A Randomized Controlled Trial on Assessment of Analgesia on Using Magnesium Sulphate by Different Routes in Patients Undergoing Arthroscopy of Knee under Spinal Anaesthesia

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ABSTRACT

BACKGROUND

Adequate pain management has a great importance for smooth postoperative recovery, early hospital discharge and early rehabilitation. In this study, we compare the analgesic effect and possible side effects of different routes of magnesium sulphate administration in cases of spinal anaesthesia for knee arthroscopy.

METHODS

This is an experimental prospective randomized control study. 196 patients undergoing knee arthroscopy were divided into 4 groups (49 each): Group A: Given bupivacaine intrathecally during spinal anaesthesia. Group B: Given magnesium sulphate 50 mg with bupivacaine intrathecally. Group C: Given magnesium sulphate IV 10 min after intrathecal injection (30 mg/kg MgSO₄). Group D: Given magnesium sulphate intra-articular route, 10 min before the end of surgery (800 mgSO₄ diluted in 12 ml normal saline (0.9 % NaCl). Operative time in minutes, VAS at rest and after procedure, time lapse before first analgesic dose after surgery, total dose of rescue analgesics used, pulse rate, mean arterial pressure and side effects were observed and analysed.

RESULTS

In regards to the lapse of time between end of surgery and first rescue analgesic given, total doses of tramadol used during the 24 hours after the procedure were significantly better in patients given intra-articular magnesium sulphate than other groups ($P = 0.001$). Patients of Group C who received IV magnesium sulphate were significantly better than patients who were given intrathecal magnesium sulphate in relation to time taken from end of surgery until first analgesic dose. VAS at rest and during the period of first 24 hours followed by surgery was statistically significant in patients who received intra-articular magnesium sulphate ($p < 0.001$).

CONCLUSIONS

Intra-articular administration of magnesium sulphate was observed to be superior to other routes of administration or not using at all. Next to intra-articular route, intravenous magnesium sulphate was found to be superior to intrathecal route in providing post operative analgesia in arthroscopy patients.

KEY WORDS

Analgesia, Knee Arthroscopy, Pain, Magnesium Sulphate, Intrathecal, Intra-articular

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BACKGROUND

Magnesium sulphate is used as an analgesic intraoperatively or during immediate postoperative period, as it plays a vital role in pain management.¹ Its action is on receptors in central nervous system as an antagonist of N-methyl-D-aspartate (NMDA).² Though magnesium sulphate is used as an analgesic for decades, the first randomized control study was conducted only in 1996 when it was used as an adjuvant to other postoperative pain management drugs.³ The earlier studies in 2007 gave conflicting opinions.^{4,5} But the recent meta-analyses and systematic review studies proved its positive pain alleviating role in several surgeries.^{6,7} Usage of magnesium sulphate reduces the dosage and frequency of schedules of opioid drugs according to Albrecht et al. who reviewed 25 randomized controlled studies which include 1461 patients. They concluded that perioperative intravenous magnesium reduced opioid analgesics in the first 24 hours postoperative period without any reported serious adverse effects. The analgesic effects of magnesium in orthopaedic surgery were also extensively studied by Koenig et al.⁸ in 1997 and concluded that magnesium sulphate given intravenously for knee arthroscopic surgery was very useful. The adverse effects of IV use of MgSO₄ were also studied by many authors who concluded that they were minimal.^{9,10,11} Preventive analgesia always reduces pain impulse transmission in the central nervous system and reduces pain felt by the patient.¹² Magnesium acts as a physiological and pharmacological blocker of NMDA receptors in central nervous system & can be used in both acute and chronic pain.¹³ The routes of administration of magnesium sulphate were chosen by different authors as intravenous, intrathecal, and epidural given as an adjuvant in regimens of analgesic drugs.¹⁴ Intra-articular magnesium sulphate was also used in many studies and demonstrated to produce effective postoperative analgesia.^{15,16} Review of literature showed many studies on the role of magnesium sulphate as an analgesic but the studies on the role of different routes of administration of magnesium sulphate are but a few in number.

