

Comparative Study Between Dexmedetomidine And Magnesium sulfate Added to Bupivacaine In Spinal Anesthesia For Postoperative Analgesia In Patients Undergoing Perianal Surgeries

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Abstract

Introduction: Spinal anesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer. A number of adjuncts, such as Opioids, Clonidine, and Midazolam have been studied to prolong the effect of spinal anesthesia (ELIA, et al 2008).

Dexmedetomidine (Dex) a new highly selective α_2 -agonist is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and postoperative analgesia with minimal side effects (Kanazi and Al-Ghanem 2009).

Magnesium sulfate (MgSO₄) is an antagonist of N-methyl D Aspartate receptor (NMDA) improves postoperative analgesia after intrathecal administration as an effective adjuvant to bupivacaine (Soave and Arcangeli 2009).

Aim of the work: To compare the postoperative analgesic effects and any side effects of dexmedetomidine and magnesium sulfate (MgSO₄) when added to bupivacaine in spinal anesthesia in patients undergoing perianal surgeries.

Patients and methods: Ninety ASA physical status I and II patients aged 18-70 years, of either sex, scheduled for perianal surgeries under spinal anesthesia in this prospective randomized, double-blinded study.

Results: All the MgSO₄ cases needed analgesia within 4 hours postoperative, while for all the Dex cases needed analgesia within 5 hours postoperative. The difference between the two groups was highly significant.

Conclusion: Addition of dexmedetomidine prolongs the sensory and motor block significantly when used with hyperbaric bupivacaine intrathecally, without increasing the incidence of significant adverse effects. Intrathecal Magnesium also prolongs the duration of sensory and motor block, but lesser than dexmedetomidine.

Key words: Spinal Anesthesia - Postoperative Analgesia - Dexmedetomidine - Magnesium sulfate - Perianal Surgeries.

Introduction

Pain is defined by the International Association for the Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage, (Merskey and Bogduk, 1994).

Pain assessment can be straight forward and brief in the setting of acute pain related to trauma or surgery. It increases in complexity and the time required as the pain becomes persistent, fails to respond to conventional therapy, (Portenoy and Kanner, 1996).

Pain assessment is done by: a) Numeric rating scale: Patients indicate their pain intensity on a scale of 0 to 10, with 0 indicating no pain and 10 the worst pain imaginable.

b) Verbal rating scales consist of a series of words commonly used to describe pain (e.g., no pain, mild pain, moderate pain, severe pain).

c) Visual analog scale consists of a 10-cm line with one end labeled "no pain"

other end labeled “worst pain imaginable.”

d) Faces pain scale presents pictures of 6 to 8 different facial expressions depicting a range of emotions,(Jensen and McFarland, 1993), (Bieri et al, 1990).

Dexmedetomidine is a potent and highly selective α -2 adrenoceptor agonist with sympatholytic, sedative, amnestic, and analgesic properties which has been described as a useful and safe adjunct in many clinical applications. It is the most recently developed and commercialized agent in this pharmacological class,(Carollo and Nossaman 2008).

The hypnotic effect of dexmedetomidine is mediated by the hyperpolarization of noradrenergic neurons in the locus ceruleus of the brain stem. When the α -2 adrenergic receptor is activated, it inhibits adenylyl cyclase. This latter enzyme catalyzes the formation of cyclic AMP (cAMP), a crucial second messenger molecule that acts in many catabolic cell processes. By reducing the amount of cAMP in the cell, dexmedetomidine favors anabolic over catabolic pathways. Simultaneously, there is an efflux of potassium through calcium-activated potassium channels and an inhibition of calcium entry into calcium channels in nerve terminals, (Khan and Ferguson 1999).

The incidence of postoperative bradycardia has been reported to be as high as 40% in healthy patients. These temporary effects have been managed with atropine, ephedrine, and volume infusion. Caution should be taken in those clinical situations where the sympatholytic actions of α -2 receptor agonists prove detrimental, such as in patients with left ventricular dysfunction and when administered to patients who are volume depleted, vasoconstricted, or have severe heart block,(Haselman 2008).

MgSO₄ was first used to prevent eclamptic seizures in 1906 by Horn in Germany, who injected it intrathecally. An intramuscular regimen was used in 1926 to prevent recurrent seizures in women with eclampsia² and the drug was given

intravenously in 1933 to women with pre-eclampsia and eclampsia,(Lazard 1933).

