ORIGINAL RESEARCH PAPER

Anesthesiology

A COMPARATIVE STUDY BETWEEN DEXMEDETOMIDINE AND MIDAZOLAM AS AN ADJUVANT TO INTRATHECAL BUPIVACAINE

KEY WORDS:

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ABSTRACT

Background: Subarachnoid block(SAB) is the common mode of anaesthesia. To prolong its action various adjuvants are being added to local anaesthetics(LA). In this study we compared the efficacy and safety of midazolam and dexmedetomidine as an adjuvant to intrathecal 0.5% hyperbaric (H) bupivacaine.

Material & Methods: 80 ASA grade I or II patients of either sex scheduled for lower limb or lower abdominal surgeries were randomly allocated into two groups, Group D & Group M. In group D, patients received 3ml of 0.5% (H) bupivacaine + dexmedetomidine 5mcg in 0.5ml normal saline(NS). While group M received 3ml of 0.5% (H) bupivacaine + 2mg midazolam (0.4ml of 5mg/ml) + 0.1ml of NS. Onset of sensory & motor block and duration of sensory & motor block were recorded. Patients were monitored for any haemodynamic changes and side effect.

Result: Duration of both sensory & motor blockade was significantly prolonged in group D as compared to group M. There was no clinically significant difference observed among both the groups in respect to hemodynamic parameters, sedation and side effect.

Conclusion: Dexmedetomidine as an adjuvant to intrathecal bupivacaine (H) was better as compared to midazolam. It significantly prolongs the duration of analgesia postoperatively without any significant side effect.

INTRODUCTION

Regional anaesthesia is always preferred over general anaesthesia as it avoids the polypharmacy and side effects associated with general anaesthesia like prolonged sedation and hospitalization, sore throat, cough, nausea and vomiting etc. For lower limb and lower abdominal surgeries, subarachnoid block is most preferred mode of anaesthesia[1]. Short duration of action is biggest disadvantage of SAB. To overcome this disadvantage, various adjuvant drugs are being used [2,3,4] and the search for an ideal adjuvant (drugs which prolongs the duration of analgesia without any significant side effects) is still going on. Various drugs like opioids (morphine, fentanyl etc.), ketamine, neostigmine etc. are being used as an adjuvant[2,3,4]. But most of these drugs are associated with various side effects like nausea, vomiting, pruritis, sedation etc[5].

Midazolam is a water soluble benzodiazepine with the short duration of action. Analgesic effect of intrathecal midazolam is mediated through GABA receptors present in lamina 2 of dorsal horn ganglia of spinal cord[6,7,8]. It also releases endogenous opioids which acts on the spinal delta receptor[9]. Various studies done in the past have demonstrated that midazolam as an adjuvant to intrathecal bupivaicaine significantly prolongs the duration of post operative analgesia without any significant side effects[10,11]. **Kim & Lee**[12] and **Prakash et.al.**[13] concluded that the duration of post-operative analgesia was prolonged in a dose dependent manner with the addition of intrathecal midazolam. Many studies conducted on animals & humans have demonstrated that intrathecal midazolam does not shows the signs of neurotoxicities[14,15]. **Bharti et. al.** had shown prolongation of motor blockade along with increased duration of analgesia with intrathecal midazolam[16].

Dexmedetomidine is a selective alpha-2 adrenoceptor agonist[17,18]. When used as an adjuvant to intrathecal LA it significantly prolongs the postoperative analgesia with stable haemodynamics and minimal side effects[19,20]. Activation of alpha-2 receptor in brain and spinal cord results in sympatholytic effects resulting in hypotension , bradycardia, sedation and analgesia[21]. Intrathecal administration of alpha-2 agonist results in analgesic effect without deep sedation due to sparing of supraspinal CNS site from excessive drugs exposure, leading to analgesia without deep sedation[22]. Animal studies have shown that intrathecal dexmedetomidine has no adverse neurotoxicity or neurological deficit[23]. Previous studies have shown that intrathecal Dexmedetomidine has dose dependent favorable effect on the onset and regression of sensory and motor blockade[24].

