

Dexmedetomidine vs. Magnesium Sulfate as Anesthetic Adjuvants in Spine Surgery: Effects on Inflammatory Response, Hemodynamics, Recovery, and Opioid Use in a Randomized Controlled Trial

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ABSTRACT

Background: Non-cardiac surgery in patients with cardiovascular risk can lead to Spine surgery often leads to significant postoperative pain, inflammation, and hemodynamic instability, necessitating opioid use, which increases the risk of side effects. Dexmedetomidine (DEX) and magnesium sulfate ($MgSO_4$) are anesthetic adjuvants that may enhance recovery and reduce opioid consumption. This study aimed to compare the effects of DEX and $MgSO_4$ as an anesthetic adjuvant on interleukin-6 (IL-6) levels, hemodynamic stability, postoperative recovery, and opioid consumption in spine surgery.

Methods: A randomized controlled trial was performed on 24 patients undergoing spine surgery under general anesthesia. Participants were randomly divided into two groups: Group 1 received DEX (a 1 $\mu g/kg$ bolus followed by a continuous infusion of 0.3–0.5 $\mu g/kg/h$), while Group 2 was given $MgSO_4$ (a 30–50 mg/kg bolus followed by an infusion of 10–20 mg/kg/h). Hemodynamic parameters, IL-6 levels (pre- and postoperatively), opioid use, and recovery outcomes were analyzed.

Results: IL-6 levels decreased significantly in both groups ($p=0.001$), with a greater reduction in the DEX group (-60.5 pg/dL vs. -24.9 pg/dL), though not statistically significant. Hemodynamic stability was comparable, but DEX provided better pulse rate control. Opioid consumption was lower in the DEX group at 24 and 48 hours postoperatively ($p < 0.05$). The DEX group also showed higher Aldrete scores ($p<0.05$) and shorter hospital stays (3.75 vs. 4.83 days, $p<0.05$).

Conclusion: DEX provides superior anti-inflammatory effects, hemodynamic stability, reduced opioid use, and improved recovery compared to $MgSO_4$ as an anesthetic adjuvant in spine surgery patients.

Introduction

Spine surgery often results in severe postoperative pain, hypotension, and hemodynamic problems. Recovery is prolonged with the use of opioids,

which carry the risk of side effects, including addiction [1–3]. In addition, the procedure causes postoperative inflammation, characterized by an increase in interleukin-6 (IL-6), which can also exacerbate pain and inhibit recovery [4].

The Enhanced Recovery After Surgery (ERAS) protocol was introduced to accelerate recovery with

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multimodal analgesia, including dexmedetomidine (DEX) and magnesium sulfate (MgSO_4) as anesthetic adjuvants. DEX has sedative and analgesic effects without causing respiratory depression, maintains hemodynamic stability, and reduces the need for opioids [2, 5–7]. Meanwhile, MgSO_4 inhibits calcium channels and N-methyl-D-aspartate (NMDA) receptors to inhibit pain and increase the duration of analgesia. Magnesium also has the effect of lowering blood pressure and heart rate and can reduce anesthetic consumption [6–9].

This study aims to evaluate the effects of low-dose DEX and MgSO_4 on IL-6 levels, hemodynamic stability, postoperative recovery, and opioid consumption in patients undergoing spine surgery. The findings are expected to offer evidence-based recommendations for improving anesthesia safety and optimizing postoperative pain management.

Methods

Study Design

This single-blind randomized controlled trial was conducted from July to December 2024 at a tertiary care teaching hospital in Makassar, Indonesia. The study received approval from the Ethics Committee for Biomedical Research (No: 629/UN4.6.4.5.31/PP36/2024). All participants provided written informed consent before enrollment.

Participants

Eligible patients were those aged 18–60 years undergoing spine surgery under general anesthesia, with an American Society of Anesthesiologists (ASA) physical status of I–II and a body mass index (BMI) below 30 kg/m^2 [10].

