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Original Research Article

Prospective Randomized Clinical Study to Assess the Effect of Intrathecal Dexmedetomidine and Magnesium as Adjuvants to Bupivacaine in Patients Undergoing Total Hip Replacement

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Conflict of interest: Nil

Aim: To compare the effect of intrathecal dexmedetomidine and magnesium as adjuvants to bupivacaine in patients undergoing total hip replacement.

Methodology: In this prospective randomized, double-blinded study in Department of Anesthesia and critical care, Patna Medical college and hospital, Patna, Bihar, India for one year. 90 ASA physical status I and II patients aged 18–45 years, of both the genders scheduled for total hip replacement surgery under spinal anesthesia were included. Patients received no premedication and, upon arrival of patients into the operating room, ECG, pulse oximetry (SpO2) and noninvasive blood pressure (NIBP) were monitored. Following infusion of 500 mL lactated Ringer's solution and with the patient in the sitting position, lumbar puncture was performed at the L3-L4 level through a midline approach using a 25G Quincke spinal needle. Using computer-generated random numbers, patients were allocated into three groups. Group D received 15 mg hyperbaric bupivacaine and 0.1 ml (10 μg) DXM. Group M received 15 mg hyperbaric bupivacaine and 0.1 ml (50 mg) Mg. Group C received 15 mg hyperbaric bupivacaine and 0.1 ml normal saline as control.

Results: The onset time of block, both sensory up to T10 dermatome and motor to Bromage 3 scale, was rapid in the DXM group D (2.83 ± 1.23 and 4.12 ± 1.26) and delayed in the Mg group M (6.73 ± 1.93 and 7.38 ± 1.47) in comparison with the control group C (4.72 ± 1.73 and 4.73 ± 1.27). The difference between the groups was statistically significant in both sensory and motor (P<0.0001). The regression time of block, both sensory up to T10 dermatome and motor to bromage 3 scale, was prolonged in the DXM group D (349 ± 45 and 329 ± 34) and in the Mg group M (278 ± 66 and 258 ± 55) when compared with the control group C (199 ± 57 and 137 ± 53). However, the duration was longest in the DXM group among the three groups. The difference between the groups was statistically significant in both sensory and motor (P<0.0001). The SpO_2 was higher than 95% in all patients in the three groups, either in the intraoperative or in the PACU time.

Conclusion: Dexmedetomidine leads to faster onset and prolonged duration of both sensory and motor block, prolonged duration of analgesia with minimal hemodynamic changes and side effects in comparison to magnesium sulfate when used as an adjuvant with hyperbaric bupivacaine in spinal anesthesia.

Keywords: Dexmedetomidine, Magnesium Sulfate, Bupivacaine.

Introduction

Regional anesthesia (spinal or epidural) is considered to be safer than general anesthesia for lower abdominal and lower limb surgeries. It avoids general anesthesia-related problems such as airway manipulation, misplacement of endotracheal tube, hypo or hyperventilation, pulmonary aspiration and metabolic complications. It reduces surgical stress response by attenuating increase in the levels of plasma catecholamines and other hormones, reduces the risk of postoperative thromboembolic events with decreased intraoperative blood loss. In addition to this, regional anesthesia provides intra and postoperative analgesia [1, 2].

Total hip replacement surgeries may be performed under regional (spinal or epidural) or general anesthesia, but neuraxial blockade is the preferred mode of anesthesia. Spinal block is still the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter in situ, less failure rates and cost effectiveness, but has the drawbacks of shorter duration of block and lack of postoperative analgesia. In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anesthesia and faster recovery [3].

Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, enabling patients to return to their normal activity more quickly. The quality of the spinal anesthesia has been reported to be improved by the addition of opioids (such as morphine, fentanyl and sufentanil) and other drugs [such as dexmedetomidine (DXM), clonidine, magnesium sulfate (Mg), neostigmine, ketamine and midazolam], but no drug to inhibit nociception is without associated adverse effects. DXM, a highly selective a-2 agonist drug, is approved as an intravenous sedative and co-analgesic drug. Its use is often associated with a decrease in heart rate and blood pressure [4]. Intrathecal and epidural characteristics of DXM have been studied in animals [5, 6].

Magnesium, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, whose efficacy or safety as an intrathecal adjuvant has been studied in recent years. Magnesium blocks calcium influx and non-competitive NMDA channel antagonism. The antinociceptive effect of magnesium seems to be effective in management of chronic and post-operative pain. The addition of magnesium as intrathecal adjuvant to LA has been reported to improve the post-operative analgesia [7, 8].

