ORIGINAL ARTICLE

Comparative Study on Various Adjuvants used during Spinal Anaesthesia in Infraumbilical Surgeries

Basheer Ahmed Khan[1], Md Mohib Hussain[2], Javed ZS[3], Naseeba Fatima[4], Santosh Singh[5]

[1]-Professor and Head, Dept. of Anaesthesiology, Deccan College of Medical Sciences
[2,3]- Senior Residents, Dept. of Anaesthesiology, Deccan College of Medical Sciences
[4,5]- Post graduates, Dept. of Anaesthesiology, Deccan College of Medical Sciences

Abstract

This prospective randomized double-blind study was conducted to evaluate the onset and duration of sensory and motor block as well as perioperative analgesia and adverse effects of various adjuvants like dexmedetomidine, magnesium sulphate, fentanyl given during spinal anaesthesiawith 0.5% hyperbaric bupivacaine for central neuraxial block. A total of 120 patients were randomly allocated into four groups to receive intrathecally either 15 mg hyperbaric bupivacaine plus 10 µg dexmedetomidine (group A, n =30) or 15 mg hyperbaric bupivacaine plus 50 mg magnesium sulfate (group B, n =30) or 15 mg hyperbaric bupivacaine plus 25 µg fentanyl (group C, n =30) or 15 mg hyperbaric bupivacaine plus 0.1 ml saline (group D, n =30) as control. The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side-effects were noted. The time of onset to reach T10 dermatome level and to reach peak sensory level as well as the onset time to reach modified Bromage 3 motor block were significantly different in all the four groups. The onset time to reach peak sensory and motor level was shorter in group A as compared with the control group C, and it was significantly prolonged in group B. It was also found that patients in group A had significant longer sensory and motor block times when compared to patients in group B, which was greater than in the fentanyl group C and control group D. In this study it was found that onset of anaesthesia was rapid and of prolonged duration in the dexmedetomidine group (A). However, in the magnesium sulfate group (B), although onset of block was delayed, the duration was significantly prolonged as compared with the fentanyl group (C) and control group (D), but to a lesser degree than in the dexmedetomidine group (A). All the groups were similar with respect to hemodynamic variables and there were no significant side-effects in either of the groups.

***Keywords**: Hyperbaric Bupivacaine, Dexmedetomidine, Magnesium sulphate, Fentanyl*

Address for correspondence: Dr. Basheer Ahmed Khan, Professor and Head, Dept. of Anaesthesiology, Deccan College of Medical Sciences

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Introduction

Spinal anaesthesia is given by administering various local anaesthetic agents intrathecally and is associated with relatively short duration of action and thus early analgesic intervention is needed in post-operative period.[1] Adjuvants are drugs added to improve the quality, to accelerate the onset of action of local anaesthetic given and to overcome the problems of spinal anaesthesia. Various adjuvants like morphine, fentanyl, clonidine, midazolam, ketamine, magnesium sulfate and dexmedetomidine are added by various routes like epidural, intrathecal and intravenous.[2,3]

Opioids are the most commonly used intrathecal adjuvants. Fentanyl is a lipophilic drug and the addition of a small dose to spinal anaesthesia can produce more rapid onset and better quality of surgical block and leads to more rapid recovery of motor function and allow for earlier discharge after surgery.

Dexmedetomidine is a new highly selective drug in the group of Alpha 2 adrenergic receptor agonists. No neurological defects have been reported till date in both human and animal studies during intrathecal or epidural use. The current trends with the use of Dexmdetomidine is going to change the scenario owing to excellent results with the use of Dexmedetomidine[1,4].