In this study our aim was to compare the midazolam and dexmedetomidine used as an adjuvant to intrathecal (H)bupivacaine in terms of efficacy (prolonged analgesia) and safety (associated side effects).

MATERIAL AND METHOD:

After getting ethics committee approval and informed written consent from the patients, 80 patients of ASA physical status 1 or 2 of either sex scheduled for lower limb or lower abdominal surgeries were enrolled for the study. Patients who refused to participate in the study, patients having contraindication for SAB (coagulopathy, infection at the site of infection, neuropathy etc), patients allergic to the drugs used were excluded from the study.

Enrolled patients were randomly allocated in to two groups of 40 patients in each group, by computer generated random number table. Group D (n=40) received 3 ml of 0.5% (H) bupivacaine + 5mcg dexmedetomidine in 0.5 ml NS. Group M (n=40) received 3 ml of 0.5% (H) bupivacaine + 2mg midazolam (0.4ml of 5mg/ml) + 0.1ml NS Patient and the investigator both were blinded about the group of the patient and the drug injected. Drug was prepared by the person who was not involved in the study. After noting down the baseline parameters (heart rate, non invasive blood pressure, respiratory rate, Spo2) all patients were preloaded with ringers lactate 10ml/kg. Lumbar puncture was performed with 25 G Quincke's needle in the sitting position under all aseptic precautions. Time of drug injection was noted as zero. Immediately after injecting the drug patients were made to lie down in supine position. Haemodynamic parameters were noted down every 5 minutes till 30 minutes thereafter every 15 minutes till the end of the surgery.

Onset of sensory block (time from drug injection to the

absence of response to pin prick at T8) was noted. Onset of motor block (time from drug injection to Bromage score 3 according to modified Bromage scale[25]) was noted. Sedation was also recorded at 30 minute (0-awake, 1-sedated comfortably but responding to verbal commands, 2-deeply sedated but arousable, 3-deeply sedated, non arousable).

Intraoperatively all patients were observed for inadequate block, requirement for additional analgesia, nausea, vomiting, hypotension, bradycardia, respiratory depression. In the postoperative period pain was assessed hourly using VAS (visual analogue scale, 0- no pain to 10- worst pain) till VAS >3 at this time rescue analgesia (inj diclofenac 75mg) was given. Time to rescue analgesia was noted down. Time interval from the time of intrathecal drug injection to the time to rescue analgesia was recorded as duration of analgesia.

STATISTICAL ANALYSIS

Statistical analysis was done using MS Office excel software. Redmond, Washington: Microsoft, 2003, Computer software. Student t-test and chi –square test were applied in appropriate situations and 'P' value <0.05 was taken as significant.

RESULT:

SAB was successful in all the patients of both the groups. There was no additional requirement for the analgesic or sedative intraoperatively.

Table 1 shows the demographic parameters. Demographic parameters of both the groups were comparable in respect to age, sex, weight, ASA physical status and duration of surgery. SAB was effective in all the patients of both the groups and there was no need of additional analgesic during intraoperative period in any of the patient.

Table 2 shows the characteristics of sensory blockade. Onset of sensory blockade was comparable in both the groups. There was no statistically significant difference (P>0.05) in the onset of sensory block in both the groups. Postoperative analgesia was significantly prolonged in group D as compared to group M (P<0.05). In group D duration of analgesia was 392.0±22.0 minutes while in group M it was 243.4±11.2 minutes which was statistically significant (P<0.05).

Table 3 shows the characteristics of motor blockade. There was no statistically significant difference in the onset of motor blockade between both the groups (P>0.05). Duration of motor blockade was significantly prolonged in group D (251.0±59.0minutes) in comparison to group M (148.2±4.4) (p<0.05).