Exclusion criteria included anesthetic intolerance or allergies, pregnancy or lactation, hypertension, ischemic heart disease, renal impairment, neuromuscular disorders, liver disease, cerebrovascular disease, diabetic neuropathy, coagulopathy, use of magnesium supplements, and prior spine surgery. Participants who experienced surgical complications or required procedures exceeding four hours were excluded. After providing informed consent, patients were randomly assigned to either the DEX group or the MgSO_4 group (Figure 1). Anesthesia instructions were concealed in sealed envelopes until the time of surgery.

Interventions

Patients were positioned in a prone posture with standard hemodynamic monitoring. Baseline blood pressure, heart rate, and IL-6 levels were recorded through a 1 mL peripheral blood sample collected one hour prior to surgery. The DEX group received a $1 \text{ } \mu\text{g/kg}$ loading dose over 10 minutes, followed by a continuous infusion of $0.3\text{--}0.5 \text{ } \mu\text{g/kg/hour}$.

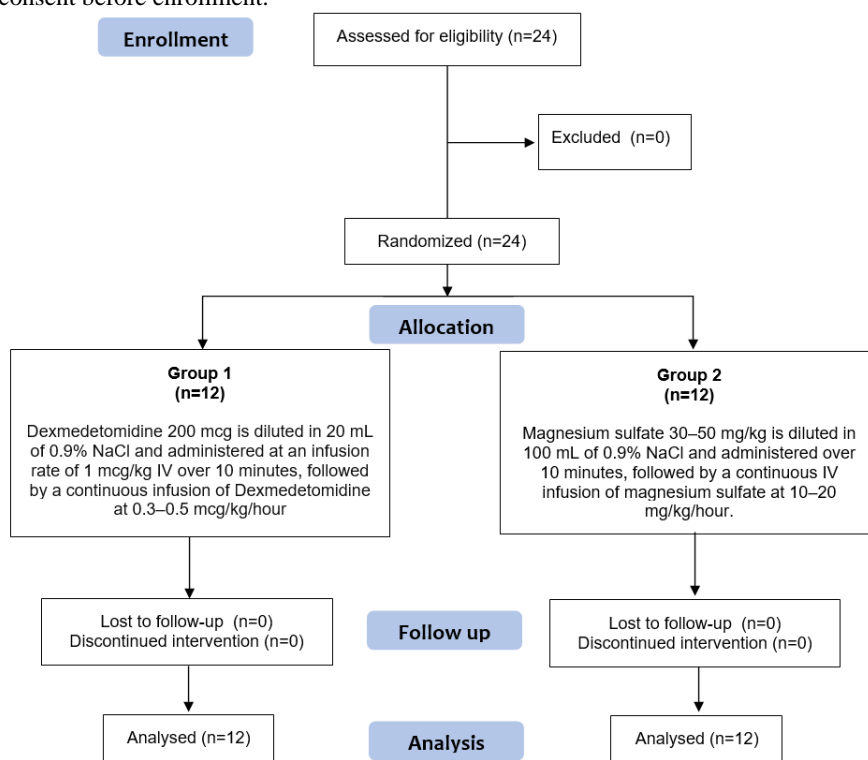


Figure 1- CONSORT flow chart

The MgSO₄ group was given a 30–50 mg/kg bolus diluted in 100 mL of normal saline over 10 minutes, followed by an infusion of 10–20 mg/kg/hour. Patients were preloaded with 10 mL/kg of normal saline. Propofol was administered at 50–200 mcg/kg/min, with hourly documentation of its usage and muscle relaxation status. In cases of hypertension (MAP > 20% above baseline) or tachycardia, a fentanyl bolus of 0.5 µg/kg was provided. Hypotension (MAP < 30% of baseline) was managed with a 200 mL bolus of normal saline or 5 mg of intravenous ephedrine, while bradycardia (HR < 50/min) was treated with atropine at 0.01 mg/kg IV. After skin closure, all infusions were discontinued, and neuromuscular blockade was reversed with neostigmine at 40 µg/kg. Extubation was performed, and recovery was assessed every two minutes using the Aldrete score. Another 1 mL blood sample was collected 6–12 hours postoperatively for IL-6 analysis. Pain levels were measured using a Visual Analog Scale (VAS), and opioid usage was documented at 2, 4, 6, 12, 24, and 48 hours post-surgery.

