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Research Article

# Comparative Effects of Ketamine Versus Magnesium Sulfate on Pain Management after Spine Surgery: A Double-Blind Randomized Clinical Trial

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**ABSTRACT**

**Background:** Spinal fusion surgery, as one of the treatment options for back pain, often results in significant postoperative pain due to complexity and multiple incisions. Glutamate receptors such as NMDA are among the main receptors involved in this process, causing central hyperalgesia and sensitization and ultimately accelerating pain processing in the CNS. Therefore, NMDA receptor antagonists such as ketamine and magnesium sulfate can be considered as suitable options for treating pain caused by these surgeries. A prospective study was conducted to compare the effects of ketamine and magnesium sulfate on pain control in these patients. This double-blind clinical trial was performed on 72 patients undergoing fusion surgery, referred to the 5th Azar Medical & Educational Center of Gorgan in 2020-2022.

**Methods:** In group A, 50mg/kg of magnesium sulfate along with CVE=5 ml/kg was infused over 20 minutes, and then 500 mg/h of magnesium sulfate was given during and up to 48 hours after surgery. In group B, 0.5 mg/kg of ketamine was given as a bolus after patient positioning and 2 minutes before surgical incision, followed by 2.5 mcg/kg/h of ketamine during and up to 48 hours after surgery. Pain was evaluated using the NRS scale from admission to recovery up to 48 hours after surgery, and the amount of opioid consumption was recorded.

**Results:** Both ketamine and magnesium sulfate led to a significant reduction in pain during the first 48 hours after surgery (P value <0.0001). The speed of pain reduction in the first 6 hours was higher in women in the ketamine group and in men in the magnesium group, although the results were reversed in the second 6 hours. Pain assessment in opium addicts indicated the superiority of magnesium in the speed of pain reduction in patients during the first 12 hours. The amount of analgesic used during recovery was statistically similar in both groups (p=0.645), but during the 24 hours after surgery, the amount of opioid consumption used in the magnesium group was significantly lower (p=0.025). After 24 hours, none of the two groups needed analgesics. No severe side effects were observed in any of the patients in the two groups.

**Conclusion:** Magnesium sulfate not only works well with ketamine in controlling postoperative pain but can also perform better than ketamine in women and opioid addicts, leading to a reduction in the use of opioids and avoidance of ketamine's side effects. In addition to reducing pain and analgesic use, considering the benefits of magnesium in stabilizing hemodynamics and reducing anesthetic use, this drug can

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be a very suitable alternative to ketamine for a wider range of patients undergoing spinal surgery, including those with heart and mental illnesses.

## Introduction

Back pain is a common problem among individuals in society, with around 10% of patients becoming disabled. As age increases, the incidence of spinal canal stenosis also increases. While non-surgical treatment is the first line of treatment, surgical methods are considered when initial treatments fail [1]. Spinal surgeries often result in significant postoperative pain, which can last for several days. Adequate pain relief is important for postoperative care in these patients. Laminectomy is a common spinal surgery [2], and laminectomy with fusion is associated with moderate to severe pain after surgery [1-2]. Severe postoperative pain can lead to central pain sensitization and increased pain sensation (hyperalgesia), which can cause patient dissatisfaction with their surgery [3]. Effective pain control leads to increased patient satisfaction and reduces the duration of hospital stays and hospital costs [4]. Postoperative pain is caused by various mechanisms, including nociceptive, neuropathic, or inflammatory mechanisms [2]. The main receptor involved in this process is glutamate receptors such as NMDA (N-Methyl-D-Aspartate) receptor, which causes central sensitization and hyperalgesia following painful stimuli during and after surgery. Furthermore, high doses of opioids during and after surgery can also stimulate these receptors [3,5]. Although opioids are widely used for postoperative pain relief, they have multiple side effects, such as respiratory depression, nausea and vomiting, hypotension, tachycardia, sweating, and pruritus [6]. So other drugs such as NMDA receptor antagonists like ketamine and magnesium sulfate are used to reduce the need for opioid consumption by regulating the activity of NMDA receptors [3-4,7-8]. These drugs can be a suitable strategy for postoperative pain control.

Ketamine, an NMDA receptor antagonist, is used as an anesthetic and for maintaining anesthesia. It is also used as an effective primary or adjunctive pain medication for postoperative pain, with several mechanisms of action: reducing central sensitization, and hyperalgesia, and reducing resistance to postoperative drug use by regulating mu, kappa, and delta opioid receptors. Researchers have indicated that combining opioids with NMDA antagonists like ketamine can provide useful analgesic effects for patients undergoing spinal surgery [8-10].

