

Original Research Article

A comparative study of low doses of intrathecal ketamine and midazolam with bupivacaine for postoperative analgesia in infraumbilical surgeries

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Received: 13 February 2019

Accepted: 20 February 2019

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ABSTRACT

Background: Infra-umbilical surgeries may be performed under local, regional (spinal or epidural) or general anaesthesia, spinal block is still a first choice, because of its rapid onset, high quality of blockade, lack of catheter related infection, less failure rate and also cost effective but the duration of block and postoperative analgesia is limited. The purpose of study was to compare the efficacy of adding ketamine to 0.5% hyperbaric bupivacaine with midazolam to 0.5% hyperbaric bupivacaine in elective infraumbilical procedures.

Methods: A randomized, single blinded, clinical study. 60 subjects were enrolled from the patients presenting for elective infraumbilical surgeries after following the inclusion and exclusion criteria laid down for the study. Sixty ASA Grade I and II patients undergoing infra umbilical surgeries were randomly divided into one of the two equal groups (n=30).

Results: Total 60 patients were included in this study. The mean time to achieve T10 sensory level and modified bromage scale III was prolonged in group M (4.33 ± 1.09 , 6.66 ± 1.26 min) as compared to group K (3.3 ± 0.7 , 4.96 ± 1.21 min) which was statistically significant (P value <0.05).

Conclusions: The present study concludes that addition of intrathecal midazolam to hyperbaric bupivacaine provide very good and prolonged post-operative analgesia without significant intra-operative and post-operative side effects compared to intrathecal ketamine.

Keywords: Intrathecal ketamine, Infraumbilical surgeries, Midazolam, Postoperative analgesia

INTRODUCTION

Infra-umbilical surgeries may be performed under local, regional (spinal or epidural) or general anaesthesia, spinal block is still a first choice because of its rapid onset, high quality of blockade, lack of catheter related infection, less failure rate and also cost effective but the duration of block and postoperative analgesia is limited. In recent years, usage of intrathecal adjuvants has gained much popularity with the benefit of prolonging the duration of

blockade, better success rate, patient satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery.¹ Adequate pain management accelerates functional recovery, facilitates rehabilitation and enables the patients to quick return to their normal activity. The quality of the spinal anaesthesia has been reported to be improved by the addition of opioids and other drugs (such as vasoconstrictors, clonidine, neostigmine, ketamine and midazolam).² The purpose of study was to compare the efficacy of adding

ketamine to 0.5% hyperbaric bupivacaine with midazolam to 0.5% hyperbaric bupivacaine in elective infraumbilical procedures.

METHODS

A randomized, single blinded, clinical study was present study was done at department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences during a period of one-year between August 2016 to August 2017.

The study protocol was approved by the Institutional Ethical Committee, CAIMS, Karimnagar, Telangana, India.

Sixty subjects were enrolled from the patients presenting for elective infraumbilical surgeries after following the inclusion and exclusion criteria laid down for the study. Written informed consent was duly obtained from all the participants in their own language.

Inclusion criteria

- Age: 18-55 years,
- ASA grade I or II,
- Patients undergoing elective infra-umbilical surgeries.

Exclusion criteria

- Extremes of age,
- Pregnancy,
- ASA grade > II,
- Patients with existing cardiac, renal, hepatic, respiratory, neurological, endocrine, coagulation and psychiatric disorders.

Procedure

Sixty ASA Grade I and II patients undergoing infra umbilical surgeries were randomly divided into one of the two equal groups (n=30).

Randomization was done by using physical method, where 60 folded papers were placed in a container, each one labelled either Group K or Group M with each label 30 in number. A third person was asked to take a folded paper before beginning the case.

This was a single blinded study as the patient didn't know what drug he was receiving. All patients were examined a day before surgery. They were kept fasting overnight. All patients were explained about visual analogue score beforehand.

Group K (n=30) patients received 0.5% heavy Bupivacaine 3 ml (15 mg) + preservative free ketamine 0.5 ml (25 mg). Group M (n=30) patients received 0.5%

heavy Bupivacaine 3 ml (15 mg) + preservative free midazolam 0.5 ml (2.5 mg).

Statistical analysis

The statistical software SPASS was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Total 60 patients were included in this study. Both the study groups were comparable with respect to age, sex, ASA grade, mean height and weight, duration of the surgical procedure.