Outcomes

The primary endpoints included hemodynamic stability (measured by mean arterial pressure and heart rate), IL-6 levels, postoperative opioid consumption, and recovery duration. IL-6 levels were assessed both preoperatively and postoperatively. Hemodynamic parameters were recorded one hour pre-surgery, after incision, one hour post-incision, and following extubation. Opioid consumption was measured at intervals of 0, 2, 4, 6, 12, 24, and 48 hours postoperatively. Total opioid requirements and length of hospital stay were also analyzed.

Statistical Analysis

SPSS version 26.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Descriptive statistics were

used to summarize baseline characteristics. Categorical variables were analyzed using the chi-squared test, whereas numerical data were expressed as mean ± standard deviation for normally distributed variables or as median with a minimum-maximum range for non-normally distributed data. Group comparisons were performed using either an independent t-test or the Mann-Whitney test, depending on the data distribution. Intra-group differences were evaluated using the Wilcoxon test. A p-value of <0.05 was considered statistically significant.

Results

Analysis showed no significant differences in baseline characteristics between the DEX and MgSO₄ groups (>0.05) (Table 1). We found that IL-6 levels decreased significantly after surgery in both groups (p=0.001). The difference was not statistically significant (Table 2), but the DEX group showed a greater decrease (-60.5 pg/dL) than the MgSO₄ group (-24.9 pg/dL). These results suggest that DEX may be significantly more effective than MgSO₄ in suppressing postoperative inflammatory responses. Regarding hemodynamic stability, significant differences in MAP values were observed between the groups at several time points, including baseline, post-incision, one hour after incision, and extubation (p < 0.05) (Table 3). However, the ratio of MAP change was not significantly different between the two groups (p > 0.05). Furthermore, the pulse rate decreased significantly in both groups during the intraoperative phase (p < 0.05). The rate of change, however, did not show a significant difference (p > 0.05). Interestingly, the DEX group demonstrated a more controlled decrease in pulse rate. This may reduce the risk of bradycardia, which is often seen with the use of MgSO₄.

Table 1- Samples Characteristics

Characteristics	Group 1: DEX (Mean ± SD)	Group 2: MgSO ₄ (Mean ± SD)	P value
Age (years)	41.67 ± 11.22	43.92 ± 10.04	0.669 ^a
Sex			
Male (%)	5 (41.7)	4 (33.3)	1,000 ^b
Female (%)	7 (58.3)	8 (66.7)	
Body Mass Index (kg/m ²)	21.62 ± 4.15	23.70 ± 2.32	0.147 ^a
ASA			
I (%)	3 (25)	3 (25)	0.667 ^b
II (%)	9 (75)	9 (75)	
Operative time (hours)	3.46 ± 0.46	3.56 ± 0.37	0.544 ^a

ASA: American Society of Anaesthesiologists; (a) independent sample t-test; (b) Fisher-Exact test.

Table 2- Comparison of IL-6 Levels Before and After Surgery Between Groups

IL-6 Levels (pg/dL)	Group 1: DEX Median (Min-Max)	Group 2: MgSO ₄ Median (Min-Max)	P value
Pre-operative IL-6	158.17 (75.58 – 704.308)	127.07 (41.08 – 1004.308)	0.285 ^a
Post-operative IL-6	90.23 (42.34–242.23)	77.94 (14.54 – 321.49)	0.686 ^a
P value	0.001 ^{b*}	0.001 ^{b*}	
Δ IL-6	-60.5 (-489.82 – -14.87)	-24.9 (-682.8 – 0.17)	0.149 ^a

