ORIGINAL ARTICLE

Effects of NMDA receptor antagonists on acute postoperative pain

Maja Stojanovic[1,2], Predrag Stevanovic[2,3], Sonja Vuckovic[2,4], Katarina Savic Vujovic[2,4]

[1]Institute for Cardiovascular Disease Dedinje, Belgrade, Serbia
[2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia
[3]University Hospital Center Dr Dragiša Mišović, Belgrade, Serbia
[4]Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

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Correspondence to:
Maja Stojanovic
Institute for Cardiovascular Disease Dedinje,
1 Heroja Milana Tepića Street, 11000 Belgrade, Serbia
Email: majastojanovic05@gmail.com

Summary

Introduction: Pain represents a multifactorial process with detrimental effects on the entire organism. This randomized, open-label pilot study investigated the effect of preemptive administration of ketamine and magnesium-sulfate on the intensity of postoperative pain after laparoscopic colon tumor resection.

Methods: Sixty patients were randomized into the ketamine-magnesium (KM) and the control (C) groups. After the introduction to anesthesia, patients in the KM group received an i.v. bolus dose of 0.5 mg/kg ketamine, followed by a continuous infusion of 0.6 mg/kg/h lasting until the end of surgery. After a bolus dose of ketamine, they also received magnesium-sulfate 20 mg/kg in an intravenous infusion (5-10 minutes). Group C received only 0.9% NaCl infusion. After the patients were awakened (0h), the pain intensity was compared (0-46h) between the two groups.

Results: The Mann-Whitney test implied significantly ($p<0.05$) lower visual analog scale (VAS) scores, in KM group at 0, 1, 2, 10, 22 and 30 hours after the surgery, and no statistical significance ($p>0.05$) for VAS scores after 6, 14, 18, 38 and 46 hours, compared to C group. Ketamine and magnesium-sulfate significantly ($p<0.05$) reduced the postoperative consumption of analgesics, increased the sedation level at 0h postoperatively, and increased the overall patient satisfaction with the treatment.

Conclusion: Preemptive administration of ketamine and magnesium-sulfate combination has a beneficial effect on postoperative pain after laparoscopic colon tumor resection.

Keywords: NMDA-antagonists, ketamine, magnesium-sulfate, acute pain

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INTRODUCTION

Pain represents a multifactorial process with detrimental effects on the entire organism. Inadequately controlled postoperative pain affects the overall outcome of patient treatment and is associated with increased morbidity, diminished quality of life, and impaired functional recovery. In the current era of surgical advancement, characterized by the use of minimally invasive procedures and a trend toward prompt discharge after surgery, it is necessary to adapt analgesic strategies to align with the rapid recovery of patients following surgical intervention (1). According to the recommendations for acute pain therapy by the American Society of Anesthesiologists (ASA), acute pain is defined as pain present in surgical patients after the procedure, a consequence of trauma caused by the procedure itself, or due to complications related to the procedure (2).

Patients undergoing major surgical procedures experience significant clinical symptoms in the form of pain both at rest and during activity. Pain at rest is usually moderate, having an average visual analog scale (VAS) score of 3 to 4 out of 10 during the first 2 to 3 days after surgery, disappearing within the first week after the surgery. In contrast, pain during activity may reach scores of 7 to 8 and can last for weeks (3).

The mechanism by which harmful peripheral stimuli are transmitted to the central nervous system is called nociception (4). It consists of transduction, peripheral and central transmission, and synaptic transmission with modulation processes. At the synaptic level, the primary mediator involved in pain transmission is glutamate. Fast synaptic excitatory transmission occurs *via* glutamate released from the central terminals of nociceptors, which acts on ligand-gated ion channels on the postsynaptic membrane of central neurons (5,6). Ionotropic glutamate receptors are cation channels that allow the entry of positively charged ions, Na^+ and Ca^{2+}, into the postsynaptic cell, eliciting an excitatory postsynaptic potential, depolarization of the postsynaptic membrane, and increased excitability of the postsynaptic neuron (7). The glutamatergic excitatory postsynaptic potential induced by low-frequency action potentials in primary afferent neurons is generated mainly by the activation of AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and kainate glutamate receptors. NMDA (N-methyl-D-aspartate) receptors, also localized on excitatory primary afferent synapses, contribute little to the postsynaptic response to low-frequency presynaptic action potentials. Such a situation is due to the presence of tonic inhibition of ion flow through the NMDA receptor ion channel, resulting from a voltage-dependent blockade by extracellular magnesium ions (Mg^2) at the resting membrane potential, and because the activity of NMDA receptors is inherently down-regulated by a shift of the kinase/phosphatase regulatory system toward dephosphorylation (8,9). NMDA receptor antagonists, such as ketamine and magnesium, reduce the central mechanism of pain impulse transmission, thereby decreasing acute pain and preventing the development of chronic pain (10,11). Previous studies have investigated the effects of ketamine and magnesium alone, or in combination with other analgesics, particularly opioids. There are limited clinical data on their combined preventive use in laparoscopic colorectal procedures (10,11).

