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COMPARISON OF EFFICACY OF INTRATHECAL DEXMEDETOMIDINE AND MAGNESIUM SULPHATE AS ADJUVANTS TO ISOBARIC LEVOBUPIVACAINE IN LOWER LIMB ORTHOPEDIC SURGERIES A PROSPECTIVE RANDOMISED DOUBLE BLIND CLINICAL STUDY

Anaesthesiology

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ABSTRACT

Introduction: Adjuvants in spinal anesthesia extends not only the duration of surgical anesthesia but also provides intraoperative hemodynamic stability and postoperative analgesia. **Aim:** In this study we compare the efficacy of addition of adjuvants Dexmedetomidine and Magnesium sulphate intrathecally with Isobaric Levobupivacaine. **Objectives:** Primary objectives of study include the sensory and motor block characteristics, secondary objectives include hemodynamic parameters, duration of effective analgesia, requirement of rescue analgesia in 24 hrs, sedation and any adverse events were monitored. **Material And Methods:** After getting Institutional Ethics Committee approval, 60 patients of either gender, ASA grade I, II and III scheduled for lower limb orthopedic surgery under spinal anesthesia were enrolled and randomly allocated in two groups. Group LD received 2.5ml of 0.5% Isobaric Levobupivacaine+10ug Dexmedetomidine(0.5ml). Group LM received 2.5ml of 0.5% Isobaric Levobupivacaine+75 mg Magnesium Sulphate(0.5ml). The two groups were compared with respect to the onset and duration of sensory and motor block, two segment regression time, hemodynamic changes, sedation score and duration of postoperative analgesia monitored for 24 hours postoperatively. **Results:** The onset of sensory and motor block were significantly faster in Group LD (4.13+1.16min and 5.46+1.30min) compared to Group LM (5.56+1.54min and 6.63+1.51min) ;(P<0.05). The time to achieve maximum level was significantly faster in Group LD (6.56+1.30) compared to Group LM (7.73+1.83) ;(P<0.05). Group LD (130.33+6.39min) showed significantly prolonged time to two segment regression compared to Group LM (90.26+8.55min) ;(P<0.001). Duration of sensory and motor block were significantly prolonged in Group LD (250.66+22.27min and 185.66±17.15min) compared to Group LM (164.33+19.06min and 122.5±16.33min);(P<0.001). Duration of effective analgesia significantly prolonged in Group LD(649.33+120.42min)than Group LM(339+71.93min);(P0.05). The patients remained hemodynamically stable in both groups without side effects;(P>0.05). **Conclusion:** As adjuvant with intrathecal Isobaric Levobupivacaine, Dexmedetomidine(10ug) leads to early onset as well as prolonged duration of both sensory and motor block, prolonged duration of postoperative analgesia in comparison to Magnesium Sulphate (75 mg).

KEYWORDS

Levobupivacaine, Dexmedetomidine, Magnesium Sulphate

1.INTRODUCTION

Acute pain is one of the most common and uncomfortable symptoms of disease, and it is frequently mismanaged. As a result, providing postoperative pain management has become a critical part of anaesthesia and a problem for anaesthesiologist.

Spinal anaesthesia is the most common central neuraxial block used in surgical setting. Commonly used agents in spinal anesthesia are Bupivacaine, Lignocaine, Levobupivacaine and Ropivacaine. Bupivacaine and Levobupivacaine has slow onset and longer duration (2-2.5 Hr) of anesthesia. spinal anaesthesia with local anesthetics not only provides adequate intraoperative anesthesia but also provide effective pain reduction in post operative period. adjuvants have been used to prolong the quality of block and duration of postoperative analgesia like opioids. However, their use has been limited by their adverse effects like respiratory depression, nausea, vomiting and pruritus especially with its neuraxial use. other nonopioid drugs like Alpha 2 adrenoreceptor agonists like Clonidine and Dexme detomedine, NMDA receptor antagonists Magnesium sulphate, Ketamine and Midazolam has been used intrathecally.[1]

Levobupivacaine, the pure S(-) enantiomer of Bupivacaine, had safer pharmacological profile with less cardiac and neurologic adverse effects than its racemic sibling, Bupivacaine. Due to those effects, Levobupivacaine was a good alternative.[2]

