Effect of Intrathecal Dexmedetomidine versus Intrathecal Magnesium Sulfate used as Adjuvants to Bupivacaine in Patients Undergoing Lower Abdominal Surgeries

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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 side effects of dexmedetomidine and magnesium sulfate given intrathecally with 0.5% hyperbaric bubivacaine for spinal anesthesia. A total 90 patients classified as ASA I and II scheduled for lower abdominal surgeries were randomly allocated to receive intrathecally either 15 mg hyperbaric bubivacaine plus 10 μg dexmedtomidine (group D) or 15 mg hyperbaric bupivacaine plus 50 mg magnesium sulfate (group M) or 15 mg hyperbaric bupivacaine plus 0.1 ml saline (group C). The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side effects were recorded. It was found that the onset of anesthesia was rapid and prolonged duration in D group. However, in M group, although onset of block was delayed, the duration was significantly prolonged as compared with C group.

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1- Introduction:

In the recent days regional techniques have come to take an upper hand in anesthesia over general anesthesia due to certain advantages like less chance of airway compromise and aspiration, facilitation of postoperative analgesia and benefits in some preexisting medical conditions and so on. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period [(1)]. A number of adjuvants, such as opioids and others have been studied to prolong the effect of spinal anesthesia. The addition of opioids to local anesthetic solution has disadvantages, such as pruritus and respiratory depression [(2)]. Dexmedetomidine, a new highly selective α2-agonist, is a proven neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects[(3)]. The mechanism by which intrathecal α2-adrenoceptor agonists prolong the motor and sensory block of local anesthetics is not well known. They may act by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons. Their analgesic action is a result of depression of the release of C-fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons[(4)].

Local anesthetic agents act by blocking sodium channels. The prolongation of effect may result from synergism between local anesthetic and α2-adrenoceptor agonist, while the prolongation of the motor block of spinal anesthetics may result from the binding of α2-adrenoceptor agonists to motor neurons in the dorsal horn [(5)]. Intrathecal α2-receptor agonists have been found to have antinociceptive action for both somatic and visceral pain [(6)]. Antinociceptive effects of Mg appear to be relevant not only to chronic pain but it also determines, in part, the duration and intensity of postoperative pain. These effects are primarily based on the regulation of calcium influx into the cell, i.e. natural physiological calcium antagonism. Mg is a noncompetitive antagonist to NMDA receptors and has the potential to prevent central sensitization from peripheral nociceptive stimulation[(7)]. Intravenous (i.v.) administration of Mg, even at high doses, is associated with limited passage across the blood–brain barrier [(8)]. In previous studies, it was demonstrated that intrathecally administered Mg prolonged spinal opioid analgesia both in rats and in humans[(9)].

2- Patients and Methods:

This is a prospective randomized double-blinded study that was approved by the Ethics Committee of Al-Azhar university hospitals, 90 ASA physical status I and II patients aged 18–45 years, of either gender, height 150–190 cm and weight 60–90 kg, scheduled for lower abdominal surgeries under spinal anesthesia were included in this study. Patients were allocated into three groups:

• Group D received 15 mg hyperbaric bupivacaine and 10 µg dexmedetomidine.

• Group M received 15 mg hyperbaric bupivacaine and 50 mg magnesium sulfate.

• Group C received 15 mg hyperbaric bupivacaine and 0.1 ml normal saline as control.

Exclusion criteria:

- Patients with a history of uncontrolled, labile hypertension.
- Patients with allergy to the study drugs.
- Patients with opium addiction, sedative drugs consumption.
- Patients with contraindication for spinal anesthesia, failure of spinal block and the need for general anesthesia.
- Patients with coagulation disorders.
- Patients with skin infection at site of injection of spinal anesthesia.
- Pregnant patients.