Loftus (2010) studied the effect of ketamine during surgery in reducing the amount of opioid consumption during surgery in 104 patients undergoing spinal surgery with a history of chronic opioid use. According to the results, the total amount of morphine consumed 48 hours after surgery and the average reported pain intensity in recovery and during the 6 weeks after surgery also decreased significantly [10]. Pacreu (2012) showed that the use of ketamine as an infusion during and after surgery in 22 patients undergoing lumbar arthrodesis significantly reduced methadone use in the first 24 and 48 hours after surgery [9]. Similarly, Remerand (2009) [11-12] and Adam (2005) [13] confirmed the early and late analgesic effects of ketamine after complete hip arthroplasty and knee arthroplasty, respectively. Finally, Jouguluelet (2015) examined 39 clinical trials and 5 meta-analyses based on low-dose ketamine infusions between 1966 and 2013. According to this study, ketamine infusion could reduce opioid use by an average of 40% and reduce pain intensity up to 48 hours after surgery [14].

Magnesium is a cation that plays an important role in normal body function. Magnesium is a non-competitive NMDA antagonist and also a calcium channel blocker. This drug has important analgesic effects, including the suppression of neuropathic pain, increasing morphine analgesic effects, and reduction of morphine resistance [4,6-7].

According to research conducted by Manna (2012), intravenous magnesium was able to reduce the total consumption of anesthesia and analgesia drugs, recovery time, postoperative pain score, and overall morphine requirement in 60 patients undergoing neurosurgery [15]. Sedighinejad (2014) also confirmed the effect of a 48-hour infusion of magnesium sulfate and sufentanil for pain control in orthopedic surgery patients [16]. However, in a further study by Ghaffaripour (2016) on 40 patients undergoing laminectomy, magnesium sulfate injection during surgery had no effect on pain control or the need for analgesic drugs during the first 24 hours after surgery [4]. Demiroglu (2016) also admitted that intramuscular magnesium reduced pain after laminectomy, but this is not true for intravenous magnesium [6]. Finally, Albrecht (2018), by reviewing 11 clinical trials from 1998 to 2016, stated that intravenous magnesium sulfate injection in orthopedic surgery can reduce the amount of painkillers used after surgery and side effects such as vomiting, nausea, and tremors, but there was no convincing evidence of a significant effect on postoperative pain intensity [7]. One of the few studies that compared the analgesic effects of magnesium and ketamine is the study by Arıkan (2016). In this clinical randomized trial, 120 patients undergoing total abdominal hysterectomy were randomly assigned to three groups of 40 patients receiving ketamine, magnesium, and normal saline. The results showed that the total morphine consumption in the ketamine group was 9.2±32.6 mg less than the magnesium and normal

saline groups, and the patient satisfaction level in the ketamine group was higher than the other two groups [11]. Another similar study by Elshalakany in Egypt in 2022 investigated the effect of analgesic infusion of ketamine and ketamine+magnesium sulfate in patients after nephrectomy. This researcher stated that the combination group had a significant success rate compared to ketamine infusion alone [17-18].

Given that there are not many studies on the comparative analgesic effects of ketamine and magnesium sulfate and that the use of each of these drugs is associated with consequences and side effects such as delirium, brain stimulation, exacerbation of muscle weakness, and respiratory depression [3], the superiority of the effect or side effects of these drugs is under discussion. In this study, we have attempted to answer the question of which drug is more effective in controlling pain in these patients and has minimal side effects.

## Methods

This study is a double-blind clinical trial that entered the clinical phase after obtaining permission from the ethics committee of Golestan University of Medical Sciences and registration in the IRCT system.

- Ethics code: IR.GOUMS.REC.1399.343
- IRCT registration number: IRCT20170413033408N6

In this study, patients with low back pain aged 18-65 years with ASA type 1 and 2 who were candidates for laminectomy, discectomy, and posterior lumbar and sacral screw and rod placement surgery were hospitalized in the neurosurgery ward of 5 Azar Teaching Hospital in Gorgan. The day before surgery, patients were visited by an anesthesiologist, and after providing complete explanations about the surgery and the purpose of this study and obtaining written consent, they were enrolled in the study.