This study aims to examine the effect of the preemptive administration of a ketamine-magnesium combination on postoperative pain intensity reduction after laparoscopic surgery for colon tumors.

MATERIAL AND METHODS

Recruitment of participants and randomization

This pilot, randomized, open-label study was conducted on 60 patients undergoing elective laparoscopic surgery for colon tumors at the Department of Anesthesia, Resuscitation and Intensive Care, University Medical Center "Zvezdara" in Belgrade, from December 1, 2022, to December 1, 2023. The study was approved by the Ethics Committee of the "Zvezdara" University Medical Center on January 13, 2022. under the number IRB00009457, and conducted in compliance with the Declaration of Helsinki. Inclusion criteria were patients with ASA I and ASA II status, aged over 18 years, of both genders, with a diagnosis of colon tumor. Exclusion criteria were patients with ASA III and ASA IV status, younger than 18 years, those with ischemic heart disease, psychiatric and neurological disorders, and renal and hepatic insufficiency. Following routine preoperative preparation and fulfillment of the inclusion criteria, the study was explained to the patients, and the VAS was presented, along with instructions on how to use it as an instrument in the study. Patients were divided into two groups by simple randomization: the ketamine-magnesium group (KM) and the control group (C).

Drugs administration

Both groups received premedication consisting of 0.07 mg/kg midazolam intramuscularly (i.m.), 0.01 mg/kg atropine i.m., and 40 mg pantoprazole intravenously 30 minutes before surgery. Induction of anesthesia was performed with propofol and remifentanil using a target-controlled infusion (TCI) pump. The pharmacokinetic Schnider model was used for remifentanil at 6 ng/ml plasma concentration and for propofol at 6 μg/ml in brain tissue until loss of consciousness, along with rocuronium at an induction dose of 0.7 mg/kg for intubation.

After induction of anesthesia, patients in the KM group first received an intravenous bolus dose of 0.5 mg/

kg ketamine, followed by a continuous infusion at 0.6 mg/kg/h (10 mcg/kg/min) until near the end of the surgery (removal of ports). After the bolus dose of ketamine, they also received 20 mg/kg of magnesium-sulfate via intravenous infusion over 5–10 minutes. The control group received an infusion of 0.9% NaCl instead of a ketamine or magnesium solution. Thirty minutes before the end of the surgery, all patients received 4 mg of ondansetron intravenously and 100 mg of tramadol diluted in 100 ml of 0.9% NaCl.

Measurements of pain, analgesics consumption, Ramsay Sedation Score (RSS) parameters, and patient satisfaction

All patients were awakened in the operating room, and pain was assessed by reading the VAS. Measurements were taken after 0, 1, 2, 6, 10, 14, 18, 22, 30, 38, and 46 hours. The "zero hour" was defined as the time of patient admission to the Intensive Care Unit (ICU).

A VAS score above four was set as the threshold for administering the analgesic ketorolac 30 mg in 100 ml 0.9% NaCl (maximum dose 90 mg/24 h); if the VAS remained above four after one hour, tramadol 100 mg in 100 ml 0.9% NaCl (maximum dose 400 mg/24 h) was administered. The total consumption of tramadol and ketorolac was measured 48 hours after the completion of the surgery. Additionally, the RSS parameters and patient satisfaction were recorded.

Statistical analysis

Depending on the nature of the data, parametric (independent sample t-test) and nonparametric (Friedman's test, Mann-Whitney U, Kruskal–Wallis) tests were used to analyze the results. Also, the assessment of the difference between the two treatments was examined using a mixed-effect linear regression model. The assessment of the normality of the distribution of numerical variables was performed using the Shapiro-Wilk test. The analysis of research data was performed using the statistical data processing program SPSS (Statistical Package for Social Sciences) version 27. A statistical significance level of 0.05 or less was considered significant.