Objectives

To compare the three different routes of administration of magnesium sulphate for its analgesic effect in patients undergoing knee arthroscopy under spinal anaesthesia and to observe for possible side effects. To measure the operative time in minutes, VAS at rest and after procedure, time lapse before first analgesic dose after surgery, total dose of rescue analgesics used, pulse rate, mean arterial pressure and side effects.

METHODS

An experimental prospective randomized control study from January 2017 to December 2019 was conducted at Viswabharathi Medical College, RT Nagar, Penchikalapadu, Kurnool, Andhra Pradesh.

After obtaining ethical committee approval the present study was conducted among 196 patients. Informed written consents were taken from all the patients.

Inclusion Criteria

1. Patients of both genders aged between 19 years and 55 years.
2. Patients with ASA I and II fitness grading.
3. Patients planned for knee arthroscopy.
4. Patients willing to join the study.
5. Patients who have not received any type of analgesic drugs 6 hours prior to the knee arthroscopy procedure.

Exclusion Criteria

1. Patients refusing to continue or join the study.
2. Patients refusing spinal anaesthesia.
3. Patients with contra indications for spinal anaesthesia.
4. Patients with previous history of allergy to any of the drugs used in the study.
5. Patients with class, IV and V ASA grading.
6. Patients under the age of 19 years.
7. Patients with cardiac, severe hepatic or renal diseases, abnormal serum electrolytes levels.

A simple random sampling using (www.randomization.com) website was used to allot the patients to the different groups in the study. For all the patients' demographic details were elicited and noted. The age, height and weight were documented. 196 patients were divided equally into four groups (each group having 49 patients). The Group A (49 patients) patients received bupivacaine intrathecally during spinal anaesthesia but no other drug was used. Group B patients (49) received 50 mg Mg sulphate in 0.5 ml (10 % Mg sulphate) along with bupivacaine intrathecally. Group C patients (49) after spinal anaesthesia with bupivacaine received intravenous injection of magnesium sulphate (30 mg/kg) in 100 ml saline over 10 min followed by 10 mg/kg intravenous infusion over one hour. Group D (49 patients) received in addition to spinal anaesthesia intra-articular injection of 800 mg Mg sulphate (8 ml of 10 % Mg sulphate) diluted in 12 ml normal saline (0.9 % NaCl) 10 min before the end of surgery. To monitor and maintain uniform clinical standard; patients whose arthroscopy procedure exceeded 2 hours period, were eliminated from the study. All the patients were trained on Visual Analogue Scale (VAS) graded from 1-10 (10: worst pain; 0- no pain) of pain prior to surgery.

Procedure

Patients of all groups were given 0.01 mg/kg atropine I.M. half an hour before the procedure. Their blood pressure, ECG and oxygenation were continuously monitored using 3 channel monitor. All Patients received 2 mg midazolam, 500 mL of lactated Ringer's solution i.v. placed in the sitting position. 15 mg bupivacaine 0.5 % was injected intrathecally by 22-gauge spinal needle placed by median or paramedian approach through L3-L4 intervertebral space. Patients were immediately turned to the supine horizontal position. Ten minutes after intrathecal injection,

The Following Parameters Were Assessed

1. Operative time in minutes.
2. VAS pain score was measured at rest as well as with passive movement at 4, 8, 12, 16, 20 and 24 postoperatively.
3. An analgesic rescue drug tramadol, dose of injection 50 mg/ ml intravenously which cannot be repeated within 6 hours was kept ready as a postoperative for analgesia. The rescue analgesic drug was used when the VAS score is more than 5.
4. Time taken for the required first dose of analgesia postoperatively.
5. Total number of rescue analgesia doses required by the patients.
6. Side effects noticed during the 24 hours post operative period such as nausea, vomiting, pruritus, shivering; fall in respiratory rate (respiratory depression).
7. Development of hypotension or bradycardia was also considered.

Statistical Analysis

All the data collected was analysed using SPSS version: 14.0. The data was expressed as mean $\pm$ SD, percentage, ANOVA, chi square test ($p < 0.05$) was considered as statistically significant.

RESULTS

The demographic data of patients of all the four groups was identical and comparable and there was statistical correlation between them (Table 1).