Based on the earlier studies, it was hypothesized that intrathecal dexmedetomidine (5 μg) or magnesium sulfate (75 mg) with hyperbaric 0.5% bupivacaine would provide the effective spinal anaesthesia in terms of prolongation of postoperative analgesia with minimal side effects. The purpose of this study was to compare the effect of intrathecal dexmedetomidine and magnesium as adjuvants to bupivacaine in patients undergoing total hip replacement.

Materials and Methods

In this prospective randomized, double-blinded study in Department of Anesthesia and critical care, Patna Medical college and hospital, Patna, Bihar, India for one year , 90 ASA physical status I and II patients aged 18–45 years, of both the genders scheduled for total hip replacement surgery under spinal anesthesia were included. Patients with a history of uncontrolled, labile hypertension, patients with allergy to the study drugs, opium addiction, and sedative

drugs consumption, contraindication for spinal anesthesia, failure of spinal block and the need for general anesthesia were excluded from the study. Patients received no premedication and, upon arrival of patients into the operating room, ECG, pulse oximetry (SpO2) and noninvasive blood pressure (NIBP) were monitored. Following infusion of 500 mL lactated Ringer's solution and with the patient in the sitting position, lumbar puncture was performed at the L3-L4 level through a midline approach using a 25G Quincke spinal needle. Using computer-generated random numbers, patients were allocated into three groups:

- Group D received 15 mg hyperbaric bupivacaine and 0.1 ml (10 μg) DXM.
- Group M received 15 mg hyperbaric bupivacaine and 0.1 ml (50 mg) Mg.
- Group C received 15 mg hyperbaric bupivacaine and 0.1 ml normal saline as control.

After intrathecal injection, patients were positioned in supine position and oxygen 2 L/min was given through a face mask. The anesthesiologist performing the block was blinded to the study drug and recorded the intraoperative data. Sensory block was assessed bilaterally by using analgesia to pin prick with a short hypodermic needle in the midclavicular line. Motor blockade was assessed by using the modified Bromage scale [9] (Bromage 0, the patient is able to move the hip, knee and ankle; Bromage 1, the patient is unable to move the hip but is able to move the knee and ankle; Bromage 2, the patient is unable to move the hip and knee but able to move the ankle; Bromage 3, the patient is unable to move the hip, knee and ankle). The time to reach T10 dermatome sensory block, peak sensory level and Bromage 3 motor block were recorded before surgery. The regression time for sensory and motor block were recorded in a post anesthesia care unit (PACU). All durations were calculated considering the time of spinal injection as time zero. Patients were discharged from the PACU after sensory regression to S1 dermatome and Bromage 0.

The three groups were monitored preoperatively, intraoperatively and during shifting for heart rate, NIBP and SpO2. Hypotension was defined as systolic blood pressure < 90 mmHg or> 30% decrease in baseline values. Tachycardia was defined as heart rate >100/min and bradycardia was defined as heart rate <60/min. Intraoperative nausea, vomiting, pruritus, additive analgesia, sedation or any other side-effects were recorded.

Results

There were no differences in age, height, body weight and body mass index (BMI) between the groups. Systolic, diastolic arterial blood pressures, heart rates and oxygen saturations remained stable, and there was no significant difference between the groups.

Table 1: Onset times of sensory blocks for sample groups

Group	Mean	Std dev	*P*-value (comparison with control group)
Dexmedetomidine (D)	2.83	1.23	<0.001
Magnesium (M)	6.73	1.93	<0.001
Control (C)	4.72	1.73	
P-value		<0.0001	

The onset time of block, both sensory up to T10 dermatome and motor to Bromage 3 scale, was rapid in the DXM group D (2.83 ± 1.23 and 4.12 ± 1.26) and delayed in the Mg group M (6.73 ± 1.93 and 7.38 ± 1.47) in comparison with the control group C (4.72 ± 1.73 and 4.73 ± 1.27). The difference between the groups was statistically significant in both sensory and motor (P<0.0001)

Table 2: Onset times of motor blocks for sample groups

Group	Mean	Std dev	*P*-value (comparison with control group)
Dexmedetomidine (D)	4.12	1.26	<0.01
Magnesium (M)	7.38	1.47	<0.01
Control (C)	4.73	1.27	
P-value		<0.01	

Table 3: Regression times of sensory blocks for sample groups

Group	Mean	Std dev	*P*-value (comparison with control group)
Dexmedetomidine (D)	349	45	<0.001
Magnesium (M)	278	66	<0.001
Control (C)	199	57	
P-value		<0.001	