Dexmedetomidine, a highly selective alpha-adrenergic agonist is being extensively evaluated as an alternative to neuraxial opioids for control of pain and has proven to be potent analgesic, free of side effects associated with opioids and other drugs. It is known to increase the sensory and motor blockade of local anaesthetics. On intrathecal administration it acts by activating the post synaptic a2 receptors in the substantia gelatinosa of spinal cord.[11]

Magnesium sulphate produces anti nociception and potentiation of opioid activity by its action as NMDA receptor antagonist when given intrathecally. The addition of magnesium reduces the activation of C type fibres by inhibiting the slow excitatory post synaptic currents produced by NMDA activation The NMDA receptor play an important role in central nociceptive transmission, modulation, and sensitization of acute pain stats. In addition to central allocation, NMDA receptors are found in the muscle and skin, knee joint and play a role in sensory transmission of noxious signal that lead to the use of Magnesium sulphate via different routes for brachial plexus block and neuraxial route.[3]

Studies have been tried to test the postoperative analgesic effect of MgSO4 when added to spinal anesthesia, combined spinal and epidural anesthesia or epidural anesthesia. These studies have concluded that it increases the postoperative analgesic period by reducing the consumption of postoperative analgesic requirements

without any side effects. Less numbers of studies had done using Dexmedetomidine and Magnesium Sulphate as adjuvants to Isobaric Levobupivacaine. Thus, we undertook this study to Compare Effect of Adding Intrathecal Magnesium Sulphate (75 mg) to 0.5% Isobaric Levobupivacaine Vs Dexmedetomidine (10 ug) to 0.5% Isobaric Levobupivacaine during lower limb orthopedic surgeries.

2.MATERIALS AND METHODS

This study was conducted in Department of Anaesthesiology, Government Medical college and SSG Hospital, Vadodara, after taking permission from Institutional Ethics Committee for Human Research..

It was prospective randomized double-blind study in which study population was selected randomly using sealed envelope method involving 60 patients, divided into 2 groups with 30 patients in each group.

Inclusion Criteria:

1. Age group of 18-60 years
2. ASA – I/II/III
3. Either Gender
4. Scheduled for lower limb Orthopedic surgery (mainly tibial surgeries)
5. Patient able to give written and informed consent.

Exclusion Criteria

1. Patients Refusal
2. Patient on beta blockers and calcium channel blockers
3. Uncontrolled systemic disease
4. Patient on anticoagulant therapy
5. Pregnant and lactating females
6. Patient with local site infection
7. Patients with allergy to local anaesthetics and adjuvants

Sample size was estimated as follows: The mean and standard deviation for parameter mean time of onset sensory block in minutes is taken from reference study by makhni at al. Effect size of mean time of onset sensory block in minutes at t10 level is 2.54. if beta 80%- and 2-sided alpha is 0.01 than sample size would be 26 in each group and after adding error of 10% (2.6) in sample, final sample size would be 28.6~29 in each group. but since minimum sample size is 30 to study any significant difference in two groups i will take 30 in both groups. It was study with total 6 0 patients divided into group of 30 each.

Thorough preanesthetic check-up of all patients including all routine investigation was done. The procedure was explained to patient and written informed consent was taken. Premedication was given as Tab Ranitidine (150 mg) the night before surgery. In the operation Theatre, a good venous access was secured with 18G IV cannula in the forearm and all the patients were preloaded with 10 ml/kg of Ringer's lactate solution. All the patients received premedication in the form of Inj. Glycopyrrolate (5 mcg/kg) I.V and Inj. Ondansetron (0.15mg/kg) iv 15 min before spinal anaesthesia. No sedative premedication was given in both the groups.

Group LD - Inj. Isobaric 0.5% Levobupivacaine 2.5 ml + preservative free Inj. Dexmedetomidine 10 mcg(0.5ml) =3 ml.

Group LM- Inj. Isobaric 0.5% Levobupivacaine 2.5 ml+preservative free Inj.Magnesium sulphate 75mg (0.5 ml) =3 ml.