Observation	Group A	Group B	Group C	Group D	P value
Mean age-years	39.5	38.20	40.15	41.50	0.328
Mean height-cms	173.40	175.35	176.60	174.25	0.287
Mean weight-kg	81.35	80.55	82.90	79.85	0.410

Table 1. Demographic Data (n-196; Group A-46, Group B-46, Group C-46, Group D-46)

Observations	Group A	Group B	Group C	Group D	HSD Value
Operation time in minutes	59.45 $\pm$ 8.60	62.45 $\pm$ 9.75	61.50 $\pm$ 8.10	60.40 $\pm$ 7.80	0.5252
Time lapse for first analgesic	285.40 $\pm$ 34.25	305.20 $\pm$ 12.40	320.70 $\pm$ 13.65	448.90 $\pm$ 10.50	-1.6811
Total doses of rescue analgesic drug used in 24 Hrs-in mg	118.30 $\pm$ 10.45	85.20 $\pm$ 8.45	91.32 $\pm$ 8.40	48.65 $\pm$ 5.45	15.033
The mean number of doses of rescue analgesic used	04.35 $\pm$ 1.10	04.25 $\pm$ 1.20	03.0 $\pm$ 2.10	02.30 $\pm$ 0.55	2.2673

Table 2. Postoperative Parameters Observed and Their Comparison among the Four Groups (n-196; Group A-49, Group B-49, Group C-49, Group D-49)

There was no statistically significant difference between the four groups regarding operative time (Table 2). As regards mean time taken from end of surgery until first analgesic dose: Group D was significantly higher than group B, C and A. However, the time taken was more among patients of Group C than Group B and A (Table 2). The mean total doses of tramadol consumed in the first postoperative 24 hours: Group D patients used tramadol significantly less than the other A, B and C groups. However, the mean total dose was significantly less in Group C patients than Group A and B patients. Among the Groups A and B, B Group patients

consumed less tramadol dose than Group A (Table 2). Post hoc Honestly Significance Difference (HSD) using one-way ANOVA method was used to test the significance and the HSD values were found to be significant.

Figure 1. VAS at 4, 8, 12, 16, 20 and 24 hrs Postoperatively in the Four Studied Groups (n-196)

The VAS score measured among the patients of all groups at 4th hourly intervals and the scores showed that the patients of Group D had a significantly lower score than other three groups at all the time intervals (Fig 1). Group C and B patients showed significantly lower VAS scores than Group A at fourth hourly intervals (Fig 1).

	Group A	Group B	Group C	Group D
2 hours	0.2	0.2	0.1	0.1
4 hours	3.5	1.85	2.6	2.1
8 hours	3.86	3.21	3.38	2.75
12 hours	3.9	3.38	3.44	2.6
16 hours	3.88	2.95	2.9	2
20 hours	2.99	2.64	2.61	1.98
P value	0.171	0.023	0.018	0.001

Table 3. VAS at 4, 8, 12, 16, 20 and 24 hrs Postoperatively in the Four Studied Groups (n-196)

There were no statistically significant differences in heart rate among the patients of the four groups (Fig. 2, Table 4).

Figure 2. Pulse Rate during the Arthroscopy among the Patients of Four Groups (n-196).

	Group A	Group B	Group C	Group D
Base line	84	85	82	83
30 minutes	89	91	92	92
1st hour	94	95	95	97
2nd hour	87	88	86	86
3th hour	81	80	80	81
4th hour	74	73	72	76

Table 4. Pulse Rate among the Patients of the Four Groups (n-196).

There were no statistically significant differences in mean arterial pressure among patients of the four groups (Fig. 3, Table 5).

	Group A	Group B	Group C	Group D
Base line	87	88	89	90
30 minutes	93	94	92	94
1st hour	94	95	96	96
2nd hour	88	86	88	86
3rd hour	88	88	89	86
4th hour	89	86	89	88

Table 5. Mean Arterial Pressure Rate among the Patients of the Four Groups (n-196)

There was no statistical significance in the heart rate, mean arterial pressure and occurrence of side effects among the patients of the four groups (Table 6).