Table 1: Age and sex distribution.

| Variables | Group B | Group M | P-value |
|-------------------------|--------------|-------------|---------|
| Mean age (years) | 39.46±9.83 | 42.36±9.79 | 0.257 |
| ASA grade | | | |
| I | 22 | 21 | |
| II | 8 | 9 | |
| Sex | | | |
| Male | 16 | 15 | |
| Female | 14 | 15 | |
| Mean Ht. (in cm) | 161.63±10.24 | 159.7±10.11 | 0.465 |
| Mean weight (in kg) | 62.7±9.59 | 63.03±9.44 | 0.894 |
| Duration of surgery | 81.5±21.66 | 79.66±23.11 | 0.751 |

Table 1 showing both the groups were comparable in terms of age, sex, mean height and weight, basal pre-operative vital parameters and duration of the surgical procedure there by eliminating the possibility of unequal patient distribution amongst the study groups and the occurrence of bias in the results.

Table 2: Onset of sensory and motor blockade.

| Group | Group K | Group M | P-value |
|--------------------------------------|-----------|-----------|---------|
| Mean onset of sensory block (in min) | 3.3±0.70 | 4.33±1.09 | 0.003 |
| Mean onset of motor block (in min) | 4.96±1.21 | 6.66±1.26 | 0.001 |

Table 2 shows the mean time to achieve T10 sensory level and modified bromage scale III was prolonged in group M (4.33±1.09, 6.66±1.26 min) as compared to group K (3.3±0.7, 4.96±1.21 min) which was statistically significant (P value <0.05).

Total duration of sensory block was significantly higher in group M (218.5±22.52 min) when compared to group

K (171.5±18.76 min). Total duration of motor block was significantly higher in group M (190.66±21.2 min) when compared to group K (152.5±11.87 min). Total duration of effective analgesia was higher in group M (435.76±24.81 min) than group K (348.5±16.56 min) and was statistically significant ($P<0.001$).

Table 3: Comparison of mean postoperative pain scores.

| Time | 0-6 hours | 6-8 hours | After 8 hours |
|------|------------------------|----------------------|-----------------------|
| VAS | Group K Group M | Group K Group M | Group K Group M |
| 0-4 | 30 (100%) 30 (100%) | 21 (70%) 13 (43%) | 0 2 (7%) |
| 5-10 | 0 0 | 9 (30%) 17 (57%) | 30 (100%) 28 (93%) |

Table 4: Comparison of pulse rate (beats per min) in both the groups.

| Time | Group K | Group M | P-value |
|---------|------------|------------|---------|
| Pre-op | 81.50±8.30 | 79.73±7.01 | 0.375 |
| 1 min | 82.16±6.79 | 78.80±6.44 | 0.054 |
| 5 min | 78.70±6.58 | 77.30±5.66 | 0.380 |
| 10 min | 78.70±6.58 | 77.30±5.66 | 0.380 |
| 20 min | 73.33±7.73 | 71.80±4.52 | 0.073 |
| 30 min | 70.00±5.52 | 72.70±6.06 | 0.391 |
| 45 min | 80.10±8.66 | 83.03±6.94 | 0.153 |
| 60 min | 84.83±6.68 | 84.00±4.93 | 0.586 |
| 90 min | 87.43±5.88 | 86.83±5.03 | 0.672 |
| 120 min | 88.56±6.10 | 86.20±5.49 | 0.120 |
| 180 min | 88.80±6.74 | 86.36±5.51 | 0.130 |
| 240 min | 88.06±4.98 | 88.23±5.47 | 0.900 |
| 300 min | 89.00±7.61 | 89.63±5.41 | 0.713 |
| 360 min | 88.33±6.08 | 90.03±6.05 | 0.282 |
| 420 min | 88.90±4.58 | 89.00±5.69 | 0.940 |
| 480 min | 87.53±6.26 | 88.93±4.98 | 0.341 |
| 540 min | 89.46±5.71 | 87.66±6.14 | 0.244 |
| 600 min | 89.26±5.83 | 86.46±7.25 | 0.104 |

Table 3 shows that 70% patients in group K had a higher pain score of >5 during 6-8 hours of postoperative period as compared to 43% in group M. The pain scores were similar in both the groups in the first four hours of postoperative period.

About 6.7% of patients (2 patients) had lower pain scores even after 8 hours of postoperative period after administration of intravenous analgesia as compared to none in group K.

Table 4 shows there was no significant difference in the both groups. The averages of the various hemodynamic parameters like pulse rate, mean arterial pressure and peripheral oxygen saturations were similar in both the groups throughout the intraoperative and postoperative period.

Table 5 shows comparison of mean arterial pressure in both the groups was statistically no significant.

