Original Research Article

Comparison of efficacy of intrathecal bupivacaine plus midazolam vs bupivacaine alone for postoperatively analgesia in the patients underwent caesarean section

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Abstract

Background: The aim of good postoperative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Adding, an intrathecal adjuvant to local anesthetics forms a reliable method to prolong the duration of anesthesia. In present study, we aimed to compare efficacy of intrathecal bupivacaine plus midazolam versus bupivacaine alone for postoperative analgesia in the patients of caesarean delivery at our tertiary care hospital. **Material and Methods:** The study was conducted in the department of anesthesiology in pregnant women, 20-40 years age, ASA grade I/II, posted for elective Caesarean section. Patients were randomly divided into group B (10 mg bupivacaine intrathecally) and group BM (10 mg bupivacaine combined with 2 mg of preservative-free midazolam intrathecally) by chit method. **Results:** During study period total 90 pregnant women were enrolled, 45 were allotted to each group B (10 mg bupivacaine) and group BM (10 mg bupivacaine combined with 2 mg of preservative-free midazolam). Baseline maternal characteristics such as age, weight, height, pulse rate, systolic BP, diastolic BP were comparable in both groups and difference was not significant. Duration of surgery was comparable in both groups. Early onset of sensory and motor block, prolonged duration sensory and motor block as well as prolonged duration of effective analgesia was noted in group BM as compared to group B, and the difference was statistically significant. No patient had failed spinal block. Complications such as bradycardia, hypotension, nausea and vomiting were noted in present study. Group B had increased number of bradycardia, hypotension and a smaller number of nausea /vomiting as compared to group BM, difference was not statistically significant. In present study respiratory depression, incomplete block, pruritus were not seen. **Conclusion:** Addition of intrathecal midazolam with bupivacaine, reduces the onset time of sensory and motor block, significantly prolongs duration of analgesia with no increase in the incidence of complications, in patients undergoing caesarean delivery.

Keywords, postoperative analgesia, caesarean delivery, **:** intrathecal, bupivacaine, midazolam

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INTRODUCTION

In this era of modern technology and facilities, caesarean delivery is remarkably safe, which is mainly due to availability of antibiotics, safe anaesthesia, blood transfusion facilities and recent improvement in surgical techniques. Spinal anesthesia for cesarean delivery is the best anesthetic technique, as it is simple to perform with rapid onset of anesthesia, complete muscle relaxation, lower incidence of failed block, less drug doses, minimal neonatal depression and decreased incidence of aspiration pneumonitis are advantages of spinal anesthesia.[1] The aim

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of good postoperative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. Adding, an intrathecal adjuvant to local anesthetics forms a reliable method to prolong the duration of anesthesia. A number of adjuvants to local anesthetics for spinal anesthesia like opioids (fentanyl and buprenorphine), benzodiazepines (midazolam), ketamine and neostigmine have been used.[2] Among the local anesthetics, 0.5% hyperbaric bupivacaine is the most commonly used drug for spinal anesthesia. The most important disadvantage of single drug spinal anesthesia is the limited duration. Adjuvants have long been used along with local anesthetics to prolong the duration of anesthesia and analgesia. Opioids like morphine and fentanyl are extensively used to potentiate analgesic effect of local anesthetics in neuraxial blockade, but adverse effects like pruritus, urinary retention, postoperative vomiting and respiratory depression limit the use of opioids.[3] Various studies have found that adding midazolam to bupivacaine significantly increases the duration of postoperative analgesia.[4] In present study, we aimed to compare efficacy of intrathecal bupivacaine plus midazolam versus bupivacaine alone for postoperative analgesia in the patients of caesarean delivery at our tertiary care hospital.

MATERIAL AND METHODS

The study was conducted in the department of anesthesiology of a XXX medical college, XXX. Study design was hospital-based comparative, interventional study, conducted for a period of 1 year (October 2019 to September 2020). The institutional ethical committee approval was taken.