RESULTS

Characteristics of patients

The study included 60 patients evenly divided into two groups (KM and C), with 30 patients in each. The distribution of patients by examined parameters is presented in **Table 1**. In both the KM and C groups, the variables age, body height, body weight, Body Mass Index (BMI), and procedure duration have satisfied the normality of the distribution. An independent t-test showed that there were no statistically significant differences between the groups for any of the examined variables.

Table 1. Distribution of patients by examined parameters

Variable	Group	N	Mean	SD	p
Age (years)	KM	30	69.00	8.81	0.670
	C	30	67.80	8.86	
Height (cm)	KM	30	172.00	8.94	0.601
	C	30	173.55	9.62	
Weight (kg)	KM	30	77.95	21.44	0.573
	C	30	81.25	14.65	
BMI (kg/m^2)	KM	30	25.99	5.02	0.512
	C	30	26.93	3.88	
Procedure duration (min)	KM	30	196.95	51.77	0.528
	C	30	207.5	52.88	

KM - ketamine-magnesium group; C- control group; BMI - Body Mass Index

In the KM group, the ratio of men to women was 16:14 (53.3%:46.7%), while in the C group, it was 18:12 (60%:40%). The mean value of the ASA score in the KM group was 1.95, while in the C group, it was 1.65. In both the KM and C groups, the variable ASA status does not satisfy the normality of the distribution. The nonparametric Mann-Whitney U test reveals statistical significance (p=0.019) in the ASA score between the two groups.

Propofol and remifentanil consumption

Propofol and remifentanil were normally distributed, so the comparison by group was tested with an independent t-test **(Table 2)**. The t-test for independent samples with homogeneous variances (p=0.296), where the condition of homogeneity of variances is satisfied, implied that Ho should be rejected with a 5% error risk and that there is significantly (p=0.001) higher propofol consumption in the C than in the KM group. The t-test for independent samples with homogeneous variances (p=0.156), where the condition of homogeneity of variances is satisfied, showed that there is significantly (p<0.001) higher remifentanil consumption in the C than in the KM group.

Table 2. Propofol and remifentanil consumption

Drug	Group	N	Mean	SD	p*
Propofol (mg)	KM	30	1054.80	405.85	0.001
	C	30	1610.00	540.15	
Remifentanil (µcg)	KM	30	1113.15	344.59	0.001
	C	30	1598.00	409.42	

