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ADVERSE EVENTS AND COMPLICATIONS OF INTRATHECAL XYLOCAINE AND MIDAZOLAM FOR POSTOPERATIVE ANALGESIA IN LOWER SEGMENT CESAREAN SECTION: A DESCRIPTIVE STUDY

Anesthesiology

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ABSTRACT

Background: Intrathecal xylocaine with midazolam is increasingly being used for postoperative pain relief. There were few concern like respiratory depression and neurotoxicity with the use of inthrathecal midazolam .

Methods: This was a descriptive study enrolling total of 90 patients of with 30 patients in each group using intrathecal drugs for postoperative pain relief in Lower segment cesarean section. The three groups were intrathecal xylocaine, intrathecal xylocaine + 1mg midazolam and intrathecal xylocaine + 2 mg midazolam respectively.

Results: the base demographic and hemodynamic variables were comparable between the three groups. Only shivering and hypotension was noted with use of midazolam which was no different from other groups.

Conclusion: Intrathecal midazolam as an adjuvant to intrathecal xylocaine was not associated with significant adverse events or complications

KEYWORDS

INTRODUCTION:

Postoperative pain relief can improve functionality, reduce physiological and emotional morbidity and improve quality of life. The distress and pain which a patient often endures in immediate post operative period is beyond description. As an anaesthesiologist it is our duty as well as priviledge to use all legitimate means to bring down the physical sufferings of patient not only during operation itself but also postoperatively.

Dr. August Bier carried out the first spinal anaesthesia in 1899 that has become the standard practice for lower extremity and abdominal surgery worldwide. (1) The most commonly used drugs for spinal anaesthesia are local anaesthetics. However, a major disadvantage of single injection spinal anaesthesia is its limited duration of action. In clinical practice, a number of adjuvants have been added to intrathecal local anaesthetics for supplementation of intraoperative anaesthesia and postoperative analgesia. They have advantages as they reduce the dose of local anaesthetic; provide long lasting postoperative analgesia with reduced incidence of central nervous system depression, motor effects or hypotension. (2) Midazolam, synthesized by Walsar and colleagues in 1976, was the first clinically used water-soluble benzodiazepine.(3) It is also the first benzodiazepine that was produced primarily for use in anaesthesia.

The benzodiazepines are used primarily for anxiolysis, amnesia, and sedation (2). The discovery of benzodiazepine receptors in the spinal cord triggered the use of intrathecal midazolam for analgesia (4). Hence we designed the study to describe the adverse events and complications of intrathecal preservative free midazolam used postoperatively in lower segment cesarean section .

MATERIAL AND METHODS

This was a descriptive study done at a tertiary care centre in north India. Institutional ethics committee approval was taken before the start of study. Patients between age groups of 20-35years who underwent lower segment cesarean section were divided into three groups of 30 each and were enrolled into the study after informed consent. All patients received a uniform premedication of injection Glycopyrrolate bromide 0.2mg I.M. Injection Ondeansetron 4mg I/V, injection Metoclopromide10mg I/V were given 30 minutes prior to operative procedure upon arrival into the operation theater. Ringer Lactate solution 500ml was infused as a preload, followed by dextrose 5%. Under all aseptic conditions lumber puncture was performed at L2-L3 space and following drugs were injected.

Group 1 received 1.2ml of 5% heavy Xylocaine Hcl, Group 2 received 1mg of midazolam in 0.2ml along with 1.2ml of 5% heavy Xylocaine Hcl and Group 3 received 2mg of midazolam in 0.4ml along with 1.2ml of 5% heavy Xylocaine Hcl.

Pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate were recorded every minute till 5 minutes, then every 5 minutes till 15 minutes, then every 10 minutes until completion of surgery.

RESULTS:

Total of ninety patients were enrolled in the study (thirty in each group). Table No 1 showing demographic profile of patients in the three groups . The mean age in group 1 was 24.5yr, in group 2 mean age was 24.6 and in group 3 mean age was 26.2.The mean weight was 66kg, 61.4kg and 62.7kg in group1, 2 and group 3 respectively . There was no significant difference between characteristics of patients in different groups.

TABLE 1: Demographic profile of patients

variance	Group1(n=30)	Group2(n=30)	Group3(n=30)
Age	24.5± 3.1	24.6±3.9	26.2±3.4
Height	156.25±3.91	157.16±3.14	156.75±3.4
weight	66.0± 3.54	61.4±4.54	62.7±2.17

Table 2 showing baseline haemodynamic values of all three groups. The mean heart rate in all groups was around 78 per minute, mean systolic blood pressure range from 128 to 131 mmHg. The mean diastolic blood pressure in all groups range from 77 to 79 mmHg. The respiratory rate in all three groups range from 14.9 to 15.9 per minute.