Inclusion criteria

- Pregnant women, 20-40 years age, ASA grade I/II, posted for elective Caesarean section

Exclusion criteria

- Bad obstetric history, medical disorders in present pregnancy such as hypertension, heart disease, renal disease, liver disease, patients with psychiatric diseases.
- Evidence of fetal compromise and anomalies.
- During surgery additional general anaesthesia required
- Contraindication to spinal anaesthesia.
- Not willing for participation in study.

A detailed history was obtained and thorough general and systemic examination was performed. Preanesthetic checkup was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations like CBC, urine routine and microscopic examination, KFT, LFT, BSL were performed prior to surgery. The procedure of spinal anesthesia was explained to the patients and written consent was obtained. Patients were randomly divided into group B and group BM by chit method.

1. The B group received 10 mg bupivacaine intrathecally
2. BM group received 10 mg bupivacaine combined with 2 mg of preservative-free midazolam intrathecally.

In operation theatre, the standard monitoring was done and baseline parameters were recorded. Each patient was preloaded with 10 mL/kg Ringer lactated solution prior to spinal anaesthesia. Under all aseptic precautions, through midline approach, spinal anaesthesia was given. Intraoperatively patients hemodynamic parameters (maternal pulse rate, non-invasive blood pressure, oxygen saturation, and respiratory rate) were measured periodically and recorded. Standard postoperative care was provided. The duration of effective analgesia was taken from the time of intrathecal drug administration to the time of first supplementation with rescue analgesic. Postoperatively blood pressure, pulse rate, intensity of pain and SPO2 were recorded at 30 min, 1 hr., 2hr, 4hr, 6hr, 8hr, 12hr, 16hr, 20hr and 24hr. Adverse effects such as hypotension, bradycardia, respiratory depression were looked for and recorded accordingly. Findings were collected in predesigned proforma, entered in Microsoft excel and analyzed with the help of SPSS version 21. The values of the two groups were compared and expressed as mean ± SD. Statistical analysis was done by using Student's paired t-test for quantitative and Chi-square test for qualitative parameters. The p value of <0.05 was considered as statistically significant.

RESULTS

During study period total 90 pregnant women were enrolled, 45 were allotted to each group B (10 mg bupivacaine) and group BM (10 mg bupivacaine combined with 2 mg of preservative-free midazolam). Baseline maternal characteristics such as age, weight, height, pulse rate, systolic BP, diastolic BP were comparable in both groups and difference was not significant.

Table 1: Baseline maternal characteristics

Maternal characteristics	group B {No. of patients (%)/ mean ± SD}	group BM {No. of patients (%)/ mean ± SD}
Age (in years)	24.27 ± 2.3	25.14 ± 3.5
Weight (in kgs)	66.4 ± 8.7	66.9 ± 5.7
Height (in cms)	153.3 ± 7.3	154.5 ± 6.1
ASA status		
I	35 (78%)	32 (71%)
II	10 (22%)	13 (29%)
Pulse Rate (per min)	83.3 ± 12.5	81.6 ± 13.1
Systolic BP (mm Hg)	112.4 ± 15.5	108.3 ± 13.4
Diastolic BP (mm Hg)	73.5 ± 6.2	75.5 ± 7.7

Duration of surgery was comparable in both groups. Early onset of sensory and motor block, prolonged duration sensory and motor block as well as prolonged duration of effective analgesia was noted in group BM as compared to group B, and the difference was statistically significant. No patient had failed spinal block.

Table 2: Comparison of sensory parameters in two groups.

Characteristics	group B (mean ± SD)	group BM (mean ± SD)	p value
Duration of surgery(min)	35.45 ± 11.2	36.21 ± 10.35	0.85
Onset of sensory block (min.)	4.13 ± 0.94	2.53 ± 0.73	0.32
Duration of sensory block (min.)	113.64 ± 16.72	135.33 ± 16.31	0.25
Onset of motor block (min.)	5.49 ± 1.31	3.28 ± 0.91	0.41
Duration of motor block (min.)	135.42 ± 21.6	109.73 ± 14.87	0.19
Mean duration of effective analgesia	155.1 ± 23.5	186.1 ± 32.1	0.15

Complications such as bradycardia, hypotension, nausea and vomiting were noted in present study. Group B had increased number of bradycardia, hypotension and a smaller number of nausea /vomiting as compared to group BM, difference was not statistically significant. In present study respiratory depression, incomplete block, pruritus were not seen.

