ORIGINAL RESEARCH PAPER
Volume - 9 | Issue - 11 | November - 2020 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MAGNESIUM SULPHATE AN ANGELIC ALLAY ALLEVIATING POSTOPERATIVE SPINAL SURGERY PAIN.

Clinical Research

Makhamreh Basel	Aneasthesia department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Jraisat Ibrahim	Aneasthesia department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Shamoun Elias	Aneasthesia department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Allouzi Rakan	Neurosurgery department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Abu kaff Mohammed	Neurosurgery department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Abu Salma Zuhair	Neurosurgery department, King Hussein Medical Center - Royal medical services, Amman-Jordan.
Alqroom Rami*	Neurosurgery department, King Hussein Medical Center - Royal medical services, Amman-Jordan.*Corresponding Author

ABSTRACT

Introduction: Magnesium sulphate used as an adjuvant for perioperative analgesia based on its properties as *N*-Methyl-d-aspartate (NMDA) receptor antagonist and calcium channel blocker, it is presumed that its antagonism of NMDA receptor prevents the induction of central sensitization due to peripheral nociceptive stimulation and abolishes hypersensitivity. In addition, calcium channel blockers have shown antinociceptive effects and morphine potentiation in patients with chronic pain.

Objectives: The aim of this study is to the emphasize the efficacy of perioperative infusion of magnesium sulphate in terms of early postoperative pain in patients underwent conventional lumber spine surgery and managed by our neuro-anesthesia team.

Methods and patients: A prospectively obtained data were assessed in a retrospective study, which was conducted by reviewing the medical records of all patients managed at King Hussein Medical Center (KHMC). Patient reports were retrieved from the electronic hospital database for a 2-year period (2018-2020). Collected data from consecutive patients who had I or II levels of degenerative lumbar spine disease (with moderate or very severe low back pain with or without radicular pain) . We excluded patients with acute deficits, spinal instrumentations spinal tumors surgery, and those who were lost follow up.

Results: Study final population included 88 men and 40 women, male to female ratio of 2.2:1, median age of 57.21±3.7 years. No statistically significant difference in mean age and sex distribution of patients. Patients showed a significant decrease in VAS scores of low back pain. The two groups had comparable VAS scores preoperatively. At the 48-hours postoperative follow-up, statistically significant improvements in VAS outcome scores were found comparing the group I to control group. No patient developed a postoperative complication related to the use of magnesium sulphate .

Conclusion: This study showed that adjunct use of perioperative magnesium sulphate to alleviate postoperative back pain in patients with degenerative spine disease could significantly improve the pain score which leads to significant decrease in working days off and the need for pain killer medications or even obviating the usage rate.

KEYWORDS

Magnesium sulphate; pain management; pain score; Visual analogue scale; multimodal analgesia; postoperative pain measurement, spinal surgery.

INTRODUCTION

Magnesium sulphate has been introduced in anesthesia as a smooth muscle relaxant. Magnesium sulphate plays this role by ruthlessly blocking intracellular calcium channels, reducing available calcium and thus impeding smooth muscle contractility. It also vies with calcium at the level of motor end plate, where it decreases excitation by preventing acetylcholine release. Magnesium sulphate has been used initially in obstetric field and in patients underwent cardiac interventions, as an adjunct drug for perioperative analgesia depending on its properties as *N*-Methyl-d-aspartate (NMDA) receptor antagonist and calcium channel blocker. It is alleged that magnesium sulphate antagonizes NMDA receptor and inhibits the induction of central sensitization due to peripheral nociceptive stimulation and obliterates hypersensitivity. In addition, calcium channel blockers have shown antinociceptive properties and morphine potentiation in patients with chronic pain [1,2].

Conventional spinal surgeries often involve wide dissection of subcutaneous tissues, bones, and ligaments and thus result in an intense postoperative pain, predominantly for the early few days. Satisfactory pain control during this period has been proved to correlate well with enhanced functional outcome [3,4]. Undeniably postoperative pain is the collective result of activation of various pain mechanisms including nociceptive, neuropathic, and inflammatory [5]. Effective postoperative pain moderation eases early mobilization as well as expedites hospital discharge [3]. This study attempts to analyze the different aspects of the perioperative magnesium sulphate infusion introduced for relief from postoperative pain following conventional spinal surgeries in terms of physiological basis of pain following spinal surgeries, and assessment of postoperative pain alleviation.