After taking the patient in operation theatre, monitors like NIBP (non-invasive blood pressure), ECG and pulse oximeter were attached. Base line pulse rate, blood pressure, and oxygen saturation were noted down. Patient was placed in sitting position, with all aseptic and antiseptic precautions, painting and draping was done. After identification of L3 –L4 intervertebral space, 23G Spinal needle was inserted by midline approach. After confirmation of free CSF flow, study drug was injected intrathecally.

For ensuring blinding, the fellow anaesthesiologist (who is not involved in the data collection) will prepare the test drugs, using sterile technique according to group allocated. The drug is then handed over to the attending anaesthesiologist (Myself) who is involved in performing subarachnoid block, would be unaware about the study groups. The patient and the anaesthesiologist (Myself) performing subarachnoid block will be blinded to the content of the drug.

Assessment of sensory block done with pin prick method Bilaterally in midclavicular line assessed every 15 sec for 2min and then every min for 10 min after completion of Intrathecal injection of the drug and then every 30 minutes during surgery. Motor block assessed using BROMAGE SCALE:

0=the patient is able to move hip, knee and ankle.
1=the patient is unable to move hip but is able to move knee and ankle.
2=the patient is unable to move hip and knee but is able to move ankle.
3=the patient is unable to move hip, knee and ankle.

Sedation was Evaluated using Ramsay Sedation Scale. Intraoperative monitoring of Vitals like Pulse Rate, Blood pressure and spo2 were monitored continuously at regular intervals (baseline, 1st,3rd, 5th,10th,15th,20th,30th than every 15 minutes till 60 minutes and then half hourly till end of surgery. Intraoperative complication like Bradycardia, Hypotension, Nausea /vomiting noted and treated accordingly. Fluid requirement and blood loss were calculated and replaced accordingly. In Postoperative monitoring Pain assessment will be done starting at the end of surgery at 0 hour and every hourly for first 4 hours, then every 2 hourly up to 12 hours and then 4 hourly till 24 hours. It is a 10 cm scale graded from 0-10 in such a way that 0 denotes no pain and 10 denote the most excruciating pain. The duration of effective analgesia was counted from the time of injection of spinal drug to VAS score of 4 or more. At this time, they were given rescue analgesic in the form of inj. Paracetamol(1gm) IV given.

3.RESULTS

All 60 patients included in the study were analyzed. There was no difference in age, sex, ASA grading, duration of surgery between the groups as seen in Table 1. Table 2 and 3 shows sensory and motor block characteristics in each group. Systolic blood pressure, Diastolic arterial blood pressure, Heart rate and Spo2 remain stable and there was no significant difference between the groups. The Mean Onset of sensory block at L1 level was statistically significant between group LD (4.13± 1.16 minutes) and group LM (5.56±1.54minutes) ;(P<0.001). Time to achieve maximum sensory level was significantly faster in Group LD (6.56+1.30 minutes) than Group LM (7.73+1.83 minutes). The time for the two-segment regression was prolonged in group LD (130.33+6.39 minutes) compared to group LM (90.26+8.55 minutes) and the difference was statistically highly significant. (P<0.001). The total duration of sensory block was prolonged in group LD (250.66+22.27 minutes)as compared to group LM (164.33+19.06 minutes) and statistically highly significant (P<0.001).onset time for sensory and motor block was earlier in group LD compared to group LM. The mean onset of motor blockage and time to achieve maximum motor blockage was earlier in group LD (5.46±1.30 and 8.25±1.58 minutes) compared to group LM (6.63±1.51 and 10.31±2.38 minutes) and the difference was stastically significant. The total duration of motor block was prolonged in group LD (185.66±17.15 minutes) as compared to group LM (122.5±16.33 minutes) and the difference was stastically highly significant(P<0.001).Table 4 shows the duration of effective analgesia was prolonged in group LD (649.33+120.42 minutes) compared to group LM (339+71.93 minutes) and difference was statistically highly significant. (P<0.001). The numbers of rescue analgesics given to patient in group LD (1.16+ 0.37) were less as compared to group LM (3.03+ 0.76) and the difference highly significant statistically(P<0.001). Sedation score were comparable in both groups. Intraoperative there were no complications except that 2 patients in Group LD and 1 patient in Group LM developed Nausea/Vomiting. Postoperatively no complications were observed.

