | (1-2) | (4-12) | (2-6) | |

**Table2: Haemodynamic parameters**

| Haemodynamic parameters | Time of recording | Group I (n = 20) Mean ± SD | Group II(n = 20) Mean ± SD | Group III(n = 20) Mean ± SD |
|---|---|---|---|---|
| **Systolic blood pressure (mm of Hg)** | **Preoperative** | 116.2±17.2 | 112.6±18.2 | 116.3±12.31 |
| | **Maximum intraoperative fall (%)** | 90.6 ± 15.5 (25.6%) | 104.6±14.4 (8%) | 92.5±14.41 (23.8%) |
| | **Postoperative** | 100.4±16.23 | 110.0±12.3 | 98.6±12.39 |
| **Heart rate (beats / min)** | **Preoperative** | 94.2±9.2 | 93.62±11.2 | 91.5±9.31 |
| | **Maximum intraoperative fall (%)** | 78.6 ± 7.59 (15.6%) | 88.6±9.44 (5.02%) | 76.4±8.91 (15.1%) |
| | **Postoperative** | 84.2 ±10.23 | 92.3±9.3 | 81.5 ±9.99 |

**Table3: Complications.**

| Complications | Group I (n = 20) | Group II (n = 20) | Group III (n = 20) |
|---|---|---|---|
| **Bradycardia** | 2 | 0 | 1 |
| **Hypotension** | 3 | 0 | 0 |
| **Post dural puncture headache** | 2 | 1 | 0 |
| **Shivering** | 7 | 1 | 3 |
| **Nausea/ vomiting** | 5 | 2 | 1 |

## DISCUSSION

Better understanding of phamacodynamics and pharmacokinetics of local anaesthetics in paediatrics age group lead to use of spinal anesthesia in childrens. Recommendation of regional anaesthesia for surgeries in children is based largely on impressions gained from clinical experience rather than on detailed and prospective outcome studies. Now with better appreciation of the technique it is becoming more popular, though it has few limitations. The main factor of concern is the duration of action of local anaesthetics in spinal anaesthesia for children.

The shorter duration of action of local anaesthetics in children is related to the larger volume of CSF (4ml/kg body weight vs. 2ml/kg body weight in adults), different diameter and surface area of spinal cord and nerve roots, higher cardiac output per kg of body weight, relatively faster uptake and elimination of drug from CSF, smaller lower extremity volume as a fraction of total blood volume and larger size of liver.

To overcome the limitations and to exploit the maximum advantages of the techniques, several studies have been done using various drug combinations to prolong the duration of spinal anaesthesia. Mohamed & Mohamed[9]in their study compared bupivacaine 0.25% only and midazolam 50µgm/kg with saline. The authors found that the mean duration of postoperative analgesia was increased up to 12 hours and the group combining midazolam and bupivacaine required less number of analgesia in postoperative period, as evident by the analgesic requirement of the patients. Study in infants using isobaric bupivacaine found that addition of epinephrine did not significantly change the duration of anaesthesia of bupivacaine[10].Preservative free ketamine with 0.5% bupivacaine heavy for spinal anaesthesis caused the duration of analgesia of 4-12 hours and was definitely batter than bupivacaine alone[11]. With the same intentions of full exploitation of the technique to obtain maximum benefits we in this study combined preservative free midazolam and or ketamine with 0.5% bupivacaine and used 0.5% bupivacaine as a control group.

***Onset of sensory block:***

In our study the mean time of onset of action of sensory block was 5.14±1.2 minutes in group I, in group II in was 4.98±1.01 and in group III was 5.06±1.31 minutes, thus there was no significant variation in the time of onset of sensory block with the addition of ketamine and midazolam to bupivacaine.

Mahe et al[10] in their study of spinal anaesthesia in infants found isobaric bupivacaine with epinephrine, the time of onset of action of bupivacaine was less than 2 minutes and miximum level of analgesia was reached at 10 minutes as judged by pinprick. Singh et al[11] found that the mean time of onset of sensory block observed by pinprick was 3.7 minutes (range 3-6 minutes) and no significant variation occurred with addition of ketamine to bupivacaine. Kokki et al[12] while studying spinal anaesthesia using isobaric and hyperbaric bupivacaine proposed that in the age group of 1-7 years, onset may be prolonged up to 30 minutes and delayed spinal anaesthesia may develop in paediatric patients. Bajaj et al[13] found that the onset of sensory and motor blockade was potentiated by intrathecal midazolam.