Table 5: Comparison of mean arterial pressure (mmHg) in both the groups.

| Time group | Group K | Group M | P-value |
|------------|------------|------------|---------|
| Pre-op | 87.20±4.60 | 85.90±6.95 | 0.396 |
| 1 min | 84.13±4.94 | 86.76±5.77 | 0.062 |
| 5 min | 78.53±5.58 | 80.06±4.41 | 0.243 |
| 10 min | 72.20±7.21 | 73.70±8.86 | 0.474 |
| 20 min | 69.50±5.23 | 71.80±4.52 | 0.073 |
| 30 min | 70.00±5.52 | 70.93±5.40 | 0.512 |
| 45 min | 69.83±6.15 | 71.13±5.99 | 0.410 |
| 60 min | 75.36±4.68 | 72.96±4.39 | 0.045 |
| 90 min | 80.93±5.28 | 81.46±7.33 | 0.749 |
| 120 min | 84.26±5.56 | 81.86±5.32 | 0.092 |
| 180 min | 87.60±4.16 | 84.43±5.89 | 0.019 |
| 240 min | 87.40±3.97 | 85.23±6.81 | 0.137 |
| 300 min | 81.76±5.65 | 78.40±7.98 | 0.065 |
| 360 min | 83.43±5.15 | 81.56±6.46 | 0.220 |
| 420 min | 85.63±5.99 | 83.36±7.25 | 0.191 |
| 480 min | 83.43±6.61 | 82.86±6.82 | 0.743 |
| 540 min | 84.16±5.63 | 84.40±6.56 | 0.870 |
| 600 min | 87.70±4.54 | 84.80±6.49 | 0.050 |

DISCUSSION

This study was undertaken to know the synergistic effects of adding 25 mg of preservative free ketamine hydrochloride or 2.5 mg of midazolam to 0.5% hyperbaric bupivacaine intrathecally in patients posted for infraumbilical surgeries.

In the present study, both the groups were comparable in terms of age, sex, mean height and weight, basal pre-operative vital parameters and duration of the surgical procedure thereby eliminating the possibility of unequal patient distribution amongst the study groups and the occurrence of bias in the results.

The mean onset of sensory block in ketamine group was 3.3 minutes and in midazolam group, mean onset of sensory block was 4.33 minutes. Similar values were obtained with regard to the onset of sensory block in midazolam group in the studies conducted by Shadangi BK et al, in 2014 and study of Hemanth N et al, in ketamine group.^{3,4} There were statistically significant differences between the two groups with respect to the onset of block as significance value obtained from student t test was less than 0.05.

According to the results of the current study, the onset of sensory blockade was slower but was similar to other study groups when compared in various other studies as those done by Gupta et al, and Sidiq S et al, who used similar doses of midazolam as adjuvant to hyperbaric bupivacaine.^{5,6} This discrepancy in the onset of sensory

blockade could be most likely due to a rapid onset of sensory blockade in the ketamine group rather than a delay in the onset with midazolam.

Krishna TM et al, who administered intrathecal ketamine 0.1 mg/kg and midazolam 0.02 mg/kg respectively observed a Mean \pm SD of pain free period of 369.7 \pm 124.2 min in ketamine group and 730 \pm 81.5 min in midazolam group. As in the present study, the pain free interval was significantly greater in midazolam group.⁷

The mean onset of motor blockade in ketamine group was 4.96 minutes and in midazolam group, the mean onset of motor blockade was 6.66 minutes. There was a statistically significant difference between the two groups with respect to the onset of motor blockade as significance value obtained from student t test was less than p-value 0.05.

The mean duration of effective analgesia was 435.76 \pm 24.81 minutes in midazolam group and in ketamine group, the mean duration of analgesia was 348.5 \pm 16.56 minutes (significantly higher in midazolam group). The incidence of hypotension was also equal in both the groups (4 patients in each group). Two patients who received intrathecal midazolam had bradycardia that responded to a single dose of 0.6 mg of atropine sulphate.

The present study assumed that there was no respiratory depression in both ketamine and midazolam groups as the peripheral arterial oxygen saturations were above 97% in all the patients at any given time in the intraoperative and postoperative period.

The limitations of the study were limited due to a small sample size which may not have represented the general population in results, computer-based randomization of the cases studied could not be done, study compared the various characteristics of block with both the additives to one another but did not compared the results to a control group.

CONCLUSION

The present study concludes that addition of intrathecal midazolam to hyperbaric bupivacaine provide very good and prolonged post-operative analgesia without

significant intra-operative and post-operative side effects compared to intrathecal ketamine.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Rajabhushanam M, Kumar SK, Aasim SA, Venkatesh S. A comparative study of low doses of intrathecal ketamine and midazolam with bupivacaine for postoperative analgesia in infraumbilical surgeries. Int J Adv Med 2019;6:197-200.