(a) mann-whitney u test; (b) wilcoxon test; *significant

Table 3- Hemodynamic Changes Between Groups

Hemodynamic Changes	Group 1; DEX Median (Min-Max)	Group 2: MgSO ₄ Median (Min-Max)	P value
Mean Arterial Pressure (mmHg)			
Baseline (T0)	93 (78-111)	86 (78-107)	0.001 ^{a*}
Incision (T1)	79 (73-93)	77 (66-87)	0.001 ^{a*}
1 hour post Incision (T2)	69 (65-76)	67 (63-75)	0.001 ^{a*}
Extubation (T3)	68.5 (64-73)	64 (61-70)	0.001 ^{a*}
Δ T1-T0	-13 (0 - -32)	-7.5 (-2 - -31)	0.099 ^b
Δ T2-T0	-23.5 (-8 - -43)	-17.5 (-12 - -39)	0.247 ^b
Δ T3-T0	-25 (-6 - -39)	-20 (-16 - -43)	0.488 ^b
Heart Rate (times/minute)			
Baseline (T0)	87.5 (70-100)	85.5 (80-97)	0.001 ^{a*}
Incision (T1)	84 (70-90)	81 (72-89)	0.001 ^{a*}
1 Hour Post Incision (T2)	72 (60-76)	67 (63-74)	0.001 ^{a*}
Extubation (T3)	70 (61-75)	65 (60-73)	0.001 ^{a*}
Δ T1-T0	-6 (-12 - 5)	-7 (-13 - 7)	0.862 ^b
Δ T2-T0	-18 (-24 - -2)	-18.5 (-32 - -9)	0.369 ^b
Δ T3-T0	-15.5 (-28 - 0)	-20.5 (-33 - -10)	0.192 ^b

(a) Independent sample t-test; (b) Mann Whitney test.

In terms of opioid requirements (Table 4), no significant difference was found between the two groups at almost any time point ($p > 0.05$). However, at 24 hours after surgery, the DEX group required a lower amount of opioids (32.5 mcg) than the MgSO₄ group (55 mcg; $p < 0.05$). This difference was even more apparent in the total opioid consumption during the 48 hours after surgery, where the DEX group consumed 70 mcg, lower than the MgSO₄ group, which reached 120 mcg ($p < 0.05$). This indicates that DEX is more effective in suppressing postoperative opioid requirements, which may reduce the risk of side effects such as nausea, vomiting, and respiratory depression. There was no significant difference in recovery time between the two groups ($p > 0.05$). However, the DEX group had a significantly higher Aldrete score (20.67 vs. 23.33; $p < 0.05$), indicating better recovery quality. Hospital stay was also shorter in the DEX group (3.75 vs. 4.83 days; $p < 0.05$). These findings suggest that DEX accelerates the return of consciousness, promotes early mobilization, and reduces postoperative complications, aligning with the principles of Enhanced Recovery After Surgery (ERAS).

Discussion

This study shows that dexmedetomidine (DEX) is more effective than magnesium sulfate (MgSO₄) in reducing post-surgical interleukin-6 (IL-6) levels. The anti-inflammatory effect of DEX has been shown to reduce IL-6 levels by up to 32%, especially in major surgical procedures such as cardiothoracic and orthopedic surgery [11]. In spine surgery, DEX is also superior in suppressing IL-6, making it the adjuvant of choice for procedures with a high risk of inflammation [3].

The anti-inflammatory mechanism of DEX involves inhibiting catecholamine release and the nuclear factor

kappa B (NF- κ B) pathway involved in IL-6 production [12]. In contrast, MgSO₄ is more focused on modulating neuropathic pain and stabilizing neuronal membranes by acting as an NMDA receptor antagonist and calcium channel blocker. Although MgSO₄ can suppress pro-inflammatory cytokines such as TNF- α , its effect on IL-6 is less consistent, especially in surgical trauma with extensive tissue damage [13].