Table 3: Complication

Complications	group B (n=45)	group BM (n=45)
Bradycardia	2 (4%)	1 (2%)
Hypotension	2 (4%)	1 (2%)
Nausea and vomiting	1 (2%)	2 (4%)

DISCUSSION

Post-operative pain in caesarean delivery is mainly related to extent and duration of the block, visceral pain on exteriorization of uterus and handling of other abdominal contents. To increase the extent and duration of block, large dose of the local anaesthetic might result in an intensive block with the resultant hypotension, bradycardia and sometimes even cardiac arrest. Decreasing the dose of local anesthetic decreases the magnitude of hypotension but compromises upon the quality of anesthesia. Recently, intrathecal midazolam has been shown to potentiate the effect of local anesthetics in SAB by acting through BZD-GABA receptor complex at spinal cord level leading to segmental analgesia, without any neurotoxic effects.[5] Midazolam belongs to benzodiazepine group of drugs, shown clear analgesic effects in intrathecal anesthesia. There are benzodiazepine receptors throughout the nervous system, including the spinal cord, which show connections with gamma-aminobutyric acid (GABA) receptors.[6] The addition of Midazolam in doses of 1 to 2 mg intrathecally has a positive effect on post-surgical pain and in chronic pain therapy. Intrathecally administered midazolam does not have any neurotoxic effects as demonstrated by animal studies.[7] In a study by Sharifi *et al.* it was shown that adding midazolam to bupivacaine reduced the time required for spinal anesthesia. In that study it was shown that adding midazolam to bupivacaine reduced the time required for motor block. They also showed that adding midazolam to bupivacaine increased the time of spinal anesthesia.[8] In another study conducted by Imani *et al.* it was found that adding midazolam to bupivacaine significantly reduced the time required for spinal anesthesia. It was also found that adding midazolam to bupivacaine reduced the time required for motor block.[4] Similar findings were noted in present study.

Karbasfrushan *et al.* noted that the combination of bupivacaine and intrathecal midazolam generated an effective anesthetic drug, which was used to reduce pain.

Although the onset of sedation was faster, yet the incidence of nausea and vomiting was higher in the experimental group. The duration of effective analgesia and the time for regression of sensory analgesia was the same in both groups.[9] Present study results were similar with those of Chavda *et al.*,[10] and Prakash *et al.*[11] who conducted a study to investigate analgesic efficacy of two doses of intrathecal midazolam as adjunct to bupivacaine for spinal anaesthesia in patients undergoing caesarean delivery. They concluded that intrathecal midazolam 2 mg provided a moderate prolongation of postoperative analgesia when used as adjunct to bupivacaine. In a meta-analysis Ho KM *et al.* concluded that adding intrathecal midazolam to other spinal medications improves perioperative or peripartum analgesia and reduces nausea and vomiting during caesarean delivery. Midazolam is known to produce antinociception and potentiate the effect of local anaesthetic when given in neuraxial block, without having significant side effects. A small diluted dose of intrathecal midazolam (1 to 2.5 mg) does not appear to increase the duration of motor blockade, the risk of respiratory depression or of short-term neurological deficits.[12] Sanwal MK *et al.*,[13] studied bupivacaine sparing effect of intrathecal midazolam in sub-arachnoid block for cesarean section and concluded that, 7.5 mg bupivacaine with 2 mg midazolam is the optimum dose ratio combination to be used in subarachnoid block for caesarean section. intrathecal midazolam 2 mg, it is possible to reduce the dose of bupivacaine from 2.2 mg to 1.5 mg to provide the same surgical anesthesia but with fewer incidence of hypotension and other side effects. Intrathecal administration of drugs in combination results in prolonged and better analgesic effect as compare to individual drug administration. In combination drug usage, doses of drugs also reduce which gives another advantage in avoiding their dose-related adverse effects.

CONCLUSION

Addition of intrathecal midazolam with bupivacaine, reduces the onset time of sensory and motor block, significantly prolongs duration of analgesia with no increase in the incidence of complications, in patients undergoing caesarean delivery.

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