Due to the lack of a related article on orthopedic surgeries that reports the comparative results of both drugs, based on the mean and standard deviation obtained from a preliminary study with a sample size of 8 individuals in each group, at a confidence level of 0.95 and a test power of 0.80, and using the following formula, the sample size for each group was calculated to be 36 individuals:

$$n = \frac{[t_{1-\frac{\alpha}{2},n_0-1}+t_{1-\beta,n_0-1}]^2(sd_1^2+sd_2^2)}{(\bar{x}_1-\bar{x}_2)^2} \quad (1)$$

$$n_0 = 8, \alpha = 0.05, \beta = 0.20 \quad (2)$$

$$n = \frac{[1.895+0.896]^2[(2.79)^2+(2.27)^2]}{(7.65-5.95)^2} = 36 \quad (3)$$

Patient allocation to one of the two drug groups was done based on the permuted block randomization method. A random sequence of letters A and B was generated in blocks of four, and 18 blocks were made available to one of the research team members who had no involvement in selecting the samples. Sequentially numbered, sealed, opaque envelopes (SNOSE) were used to conceal the random sequence.

**Inclusion criteria**

- Patients aged 18-65 years with ASA type 1 and 2
- Candidates for spinal fusion surgery

**Exclusion criteria**

- History of previous surgery in the lumbosacral area
- History of schizophrenia and use of antipsychotic drugs
- History of calcium channel blocker use
- History of neuropathy and myopathy
- History of kidney injury requiring dialysis in the past
- Presence of conduction system disorders in the patient's ECG
- Allergy to anesthesia drugs
- Less than 48 hours hospital stay after surgery

**Withdrawal criteria**

- Surgery duration exceeding four hours
- Need for transfusion of more than four units of packed red blood cells
- Occurrence of air embolism during surgery
- Severe agitation and delirium in the recovery and ward that did not respond to usual doses of benzodiazepines or lasted more than two hours and required further interventions.

**Intervention procedure**

After entering the operating room, all patients underwent sedation with 0.05 mg/kg midazolam. For all patients, a 5 ml/kg normal saline infusion along with 15 mg/kg tranexamic acid (to reduce bleeding) was performed over 20 minutes before inducing anesthesia. Then anesthesia induction was performed with 1-2 mg/kg propofol, 1 mg/kg lidocaine, 3 mcg/kg fentanyl, and 0.5 mg/kg atracurium, and the patient was intubated with a suitable-sized spiral tube. Isoflurane volatile anesthesia at 1-1.5 MAC and $N_2O$:$O_2$ gas with a ratio of 1:1 were used for maintenance of anesthesia. Normal saline infusion at a rate of 5-10 ml/kg/h was used for fluid therapy during surgery. In case of bleeding exceeding MABL (Maximum Allowable Blood Loss), packed red blood cells were replaced. During surgery, the mean arterial pressure was maintained within 30% of the patient's baseline pressure range. If there was a history of chronic opioid use, we used 5 mg of methadone intramuscularly after anesthesia induction. After intubation, a central

venous catheter, an arterial catheter, and a Foley catheter were inserted and fixed for the patient.

In the magnesium group, along with initial fluid therapy, 50 mg/kg magnesium sulfate was infused, and in the ketamine group, 0.5 mg/kg ketamine was injected about 2 minutes before incision after achieving a suitable surgical position and preparing the surgical site.

After the start of surgery, in the magnesium group, the prescription was continued at a rate of 500 mg/h, and in the ketamine group, it was continued at a rate of 2.5 mcg/kg/h via infusion pump for 48 hours.

Anesthesia induction was performed by an anesthesiologist who was not involved in the study design or outcome assessment. The pumps, which were similar in appearance (size, shape, volume, and manufacturer), were prepared by the recovery nurse, and the responsible physician had no knowledge of their contents.

The patient's hemodynamics were measured and recorded before and after induction and then every 5 minutes during surgery. The monitoring used for these patients included ECG, heart rate, systolic and diastolic blood pressure, mean arterial pressure, and capnography from the Saadat monitoring device. The patient's urine output was also checked and recorded every hour.