TABLE 2: Mean +SD of basal heart rate, systolic and diastolic blood pressure and respiratory rate of patients

variable	Group 1(n=30)	Group2(n=30)	Group3(n=30)
Heart rate(per minute)	78.7± 7.5	78.9± 7.7	78.7± 7.9
SPB(mmHg)	128±11.1	131.5± 16.9	128± 11.1
DBP(mmHg)	79.5 ±5.7	77.9± 7.4	78.4 ± 5.8
RR(per minute)	15.9± 1.2	14.9± 1.2	14.9± 1.2

TABLE 3: Incidence of adverse events/ complication of in all the three groups

Complications	Group 1(n=30)	Group 2(n=30)	Group 3(n=30)
Nausea and vomiting	2(6.7%)	-	-
Headache	-	-	-
Backache	-	-	-
Shivering	2(6.7%)	2(6.7%)	2(6.7%)
Hypotension	1(3.3%)	1(3.3%)	-
Hypertension	-	-	-
Bradycardia	-	-	-

Respiratory depression	-	-	-
Pruritis	-	-	-
Motor &sensory deficit	-	-	-
Bowel dysfunction	-	-	-
Urinary retention	-	-	-

Two patients in group 1 had nausea and vomiting, 6 patients (2 in each group) developed shivering, hypotension occurred in 2 patients one each in group 1 and 2. There were no episodes of bradycardia, sedation, respiratory depression, pruritus and neurological deficit.

DISCUSSION:

A pain-free postoperative period is essential following a caesarean section so that the mothers may care for and bond with their newborns. Intrathecal adjuvants are often administered during this procedure to provide significant analgesia.

Local anesthetics with opioids demonstrate significant synergy (5). Spinal opioids are effective but do produce adverse effects, like respiratory depression, urinary retention, nausea and pruritus. Furthermore, the single administration of an opioid may induce a long-lasting increase of threshold pain sensitivity, leading to delayed hyperalgesia (6). Recent techniques for postoperative management in abdominal surgeries include ultrasound-guided TAP block, which has produced promising results (7). Similarly, TAP blocks are effectively used for post-caesarean analgesia (8). Providing high-quality analgesia is of paramount importance in developing countries and in all hospital settings. Therefore, intrathecal adjuvants are one of the easiest and most accessible methods for offering pain relief. Midazolam is a relatively water-soluble benzodiazepine (9) and is extensively used in both critical care medicine and in the operating room for its sedative, anxiolytic, and amnesic effects.

Local anaesthetic agents used for this purpose provide good intraoperative analgesia. However, they provide a very limited postoperative duration of action. In order to overcome this problem and to maximise the duration of anesthesia-analgesia, many adjuvants, such as intrathecal opioids and non-opioids, have increasingly been tried in the last two decades to relieve postoperative pain.

Among the various methods available for providing postoperative analgesia, the benefits of intrathecal opioids and non-opioids as adjuncts in spinal anaesthesia are well documented. Unfortunately the addition of intrathecal opioids is associated with dose related adverse effects such as respiratory depression, nausea, vomiting, urinary retention, pruritus, and sedation. Therefore, the use of non-opioids such as ketamine, clonidine, neostigmine, magnesium sulfate, and midazolam have become popular adjuncts for post-operative analgesia. However, side effects in the postoperative period render most adjuvants less than ideal.

The delta selective opioid antagonist naltrindole, suppress the antinociceptive effect of intrathecal midazolam suggesting that intrathecal midazolam is involved in the release of an endogenous opioid acting at spinal delta Receptor (10). The most serious side effect of intrathecal midazolam is its possible neurotoxicity . So far animal studies have revealed no damage to spinal cord, nerve root or meninges.(11) In our study we paid special attention to any potential side effects or complications during peri operative period. There were no neurological complications of intrathecal midazolam in present study.

Study done by Kim M.H and Lee Y M et al (12) have reported urinary retention in 3 of the 15 patients where control group received intrathecally 1 ml of 0.5% heavy bupivacaine plus 0.2ml of 0.9% saline; and the study group received intrathecally 1ml 0.5% bupivacaine plus midazolam (1mg of midazolam in 0.2 ml &2mg of midazolam in 0.4 ml). No neurological deficits were detected at discharge, which is similar to our study. None of the patients in midazolam group had nausea and vomiting. It has been postulated that a possible mechanism for the anti-emetic effect of benzodiazepines could be an action at the chemoreceptor trigger zone, which reduce the synthesis, release, and postsynaptic effect of dopamine (13). Shivering was present in 6 patients all groups in plain xylocaine group(group 1) 4 in midazolam group(two in each group 2 and group 3).

CONCLUSION:

Intrathecal midazolam provides significant and effective postoperative analgesia along with stable intraoperative hemodynamics. Adequate postoperative analgesia can be achieved without significant side effects using intrathecal midazolam.

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