ORIGINAL RESEARCH

A Hospital Based Study to Evaluate the Comparison of Effectiveness of Using Bupivacaine Fentanyl Magnesium Mixture with Magnesium Using Intrathecal and Epidural in Reducing Intra and Postoperative Analgesic Requirements

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ABSTRACT

Background: Post operative pain relief can be provided by pharmacological and non-pharmacological methods. Magnesium is the fourth most plentiful cation in the body. This study is designed to assess the effectiveness of using intrathecal and epidural magnesium (Mg) in reducing intra and post operative analgesic requirements and to compare the quality of analgesia of intrathecal bupivacaine-fentanyl-magnesium mixture with intrathecal bupivacaine-fentanyl mixture. **Material & Methods:** A Hospital based prospective single center study done on 30 ASA I & ASA II patients in the age group of 18 years to 65 years admitted undergoing elective orthopaedic lower limb surgeries at government medical college, Amritsar, Punjab, India during one year period. Patients with duration of surgery between 1-2:30 hours were only included in the study. Unanticipated prolonged duration of surgery was excluded from the study. Intra-operatively the patient was monitored with ECG, BP and SpO2. Ramsay sedation scale (RSS) was also noted every 30 min during intraoperative period. Urine output was monitored hourly. Qualitative variables were compared with `Chi-square test' and quantitative variables were compared with 'the student 't' test'. The level of statistical significance was set at $P < 0.05$. **Results:** The demographic profile was compared and there was no statistical significance in between the groups. Time of first rescue analgesia (hrs.) was 3.16±0.54 in group P and 6.03±0.62 in group M. Which was statistically significant (P<0.001***). Average no. of epidural top up was higher in group P as compared to group M. **Conclusion:** We concluded thatSingle dose administration of intrathecal and epidural magnesium to intrathecal bupivacaine-fentanyl mixture provides effective postoperative analgesia in patients undergoing elective orthopaedic lower limb surgeries, without any hemodynamic instability.

Keywords: Intrathecal, Epidural, Fentanyl, Bupivacaine, Pain score, Magnesium.

INTRODUCTION

Recent advances in neurosciences have demonstrated that peripheral tissue injury may lead to long alterations in central processing with reduction in pain threshold, amplification of response to pain. Comparable alterations may also occur following surgical trauma, resulting in amplification and prolongation of postoperative pain.

Post operative pain relief can be provided by pharmacological and non-pharmacological methods. Nonpharmacological methods include hypnosis, cold or heat, relaxation therapy, splinting of wounds, Transcutaneous Electrical Nerve Stimulation and pre-operative explanation and education. The pharmacological methods include simple analgesics, non-steroidal anti- inflammatory drugs, Opioids (oral, intramuscular, intravenous, Patient Controlled Analgesia, Epidural or intrathecal) and Local anaesthetic agents (wound infiltration, nerve blockade, epidural, intrathecal).

Regional anaesthesia is a safe, inexpensive technique with the advantage of prolonged postoperative pain relief. Effective treatment of postoperative pain blunts autonomic, somatic, and endocrine responses. It has become a common practice to use a polypharmacological approach for the treatment of postoperative pain, because no drug has yet been identified that specifically inhibits nociception without associated side effects.[1]

Magnesium is the fourth most plentiful cation in the body. It has anti-nociceptive effects in animal and human models of pain.[2,3] These effects are primarily based on the regulation of calcium influx into the cell, that is natural physiological calcium antagonism and antagonism of N-methyl-D-aspartate receptor.1 It has been reported that intrathecal magnesium enhances opioid anti-nociception in an acute incisional model.[3] These effects have prompted the investigation of magnesium as an adjuvant for postoperative analgesia. There are studies concerning different routes of magnesium administration such as i.v or intrathecally or epidurally that improve anaesthetic and analgesic quality.[4,5]

This study is designed to assess the effectiveness of using intrathecal and epidural magnesium (Mg) in reducing intra and post operative analgesic requirements and to compare the quality of analgesia of intrathecal bupivacaine-fentanyl-magnesium mixture with intrathecal bupivacaine-fentanyl mixture.

MATERIALS& METHODS

A Hospital based prospective single center study done on 30 ASA I & ASA II patients in the age group of 18 years to 65 years admitted undergoing elective orthopaedic lower limb surgeries at government medical college, Amritsar, Punjab, India during one year period.