After awakening and extubation, vital signs, including heart rate, blood pressure, respiratory rate, patellar reflex (muscle twitch), and level of consciousness, were measured and recorded every hour for the first four hours and then every two hours for the next four hours, and then every four hours by the collaborating resident. In the magnesium group, if the patellar reflex decreased for two hours, the pump was stopped and re-infused once symptoms subsided. If the patient became restless without any alarming cause, 3-5 mg of midazolam was injected intravenously. If there was no response and further intervention was needed, the patient was excluded from the study.

For postoperative pain control, with the coordination of the surgeon, 30 mg/6 h ketorolac with a maximum daily dose of 120 mg and 15 mg/kg/6h intravenous acetaminophen with a maximum daily dose of 4 grams were used with a 3-hour interval between ketorolac and intravenous acetaminophen. In patients with a history of long-term narcotic use, the equivalent dose of the narcotic was prescribed based on methadone. Pain was measured and recorded based on the Numeric Rating Scale (NRS). In case of NRS≥4 despite receiving acetaminophen and ketorolac, morphine was used for postoperative pain control. Then the total amount of morphine used during the first and second 24 hours was measured and recorded.

The intensity of pain was described by calculating the mean and standard deviation. The normality of the data distribution was examined using the Shapiro-Wilk test. The sphericity condition was examined using Mauchly's Test of Sphericity. Repeated Measure ANOVA and Repeated Measure ANCOVA were used to analyze the data. The significance level of the tests was considered to be 0.05. The data were analyzed using R software version 4.0.2.

## Results

In this study, 36 patients were in both the magnesium and ketamine groups, with mean ages of 47.66 ± 10.91 and 45.05 ± 14.80 years, respectively, and this difference was not statistically significant (P value = 0.397). The consort flow diagram of this study has been shown in (Figure 1).

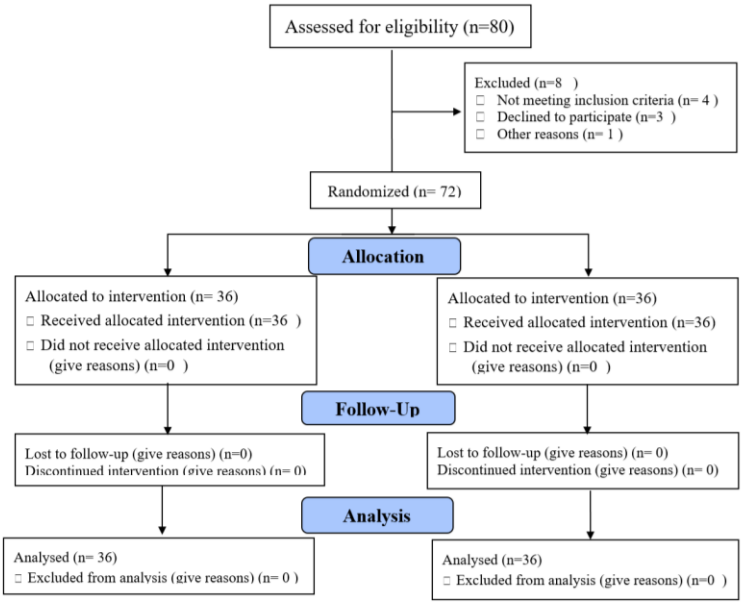


**Figure 1- Consort Flow Diagram**

Of the 72 patients in the study, 26.4% were opioid addicts, with 22% of them in the magnesium group and 29% in the ketamine group.

The results of Repeated Measure ANCOVA showed that the mean pain intensity during recovery was somewhat higher in the magnesium group than in the ketamine group, but both drugs significantly reduced pain intensity over 48 hours (P value < 0.0001). The rate of pain reduction was slightly higher in the magnesium group initially, but after 36 hours, the results were completely equal for both drugs (Figure 2). To adjust for the effect of age on pain reduction, Repeated Measure ANCOVA was used, and the results showed that patient age had no effect on how the drugs affected pain reduction (P value = 0.199). To determine the effect of patient gender on pain in the two groups under study, we used a classification method, and the results showed that the pattern of pain reduction in women and men in the magnesium and ketamine groups was not similar. In women, the rate of pain reduction during the first 6 hours of recovery was higher in the magnesium group, but for men, it was higher in the ketamine group. This behavior was reversed between 6 and 12 hours, with men showing a higher rate of pain reduction in the magnesium group and women showing a higher rate in the ketamine group (Figure 3,4). To determine the effect of opium addiction on pain in the two groups under study, we also used a classification method, and the results showed that pain during recovery was higher in opium addicted patients than in non-addicted patients, and over time, both groups experienced a significant reduction in pain (P value < 0.01). The rate of pain reduction during the first 12 hours of recovery was somewhat higher in the magnesium group for addicted patients, but in non-addicted patients, the rate of pain reduction was the same in both groups (Figure 5,6).