Although it is recognized as an anticonvulsant, significant falls in blood pressure have been observed during use of the recommended therapeutic doses of MgSO₄, the hypotensive action was transient. This transient hypotensive effect has been consistently noted with a bolus infusion and high dose continuous infusion by some authors, (Scardo and, Hogg 1995).

The first sign of magnesium toxicity is usually the loss of tendon (patella) reflexes. This occurs with plasma levels > 5 mmol/L with respiratory depression occurring at levels > 6 mmol/L, (Winkler and Smith 1942).

Other early signs and symptoms of toxicity include nausea, feeling of warmth, flushing, somnolence, double vision, slurred speech and weakness (usually at 3.8 to 5 mmol/L), Muscular paralysis and respiratory arrest will develop at plasma levels of 6.3 to 7.1 mmol/L, Cardiac arrest will develop at plasma levels of 12.5 to 14.6 mmol/L, (Sibai 1990).

Patients and methods

We included 90 ASA physical status I and II patients aged 18-70 years, of either sex, scheduled for perianal surgeries under spinal anesthesia in this prospective randomized, double-blinded study.

Exclusion criteria:

Patients with a history of

- 1- Uncontrolled hypertension.
- 2- Heart block/dysrhythmia.
- 3- Therapy with adrenergic receptor antagonist, calcium channel blocker, opium addiction, and sedative drugs consumption.
- 4- Contraindication for spinal anesthesia .

The patients were preloaded with Lactated Ringer's solution 15ml/kg, lumbar puncture was performed at the L4-L5 level in the sitting position through a midline or lateral approach using 25G spinal needles under complete aseptic precautions.

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

(Group Mg) to receive 2.5ml volume of

0.5% hyperbaric bupivacaine and 50mg magnesium sulfate (0.5ml magnesium sulfate, ampule 1000mg in 10ml-Epico) plus 0.5ml of normal saline. (Group Dex) to receive 2.5ml volume of 0.5% hyperbaric bupivacaine and 10ug dexmedetomidine in 1ml of normal saline Intrathecal injection was given over approximately 10-15s. Patients were positioned in sitting position 5- 10m after completion of the injection as trial for achievement of saddle block and oxygen 2L/min was given through a face mask if the pulse oximeter reading decreased below 90%.

We will measure pulse and blood pressure (systolic and diastolic) after intrathecal injection at 1min, 5min, 10min, 15min, 20min, 25min, and 30 min intraoperative and 2hrs, 4hrs, 6hrs, and 12hrs postoperative.

Sensory block was assessed bilaterally by using sensory response to pin prick with a short hypodermic needle in the midclavicular line to be sure we reach the target sensory level and we measure sensory regression to S1 postoperative .

Motor block assessed by Modified

Bromage scale,(Bromage et al 1969):

0=Able to raise legs above table.

1=Inability to raise extended legs.

2=Inability to flex knees.

3=Inability to flex ankles.

Introduce dexmedetomidine 100ug/ml should be noted like Respiratory Depression, Itching, Shivering, Nausea, Vomiting, Desaturation, Hypotension, Bradycardia.

Duration of complete analgesia was defined as the time from spinal injection to the first report of pain when VAS > 0 and duration of effective analgesia was defined as the time from spinal injection to the first rescue analgesics requirement when VAS reached 4 or more it is the end of spinal analgesia and need to additional analgesia (0=No pain, 10=Most severe pain), (Scardo and Hogg 1995).

The rescue analgesics consisted of intravenous infusion of ketolac 30mg\2ml (Alamrya pharm) (maximum daily dose 60mg) when VAS reached 4 or more. Patients were discharged at Bromage 0 to home.

Results

Table 1 (the onset of sensory and motor block of study group)

	Dex group Mean±SD	Mg group Mean±SD	T Test	P Value
Duration of Surgery (Minutes)	20.11±4.825	16.22±2.173	4.930	<0.001
Onset of Sensory Block (Minutes)	1.33±0.505	1.31±0.468	2.166	0.063
Onset of Motor Block (Minutes)	3.04±0.520	2.58±0.499	4.340	<0.001

This table shows that the surgical duration was nearly 20 minutes in Dex group and 16 minutes in Mg group with highly significant difference between the two groups.