Methods and patients

The study was approved by the Royal Medical Services Institutional ethics committee (37/8/2020). As this study was a retrospective review, the requirement for consent was waived.

A prospectively routinely obtained data were assessed in a retrospective study, which was conducted by reviewing the medical records of all patients managed at King Hussein Medical Center (KHMC). Patient reports were retrieved from the electronic hospital database for a 2-year period (2018-2020). We prospectively collected data from 433 consecutive patients who had I or II levels of degenerative lumbar spine disease (viz. canal stenosis, foraminal stenosis, or disc herniation) with moderate or very severe low back pain with or without radicular pain (visual analogue scale (VAS) between 4 and 10) for low back pain and leg pain, as well as persistent pain more than 6 weeks despite the use of other conservative treatment options (physical therapy, medication, etc.). We excluded patients with acute deficits, spinal instrumentations (either as primary or secondary

procedure), spinal tumors surgery, and those who were lost follow up.

Inclusion/ exclusion criteria

***Inclusion criteria*:**

1) One or more levels of degenerative lumbar spine disease.
2) persistent pain more than 6-weeks
3) A minimum follow-up of 2-months.

***Exclusion criteria were*:**

1) Inadequate documentation of follow up.
2) Oncology cases scheme.
3) The presence of severe systemic disease(heart disease, thromboembolism, bleeding tendency, renal malfunction)
4) Age <18
5) Patients with acute deficits, spinal instrumentations.

Intraoperative standard monitoring includes pulse oximeter usage, electrocardiography recording, noninvasive blood pressure device application, and temperature monitoring. In addition, to end tidal carbon dioxide measurement, inspired oxygen concentration, and the use of low oxygen concentration and ventilator disconnect alarms. Quantitative monitoring of the volume of expired gas arterial pressure monitored. Population included in the final stage of analysis allocated into two groups. The magnesium sulphate study group (Group I) encompassed 128-patients, our protocol of intravenous magnesium sulphate is to infuse 50 mg per kilogram for 15 min after induction and general anesthesia followed by continuous intravenous infusion at rate of 15 mg/ kg/hour till the end of surgery. In patients allocated in (Group II), the control group, the same volume of isotonic saline was administered with the same infusion rate. If any major changes observed in the systolic arterial pressure (declined to lower than 90 mm Hg) or if mean arterial pressure reduced >20% from baseline, ephedrine 5 mg was administered. While in the case scenario the heart rate lessened to <45 beats/min, atropine 0.5 mg was infused intravenously.

Patients' demographical data were collected (viz., sex, age, duration of symptoms, medical history, and social history), while post perioperatively we documented if any side effects observed in addition to the data regarding patients

To minimize bias, independent reviewers collected the data, including side effects, when patients visited the hospital for follow-up. All patients were operated on by one neurosurgeon (Al. R) with the same technique. The surgeon was completely aware of the allocated group, but the assistant neurosurgeons who was responsible for follow up and analysis of the data was completely blind to the group.

At the end of surgery, the patients were transferred to the ward and evaluated for outcome measurements. VAS evaluations of low back pain were collected pre-operatively and at 8-hours, at 24-hours at 48-hours, after the initial surgery.

Surgical technique

The microsurgical procedure with bilateral decompression was performed in a standardized manner, surgical steps were as follows. Patient under general endotracheal anesthesia placed in prone position on Wilson frame, the ailing level is marked with X-ray control. The region is draped in a sterile fashion, then a vertical midline incision over the appropriate interspace marked using anatomical landmarks and fluoroscopy, subsequently, skin incised and the subcutaneous tissues are dissected , with sub periosteal dissection done down to the specified level to expose the spinous process and the lamina bilaterally. Fluoroscopy is used to reconfirm the level. Bilateral flavectomy performed in addition to bilateral foraminotomy. When dealing with herniated lumbar disc, inter-laminar approach was used preserving the lamina as possible, the exposed nerve root was retracted medially or laterally, depending on the position of the disc and through a transverse annulotomy, all the loose disc material is removed, the disc space washed with normal saline to remove out any remaining free fragments. Facets were left undisturbed. The operating microscope was used in all the cases.