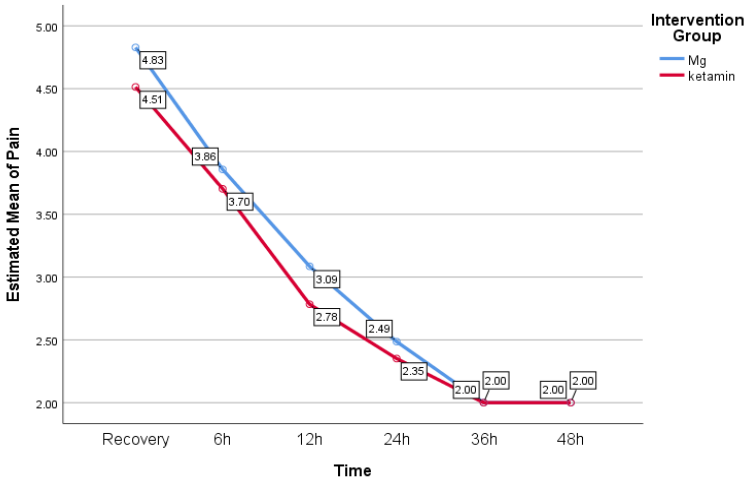


**Figure 2- Comparison of the trend of pain reduction in two groups of magnesium and ketamine during 48 hours after surgery.**

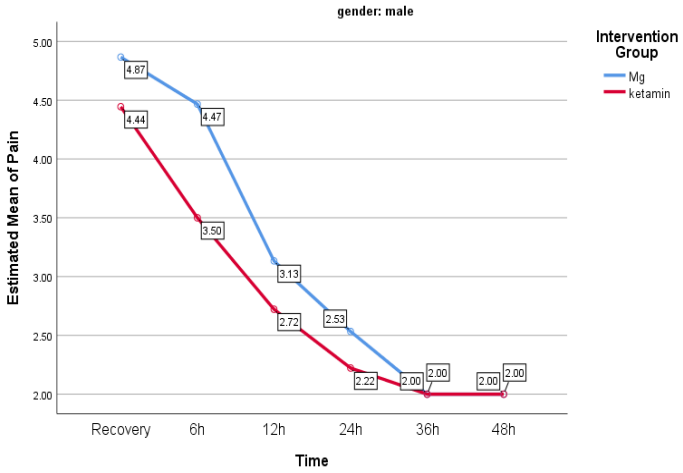


**Figure 3- Comparison of the trend of pain reduction in two groups of magnesium and ketamine for men during 48 hours after surgery.**

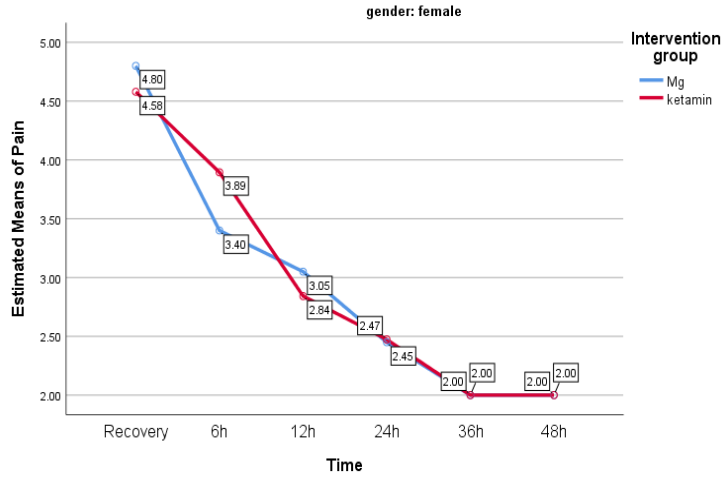


**Figure 4- Comparison of pain reduction process in two groups of magnesium and ketamine in women during 48 hours after surgery.**