***Height of sensory block:***

In our study the mean height of sensory blockade in group I was T 5.4±1.02 after 15 minutes after injection of drug. While in group II was T 5.8±1.11 and in group III it was T 5.2±1.15.Mahe et al[10] concluded that addition of epinephrine made no significant difference in the height of sensory blockade. Kokki et al [12] found the mean height of the sensory blockade was T4 and the cephalic spread was variable and unpredictable in both isobaric and hyperbaric bupivacaine. Also Kokki et al[14] found that mean height of sensory blockade with spinal anaesthesia using 0.5% bupivacaine, isobaric and hyperbaric was T4.8±2.7 while epidural anaesthesia yielded level of T6.5±3.0.

The height of spinal anaesthesia blockade is altered by important factors being position of patients, baricity of the drug injected, rate of injection of drug, direction of injection needle, dosage (mass of drug), and temperature of the drug injected. The mean height of sensory blockade was slightly (1-2 segment) less than previous studies. This might be due to slower rate of injection of drug intrathecally and placing a pillow under the shoulders after the patient was made supine. Thus the additive drugs in our study did not alter the mean height of sensory blockade of bupivacaine.

***Degree of motor blockade and duration of motor blockade:***

Mahe et al[10] found complete motor blockade for 70±25 minutes in both groups using isobaric 0.5% bupivacaine with or without epinephrine and addition of epinephrine made no significant difference. Singh et al[11] observed excellent relaxation, and duration of motor blockade was adequate for surgical procedure using preservative free ketamine 50mg with 0.5% bupivacaine. Kokki et al[12] studied in children found adequate relaxation for surgery below the level of umbilicus.

Marhofer P[8] concluded that ketamine produces muscle relaxation equivalent to bupivacaine. The analgesia produced by ketamine was equivalent to the combination of bupivacaine and epinephrine and only 30% of the patients required additional analgesics during postoperative period. Bajaj et al[13] found that midazolam with 5% xylocaine for spinal anaesthesia potentiated the onset and prolonged the duration of motor blockade.

In our study the duration of motor blockade in group I was 83.2±8.2 minutes which is consistent with

previous studies using bupivacaine heavy in children's. The duration of motor blockade was 120.1±7.01 minutes in group II and 103.9±9.31 in group III. The duration of motor blockade in group II and group III was significantly more than group I. Thus the preservative free addictive drugs have prolonged the duration of motor blockade which was consistent with previous studies.

***Time to two segment regression:***

The time of two segment regression in group I was 84.2±8.2 minutes, 106.6±7.01 minute in group II and 100.1±7.31 minutes in group III. Thus there was significant prolongation of time to two segment regression in group II and group III as compared to control group I. Kokki et al[12] found that the time to two segment regression of block was 80 min (55-90 min) in isobaric bupivacaine and 80 min (30-190 min) in hyperbaric bupivacaine. Authors[15] while studying hyperbaric bupivacaine in 7 to 18 years found time for regression of block by two segments was 83 minutes (50-143) in group I and 85 minutes (53-150) in group II. Marhofer P et al[8] concluded that ketamine 1mg/kg for caudal block in children produced surgical and postoperative analgesia equivalent to that of bupivacaine. The mean duration of analgesia in this group was 273±123 minutes. Bajaj et al[13] found the duration of sensory block with xylocaine was 55.2±2.35 minutes while when xylocaine with midazolam was used it was 99.9±3.14 minutes.

Thus the prolongation of time of two segment regression of bupivacaine by addition of midazolam and ketamine in our study was consistent with the similar previous studies in paediatric and adult patients.

***Duration of postoperative analgesia:***

In our study patients remained pain free i.e. VAS of 0 to 3 (analgesia-60-90%) was noted. the duration of postoperative analgesia, was significantly prolonged in group II and III. The duration was maximum in group II 6.2±1.2 hours, in group III it was 2.9±1.31 hours as compared to 1.34±.052 hours in group I. Valentine et al[16] found that postoperative analgesia was better in the groups containing midazolam and diamorphine with bupivacaine. The adverse effects were minimal in a group containing midazolam.

Singh et al[11] found that the combination ketamine to bupivacaine provided postoperative analgesia for 4-12 hours and was definitely better than bupivacaine alone. Kokki et al[12] found that the duration was 110 min (53-270).Bajaj et al[13] concluded that addition of midazolam through intrathecal infusion produced better analgesic and sedation than local anaesthetic alone with minor adverse effects.

