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EFFICACY OF INTRATHECALLY ADMINISTERED ADJUVANTS MIDAZOLAM AND CLONIDINE WITH BUPIVACAINE ON HEMODYNAMIC STABILITY

Anesthesiology

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ABSTRACT

We conducted a double blinded randomized control study in 60 patients belonging to ASA I and II undergoing elective lower abdominal surgeries. Patients of both sexes ranging between 22 to 65 years of age were included. Our aim was to evaluate the effects of intrathecal midazolam 2mg and clonidine 30 mcg as adjuvant to bupivacaine for hemodynamic stability and postoperative analgesia. Patients were divided randomly using closed cover technique into two groups of 25 each.Group BM received 3ml of 0.5% heavy bupivacaine 0.4ml midazolam (preservative free) and 0.1ml of normal saline. Group BC received 3ml of 0.5% heavy bupivacaine, 0.2ml clonidine and 0.3 ml of normal saline. The total volume of the injected solution was 3.5ml in both groups. The onset of sensory and motor blockade, the duration of sensory and motor blockade, peak sensory level, time to achieve maximum sensory level, changes in pulse rate, changes in mean arterial pressure, duration of analgesia, respiratory rate, o2 saturation, sedation score and adverse effects were noted in both groups. The data collected were analyzed by Chi square test and students't' tests. We found that onset of sensory and motor blockade, time to achieve maximum sensory level, and duration of complete motor recovery was earlier in BM group than BC group. Duration of Sensory block and duration of analgesia were prolonged in BM group than BC group. In both groups, no significant changes were observed in respiratory rate, O2 saturation and sedation in our study. Intrathecal Midazolam as an adjuvant to bupivacaine comparing to Clonidine resulted Rapid onset of sensory and motor blockade, Achieves maximum sensory level at a shorter interval, Increased duration of sensory blockade and decreased duration of Motor blockadeIt gives stable mean arterial pressure and pulse rate.

KEYWORDS

Anesthesia,Adjuvants,Midazolam,Bupivacine,Clonidine

1. INTRODUCTION:

Spinal anaesthesia was first performed by August Bier on 16th August 1898 when he injected 3 ml of 0.5% Cocaine intrathecally. It is a simple technique which has many advantages over epidural anesthesia. In addition, correct placement of the needle in the subarachnoid space is confirmed by a clearly defined end point (appearance of CSF).Spinal anaesthesia with local anaesthetic agents is extensively used for lower abdominal surgeries. It provides the excellent pain relief as compared to intravenous or epidural route. There are many advantages for spinal anesthesia over general anaesthesia which makes it the anesthesia of choice in current surgical practice. Many clinical studies support the fact that Postoperative morbidity and mortality may be reduced when neuraxial blockade is used either alone or in combination with general anaesthesia. Since it decreases the stay, it is cost effective for both patient and hospital. It is suitable for patients with respiratory diseases and helps preventing intubation related problem like laryngospasm. It is also helpful in maintaining the airway patency and reduced blood loss. Early return of gastro intestinal function following surgery can be considered as an added advantage. Other advantage may be reduced hypercoagulable state associated with surgery, increased tissue blood flow due to sympathectomy, decreased splinting which improves oxygenation, enhanced peristalsis, and reduced stress response to surgery due to suppression of neuroendocrine system.Apart from the theoretical risk of infection to the brain, difficulty in finding the space in old age and bony abnormalities can pose a challenge to the anesthesiologist. The serious complication associated with spinal anaesthesia includes bradycardia, hypotension, prolonged motor block and high spinal. It is related to the sympatholytic effect of local anaesthetic agents. If the level of the block is higher, the sympatholytic effect will be more and leads to more serious complications. Though these effects cannot be abolished completely, they can be considerably minimized by using either low dose or low concentration of local anesthetics. One of the main disadvantages is the limited duration of block achieved with local anaesthetics.In the last decades benzodiazepines, alpha 2 agonist, acetylcholine esterase inhibitors like neostigmine and NMDA receptor antagonist like ketamine are all used as adjuvants to local anaesthetics.