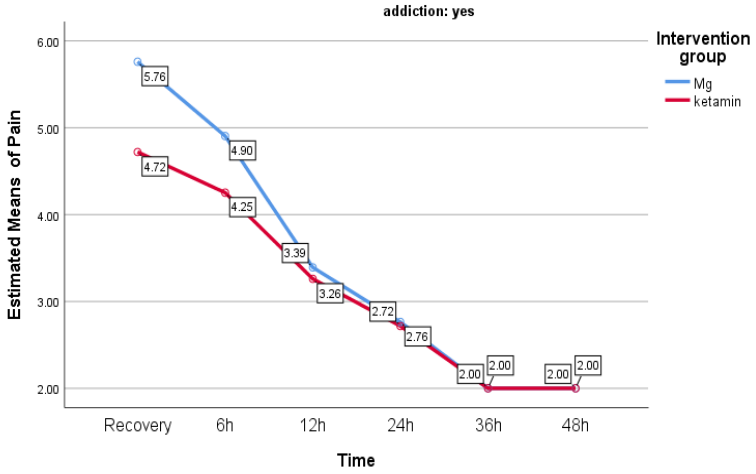


**Figure 5- Comparison of the trend of pain reduction in two groups of magnesium and ketamine for opium-addicted patients during 48 hours after surgery.**

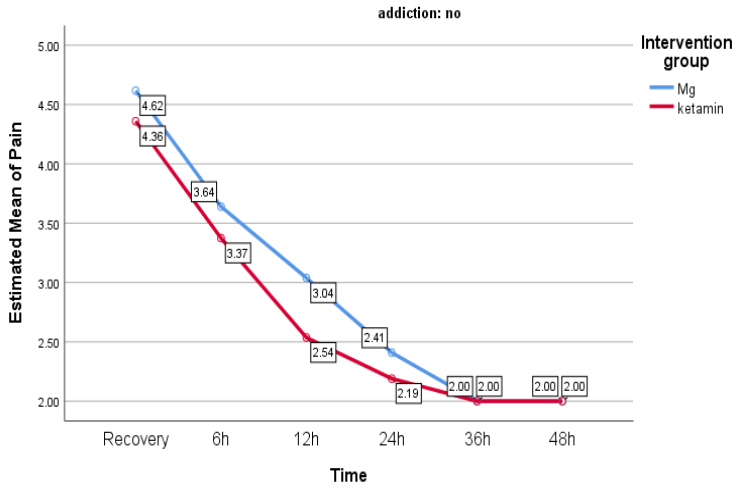


**Figure 6- Comparison of the process of pain reduction in two groups of magnesium and ketamine for non-addicted patients during 48 hours after surgery.**

After appropriate pain score evaluation, if necessary, morphine was considered for patients. Therefore, we continued to investigate the amount of drug consumption in the two groups. Despite the use of ketamine, magnesium, acetaminophen, and ketorolac, including opioid addicts, none of the patients needed morphine in the second 24 hours of hospitalization. The distribution of drug consumption in the two treatment groups during recovery was as follows: 2.08 ± 2.34 mg in the magnesium group and 2.33 ± 2.27 mg in the ketamine group (P value = 0.645). However, in the first 24 hours after surgery, the amount of drug consumption in the magnesium and ketamine groups was 2.44 ± 3.85 and 5.27 ± 6.34 mg, respectively, which was statistically significant (P value = 0.025); although the amount of drug consumption in addicted patients in the magnesium and ketamine groups was 6.18 ± 4.62 and 10.63 ± 8.04 mg, respectively, which was not statistically significant (P value = 0.147).

Regarding the total drug consumption during the first 48 hours after surgery, it was 4.53 ± 4.58 mg in the magnesium group and 7.61 ± 8.10 mg in the ketamine group, which was statistically significant (P value = 0.04). We also examined the amount of drug consumption in the two groups of addicted and non-addicted patients during 48 hours. According to the results, despite taking methadone for addicted individuals, the amount of drug consumption in addicted and non-addicted groups in the magnesium group was 8.76 ± 7.02 and 5.16 ± 6.43 mg, respectively, which was statistically significant (P value = 0.045).

In our study, we also evaluated the simultaneous effect of opium addiction in the two drug groups under study. According to the results, in the magnesium group, the difference in the amount of drug requirement between addicted and non-addicted groups was 6.18 ± 4.62 and 4.04 ± 4.53 mg, respectively, which was not statistically significant (P value = 0.12). In the ketamine group, the amount of drug consumption in addicted and non-addicted groups was 10.63 ± 8.04 and 6.32 ± 7.87 mg, respectively, which was not statistically significant (P value = 0.067).