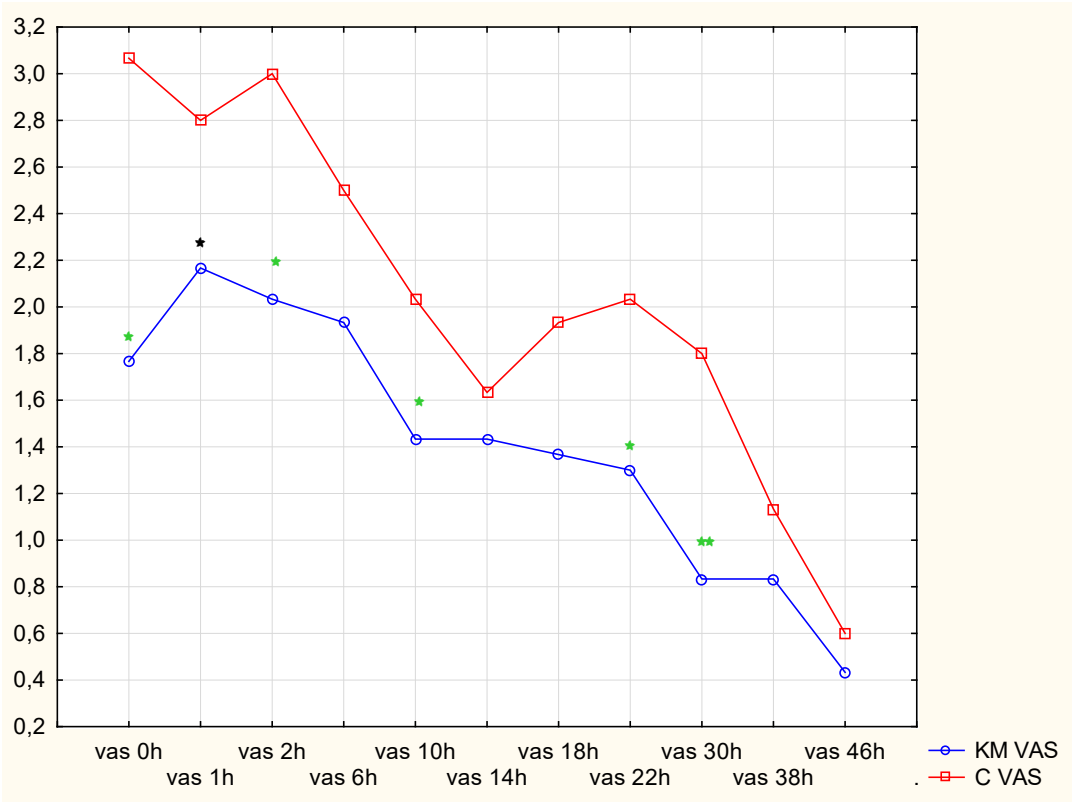
*t-test for independent samples

Postoperative VAS scores

VAS score measurements were taken after 0, 1, 2, 6, 10, 14, 18, 22, 30, 38, and 46 hours. Figure 1 illustrates the time interval dependence of VAS scores for the KM and C groups, respectively.

The Friedman test for repeated measurements for all the examined patients indicates a difference in pain

Figure 1. Mean of visual analog scale scores at different time intervals in ketamine-magnesium and control groups. *p<0.05, ** p<0.01



VAS - visual analog scale; KM - ketamin-magnesium; C – control

intensity in the examined groups over time. In other words, during the 11 time periods, patients' pain intensity significantly changed in both the KM (p<0.001) and C (p<0.001) groups. Also, the mixed-effect linear regression model showed that there were statistically significant differences (p<0.001) between the KM and C groups in terms of VAS scores. The C group displayed the highest mean VAS score of about 3 during the first 2 hours and then showed a fall to 2.03 at the 10-hour period. However, the KM group displayed a mean VAS score of about 2 during the first 6 hours, followed by a VAS of 1.43 at 10 10-hour period. During the rest of the time, VAS scores decreased slowly, and they are consistently lower in the KM group than in the C group.

Considering that the VAS scores do not satisfy the normality of the distribution, the nonparametric Mann-Whitney U test showed the existence of a statistically significant difference for the VAS scores between groups by time: VAS 0h (p<0.034), VAS 1h (p<0.029), VAS 2h (p<0.043), VAS 10h (p<0.019), VAS 22h (p<0.017) and VAS 30h (p<0.001), while there was no statistically significant difference in VAS 6h (p<0.340), VAS 14h (p<0.185), VAS 18h (p<0.147), VAS 38h (p<0.198) and VAS 46h (p<0.865). **Table 3** presents descriptive statistics of VAS scores of KM and C groups and the comparison of VAS scores between KM and C groups in the examined time intervals.

According to VAS scores, significantly higher pain intensity was found in the C group compared to the KM group at time intervals 0h, 1h, 2h, 10h, 22h, and 30h. No statistically significant difference in pain between groups was shown at 6h, 14h, 18h, 38h, and 46h time intervals **(Table 3)**.

Consumption of analgesics

The variables tramadol and ketoprofen consumption do not conform to a normal distribution. The Mann-Whitney U test in both groups implies that Ho should be rejected with a 5% error risk and that there is a significantly higher consumption of tramadol and ketoprofen in the C group compared to the KM group (p<0.001) **(Table 4)**.

Postoperative RSS scores

RSS measured at 0h, 1h and 4h postoperatively was used to determine the level of sedation. Friedman's repeated measures test shows that there are statistically significant differences within groups, in the KM group (p=0.001), while in the C group, there are no statistically significant differences (p=0.513). *Post hoc* tests in the KM group revealed statistically significant differences between RSS 0h and RSS 1h (p=0.001) and between RSS 0h and RSS 4h (p=0.001). In contrast, the C group showed no differences. The normality of the distribution was not satisfied in the variable RSS. Testing between groups, the Mann-Whitney U test showed that there were statistically significant differences between RSS 0h (p=0.001), and that there were no differences between RSS 1h (p=0.157) and RSS 4h (p=1.000) **(Table 5)**.