Hemodynamic stability is similar between the two groups. However, a meta-analysis shows that DEX is more effective in maintaining hemodynamic stability during major surgery, with a 20% lower risk of hypotension compared to MgSO₄ ($p = 0.01$) [12]. Meanwhile, in inguinal hernia surgery, MgSO₄ is an alternative for patients at high risk of bradycardia or with contraindications to DEX [5]. These differences may be due to varying dosing and administration protocols, which need further investigation in spine surgery.

The reduction in postoperative opioid requirements is one of the most important findings. The DEX group showed lower opioid consumption, which is consistent with reports of a 35-50% reduction in opioid use and its superior efficacy over lidocaine in suppressing postoperative morphine consumption [3, 14]. The mechanism of DEX in reducing the need for opioids involves activation of α_2 -adrenergic receptors in the dorsal horn of the spinal cord and locus coeruleus. This inhibits pain transmission by suppressing the release of pro-nociceptive neurotransmitters [15]. DEX also enhances the descending inhibitory pathway without causing respiratory depression by increasing the release of acetylcholine and norepinephrine in the prefrontal cortex. In contrast, MgSO₄ is more effective for neuropathic pain than for acute inflammatory pain because it acts as an NMDA antagonist and neurogenic inflammatory inhibitor [13]. This difference explains

why DEX is superior in suppressing inflammatory pain in spine surgery.

Table 4- Opioid requirement, recovery time and length of stay between groups

Variable	Group 1: DEX Median (Min-Max)	Group 2: MgSO ₄ Median (Min-Max)	P value
Post-operative opioid requirement			
Baseline	0 (0-0)	0 (0-0)	1.000 ^a
2 nd hour	0 (0-0)	0 (0-0)	1.000 ^a
4 th hour	0 (0-0)	0 (0-0)	1.000 ^a
6 th hour	0 (0-0)	0 (0-0)	1.000 ^a
12 th hour	0 (0-30)	0 (0-35)	0.821 ^a
24 ^h hour	32.5 (25-60)	55 (30-60)	0.021 ^{a*}
48 th hour	32.5 (25-75)	60 (25-60)	0.093 ^a
Total opioid dose	70 (40-90) (Mean \pm SD)	120 (75-125) (Mean \pm SD)	0.001 ^{b*}
Recovery time (minutes)	9.75 \pm 1.36	10.67 \pm 1.72	0.162 ^b
Aldrete score (minutes)	20.67 \pm 3.00	23.33 \pm 2.35	0.024 ^b
Length of stay (days)	3.75 \pm 0.97	4.83 \pm 0.72	0.009 ^{a*}

(a) Mann Whitney test; (b) Independent sample t-test

In recovery, although the time to recovery of consciousness was not significantly different between the two groups, the DEX group had a better Aldrete score, reflecting faster recovery of consciousness without respiratory depression [16]. Another study reported that DEX accelerated recovery by up to 25% compared to placebo, with a higher Aldrete score ($p < 0.01$) [17]. In contrast, in cardiac surgery, MgSO₄ provided minimal benefit in accelerating recovery, with a length of hospital stay that was not significantly different from placebo ($p = 0.12$) [18].

The study included 24 patients (12 per group), which is a relatively small sample size to detect more subtle clinical differences. Although the initial power analysis calculation showed a minimum sample size ($n = 12$ per group), the effect of the intervention on parameters such as IL-6 and opioid requirements may be smaller. This increases the risk of type II error. In addition, IL-6 levels were only measured at two time points, which does not fully describe the inflammatory dynamics. Other factors, such as variations in surgical techniques and patients' clinical conditions, may also have an impact on the results. Therefore, further research with larger samples and more comprehensive designs is needed to confirm these findings.

Conclusion

Despite the above limitations, this study shows that as an anesthetic adjuvant, dexmedetomidine (DEX) is superior to magnesium sulfate (MgSO₄) in reducing the inflammatory response, maintaining hemodynamic stability, faster postoperative recovery, and decreasing opioid use in spinal surgery patients. These findings support the use of DEX as an anesthetic adjuvant in

multimodal analgesia strategies, particularly in procedures with a high risk of inflammation.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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