Statistical analysis

For statistical analysis, patients' data was registered and kept on Microsoft Excel 2010 Spreadsheets. We extracted the relevant information and analyzed it on SPSS version 23.0. Data are reported as median (and ranges), or mean values +/- standard deviation. To compare clinical outcomes in the different periods, we conducted an unpaired sample t-test using Excel 2010 for 3 scenarios: pre-operation vs. 8-hours post-operation, pre-operation vs. 24-hours post-operation, and pre-operation vs 48-hours post- operation. An unpaired student's t-test was used to compare between groups. Statistically significant value was documented at $p<0.05$.

RESULTS

The study final population included 88-males and 40-females who met the inclusion/exclusion criteria, and the male-to-female ratio was 2.2:1. The age of patients was between 34 and 63 years with a median age of 57.21±3.7years. Statistically, there was no significant difference between the two groups recruited for the analysis in terms of: mean age; levels operated; gender; body mass index; preoperative VAS(back pain); preoperative VAS(Leg pain); mean follow up duration and sex distribution of the patients between the two groups (Table1). The two groups had comparable VAS scores preoperatively. At the 48-hours postoperative follow-up, statistically significant improvements in VAS outcome scores were found comparing the two groups, patients demonstrated a substantial decrease in VAS scores of low back pain (Table 2). On the hand, comparing the two groups in terms of leg pain scores, there were no significant differences (Table 3). Clinically, the mean symptom duration was 8.4 ± 4.2 months. The average follow-up duration was 4.41±2.68 months. There were no technical difficulties in the procedure and no procedure-related major complications. No patient had early postoperative complications. No patient developed postoperative infections or other complications related to magnesium sulphate infusion. There was no significant difference in haemodynamic variables (mean arterial pressure and heart rate) during the intra- or early postoperative period. Seven patients in Group I and five patients in Group II developed hypotension, and two patients in Group I and one patient in Group II experienced bradycardia during surgery. In accordance with the study protocol, ephedrine 5 mg and atropine 0.5 mg were administered in each event, and in all cases, arterial pressure and heart rate were normalized.

Table 1: Patient demographical data and characteristics.

Parameter	Group I	Group II	*p* value
Number of patients	128	72	
Levels (1 level/ 2 levels)	159 (97/31)	84 (60/12)	
Average Age (years)	57.21±3.7	58.22±8.27	0.93
Gender (Female/Male)	40/88	21/51	0.7
BMI	28.1±3.2	27.2±3.6	0.07
Preoperative VAS(back pain)	6.97±2.77	6.09±2.84	0.36
Preoperative VAS(Leg pain)	7.01± 2.31	6.47±2.73	0.66
Mean follow up duration (months)	4.41±2.68	6.14±3.6	0.95
NS= Not significant, BMI = body mass index			

Table II: Average VAS pain scores of low back pain. Values are presented as medians and SD. Group I, Mg group; Group II , control group. *$P<0.05$*

	Group I	Group II	P value
Preoperative	6.97±2.77	6.09±2.84	0.36
Postoperative 8-h	5.7 ± 1.64	5.88±2.44	0.69
Postoperative 24-h	4.1± 2.4	5.36±2.24	*0.013
Postoperative 48-h	2.6±2.1	4.56±1.88	*0.002

Table III: The average visual analogue scale (VAS) of leg pain

	Pre-operative	8-hours	24-hours	48-hours
Average VAS Group I	7.56 ± 1.32	1.96 ± 1.12	1.63 ± 1.21	0.95 ± 1.09
Average VAS Group II	7.24 ± 1.57	2.42 ± 1.04	2.18 ± 1.25	1.36 ± 1.25
p value	0.48	0.015	0.33	0.226

DISCUSSION

The postoperative pain in the vast majority of patients who had spine surgery is a mixed pain, has an element of the already preexisting suffered chronic pain that had been treated with conventional analgesics or narcotics beside the long-term consumption of analgesics which alters pain perception in these patients thereby complicating pain management[6,7]. Effective pain controls facilitate early mobilization as well as expedites hospital discharge. Pain

following spine surgery provoked by a variety of dynamics such as soft tissue disturbance and direct nerve root handling, which trigger the inflammatory cascade [8-10].