Mild hypotension and bradycardia was observed in both the groups which was more in group D (4 patients) than group M (2 patients) . The sedation score of all the patients in both the groups was between 0 and 1. None of the patients exhibited deep sedation. In group M two patients had intra-operative shivering and two patients had nausea. While in group D two patients had nausea while none of the patient had shivering. Both the groups were comparable in respect to haemodynamic parameters and side effects.

DISCUSSION:

Post-operative pain is the main concern during anaesthasia care of the patients. To increase the duration of post-operative analgesia, various drugs are being used an adjuvant to intrathecal LA[2,3,4]. Previous studies have shown dose dependent prolongation of postoperative analgesia with intrathecal midazolam[12,13] and dexmedetomidine[23] without any significant side effect or neurotoxicity[14,15,24] . In this study we compared both the drugs for the efficacy (prolonged postoperative analgesia) and safety (side effects) when used as an adjuvant to intrathecal bupivacaine (H).

In our study we compared both the drugs and did not found any significant difference in the onset of both motor and sensory block in both the groups. Earlier literature suggest that both the drugs prolongs postoperative analgesia as compared to bupivacaine alone[10,11,16,19,20]. In this study we found dexmedetomidine is more effective in respect to duration of analgesia in comparision to midazolam. We found statistically significant prolongation of duration of analgesia in group D, 392.0± 22.0 minutes, as compared to group M, 243.4±11.2 minutes. We can say that dexmedetomidine is more efficacious than midazolam in respect to postoperative analgesia, as a result in this study. We also found statistically significant prolongation of duration of motor block with dexmedetomidine in comparison to midazolam, which may delay the postoperative mobilization of patients.

In our study none of the patient had any requirement of additional analgesics or sedative intraopertively, which shows both the drugs improve the quality of SAB in respect to intraoperative analgesia. Previous studies also depicts that both the drugs when used intrathecally significantly reduces somatic and visceral pain during intraoperative period. **Ghanem et al**[26] and **kalso et al**[27] reported that addition of aloha 2 agonist to intrathecal LA reduces the visceral and somatic pain. Bharti et al[16] has reported reduced visceral and somatic pain with intrathecal midazolam.

Both the drugs produce sedation when used by parenteral route but this effect is not profound with intrathecal route. In our study none of the patient was in deep sleep and all the patient were in sedation score between 0 or 1, which was consistent with previous studies[16,28].

Most feared complication of using alpha-2 agonist is bradycardia and hypotension. In our study 4 patients developed hypotension and two patient developed bradycardia in group D, which responded to ephedrine and atropine. In group D three patients felt nausea while in group M two patients had nausea. Three patients of group M had intraoperative shivering while in group D none of the patient experienced shivering. **Usha et al** and **Karaman and colleague** have found in their study that admnisteration of dexmedetomidine infusion decreases the incidence of shivering intraoperatively[31,32]. There was no significant side effect observed in both the groups as consistent with earlier studies[16,28].

Earlier studies[29,30] also suggests that intrathecal dexmedetomidine is an better alternative to midazolam as an adjuvat to LA, as dexmedetomidine produces more prolonged postoperative analgesia without any significant adverse outcome.

CONCLUSION:

As an adjuvant to intrathecal bupivacaine (H), dexmedetomidine is a better choice over midazolm. It produces significantly prolonged postoperative analgesia without any significant side effect in comparision to midazolam. This study was conducted in a small group of relatively healthy young patients. For more conclusive results it requires further study in a bigger number of patients with different type of co-morbidities.

Table 1: Patient Demographic Profile
PATIENT DEMOGRAPHIC PROFILE

Variables	Group D (n=40) Mean ± SD	Group M (n=40) Mean ± SD	p value
Age (years)	38.4± 6.6	37.8± 6.8	> 0.05
Weight (Kg)	57.8 ± 8.0	58.2 ± 8.8	> 0.05
ASA I/II	25/15	24/16	
Duration of Surgery (Min)	77.7 ± 8.5	78.6 ± 9.0	> 0.05