Table 3. Visual analog scale scores of the ketamine-magnesium and control groups and their comparison in the examined time intervals

Time interval	Group	N	Mean	Median	Min	Max	p
VAS 0h	KM	30	1.77	2	0	6	0.034
	C	30	3.07	3	0	6	
VAS 1h	KM	30	2.17	2	0	6	0.029
	C	30	2.80	3	0	6	
VAS 2h	KM	30	2.03	2	1	7	0.043
	C	30	3.00	3	1	7	
VAS 6h	KM	30	1.93	2	0	4	0.340
	C	30	2.50	2	1	4	
VAS 10h	KM	30	1.43	2	0	4	0.019
	C	30	2.03	2.5	1	3	
VAS 14h	KM	30	1.43	2	0	4	0.185
	C	30	1.63	1.5	0	2	
VAS 18h	KM	30	1.37	2	0	4	0.147
	C	30	1.93	2	1	2	
VAS 22h	KM	30	1.30	1	0	3	0.017
	C	30	2.03	2	1	3	
VAS 30h	KM	30	0.83	1	0	2	0.001
	C	30	1.80	2	0	2	
VAS 38h	KM	30	0.83	1	0	2	0.198
	C	30	1.13	2	0	2	
VAS 46	KM	30	0.43	1	0	2	0.865
	C	30	0.69	1	0	2	

VAS - visual analog scale; KM - ketamin-magnesium; C – control

Table 4. Tramadol and ketoprofen consumption

Drug	Group	N	Median	Min	Max	p*
Tramadol (mg)	KM	30	200.00	200.00	300.00	0.001
	C	30	400.00	200.00	400.00	
Ketoprofen (µcg)	KM	30	60.00	30.00	90.00	0.001
	C	30	90.00	60.00	90.00	

*Mann-Whitney U test

Table 5. Postoperative Ramsay Sedation Scores

	Group	N	Median	Min	Max	p*
RSS 0h	KM	30	3.00	2.00	4.00	0.001
	C	30	2.00	1.00	3.00	
RSS 1h	KM	30	2.00	2.00	3.00	0.157
	C	30	2.00	2.00	2.00	
RSS 4h	KM	30	2.00	2.00	2.00	1.000
	C	30	2.00	2.00	2.00	

*Mann-Whitney U test
RSS - Ramsay Sedation Scores; KM - ketamine-magnesium; C - control

Patient satisfaction with analgesia

In the KM group, 90% of patients were very satisfied with analgesia; the other 10% were satisfied. In the C group, 50% of patients were very satisfied with analgesia, 40% were satisfied, and 10% were dissatisfied. The Kruskal–Wallis test shows a statistically significant difference in the quality of analgesia between the two examined groups (p=0.003) **(Table 6)**. It is concluded that the KM group has a higher level of analgesia quality than the C group.

Table 6. Patient satisfaction with analgesia

Group		Very satisfied	Satisfied	Dissatisfied	p*
KM	N	27	3	0	0.003
	%	90	10	0	
C	N	15	12	3	
	%	50	40	10	

*The Kruskal–Wallis test

DISCUSSION

Patients undergoing laparoscopic surgical interventions for intestinal tumors were examined in the conducted study. The study included a total of 60 patients, evenly divided into two groups. Both groups were homogeneous regarding age, body height, weight, BMI, and procedure duration, meaning that the patients in the studied groups were similar in characteristics, rendering the groups comparable concerning the other examined parameters.

The laparoscopic approach in colorectal surgery is widely accepted because it is associated with lower pain intensity and reduced analgesic consumption, lower morbidity, including a lower incidence of wound infections, faster recovery, and a shorter hospital stay, all without compromising the surgical outcome. However, the laparoscopic surgical technique carries a higher risk of high-intensity pain compared to open surgery because it involves three main surgical principles that increase the risk of pain occurrence (12,13). These are the penetration of surgical instruments into the abdominal cavity, the creation of pneumoperitoneum, and the actual manipulation of surgical instruments.

Tissue trauma at the incision site is the principal source of pain following laparoscopy (14). Patients may develop nociceptive pain, inflammatory pain in response to tissue trauma, as well as neuropathic pain. Pain intensity is highest during the first 4-12 postoperative hours. Laparoscopic surgery is also associated with the risk of developing chronic pain. A large number of patients describe persistent postoperative pain as a constant, deep, dull pain in the abdomen or as persistent shoulder pain (15).