Table 1: Demographic Data

GROUP	GROUP LD (Mean±SD.)	GROUP LM (Mean±SD.)
Age in years (Mean±SD)	37.93+11.02	36.23+12.59
Sex (Mean±SD)	17:13	18:12
ASA grading (I:II:III)	17:08:05	17:09:04
Mean duration of surgery	100.66+20.16	91.33+19.95

Table 2: Sensory Block Characteristics

PARAMETERS	GROUP LD MEAN + SD	GROUP LM MEAN + SD	P VALUE
Onset of sensory block at L1 (min)	4.13±1.16	5.56±1.54	P <0.001

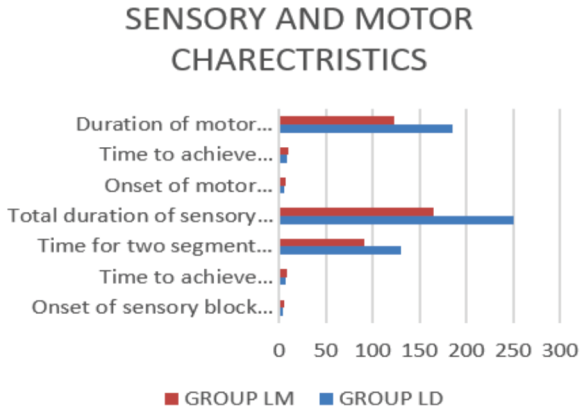
Maximum level achieved			
T8	06(20%)	04(13.33%)	
T10	T10 24(80%)	26(86.66%)	
Time to achieve maximum level(min)	6.56+1.30	7.73+1.83	P<0.05
Time for two segment regression (min	130.33+6.39	90.26+8.55	P<0.001
Total duration of sensory block(min)	250.66+22.2	164.33+19.0	P<0.001

Table 3: Motor Block Charecteristics

PARAMETERS	GROUP LD MEAN + SD	GROUP LM MEAN + SD	P VALUE
Onset of motor blockage (min)	5.46±1.30	6.63±1.51	P<0.05
Time to achieve maximum motor blockage(min)	8.25±1.58	10.31±2.38	P<0.001
Duration of motor blockage (min)	185.66±17.15	122.5±16.33	P<0.001

Table 4: Duration Of Effective Analgesia And Total Number Of Rescue Analgesia

PARAMETERS	GROUP LD MEAN + SD	GROUP LM MEAN + SD	P VALUE
DURATION OF EFFECTIVE ANALGESIA (MINUTES)	649.33+120.42	339+71.93	P<0.001
Total no. of rescue analgesic required in postoperative (24 hrs)	1.16+ 0.37	3.03+ 0.76	P < 0.001



4.DISCUSSION

Spinal anesthesia for lower limb Orthopedic surgeries is the best anaesthetic technique as it is simple to perform with rapid onset of anesthesia, preserved consciousness of patient during surgery, desirable sensory and motor block, complete muscle relaxation and prolonged postoperative analgesia. Spinal anesthesia with Levobupivacaine, the pure S (−) -enantiomer of bupivacaine, has strongly emerged as safer alternative for regional anesthesia than bupivacaine. Levobupivacaine has a safer pharmacological profile with less cardiac and neurologic adverse effects compared to Bupivacaine. Due to decreased cardiovascular and central nervous system toxicity, Levobupivacaine is a good alternative. (Bajwa and Kaur et al,2013)[2]The efficacy of local anesthetics can be enhance using adjuvants such as opioids, Alpha 2 adrenoreceptor agonists, magnesium, neostigmine, ketamine.

Dexmedetomidine is a highly selective α 2 adrenergic agonist which has been used as a premedication as well as adjuvants to LA agent in spinal anesthesia and general anesthesia. **Kapinegowda, et al**[6] studied 5 mcg, 10 mcg, and 15 mcg of Dexmedetomidine with Bupivacaine intrathecally and concluded that significant hypotension and bradycardia noticed with the intrathecal use of 15 mcg of Dexmedetomidine and also concluded that ideal intrathecal dose of Dexmedetomidine is 10 mcg with minimal side effects and hemodynamic response with prolonged postoperative analgesia.