Among the neuraxial adjuvants, Midazolam and Clonidine are becoming increasingly popular, because of their prolonged duration of analgesia, good intraoperative comfort like anxiolysis, sedation and sparing effect on postoperative analgesic consumption. Comparative studies with Midazolam and Clonidine as adjuvants to intrathecal bupivacaine are very few.In order to address these existing problems we need better pain management which is helpful for early recovery of motor function and reduction in requirement of postoperative analgesics.This research is designed to study the efficacy of such combination in our setup and compare the results with the previous studies done at other institutions.

2.AIM

To evaluate the efficacy of intrathecally administered adjuvants Midazolam and Clonidine with Bupivacaine for hemodynamic stability

3.MATERIALS AND METHODS

Study Design: Double blinded randomized case control study.

After obtaining approval from the institutional ethics committee, Thanjavur Medical College, Thanjavur, the study was conducted in 60 ASA grade I or II patients undergoing elective lower abdominal surgeries like Hernia repair and appendicectomy under spinal anesthesia. Before including the patients for the study, all patients were explained about the procedures and a written informed consent was obtained.

INCLUSION CRITERIA

- Adult Patients aged 20-60 years of either sex
- ASA I & II Patients
- Weight: 35- 70 kg
- Height : 150-170 cm

EXCLUSION CRITERIA

- Infection at the site of injection
- Spinal deformity
- H/o Bleeding diathesis

H/o Chronic pain and on analgesics
H/o Drug Allergy.
H/o Psychiatric illness

PREOPERATIVE PREPARATION: After routine preoperative assessment all patients were familiarized with Visual Analog Scale (VAS). The patients were shown a 10 cm long scale marked 0-10 on a blank paper and told that 0 represented "no pain" and 10 represented worst possible pain.At the patient's waiting room in the OT, basal line readings of the vital parameters were recorded. Intravenous line started. Each patient received inj. ranitidine 50 mg and inj. metoclopromide 10 mg before shifted to theatre. The patients were randomly allocated into two groups of 30 each by using closed cover technique. In the operating room, appropriate equipment for airway

management and emergency drugs were kept ready. The horizontal position of the operating table was checked. Patients were shifted to the operating room and positioned.Noninvasive blood pressure monitor, pulse oximeter and ECG leads were connected to the patient. Preoperative baseline systolic and diastolic blood pressure, mean arterial pressure, pulse rate, respiratory rate and oxygen saturation were recorded. Patients were preloaded with 10ml/ kg of ringer lactate 15min prior to the subarachnoid block. The Patient was placed in right lateral position. The skin over the back was prepared with antiseptic solution and draped with sterile towel.

BM GROUP

Patients received 3ml 0.5% bupivacaine (15mg)
0.4 ml Midazolam (2 mg) preservative free
0.1 ml normal saline

BC GROUP

Patients received 3 ml 0.5% bupivacaine (15mg)
0.2 ml clonidine (30 g)
0.3 ml normal saline
Lumbar puncture performed with a 25G Quincke's spinal needle at L3 – L4 inter space via midline approach. After confirming free flow of CSF, the prepared solution was injected. The patients were made to lie supine immediately after injection and the time at which the spinal anaesthesia performed was noted.

The following parameters were recorded.

- Time of injection of subarachnoid Block.
- Time of onset of sensory block at T10 level.
- Maximum level of sensory block achieved (by pinprick method)
- Time to achieve maximum level of sensory Block.
- Two segment regression time.
- Onset of Motor Block
- Duration of Complete motor recovery.
- Duration of Surgical procedure
- Sedation score
- Systolic and diastolic blood pressure, mean arterial Blood pressure pulse rate and oxygen saturation were recorded every 2 minutes for the first 10 minutes and thereafter every 5 minutes up to one hour.
- Hypotension is said to have occurred if the MAP falls less than 70mmHg and was treated with 100% 02, increasing the infusion rate of IV fluids and inj. Ephedrine in incremental doses of 6 mg at an interval of 2 minutes.
- Bradycardia was defined as heart rate less than 60/min and was planned to be managed with intravenous atropine in incremental doses.
- Respiratory depression was said to be present if respiratory rate was less than 8 per minute and / or SpO2 <90%. It was planned to be managed with mask ventilation or intubation and IPPV.