Standardized enhanced recovery programs combined with laparoscopic surgery have revolutionized clinical outcomes in elective colorectal surgery. Optimal pain control is central to the success of enhanced recovery programs (16). Pain management in colorectal surgery requires multimodal analgesia, utilizing complementary mechanisms to improve pain control while reducing exposure to high-risk medications.

One method of implementing multimodal analgesia in laparoscopic colorectal surgery is the use of ultra-short-acting opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and NMDA receptor antagonists, along with the administration of weak opioids to reduce the need for potent opioids (1,17,18).

Ketamine acts through the noncompetitive antagonism of NMDA receptors. It binds to the phencyclidine site in the NMDA receptor ion channel when the channel is open. When glutamate dissociates from its binding site, ketamine remains trapped in the now-closed channel, causing a prolonged tonic blockade (19). Ketamine exerts its antinociceptive effect by antagonizing NMDA receptors at the level of the spinal cord and brain.

The use of magnesium as an adjuvant in perioperative analgesia is relatively new. Its application is based on magnesium's properties as an NMDA receptor antagonist and its inhibitory effect on calcium channels, which leads to secondary neuronal changes. This mechanism may prevent central sensitization associated with nociception and reduce the increased activity of wide dynamic range neurons in the dorsal horn after prolonged stimulation (1,20).

A large percentage of patients undergoing laparoscopic bariatric surgery develop postoperative apnea due to the use of high amounts of opioids, as well as due to concomitant sleep apnea. To ensure a safer postoperative course and reduce both opioid doses and their harmful effects, ultra-short-acting opioids such as remifentanil are increasingly being used (21). In the examined patient groups, the consumption of propofol and remifentanil was analyzed. It was found that the consumption of both drugs was significantly higher in the control group than in the KM group. Considering that both groups were dosed according to the TCI model and that the depth of anesthesia and pain level were monitored by entropy and the SPI index, it can be concluded that the addition of ketamine and magnesium-sulfate reduces consumption of propofol and remifentanil.

NMDA receptor antagonists (ketamine and magnesium-sulfate) have an analgesic effect, reducing central sensitization and preventing the development of chronic postoperative pain. When administered in sub-dissociative doses, ketamine contributes to better pain control and a reduced need for opioids, particularly in patients with high opioid tolerance. In addition to its analgesic and opioid-sparing effects, ketamine administration has led to a reduction in the incidence of nausea and vomiting, a lower occurrence of hyperalgesia, and reduced residual pain in the first six postoperative months (22).

Numerous studies have investigated the use of magnesium in various types of pain and at different doses. One meta-analysis demonstrated that perioperative intravenous magnesium administration can improve postoperative pain (23). Additionally, in patients undergoing septorhinoplasty surgery or laparoscopic cholecystectomy, magnesium reduced the use of opioid analgesics and postoperative pain (24,25). Although the maximal analgesic benefit of magnesium is often achieved in major upper abdominal, thoracic, and orthopedic surgery, magnesium can also be used with good results in colorectal surgery (16).

Upon leaving the operating room and arriving in the ICU, all patients had their pain levels assessed using the VAS scale. The pain intensity was higher in patients in the C group and over a longer time interval (in the first 10 h) postoperatively compared to the KM group, in which the pain intensity was lower. In other time intervals, up to 30 hours postoperatively, the pain intensity in patients in the KM group showed a faster decline compared to the C group. In later time intervals, the pain intensity did not differ. In general, a lower level of pain was observed in the KM group than in the control group, which means that preemptive ketamine-magnesium treatment significantly reduced pain intensity in patients with laparoscopic colon tumor surgery. In the present study, this effect lasted up to 30h postoperatively.

For postoperative analgesia, tramadol and ketoprofen were administered based on the pain level as interpreted *via* the VAS scale. The consumption of tramadol and ketoprofen was measured in the examined groups, with greater consumption observed in the control group compared to the group that received ketamine and magnesium-sulfate.

In the present study, the RSS scores evaluation demonstrates that ketamin-magnesium treatment significantly increases the level of sedation only in the immediate postoperative period (RSS 0h), without affecting RSS later postoperatively. This is consistent with the well-known sedative effects of both NMDA antagonists (8). However, other studies have shown that subanesthetic doses of ketamine in the perioperative period do not cause an increased level of sedation and may even reduce it, likely due to decreased opioid consumption (26).

At the end of the study, all patients were evaluated for their overall satisfaction with the treatment and the quality of analgesia. Higher levels of satisfaction and quality of analgesia were noted in the KM group than in the C group.