INCLUSION CRITERIA

1. Age Group 18 – 65 years
2. ASA I and ASA II
3. Elective orthopaedic lower limb surgeries

EXCLUSION CRITERIA

1. Patient refusal
2. Patients with preexisting renal problems
3. Allergy to any of the study medications
4. Preoperative hypotension
5. Local infection at lumbar area
6. Pre-existing neurological disorders
7. Coagulation defects and patient on anticoagulants

CONDUCT OF ANAESTHESIA

Patients were allocated randomly into two equal groups (20 in each group). Group P (placebo) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2ml) plus 25 µg of fentanyl (0.5 ml) plus 0.9% NaCl solution (1 ml). Total intrathecally injected volume is 3.5 ml.

Epidural infusion of 0.9% NaCl solution is given in first hour of surgery at the rate of 5 ml/hr. Group M (Magnesium) received intrathecal 10 mg of hyperbaric bupivacaine 0.5% (2 ml) plus 25 µg of fentanyl (0.5 ml) plus 50 mg of 5% magnesium sulphate (1 ml).

Total intrathecally injected volume is 3.5 ml. Epidural infusion of 2 % magnesium sulphate is given at the rate of 100 mg/hr (5 ml/hr) during first hour of surgery. 5 % magnesium sulphate solution is prepared by mixing 1 ml of 50% magnesium sulphate with 9 ml of preservative free sterile water. 2% magnesium sulphate is prepared by mixing 1 ml of 50% magnesium sulphate with 24 ml of preservative free sterile water. No premedication was given.

On arrival in the operating room, baseline cardio-respiratory parameters viz., Heart Rate(HR), Systolic blood pressure(SBP), Diastolic blood pressure(DBP), Mean arterial pressure(MAP), Respiratory rate(RR) and Ramsay Sedation Score(RSS) were recorded. A good intravenous access was established using 18G IV cannula. Preloading was done with crystalloids (10 ml/kg).

A standard anaesthetic technique was followed in all patients.

With the patient in sitting posture, after informing the procedure to the patient & under strict aseptic precautions, epidural space was identified at L2-L3 interspace using 16G Tuohy needle by loss of resistance technique. 18G epidural catheter was threaded in a cephalad direction & 3 cm catheter length was kept inside the epidural space. A test dose of 3 cc of 1.5 % lignocaine with adrenaline (5µg/ml) was given. Spinal anaesthesia is performed at L3-L4 interspace. Epidural catheter was fixed and secured with tapes.The epidural catheter is then connected to infusion pump that is disconnected after first hour of surgery. Patients with duration of surgery between 1-2:30 hours were only included in the study. Unanticipated prolonged duration of surgery was excluded from the study. Intra-operatively the patient was monitored with ECG, BP and SpO2.

Ramsay sedation scale (RSS) was also noted every 30 min during intraoperative period. Urine output was monitored hourly. All patients were given oxygen supplementation (4-5 L/min) through Hudson's face mask. No intravenous opioid analgesics were supplemented during the study. Intravenous fluid management was done based on mean arterial blood pressure and surgical blood loss.

POST- OPERATIVE MONITORING

The epidural catheter was retained in position. Postoperatively the patient was transferred to the Post Anesthetic Care Unit (PACU) where PR, SBP,DBP, SPO_2& RR monitored continuously and recorded every hour. The intensity of pain was measured by using the verbal rating pain scale.

The time of first rescue analgesia(TFA) was calculated from the time of injection of study drug in

the central neuraxial block to the time when the verbal rating pain score reached 1 in the postop period. Number of epidural top-ups (6 ml of 0.125% bupivacaine) required by each patient for a period of 48 hours was noted in both the groups.

STATISTICAL ANALYSIS

All the data were expressed as mean ± standard deviation (SD). Qualitative variables were compared with `Chi-square test' and quantitative variables were compared with 'the student 't' test'. The level of statistical significance was set at $P < 0.05$.

Table 1: Demographic data &Characteristics

Demographic profile	Group P	Group M	P-value
Mean Age (yrs)	40.54±7.38	37.98±10.12	>0.05
Weight (kg)	59.32±6.24	60.65±6.18	>0.05
Height (in cm)	164.60±6.48	167.24±6.15	>0.05
Gender (Male/Female)	10/5	12/3	1.00
Duration of surgery (hr.)	2.15±0.08	2.13±0.06	1.00
Time of first rescue analgesia (hrs.)	3.16±0.54	6.03±0.62	<0.001***

Table 2: No. of Post Operative Epidural Top-Ups

Groups	No. of Epidural Top Ups				Average No. of Epidural Top Up
	4	5	6	7	
Group P	-	-	11	4	6.15
Group M	14	1	-	-	3.95

RESULTS

The demographic profile was compared and there was no statistical significance in between the groups. Time of first rescue analgesia (hrs.) was 3.16±0.54 in group P and 6.03±0.62 in group M. Which was statistically significant (P<0.001***) (table 1). Average no. of epidural top up was higher in group P as compared to group M (table 2).