SENSORY BLOCK

The onset of sensory block was defined as the time between the injection of anaesthetic solution and the absence of pain at the T10 dermatome. Sensory block was assessed by loss of sensation to pinprick using 21G Sterile needles bilaterally along the midclavicular line. This assessment started immediately after turning the patient to supine position and continued every minute till loss of sensation to pinprick at T10 level was noted. This pinpricking continued till the peak block height was reached and the time was noted. The duration of sensory block was defined as the time for regression of two segments from the maximum block height evaluated by pin prick. Sensory block was checked every 15 minutes till it reached two segment regression levels.

MOTOR BLOCK

Motor Block was assessed bilaterally using Modified bromage scale.

DURATION OF ANALGESIA

The time at which the patient first complained of pain was noted. The duration of effective analgesia was defined as the period from the spinal injection to the first occasion when the patient complained of pain in the postoperative period.

4. RESULTS :

We conducted a double blinded randomized control study in Thanjavur medical college, Thanjavur to evaluate the effects of two adjuvants added to intrathecal bupivacaine.The collected data were analyzed by chi square test and results obtained in the form of range, mean and standard deviation. The probability value 'P' of less than 0.05 considered statistically significant.

Patient's demographic data that includes age, sex and duration of surgery between two groups were comparabl

Figure : 1
Onset Of Sensory And Motor Block

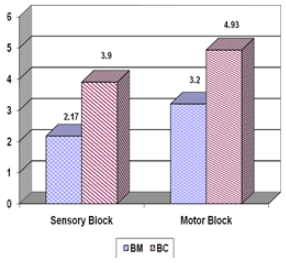


Figure : 2
Time To Achieve Maximum Sensory Level

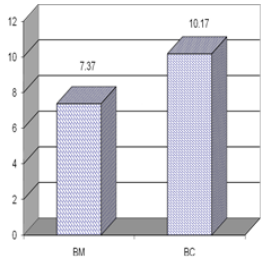


Figure : 3 Two Segment Regression Time And Duration Of Complete Motor Recovery

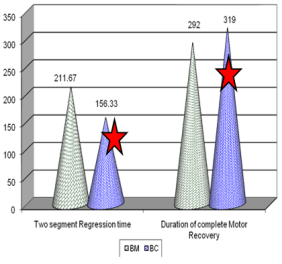
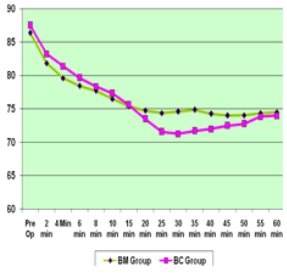


Figure : 4 Comparison Of Pulse Rate



5.DISCUSSION& CONCLUSION

The study was conducted to evaluate the effects of intrathecal midazolam and clonidine as adjuvant to bupivacaine to assess hemodynamic stability in spinal anaesthesia. Sixty patients were randomly selected and equally divided into two groups. BM group received 3ml of 0.5% heavy bupivacaine, 0.4ml (2mg) of midazolam (preservative free) and 0.1ml of normal saline. BC group received 3ml of 0.5% heavy bupivacaine, 0.2 ml (30 mcg) of Clonidine and 0.3ml of normal saline. Prakash et al, [1]conducted a placebo controlled study to evaluate the two different doses of intrathecal midazolam (1 mg and 2 mg) with 0.5% bupivacaine (10 mg) and concluded that intrathecal midazolam 2 mg with bupivacaine provided a moderate prolongation of postoperative analgesia and reduced requirement of Postoperative