Table 4: Regression times of motor blocks for sample groups

Group	Mean	Std dev	*P*-value (comparison with control group)
Dexmedetomidine (D)	329	34	<0.001
Magnesium (M)	258	55	<0.001
Control (C)	137	53	
P-value		<0.001	

The regression time of block, both sensory up to T10 dermatome and motor to bromage 3 scale, was prolonged in the DXM group D (349 ± 45 and 329 ± 34) and in the Mg group M (278 ± 66 and 258 ± 55) when compared with the control group C (199 ± 57 and 137 ± 53). However, the duration was longest in the DXM group among the three groups. The difference between the groups was statistically significant in both sensory and motor (P<0.0001).

There was no significant difference in the mean values of heart rate and mean arterial pressures in the first hour after performing the spinal anesthesia and the first hour in the PACU between the three groups. The SpO_2 was higher than 95% in all patients in the three groups, either in the intraoperative or in the PACU time.

Discussion

The present study was conducted to compare intrathecal 0.5% bupivacaine with either dexmedetomidine or magnesium sulfate in patients undergoing total hip replacement surgeries under spinal anesthesia. The intrathecal dose of dexmedetomidine (5 μg) was chosen based on previous study by Al-Mustafa et al. [10] where in no neurotoxic effects have been observed or reported in their study. Similarly the dose of intrathecal magnesium sulfate (75 mg) in our study was based on previous studies like Kathuria B et al. [11] and Jabalameli M et al. [12] that the use of this particular dose could prolong the duration of analgesia without added side effects.

The mechanism by which intrathecal alpha 2-adrenergic agonists prolong the motor and sensory block of local anesthetics is not clear. It may be an additive or synergistic effect secondary to the different mechanisms of action of local anesthetic and alpha 2 adrenergic agonist. The local anesthetics act by blocking sodium channels, whereas the alpha 2 adrenergic agonist acts by binding to pre synapyic C fibre and post synaptic dorsal horn neurons. Intrathecal alpha 2 adrenergic agonist produce analgesia by depressing the release of C fiber transmission by hyperpolarization of post synaptic dorsal horn neurons [13]. Li et al observed that Glutamate is involved in excitatory neurotransmission nociception

and plays an essential role in relaying noxious stimuli in the spinal cord. Intrathecal injection of alpha 2 adrenergic agonists produces potent antinociceptive effects by altering spinal neurotransmitter release and effectively treats acute pain [13, 14].

The mean time for onset of both sensory and motor block were found to be significantly faster in dexmedetomidine group when compared to magnesium sulfate group. Wapang A et al. [15] had conducted a study to compare dexmedetomidine (10 μg) and magnesium sulfate (50 mg) with intrathecal bupivacaine (12.5 mg) for various block characteristics under spinal anesthesia and found that mean onset time of sensory block was significantly faster in the Group D (2.53 ± 0.57 min) compared to Group M (8.00 ± 1.29 min) which concurs with our study. On the contrary, Farooq and Gupta [16] studied the effect of adding (50 mg) magnesium VS (10 μg) dexmedetomidine intrathecal as adjuvant to bupivacaine on efficacy of block on 90 patients undergoing lower abdominal and lower limb surgeries. They founded that onset time of sensory and motor block was shorter in dexmedetomidine group when compared with the other group, but the difference was statistically insignificant, which is not consistent with our results.

Khezri et al [17] found that increase in metabolism of bupivacaine due to activation of cytochrome P450 by magnesium may be responsible for delayed onset of sensory block. Aamir Laique Khan, Raj Bahadur Singh observed in their study that adding intrathecal dexmeditomedine to bupivacaine in spinal anaesthesia which reduces the time for onset of sensory blockage and prolongs the duration of action similar to this study [18]. No significant complications were observed in both the groups. Wapang A et al. [15] reported side effects like nausea, vomiting, hypotension, bradycardia, and shivering after addition of dexmedetomidine and magnesium sulfate to spinal anesthesia but found to be not significant.

Conclusion:

Dexmedetomidine leads to faster onset and prolonged duration of both sensory and motor block, prolonged duration of analgesia with minimal hemodynamic changes and side effects in comparison to magnesium sulfate when used as an adjuvant with hyperbaric bupivacaine in spinal anesthesia. So it can be said that Intrathecal DXM supplementation of spinal block can be a good alternative to intrathecal magnesium sulfate.

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