DISCUSSION

Our knowledge of acute pain mechanisms has advanced sufficiently over the past decade so that rational rather than empirically derived therapy can be used by aiming specifically at interrupting the mechanisms responsible for the generation of clinical pain. Breakthrough pain after surgical procedures is now beginning to be recognized as constituting suboptimal management. The use of epidural techniques also offer the advantage of effective prolonged postoperative analgesia as compared to nerve blocks and local infiltrations.

Noxious stimulation leads to the release of neurotransmitters which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. So NMDA receptor antagonists may play a role in the prevention and treatment of post injury pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels.[6] Non competitive NMDA receptor antagonists can have an effect on pain when used alone, but it has also been shown that they can reveal the analgesic properties of opioids.[2, 6]

The safety of intrathecal and epidural magnesium administration has been evaluated in animal and human studies that concluded that magnesium has a good safety profile with no serious side effects.[7,8] Since the amount of magnesium used in this is study is only 150 mg (50 mg intrathecally and 100 mg through epidural infusion), serum magnesium levels was not monitored during the study. In this study we found that magnesium administered intrathecally and epidurally reduced the amount of analgesic that patients required postoperatively suggesting that magnesium may enhance the analgesic effect of bupivacaine and fentanyl.

Duration of analgesia was significantly more in group M patients receiving bupivacaine, fentanyl and magnesium mixture (6.03±0.62 hrs) as compared to group P (3.16±0.54hrs). The demand for supplementary epidural top-ups over 48 hours postoperatively was significantly low in group M than group P.

S. Malleeswaran et al[9] have concluded that addition of 50 mg MgSO4 intrathecally in pre-eclamptic pregnant undergoing caesarean sections delayed the onset of sensory & motor blockade in magnesium group (8.7±0.9, 8.9±1min)compared to control group (7.7±0.8,9.2±0.8 min) $p < 0.001$. Sensory regression to T12& motor to modified Bromage '0' was more in magnesium group(197.8±13.8, 200±17.8 min) than control group (165.7±12, 175.3±18.3min) comparable to the results of present study.

Deepika Shukla et al[10] concluded that addition of 50 mg intrathecal MgSO4 prolonged the onset of sensory block & motor block in magnesium group(6.46 ± 1.33 and 7.18 ± 1.38min) in comparison with control group 4.14± 1.06 and 4.81 ± 1.03 min) in lower abdominal surgeries. The regression time of block, both sensory up to T10 dermatome and motor to bromage 3 scale, was prolonged in the Mg group (265 ± 65 and 251 ± 51 min) when compared within the control group (194 ± 55 and 140 ± 34 min). The findings of the present study were correlating with this study.

Khalili G et al[11] concluded that addition of 100 mg MgSO4 intrathecally prolongs onset & duration of sensory block in magnesium group(13.3, 106.5 min)

compared to control group (11.6,85.5 min) $p < 0.01$. These results were entirely different from the present study. Probably the methodology chosen in the present study may be different from this one. Analgesia requirement was less in magnesium group which correlates present study.

The significant decrease in postoperative analgesic use obtained in this study is comparable with other studies[9-11]that proved that intrathecal and epidural magnesium prolongs opioid analgesia and reduces postoperative analgesic requirements.

Marzieh-BeigomKhezri et al[12] concluded that addition of 50 mg MgSO4 intrathecally has prolonged onset of sensory block in magnesium group (5.86±1.25 min) compared to a control group (2.7±0.7 min). There was no difference in sensory & motor block duration in both magnesium &control groups. The similar results were obtained by Mridu Palan Nath et al (2012)[8] regarding regression of motor block time for 1st analgesia was low in magnesium group (318.33±74.62 min) than control group (343.76±76.32min). But the total Pethedine consumption was less in magnesium group than control group. In the present study onset and duration of sensory and motor block both were prolonged in group M.

CONCLUSION

We concluded thatSingle dose administration of intrathecal and epidural magnesium to intrathecal bupivacaine-fentanyl mixture provides effective postoperative analgesia in patients undergoing elective orthopaedic lower limb surgeries, without any hemodynamic instability.

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