Antinociceptive action of Magnesium (Mg) effects appear to be relevant not only to chronic pain[5] but it also determines the duration and intensity of postoperative pain[6]. These effects are primarily based on the regulation of calcium influx into the cell. Mg is a non competitive antagonist to NMDA receptors and has the potential to prevent central sensitization from peripheral nociceptive stimulation. Intravenous (i.v.) administration of Mg, even at high doses, is associated with a limited passage across the blood–brain barrier[7]. In previous studies, it was demonstrated that intrathecally administered Mg prolonged spinal opioid analgesia both in rats and in humans[8,9]. The addition of Mg to spinal anaesthesia improved postoperative analgesia in an orthopedic setting[10,11]. The addition of intrathecal magnesium sulfate (MgSO4) to 10 mg bupivacaine plus 25 µg fentanyl prolonged spinal anaesthesia in patient sunder going lower extremity surgery[11]

Materials & Methods

After obtaining institutional ethical committee approval and written informed consent, 120 ASA physical status I and II patients aged 18–50 years, of either gender, height 160–180 cm and weight 50–90 kg, scheduled for infraumbilical surgeries (excluding caesarean sections) under spinal anaesthesia were included in this prospective randomized, double-blinded study carried out at Princess Esra Hospital, Deccan College of Medical Sciences.

Inclusion criteria:

1. American Society of Anaesthesiologists Grade 1 and 2 patients.
2. Age 18-50 years of either gender.
3. Patients undergoing infraumbilical surgeries.
4. Patients free from cardiac and respiratory dysfunction.

Exclusion criteria:

1. American Society of Anaesthesiologists Grade 3 and 4 patients.
2. Patients with known contraindications for spinal anaesthesia.
3. Patients with haemodynamic instability.
4. Patient on antihypertensive and antidepressants.
5. Patients who refused for spinal anaesthesia.
6. Patients undergoing Caesarean section.

Patients received no premedication and, upon arrival of patients into the operating room, routine standard monitoring with ECG, pulse oximetry (SpO2) and non invasive blood pressure (NIBP) were connected. Following infusion of 500 ml lactated Ringer's solution and with the patient in the sitting position, lumbar puncture was performed under strict aseptic precautions at the L3-L4 level through a midline approach using a 25G Quincke spinal needle.

Using computer-generated random numbers, patients were allocated into four groups:

- Group A received 15 mg hyperbaric bupivacaine and10 µg DXM
- Group B received 15 mg hyperbaric bupivacaine and50 mg Magnesium
- Group C received 15 mg hyperbaric bupivacaine and 25 µg fentanyl
- Group D received 15 mg hyperbaric bupivacaine plus 0.1 ml normal saline as control.

After intrathecal injection, patients were positioned in supine position and all patients were given oxygen at 2 L/min through a face mask. The anaesthesiologist performing the block was blinded to the study drug and recorded the intra-operative data. Sensory block was assessed bilaterally by using analgesia to pin prick.

Motor blockade was assessed by using the modified Bromage Scale[12]

Modified Bromage Scale

0= Free movement of legs, feet with ability to raise extended legs.

1= Inability to raise extended legs, but able to move knees & feet.

2= Inability to raise extended legs or move knee. Able to move feet.

3= Inability to raise extended legs, flex knees, ankle or move toes

The time to reach T10 dermatome sensory block from the onset, peak sensory level and Bromage 3 motor block were recorded before surgery. The VAS score was used to assess pain. Time of rescue analgesia is defined as the time from sensory block to the time when patient complains of pain or VAS score of >3. Injection tramadol 50mg i.v. was given as rescue analgesia.

The regression time for sensory and motor block were recorded in our post anesthesia care unit (PACU). All durations were calculated considering the time of intrathecal injection as time zero. Patients were discharged from the PACU only after sensory regression to S1 dermatome and Bromage 0.

The four groups were monitored preoperatively, intra-operatively and during shifting for heart rate, NIBP and SpO2 . Hypotension was defined as systolic blood pressure <90 mmHg or >30% decrease in baseline values which was treated with mephentermine 6mg i.v. in incremental doses.

Bradycardia was defined as heart rate <60/min which was treated with atropine 0.6 mgi.v. Intraoperative nausea, vomiting was treated with Ondansetron 4 mg. Also pruritus, additive analgesia, sedation or any other side-effects were noted and recorded.

Results

The time of onset of block, both sensory up to T10 dermatome and motor to Bromage 3 scale, was rapid in the DXM group A (2.27 ± 1.09 and 3.96 ± 0.92), fentanyl group C (3.12 ± 1.16 and 4.16 and 0.98) and delayed in the Mg group B (6.46 ± 1.33 and 7.18 ± 1.38) in comparison with the control group D (4.14 ± 1.06 and 4.81 ± 1.03). The statistical tests for difference between the groups was conducted through one way ANOVA, with post tests being statistically significant in both sensory (F=97.118, P <0.0001) and motor (F=65.7, P <0.0001) [Tables 1 and 2].