Thus in all the above studies, the duration of postoperative analgesia was significantly prolonged by addition of preservative free midazolam and ketamine. And the results are consistent with our study.

***Haemodynamic Parameters:***

In group I 15.6% of fall in heart rate and 25.6% of fall in systolic blood pressure intraoperative occurred. In group II 5.02 % of fall in heart rate 8%. In group III percentage fall in heart was 15.1% while systolic blood pressure decreased by 23.8%.

Thus, haemodynamic variations occurred in children with maximum haemodynamic stability was maintained in group II in which ketamine was added. While the changes occurred in group I and III were comparable. Mahe et al[10] foundisobaric bupivacaine in infants with or without epinephrine decreases in arterial blood pressure and moderate changes in heart rate occurred in both the groups. The maximum decrease in systolic blood pressure observed was at 12±6 minute in group I and was averaged 24±13% and in group II it was observed at 10±5 minutes and averaged 23±11%.

Kokki et al[12] remarkable stability was observed, but the same authors[15] found children having hypotension and bradycardia and concluded that 7-18 years children were not as haemodynamically stable as infants during spinal anaesthesia. Valentine et al[16], Bajaj et al[13] used preservative free midazolam with bupivacaine in patients and found minimal effects of midazolam on intraoperative haemodynamics.

Thus, in the age group of 7-12 years haemodynamic changes do occur with bupivacaine spinal anaesthesia but to a lesser extent than adults which correlates with our study. While midazolam produced no effect on haemodynamics changes, addition of ketamine helped to maintain stable haemodynamic parameters intraoperatively.

***Complications:***

In our study in group I, 2 patients out of 20 had bradycardia and required treatment with atropine and 1 patient on group III required similar treatment for bradycardia. No patients from group II in which ketamine was added had bradycardia requiring treatment. Likewise, 3 patients in group I had hypotension intraoperatively and no patients in group II and III had hypotension.

The headache was typically postural in nature and in one case was associated with nausea and vomiting. Postoperative shivering was most common adverse effect in our study. In group II No patient from this group had any additional adverse effects like hallucinations or emergence attributed to ketamine. The dose of ketamine used was very low. Use of midazolam in the dose of 0.03-0.05 mg/kg body weight intravenously as a premedication could have contributed to the absence of emergence reaction or hallucination. In our study in group III preservative free midazolam also no adverse effects attributable to midazolam were reported except some cases in which

patients remained sedated for some period postoperatively. The haemodynamic stability seen during paediatric spinal anaesthesia is well established.

Dohi et al[5] attributed it to proportionally smaller volume of blood in lower limbs to total blood volume. Also children have relatively immature sympathetic system. The authors in there study found patients with bradycardia and hypotension requiring treatment. Singh et al[11] found very low incidence of systemic toxicity of ketamine. Only 6% patients had mild delirium and hallucinations which were easily managed by i. v. diazepam. Kokki et al[12] on paediatric spinal anaesthesia found that the incidence of postdural puncture headache in children was low and various needles used yielded similar results. The authors found isobaric and hyperbaric bupivacaine found only three children developed position dependant headache with duration of 2-3 days. All cases had mild headache and no epidural blood patch was done. Kokki et al[15] found few cases of bradycardia and hypotension requiring treatment and shivering in post anaesthesia care unit. The authors concluded that the cardiovascular stability was more in smaller children than the school age children and avoidance of extended block was also essential to avoid hypothermia. Marhofer P et al (8) found no systemic adverse effect at low ketamine dose.

Thus the overall incidence of complications in our study was less and it was consistent with the previous studies. The addition of preservative free drugs to bupivacaine in very low doses did not produce any significant adverse effects in patients.

## CONCLUSIONS

The time of onset of sensory block of bupivacaine was not significantly affected by the addition of adjuvants namely ketamine and midazolam. There was no significant variation in the mean height of sensory blockade of bupivacaine on addition of adjuvant drugs. There was no significant difference in the degree of motor blockade in all 3 groups. The group receiving ketamine remained more hemodynamically stable as compared to bupivacaine or bupivacaine with midazolam. The duration of postoperative analgesia was significantly prolonged by addition of ketamine and midazolam. Supplementation of general anaesthesia not needed in any case of group II and group III. Minimal intraoperative and postoperative complications occurred in all 3 groups and no significant variation was found in the three group's. Thus, the addition of ketamine and midazolam to bupivacaine did not produce significant complications attributable to them.

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