analgesic supplements. M.H Kim and Y.M Lee [2] evaluated 2 mg of intrathecal midazolam with 5 mg of bupivacaine and proved prolonged Postoperative analgesia than 1 mg of intrathecal midazolam. Adam. P Tucker et al,[3] has proved that the 2 mg of intrathecal midazolam will not increase the incidents of neurological side effects. Hence in our study we have chosen 2 mg intrathecal midazolam as adjuvant with bupivacaine.Hema Suxena et al,[4] evaluated 3 different doses of clonidine (15, 30, 37.5 mcg) as adjuvant with bupivacaine (13.5 mg) in spinal anaesthesia. Even with small doses of clonidine, there was significant improvement in onset and duration of sensory and motor block with relative hemodynamic stability. They have concluded 30 mcg dose provides maximum benefit and minimum side effects. Hence we have selected 30 mcg of clonidine as adjuvant with bupivacaine for comparative study In our study the level of sensory block varied from T4 to T8 level. Among all patients, 46 patients attained maximum level of sensory blockade at T6 level. Nine patients attained up to T8 level and five patients attained T4 level. Any patient in either group does not complain of discomfort related to the sensory levels. The results of Nanji Gowda et al[5] study, has shown that 2 mg midazolam to intrathecal bupivacaine did not have any effect on peak level. In BM group the time to achieve maximum sensory level was 7.37 minutes and in BC group was 10.17 minutes.

In our study the duration of sensory block was 211.67 minutes in BM group and 156.33 minutes in BC group. This is very similar to the findings of BM groups (211.67±15.44 Vs 210.84±68.44) and BC groups (156.33±12.03 Vs 169.28±63.69.In our study, in BM group the duration of complete motor recovery was 292 minutes whereas in BC group it was 319 minutes. This shows that the duration of motor block was longer in clonidine group

In our study, the duration of analgesia (from the time of intrathecal injection to the first dose of postoperative analgesia) was 486.17 minutes in BM group and 306.17 minutes in BC group. This has shown that intrathecal midazolam result in prolongation of duration of analgesia than intrathecal clonidine.The average dose of Postoperative analgesia in BM group was 87.5mg whereas in BC group it was 132.5mg. This shows that intrathecal midazolam significantly lowers the need for supplementary Postoperative analgesia than intrathecal clonidine. In our study also BM group (2mg midazolam + Bupivacaine 0.5% 15mg has the similar duration of analgesia (486.17 or 8.1 hrs). We observed the duration of analgesia was prolonged in BM group than BC group because of multimodal analgesic action of midazolam, mild sedation mediated by alpha 1 $GABA_A$ receptor and anxiolysis mediated by alpha 2 $GABA_A$ receptor. Various studies have demonstrated the hemodynamic stability when midazolam and clonidine are added as adjuvants to intrathecal bupivacaine. In our study there was a statistically significant reduction of pulse rate at 4^{th} minute interval in BM group comparing to BC group which could be explained by the earlier action of midazolam on α_1 and α_2 $GABA_A$ receptors producing sedation and anxiolysis. There were statistically significant reductions of pulse rate at 25^{th}, 30^{th}, 35^{th} and 40^{th} minutes in BC group comparing to BM group. This could be explained by the presynaptic inhibition of norepinephrine release and direct depression of AV node conduction after systemic absorption of clonidine In our study in BC group, six (20%) patients developed bradycardia while none of the patients in BM group developed the same. Seven patients in BC group (23.3%) developed hypotension whereas in BM group only two (6.7%) patients. This shows that intrathecal clonidine had statistically significant adverse effects comparing to BM group Intrathecal Midazolam as an adjuvant to bupivacaine comparing to Clonidine resulted Rapid onset of sensory and motor blockade, Achieves maximum sensory level at a shorter interval, Increased duration of sensory blockade and decreased duration of Motor blockadeIt gives stable mean arterial pressure and pulse rate.

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