The time of regression of block, both sensory up to T10 dermatome and motor to Bromage 1 scale, was prolonged in the DXM group A (352 ± 45 and 331 ± 35) and in the Mg group B (265 ± 65 and 251 ± 51) when compared with the fentanyl group C (202 ± 50 and 192 ± 40) and control group D (194 ± 55 and 140 ± 34). However, the duration was longest in the DXM group among the four groups. The statistical difference between the groups conducted through one-way ANOVA with post tests was statistically significant in both sensory (F=60.3, P <0.0001) and motor (F=166.9, P <0.0001) [Tables 3 and 4].

Table 1: Onset times of sensory blocks for sample groups

Group	Mean	SD	P-value (comparison with control group)
Dexmedetomidine (A)	2.27	1.09	<0.001
Magnesium (B)	6.46	1.33	<0.001
Fentanyl (C)	3.12	1.16	<0.001
Control (D)	4.14	1.06	
ANOVA summary			
F-value		97.118	
P-value		<0.0001	
Assumption tests			
KS test for normality		Passed	
Bartlett test		Passed	

Table 2: Onset times of motor blocks for sample groups

Group	Mean	Std dev	P-value (comparison with control group)
Dexmedetomidine (A)	3.96	0.92	<0.05
Magnesium (B)	7.18	1.38	<0.001
Fentanyl (C)	4.16	0.98	<0.05
Control (D)	4.81	1.03	
ANOVA summary			
F-value		65.7	
P-value		<0.0001	

Assumption tests		
KS test for normality	Passed	
Bartlett test	Passed	

Table 3: Regression times of sensory blocks for sample groups

Group	Mean	Std dev	P-value (comparison with control group)
Dexmedetomidine (A)	352	45	<0.001
Magnesium (B)	265	65	<0.001
Fentanyl (C)	202	50	<0.001
Control (D)	194	55	
ANOVA summary			
F-value			60.3
P-value			<0.0001
Assumption tests			
KS test for normality			Passed
Bartlett test			Passed

Table 4: Regression times of motor blocks for sample groups

Group	Mean	Std dev	P-value (comparison with control group)
Dexmedetomidine (A)	331	35	<0.001
Magnesium (B)	251	51	<0.001
Fentanyl (C)	192	40	<0.001
Control (D)	140	34	
ANOVA summary			
F-value		166.9	
P-value		<0.0001	
Assumption tests			
KS test for normality		Passed	
Bartlett test		Passed	

There was no significant difference in the mean values of heart rate and mean arterial pressures in the first hour after performing the spinal anaesthesia and the first hour in the PACU between the four groups. The SpO 2 was higher than 95% in all patients in all the groups, either in the intra-operative or in the PACU. There was no case report of neurological deficit due to spinal anaesthesia during the follow up of these cases.

Discussion

DXM reduces opioid and inhalational anaesthetic requirements when used intravenously during anesthesia[13].Compared with clonidine, the affinity of DXM to a-2 receptors has been reported to be 10-times more than clonidine[14]. Kalso et al[15]and Post et al[14]reported a 1:10 dose ratio between intrathecal DXM and clonidine in animals. Intrathecal DXM when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons[16]. Motor block prolongation by a-2 adrenoreceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the spinal cord[17].Intrathecal a-2-receptor agonists have antinociceptive action for both somatic and visceral pain[18].

Kanaziet al[19]found in their study that the supplementation of bupivacaine (12 mg) spinal block with a low-dose DXM (3 µg) produces a significantly shorter onset of motor block and a significantly longer sensory and motor block than bupivacaine alone. The results of Al-Mustafa et al[20]and Al-Ghanem et al[21] used higher doses of DXM (5 µg and 10 µg), and found that its effect is dose-dependent and that the onset of sensory block to reach T10 dermatome was shorter with the use of DXM.