## Discussion

Numerous studies have investigated various methods and drugs to reduce pain after spinal surgery. The aim of this study was also to compare the effect of two similar and yet different drugs in the treatment of these patients; ketamine and magnesium sulfate are both NMDA receptor antagonists, and their effect on reducing postoperative pain and faster recovery and reducing opioid consumption has been confirmed or rejected in various studies. Most studies on ketamine, such as Pacreu [9], Remerand [12], and Adam [13], have supported the positive effect of this drug on postoperative pain, while studies on magnesium have had more contradictions, and although Ghaffaripour [4] and Demiroglu [6] have rejected the effect of magnesium on postoperative pain, studies such as Manna [15] and Sedighinejad [16] have indicated its positive effect. Our study confirmed the majority of studies, indicating that both ketamine and magnesium sulfate are effective in reducing postoperative pain after spinal surgery.

Spinal surgery is often associated with severe pain, and the main treatment for this pain is usually narcotic drugs. In a relatively similar study, Etezadi [17] and colleagues in 2020 investigated the effect of adding ketamine and magnesium in combination in the treatment of pain in patients undergoing lumbar orthopedic procedures. Elshalakany [18] also compared the analgesic effect of ketamine infusion and ketamine & magnesium sulfate in patients after nephrectomy. Since both drugs are NMDA receptor antagonists, we decided to compare these two drugs individually and evaluate the effect of other drugs such as acetaminophen and ketorolac on reducing narcotic consumption.

In contrast to most studies, such as Loftus [10] and Demiroglu [6], we did not consider narcotic drugs as the first line of treatment for postoperative pain in our study and used a multimodal approach to compensate for it, an approach that has been a very suitable alternative to narcotics with fewer side effects.

Elshalakany [18] and Etezadi [17] found the combination of ketamine and magnesium to be very effective, but in this study, we examined both drugs individually and found that about 36 hours after surgery, the level of pain in both groups of patients had decreased similarly. These findings, despite agreement with Arıkan [11] about ketamine, are in contrast with him about magnesium effects. In fact, in contrast with Arıkan [11], Ghaffaripour [4], and Demiroglu [6], we suggest that magnesium is also effective in controlling postoperative pain.

However, the rate of pain reduction during the first 36 hours and its relationship with gender and addiction were noteworthy and distinguished findings in this process. Our studies showed that the level of pain in recovery was higher in men than women and in opium addicts than healthy individuals. The rate of pain reduction in the ketamine group was higher in men than women in the first 6 hours, but this parameter was in favor of magnesium between 6 and 12 hours. These differences in hours and gender can be evaluated more accurately by designing more extensive studies. In examining opium-addicted patients, pain reduction was almost equal in both the ketamine and magnesium groups from 12 hours after surgery, and it was clearly consistent with non-addicted patients. However, during the first 12 hours, the rate of pain reduction for magnesium was higher, while non-addicted individuals did not show any significant differences in drug type.

In addition, another noteworthy point is the need and response of patients to narcotics. Although no difference was observed in the need for narcotics in recovery between the two groups, the results of the 24-hour follow-up showed a significant statistical difference in the amount of morphine consumption in the two groups of patients. Since no need for narcotics was observed in any of the patients from 24 hours after surgery, it can practically be concluded that, contrary to expectations, magnesium plays a better role than ketamine in controlling postoperative pain and reducing the need for narcotics and their side effects.

**Limitations**

One of the limitations of this study is its duration. We only examined patients in the first 48 hours after surgery and during drug infusion. Although at the time of discharge, all patients were stable and their pain was controlled with oral medications, more extensive and longer studies can be designed to measure the effect of NMDA receptor antagonist drugs on postoperative pain reduction after discontinuation of drug infusion and obtain a more comprehensive clinical view of the results of this study. In addition, due to the limited sample size, the interpretation of results related to addiction and gender will require further investigation.

## Conclusion

The results of this study showed that both magnesium sulfate and ketamine are effective in controlling postoperative pain and reducing the use of narcotics and their side effects. In other words, magnesium sulfate not only works well alongside ketamine in controlling postoperative pain but can also perform better than ketamine and reduce narcotic use in spinal surgery patients, especially women and opioid addicts. Therefore, with further studies in this area, if this finding is confirmed, magnesium can be considered a suitable and safe alternative to ketamine for a wider range of spinal surgery patients, including those with heart and mental illnesses and opium addicts.