Shagufta Naz et al[7] studied 5 mcg,10mcg,15mcg and 20 mcg of Dexmedetomidine intrathecally and concluded that weighing the prolongation of anesthesia and analgesia and side effects, use of 10 mcg of intrathecal Dexmedetomidine is optimum intrathecal dose. So, we have chosen 10 mcg dexmedetomidine dose intrathecally. In our study

Intrathecal Magnesium Sulphate was first used in humans in 1906(A.P. Morrison et al). [5] Magnesium Sulphate is noncompetitive antagonist to NMDA receptor and thus prevents central sensitization from peripheral nociceptive stimulation. Recent studies suggest the role of magnesium sulphate as an adjuvant to local anaesthetic in spinal anaesthesia in different doses. **Binesh Kathuria et al**[9], studied adding two different doses of intrathecal magnesium sulphate 50 mg and 75 mg to bupivacaine in subarachnoid block and recommend that a dose of up to 75 mg can be used safely without any episode of respiratory depression. **Mitra jabalameli et al**[10]**,** studied adding different doses of 50mg, 75 mg and 100 mg of intrathecal magnesium sulphate to bupivacaine in the cesarean section found that 75 mg of this drug increases duration of postoperative analgesia and prolong sensory and motor block without significant side effects.100mg magnesium sulphate does not have more desirable effect than 75 mg and 50 mg. So, we have chosen 75 mg of magnesium sulphate intrathecally.

In our study, Onset of sensory block was faster in Group LD compared to Group LM which was stastically significant. This was supported by study conducted by Reena makhni et al[11], Kataria et al[12], Joshi et al[13], Shukla et al[14], Jain K et al[4], Kapinegowda ST et al[6].

In our study Group LD achieved faster motor block which was stastically significant compared to Group LM. Similar results found by Reena makhni et al[11], Kataria et al[12], Joshi et al[13], Shukla et al[14], Jain K et al[4], Kapinegowda ST et al[6].

In our study, addition of Dexmedetomidine and Magnesium sulphate both prolonged duration of sensory and motor block when added to Levobupivacaine intrathecally. But prolongation was more in Group LD than in Group LM which was stastically significant. This was supported by Reena makhni et al[11], who used Ropivacaine instead of Levobupivacaine in their study.This results also supported by Kataria et al[12], Joshi et al[13], Shukla et al[14], Jain K et al[4], Kapinegowda ST et al[6].

In this study, total duration of effective analgesia was prolonged in Group LD when compared to Group LM, which was stastically significant and supported by makhni et al[11], Kataria et al[12], Joshi et al[13], Shukla et al[14], Jain K et al[4], Kapinegowda ST et al[6]. The number of rescue analgesia required in 24 hrs were also less in Group LD compared to Group LM which was statstically significant.similar results also found by makhni et al[11], Kataria et al[12], Joshi et al[13], Shukla et al[14], Jain K et al[4], Kapinegowda ST et al[6]. We observed nausea/vomiting in 2 patients in Group LD and 1 patients in Group LM. No postoperative complications were observed.

CONCLUSSION

Comparing the effect of addition of Dexmedetomedine(10mcg) to intrathecal Isobaric Levobupivacaine (0.5%) vs addition of Magnesium Sulphate (75 mg) to intrathecal Isobaric Levobupivacaine (0.5%), following conclusion were drawn: -

In Dexmedetomidine Group early onset of sensory as well as motor block as compared to Magnesium Sulphate Group achieved.

Addition of Dexmedetomidine prolongs duration of sensory and motor block more as compared to Magnesium Sulphate.

Sedation score (2 and 3) achieved only in Dexmedetomidine Group. Addition of Dexmedetomidine provided significantly prolonged effective analgesia postoperatively and also reduced requirement of rescue analgesics as compared to Magnesium Sulphate.

Thus, mixture of Dexmedetomedine 10 mcg and Isobaric 0.5% Levobupivacaine given intrathecally provide early onset of sensory and motor blockade and prolong duration of post operative analgesia when compared to mixture of Magnesium Sulphate 75 mg and Isobaric 0.5% Levobupivacaine.

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