The onset of motor block was much faster in the Mg group (Mean 2.58 ± 0.499) compared to the Dex group (Mean 3.04 ± 0.520), with a highly significant difference motor block and no significant difference in sensory block between the two groups.

Table 2 (postoperative pain assessment)

	Dex group	Mg group	P value
Time when VAS exceeded 0 (complete analgesia)(Min)	240	200	< 0.001
Time when VAS exceeded 4 (effective analgesia) (Min)	300	240	< 0.001
Sensory regression to S1(Min)	200	180	0.466
Bromage 0(Min)	220	200	0.354

This table shows that all of the Mg cases needed analgesia within 4 hours postoperative, while for all of the Dex cases needed analgesia within 5 hours postoperative. The difference between the two groups was highly significant.

Table 3 (complications may appear in the study groups)

	Dex group	Mg group	Chi square	P value
Respiratory Depression	0	0		
Itching	0	0		
Shivering	8	11	0.6	0.438
Nausea	0	0		
Vomiting	13	7	2.314	0.128
Desaturation	0	0		
Hypotension	17	22	1.131	0.288
Bradycardia	34	6	35.280	< 0.001

This table shows shivering, vomiting, hypotension & bradycardia complications are recorded in both groups. Shivering occurred in 8 cases in the Dex group, compared to 11 cases in Mg group, with no significant difference.

Vomiting occurred in 13 cases in the Dex group, compared to 7 cases in Mg group, with no significant difference. Hypotension occurred in 17 cases in the Dex group, compared to 22 cases in Mg group, with no significant difference, while bradycardia occurred in 34 cases in the Dex group, compared to 6 cases in Mg group, with highly significant difference.

Analgesic Administration

Total dose of rescue analgesic on both groups when vas exceed >4 was 2 Amp Ketolac(60mg) on both groups. Quality of intraoperative analgesia was excellent and postoperative analgesia was good.

Discussion:

Gupta et al and ALghanem et al found intrathecal Dexmedetomidine with

bupivacaine is associated with prolonged motor and sensory block with hemodynamic stability and in our study we found that Dexmedetomidine actually prolong sensory and motor block and the blood pressure was stable but there is noticed bradycardia in 70% of cases and these bradycardia may be dose dependent as we used 10µg Dexmedetomidine but Gupta et al and ALghanem et al used 5µg, (Gupta et al 2011) (Al ghanem et al 2009).

Arcioni observed also that intrathecal Mg sulfate prolonged sensory and motor block with hemodynamic stability and this is agree with our study as Mg sulfate when added to bupivacaine prolong sensory and motor block and the pulse and blood pressure were stable, (Arcioni and Palmisani 2007).

On the other hand in Magnesium group the onset of motor block was faster than Dex group (Mean onset of motor block 2.58 minutes) but against our study, Ozalevli et

al observed a delay in onset of motor block when adding intrathecal Mg sulfate (Mean onset of motor block 2.8 min) but this may be dose dependent also as Ozalevli et al used 0.1ml Mg sulfate and we used 0.5ml Mg sulfate in our study, (Ozalevli et al 2005).

Malleeswaran et al found that the onset of sensory block was statistically prolonged in Mg sulfate group compared to Dexmedetomidine group but this is against our study as we found the onset of sensory block was nearly the same in both groups (Mean onset of sensory block in Mg group 1.31 min and in Dex group 1.33 min), (Malleeswaran et al 2010).

Haselman found that the incidence of bradycardia with clonidine (an α -2 agonist similar to dexmedetomidine) has been reported to be as high as 40% in healthy patients, but in our study bradycardia was reported in 70% of cases (Haselman 2008). Khezri et al and Singh et al found that the addition of clonidine to bupivacaine increases the duration of postoperative analgesia significantly more than Mg sulfate, and these results agree with our study as we found that in Dex group VAS >4 at 300 min maximally postoperative and in Mg group VAS >4 at 240 min maximally, (Khezri et al 2014) (Singh et al 2013).

Conclusion

Addition of dexmedetomidine prolonged the sensory and motor block significantly when used with hyperbaric bupivacaine intrathecally, without increasing the incidence of significant adverse effects. Intrathecal Magnesium also prolongs the duration of sensory and motor block, but less than dexmedetomidine.

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