### References

[1] Rasras S, Safari H, Azizzadeh A. Comparison of the effects of laminectomy alone and laminectomy with fusion and fixation in the patients over 50 years of age with degenerative spinal canal stenosis. Sci J Kurdistan Univ Med Sci. 2018; 23(1):57-63.

[2] Bajwa SJ, Haldar R. Pain management following spinal surgeries: An appraisal of the available options. J Craniovertebr Junction Spine. 2015; 6(3):105-10.

[3] Richebe PH, Bollag L, Rivat C. N-Methyl-D-aspartate Antagonists. In: Lussier D, Beaulieu P, editors. Adjuvant analgesics. Oxford American Pain Library–Oxford University Pres. 2015; 59-71.

[4] Ghaffaripour S, Mahmoudi H, Eghbal H, Rahimi A. The Effect of Intravenous Magnesium Sulfate on Post-Operative Analgesia During Laminectomy. Cureus. 2016; 8(6):e626.

[5] De Kock MF, Lavand'homme PM. The clinical role of NMDA receptor antagonists for the treatment of postoperative pain. Best Pract Res Clin Anaesthesiol. 2007; 21(1):85-98.

[6] Demiroglu M, Ün C, Ornek DH, Kıcı O, Yıldırım AE, Horasanlı E, et al. The Effect of Systemic and Regional Use of Magnesium Sulfate on Postoperative Tramadol Consumption in Lumbar Disc Surgery. Biomed Res Int. 2016; 2016:3216246.

[7] Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia. 2013; 68(1):79-90.

[8] Takieddine SC, Droege CA, Ernst N, Droege ME, Webb M, Branson RD, et al. Ketamine versus hydromorphone patient-controlled analgesia for acute pain in trauma patients. J Surg Res. 2018; 225:6-14.

[9] Pacreu S, Fernández Candil J, Moltó L, Carazo J, Fernández Galinski S. The perioperative combination of methadone and ketamine reduces post-operative opioid usage compared with methadone alone. Acta Anaesthesiol Scand. 2012; 56(10):1250-6.

[10] Loftus RW, Yeager MP, Clark JA, Brown JR, Abdu WA, Sengupta DK, et al. Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery. Anesthesiology. 2010; 113(3):639-46.

[11] Arıkan M, Aslan B, Arıkan O, Horasanlı E, But A. Comparison of the effects of magnesium and ketamine on postoperative pain and morphine consumption. A double-blind randomized controlled clinical study. Acta Cir Bras. 2016; 31(1):67-73.

[12] Remérand F, Le Tendre C, Baud A, Couvret C, Pourrat X, Favard L, et al. The early and delayed analgesic effects of ketamine after total hip arthroplasty: a prospective, randomized, controlled, double-blind study. Anesth Analg. 2009; 109(6):1963-71.

[13] Adam F, Chauvin M, Du Manoir B, Langlois M, Sessler DI, Fletcher D. Small-dose ketamine infusion improves postoperative analgesia and rehabilitation after total knee arthroplasty. Anesth Analg. 2005; 100(2):475-80.

[14] Jouguelet-Lacoste J, La Colla L, Schilling D, Chelly JE. The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: a review of the current literature. Pain Med. 2015; 16(2):383-403.

[15] Manaa EM, Alhabib AF. Effect of magnesium sulfate on the total anesthetic and analgesic requirements in neurosurgery. J Neurol

Neurophysiol S11-001. 2012.
[16] Sedighinejad A, Haghighi M, Naderi Nabi B, Rahimzadeh P, Mirbolook A, Mardani-Kivi M, et al. Magnesium sulfate and sufentanil for patient-controlled analgesia in orthopedic surgery. Anesth Pain Med. 2014; 4(1):e11334.
[17] Etezadi F, Farzizadeh M, Sharifinia HR, Alimohammadi M, Khajavi MR. The effects of intraoperative ketamine and magnesium sulfate on acute pain and opioid consumption after spine surgery. Acta Med Iran. 2020; 58(5):221-4.
[18] Mohamed AK. Assessment of Analgesic Effect of Ketamine Vs Ketamine Magnesium Infusion and Their Effect on Postoperative Morphine Consumption after Surgical Nephrectomy. Egypt J Anaesth. 2023; 39(1):11-8.