Patients will not receive premedication and, upon arrival of patients into the operating room, ECG, pulse oximetry (SpO2) and noninvasive blood pressure (NIBP) will be monitored. Following infusion of 500 Ml lactated Ringer's solution and with the patient in the sitting position, lumbar puncture will be performed at the L3-L4 level through a midline approach using a 25G Quincke spinal needle (Spinocan, B Braun Medical, Melsungen, Germany).

Sensory level assessment:

After intrathecal injection, patients will be positioned in supine position and oxygen 2 L/min will be given through a face mask. The anesthesiologist performing the block will be blinded to the study drug and will be recorded the intraoperative data. Sensory block will be assessed bilaterally by using ice saline packs.

Motor assessment:

Motor blockade will be assessed by using the modified Bromagescale (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)[10]. The time to reach the highest dermatome sensory block, peak sensory level and Bromage 3 motor block will be recorded before surgery.

Regression time assessment:

The regression time for sensory and motor block will be recorded in a post-anesthesia care unit (PACU). All durations will be calculated considering the time of spinal injection as time zero. Patients will be discharged from the PACU after sensory regression to S1 dermatome and Bromage 3.

Haemodynamicobservation:

All variables of hemodynamic states of the patients including blood pressure, heart rate and oxygen saturation will be recorded in the perioperative period.

Onset time for need of anaelgaesia:

Times for first need of anaelgesia will be recorded for all patients postoperatively.

Statistical analysis: Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

- P-value $\leq$0.05 was considered significant.
- P-value $\leq$0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

3-Results:

There were no differences in age, weight, height, body mass index and duration of surgery between the groups. These groups were similar in the maximal dermatome height achieved.

The onset time of sensory block both sensory up to T10 dermatome and motor to Bromage 3 scale, was rapid in the DXM group D (2.34±1.04 and 4.08±0.87) and delayed in Mg group M (6.65±1.26 and7.4±1.31) in comparison with the control group C (4.26±1.07 and 4.95±0.98). The difference between groups was statistically high significant in both sensory and motor P-value $\leq$0.001 [table 1 and 2].

The regression time of block, both sensory up to S1 dermatome and motor to bromage 0 scale was prolonged in the DXM group D (391±42 and 324±33) and in the Mg group M (272±61 and 234±48) when compared with the control group C (199±52 and 144±10). However, the duration was longest in the DXM group among the three groups. The difference between the groups conducted through one way ANOVA with post tests was statistically significant in both sensory and motor time regression ($p < 0.001$) [table 3 and 4].

In our study there were significance difference ($p <0.05$) between the three groups as regard of sedation in both groups M and C (Magnesium and Control group) all patients were cooperative and oriented (100%) in comparison with group D (DXM) there were 25 patients (83%) who were cooperative and 6 patients (20%) show Brisk response to light glabellar tab.

As regard of hypotension there were no significance difference ($p >0.05$) in between groups; group D (DXM) 15 patients (50%) without hypotension, group M (magnesium) 15 patients (50%) without hypotension and group C (Control) 11 patients (36.7%) without hypotension.

As regard of total dose ephedrine there were significance (p<0.05) in study groups; when we compared between group M and C there were no significance difference (p<0.05) but between group D and group M there were significance difference (p<0.05) and also between group D and group C.

Total dose of ephedrine was more in magnesium group than the other two groups. There were no significance difference (p>0.05) between study groups; all patients (100%) not complained from pruritis except only 2 patients (6%) in magnesium group.

Also about the attacks of bradycardia when we compared between the three groups there were no bradycardia in all patients (100%) as shown in table [5].

Table (1): Onset times of sensory blocks for sample groups.

Groups	Sensory blocks	ANOVA	p-value
Group M	6.65±1.26	9.133	<0.001 (HS)
Group D	2.34±1.04		
Group C	4.26±1.01		

Table (2): Onset times of motor blocks for sample groups.

Groups	Motor blocks	ANOVA	p-value
Group M	7.4±1.31	11.658	<0.001 (HS)
Group D	4.08±0.87		
Group C	4.95±0.98		

Table (3): Regression times of sensory blocks for sample groups.