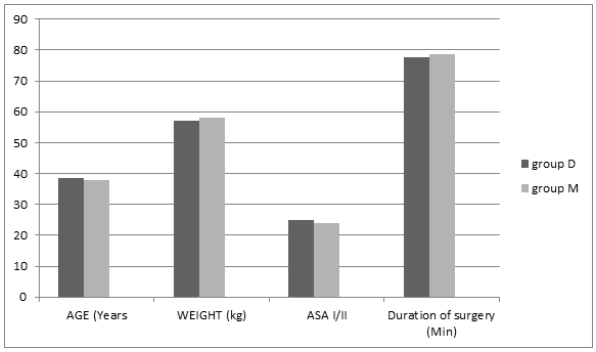


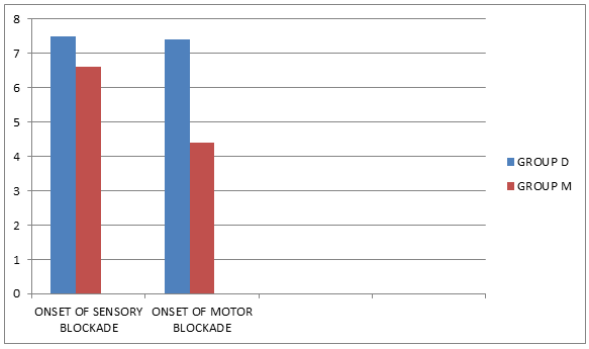
Table 2 : Characteristic of sensory blockade

Variables	Group D (n=40) Mean ± SD	Group M (n=40) Mean ± SD	p value
Onset of sensory blockade (min)	7.5 ± 1	6.6 ± 1	> 0.05
Duration of Analgesia (Min)	392.0 ± 22.0	243.4 ± 11.2	< 0.05
Pain Score (VAS)	4.7 ± 1.9	6.7 ± 1.18	< 0.05

Table 3:Characteristic of Motor blockade

Variables	Group D (n=40) Mean ± SD	Group M (n=40) Mean ± SD	p value
Onset of Motor blockade (min)	7.4 ± 0.66	7.0 ± 0.12	> 0.05
Duration of Motor blockade(Min)	251.0 ± 59.0	148.2 ± 4.4	< 0.05

ONSET OF BLOCKADE



DURATION OF BLOCKADE

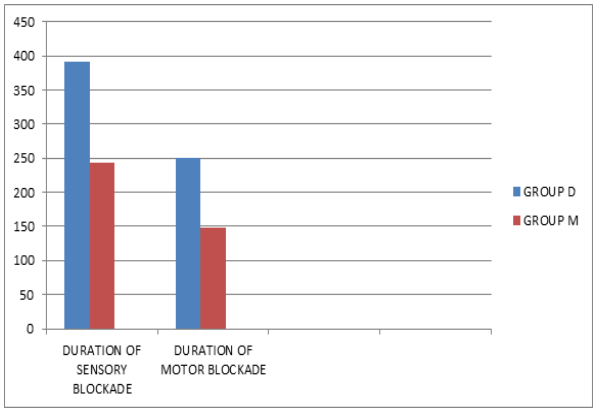
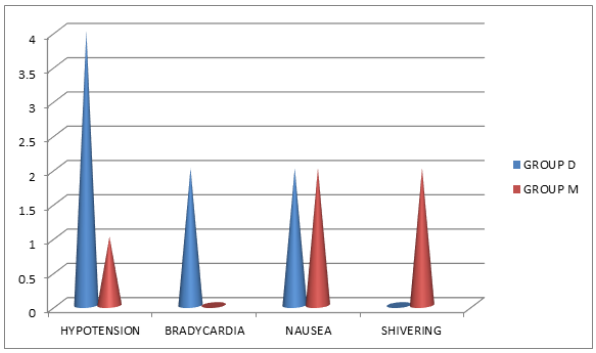


Table 4: Side Effect Profile

Variables	Group D (n=40)	Group M (n=40)
Hypotension	4	1
Bradycardia	2	0
Nausea	2	2
Shivering	0	2

SIDE EFFECTS



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