We used a higher dose of DXM and a larger volume was injected into the subarachnoid space. The most significant side-effects reported

with the use of intrathecal a-2 adrenoreceptor agonists are bradycardia and hypotension. In the present study, these side-effects were not significant probably because we used the drug intrathecally, instead of using the intravenous route.

On the other hand, in the Mg group, it was found that the onset and resolution of motor blockade and the time to attain maximum sensory level were longer. Ozalevli et al observed a similar delay in onset of spinal anaesthesia when adding intrathecal Mg to fentanyl and isobaric bupivacaine (we used hyperbaric bupivacaine in our study)[22]. They suggested that the difference in pH and baricity of the solution containing Mg contributed to the delayed onset, which may also be the case in the study by Malleeswaran et al .on mild preeclampsia patients[23]. In our study, there was prolongation of the motor and sensory block, although less than that with intrathecalDXM.

Arcioni et al .also observed that intrathecal and epidural Mg potentiated and prolonged motor block[24]. These resultsare consistent with a previous study conducted in patients undergoing lower extremity surgery during spinal anaesthesia, in which the addition of intrathecal Mg (50 mg) to 10 mg bupivacaine plus 50 μg fentanyl prolonged the period of spinal anaesthesia. Intrathecal Mg was used in order to increase the analgesic duration of opioids in humans, and they demonstrated that addition of 50 mg intrathecal Mg to intrathecal fentanyl led to better analgesia during painless delivery.

Mg blocks N-Methyl-D-aspartate (NMDA) channels in a voltage-dependent way and produces a dramatic reduction of NMDA-induced currents[25]. Noxious stimulation leads to the release of glutamate and aspartate neurotransmitters, which bind to the NMDA receptor. Activation of these receptors leads to calcium entry into the cell and initiates a series of central sensitization such as wind-up and long term potentiation in the spinal cord in the response of cells to prolonged stimuli. NMDA receptor signalling may be important in determining the duration of acute pain. Mg blocks calcium influx and noncompetitively antagonizes NMDA receptor channels[26].

Neuraxial opioids provide good analgesia similar to systemic administration, but in small doses and concentrations with less risk of systemic side effects. Intrathecal opioids exert its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have supraspinal spread and action. Fentanyl being lipophilic and more potent, addition of small doses to spinal anaesthesia can produce more rapid onset and better quality surgical block and lead to more rapid recovery of motor function and allow for earlier discharge after surgery In the present study the highest mean sensory block, the mean time taken for two segment regression and the mean time taken for regression to S1 segment was statistically significant with p value of <0.001 in group A in comparison to group C. The duration of analgesia is prolonged in dexmedetomidine group when compared to fentanyl. The mean time for rescue analgesia was significantly higher with dexmedetomidine. But dexmedetomidine produced prolonged analgesia when compared to fentanyl and MgSo4 which was statistically significant in all the studies.

The side effects like nausea, vomiting, hypotension, decrease in saturation, pruritis and shivering during intraoperative and postoperative period were comparable ($p>0.05$). Similar observations were noted in Wahlanderetal[27], Gupta et al[28], Ogan et al, Bajwa et al[29] and El-Hennawy[30]

Conclusion

Intrathecal DXM supplementation of spinal block seems to be a good alternative to intrathecal Mg and Fentanyl, as it produces earlier onset and prolonged duration of sensory and motor block without associated significant hemodynamic alterations. Ten micrograms of DXM as adjuvant to spinal bupivacaine in surgical procedures of long duration has minimal side-effects, and provides excellent quality of postoperative analgesia.

Intrathecal Mg also prolongs the duration of spinal analgesia, but this is less than intrathecal DXM and is with a delayed onset. On comparing intrathecal dexmedetomidine and intrathecal fentanyl with bupivacaine, the results indicate that dexmedetomidine provides better sensory blockade in terms of highest sensory level achieved, time of two segments regression and time of regression to S1 segment and prolonged motor blockade when compared to fentanyl. The hemodynamic stability and side

effects were similar in both the groups. Further studies are required to determine whether larger doses of intrathecal Mg can produce greater potentiation of analgesia and reduce opioid requirements.

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