Groups	Regression time of sensory blocks	ANOVA	p-value
Group M	272.95±61.75	7.196	<0.001 (HS)
Group D	391.4±42.75		
Group C	199.82±52.25		

Table (4): Regression times of motor blocks for sample groups.

Groups	Regression times of motor blocks	ANOVA	p-value
Group M	234±48	7.747	<0.001 (HS)
Group D	324±33		
Group C	144±10		

Table (5): Comparison between groups according side effects.

	Group M	Group D	Group C	ANOVA	p-value
Sedation					
Cooperative	30 (100%)	25 (83.3%)	30 (100%)	6.281	**0.029 (S)**
Brisk response to light glabellar tap	0 (0%)	6 (20%)	0 (0%)		
Hypotension	15 (50%)	15 (50%)	11 (36.7%)	2.611	0.363
T. dose ephedrine (mg)	19.83±12.18	9.45±3.93	13.5±3.95	3.369	**0.019 (S)**
Pruritus	2 (6.7%)	0 (0%)	0 (0%)	1.332	0.782
Bradycardia	0 (0%)	0 (0%)	0 (0%)	0.000	1.000

4- Discussion:

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[11]. Motor block prolongation by α2 adrenoreceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the

spinal cord[12]. Intrathecal α2 receptor agonists have antinociceptive action for both somatic and visceral pain[13]. The results of Al-Mustafa et al[6] and Al-Ghanem et al[3] used higher doses of DXM (5 µg and 10 µg) and found that its effect is dose dependent and the onset of sensory block was shorter to reach T10 dermatome with the use of DXM. Bradycardia in the dexmedetomidine group is believed to be due to postsynaptic activation of central alpha 2adrenoceptors (α2-ARs) results in sympatholytic effect, leading to hypotension and bradycardia, an effect judiciously used to attenuate the stress response of surgery[14]. In agreement with our results Sapana Joshi and Kaja Sriramamurthy showed significant reduction in hemodynamics when 15 µg dexmedetomidine was added to intrathecal bupivacaine.

Magnesium blocks N-Methyl-D-Aspatate (NMDA) channels in a voltage dependent way and produces a dramatic reduction of NMDA induced currents[15]. Noxious stimulation leads to the release of glutamate and aspartate neurotransmitters which bind to the NMDA receptor. Activation of these receptors lead to calcium entry to the cell and initiates a series of central sensitization such as wind-up and long potentiation in the spinal cord in the response of cells to prolong stimuli[16]. Mg blocks calcium influx and noncompetitively antagonizes NMDA receptor channels[17]. In our study, there was prolongation of the motor and sensory block, although less than that with intrathecal DXM. Our results were in agreement with Shukla et al[18]. Who showed that the onset time to reach peak sensory level was shorter in dexmedetomidine group as compared with the control group as his study was done on 90 patients divided into three groups, each of 30 patients. The first group was given intrathecal 15 mg hyperbaric bupivacaine plus 0.1 ml (10µg) dexmedetomidine (group D). The second group was given 15 mg hyperbaric bupivacaine plus 0.1 ml (50 mg) magnesium sulfate (group M) and the third group was given 15 mg hyperbaric bupivacaine plus 0.1 ml saline (group C) as control. He noted that The onset time of block, both sensory up to T10 dermatome was rapid in the DXM group D in comparison with M and C groups. Arcioni et al[19] also observed that intrathecal and epidural Mg potentiated and prolonged motor block.

5-Conclusion:

Intrathecal Dexmedetomedine in a dose of 10 µg supplementation of spinal block seems to be a good alternative to intrathecal Magnesium sulfate 50 µg since it produces rapid onset of motor and sensory and prolong the duration of sensory block and motor block, and it is evident that this type of block may be more suitable for major surgeries on the lower abdomen and lower extremities also it provides good quality of intraoperative analgesia, thermodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia.

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