Observations	Group A	Group B	Group C	Group D	P value
Nausea	02 (04.08%)	02 (04.08%)	03 (06.12%)	01 (02.04%)	0.761
Vomiting	01 (02.04%)	01 (02.04%)	02 (04.08%)	02 (04.08%)	0.632
Chills and rigors	01 (02.04%)	02 (04.08%)	03 (06.12%)	02 (04.08%)	0.315
Pruritus	00	00	00	01 (02.04%)	0.221
Respiratory depression	00	00	00	01 (02.04%)	0.221

Table 6. Side Effects Observed during and after arthroscopy Procedure (n-196)

DISCUSSION

The present study was to review the role of magnesium sulphate in post arthroscopy patients in providing analgesia. Diet is the only source of magnesium in human body and its level falls down after major surgeries.^{17,18} The increased levels of magnesium used in magnesium treatment regimens usually fall down by day 1 to 3.¹⁹ The increased postoperative magnesium concentrations due to such regimens could go up to 1.3–1.6 mM without any detectable complications of hypermagnesemia.²⁰ Fortunately, the increased levels of magnesium are found to prevent postoperative urinary retention.²¹ Magnesium acts as an analgesic by its antinociceptive effects on NMDA receptors to inhibit them.²² The present study was designed to compare the three different routes of administration of magnesium sulphate for its analgesic effect in patients undergoing knee arthroscopy under spinal anaesthesia and to observe for possible side effects. The results of this study showed that intra-articular administration of magnesium sulphate was found to be superior to other routes of administration when spinal anaesthesia was used for knee arthroscopy. In a similar study Elsharnouby and co-workers,²³ observed that the combination of magnesium sulphate with bupivacaine intrathecally was more effective as an analgesic than using bupivacaine alone in terms of reducing the postoperative pain. The present study also used the similar magnesium

sulphate dose as used by Radwan and co-workers,²⁴ who concluded that to increase the duration of analgesia, magnesium sulphate was very useful and it also minimizes the dose of opioids drugs for post-operative pain. A study by Liu and co-workers²⁵ proved that there were peripheral nociceptive receptors and the effect of NMDA antagonist action of magnesium sulphate inhibits them and input terminals of C-fibres which cause limitation of central processing of pain. Hence it could be concluded that magnesium sulphate has both central and peripheral action on reducing the pain. In another similar study by Banwait and co-workers,²⁶ the authors concluded that route of administration magnesium sulphate have its main role on spinal cord NMDA receptors. It could be that such a mechanism available could be the cause for the results observed in this study wherein IV and intrathecal routes of administration of MgSO₄ were equally comparable to intra-articular route of administration. But the study conducted by KO and coworkers²⁷ found the IV route and intrathecal route to be superior to the intra-articular route of administration of MgSO₄ in producing analgesia. The differences in the results of the present study and the study of KO and co-workers may be due to the different surgical procedures (abdominal hysterectomy, Caesarean operation, and other lower limb surgeries) that were included in their study, whereas the present study was conducted only for arthroscopy procedure. Among the various trials on magnesium sulphate as an analgesic drug, a study showed that the patient's total analgesic satisfaction and their experience during the night after surgery revealed VAS scores were decreased by 56% and 70%, respectively.²⁸ More than 50% of the studies failed to prove that the systemic MgSO₄ usage might be of beneficial effect on pain intensity. Majority of the randomized control studies revealed that intravenous MgSO₄ administration on patients who underwent arthroscopic or lower extremity had a positive analgesic effect, but one study showed the patients who underwent spine surgery did not have positive effect. Hence this study concluded that there need to be further investigative studies to correlate potential effects of analgesia between the types of surgeries and mode of administration of MgSO₄.²⁹ There was always a chance of perception of pain varying in different patients as pain was influenced by a variety of factors like: gender, genetic, psychological and personality behaviours.

CONCLUSIONS

While using spinal anaesthesia for knee arthroscopy, intra-articular administration of MgSO₄ was superior to IV route and intrathecal routes in regards to VAS score for pain postoperatively. The multiple usage of opioid drugs was minimized.

Limitations

Fixed dose schedules were used for IV route (30mg/Kg followed by 10mg/Kg), intra-articular route 800 mg magnesium sulphate (8 ml of 10 % Mg sulphate) and intrathecal routes (50 mg) in the study. Using higher dosage schedules could have given much better confirmatory results. The onset of sensory and motor blockades after spinal

anaesthesia was not included in intrathecal route administration in this study.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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