Conventional lumbar spine surgeries performed in patients with degenerative spine disease, are well-established surgical procedure, different surgical approaches have evolved since the first discectomy done by Oppenheim and Fedre Krause in 1906 [11-15]. But still open inter-laminar approach considered highly effective and safe[16,17].

Nowadays, efforts are steered toward the insufficiently treated postoperative pain following conventional surgical procedures. It is crucial to achieve effective postoperative pain alleviation to encourage postoperative recovery with improved functional outcome, also this will lead to early ambulation, early discharge, and preventing the development of chronic pain. Multimodal analgesia schemes were recruited for this purpose. As an essential stratagem is the combinations of different pain relief medications with different mechanisms of action, which has as a goal an accumulative analgesic effect causing fewer to no side effects compared to using a single drug [18-23]. The introduction of intraoperative epidural steroids has been applied as an additive pain treatment in lumbar spine surgery. It is main mechanism of action in reducing postoperative pain is by suppressing pain mediators and inflammation such as prostaglandins, bradykinin and histamine [20].

In this study as in other similar studies we performed to alleviate postoperative pain, we decided to infuse magnesium sulphate intravenously to decrease postoperative pain after spinal surgery. According to our early results at 8-hours, 24-hours and 48-hours postoperatively, the average VAS for LBP showed significant reduction(Figure. I), for magnesium sulphate group, also we noticed that after 48- hours postoperatively both groups were equal in terms of leg pain, this might be explained by nerve root decompression in both groups. This study encountered some limitations. The relatively small sample size and the short follow-up periods, which might limit the comparability and long-term outcomes. Socio-economic variables that might affect the study results, were not incorporated in this study.

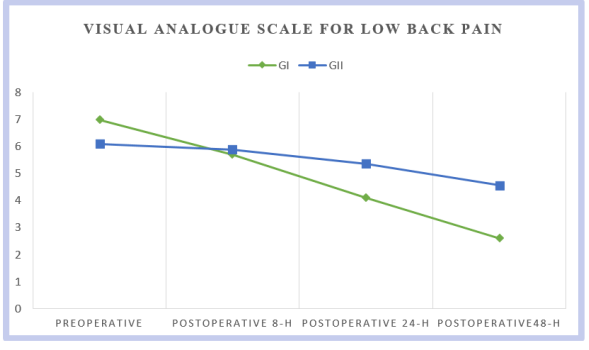

Figure. I: Pain scores on VAS, for both groups. Values plotted on mean values.

Nevertheless, there is still a noticeable lack of documentation for the consequence and the adverse side effects of these analgesic regimes. Spine surgery has been associated with significant intensities of pain compared to other surgical procedures. Therefore, we considered spine surgery to pose as adjunct pain reliever directing to improve the multifactorial methodology in pain management.

CONCLUSION

This study showed that perioperative intravenous magnesium sulphate infusion during conventional spine surgery in patients with degenerative spine disease under general anesthesia reduced postoperative pain without any notable complications. However, the study had a small sample and did not assess the mid-term or long-term complications. Nevertheless, intravenous magnesium sulphate is clinically safe. On the other hand, this relief may simply coincide with the natural course of treatment.

Future work: We need a prospective, randomized, controlled, double-blind study and a larger population.

Acknowledgments: None.
Conflicts of interest: The author certify that he has no affiliation with or any direct or indirect involvement in any organization or entity with any financial interest, or non-financial interest in the subject matter or materials discussed in this manuscript.

Funding: Authors disclose no external funding sources.

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