A limited number of studies in animals and humans examined the additive and synergistic effects of the simultaneous use of ketamine and magnesium-sulfate on postoperative analgesia. In various animal models of pain, ketamine and magnesium may display additive, antagonistic, and synergistic interactions. Ketamine and magnesium-sulfate block NMDA receptors *via* different mechanisms, achieving these effects. In most studies, the ketamine and magnesium combination is more effective in various pain conditions than ketamine alone (27-29).

It is assumed that the contradictory results in the literature are primarily due to the use of different doses of ketamine and magnesium-sulfate and the various types of pain studied. A randomized, double-blind, placebo-controlled study did not demonstrate a reduction in pain or the use of other analgesics after laparoscopic sleeve gastrectomy when given a small intravenous dose of ketamine and/or magnesium-sulfate before surgery (30). In contrast, a prospective, randomized, double-blind study following scoliosis surgery observed reduced postoperative morphine consumption in patients who received both ketamine and magnesium concurrently compared to those who received ketamine alone. Although the VAS scores did not show a statistically significant difference between the two groups, patient satisfaction and sleep quality were higher within the group that received ketamine and magnesium (31). However, what is common to all studies is that, by blocking NMDA receptor activity, ketamine and magnesium reduce the central transmission of pain impulses, thereby decreasing acute pain and preventing the development of chronic pain. Therefore, they can be used as analgesics within a multimodal pain management approach (10,11).

CONCLUSION

Analgesic techniques should aim to achieve optimal pain control and facilitate important recovery milestones, such as early oral intake of fluids and food and early mobilization. In the context of rapid patient recovery, anesthesia techniques that reduce opioid usage should be increasingly implemented to minimize the dose-dependent adverse effects of these drugs and to prevent delays in recovery. The present prospective randomized pilot clinical study demonstrated that preemptive administration of ketamine and magnesium significantly reduced postoperative VAS score, *i.e.*, pain intensity level, and the postoperative consumption of analgesics, increased RSS score, *i.e.*, sedation level, and the overall satisfaction with the treatment and the quality of analgesia after laparoscopic colon tumor surgery. NMDA antagonists should be incorporated as part of multimodal analgesia for major surgical procedures, abdominal surgery, and in patients at high risk for developing chronic postoperative pain.

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Ethical approval: This study was conducted in accordance with Declaration of Helsinki and was approved by the Ethics Committee of "Zvezdara" University Medical Center, approval number IRB00009457/2022. Written informed consent was obtained from all participants prior to inclusion in the study.

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DEJSTVA ANTAGONISTA NMDA RECEPTORA NA AKUTNI POSTOPERATIVNI BOL

Maja Stojanović[1,2], Predrag Stevanović[2,3], Sonja Vučković[2,4], Katarina Savić Vujović[2,4]

Sažetak

Uvod: Bol predstavlja multifaktorijalni proces sa štetnim efektima na ceo organizam. Randomizovana, otvorena pilot studija istražuje efekat preventivne kombinovane primene ketamina i magnezijum-sulfata na intenzitet postoperativnog bola nakon laparoskopske resekcije tumora debelog creva.

Metod rada: Šezdeset pacijenata je randomizirano u ketamin-magnezijumsku (KM) i kontrolnu (C) grupu. Nakon uvoda u anesteziju, pacijentima KM grupe primenjena je i.v. bolus doza od 0,5 mg/kg ketamina, nakon čega sledi kontinuirana infuzija od 0,6 mg/kg/h koja traje do kraja operacije. Nakon bolus doze ketamina, takođe su dobijali magnezijum-sulfat 20 mg/kg u intravenskoj infuziji (5-10 minuta). Grupa C primila je samo infuziju 0,9% NaCl. Nakon buđenja (0h), intenzitet bola je poređen (0-46h) između dve grupe.

Rezultati: Mann-Whitney test je pokazao značajno ($p<0,05$) niže rezultate vizuelno analogne skale (VAS) u KM grupi 0, 1, 2, 10, 22 i 30 sati nakon operacije, i bez statističke značajnosti ($p>0,05$) za VAS rezultate nakon 6, 14, 18, 38 i 46 sati, u odnosu na C grupu. Ketamin i magnezijum-sulfat su značajno ($p<0,05$) smanjili postoperativnu potrošnju analgetika, povećali nivo sedacije u 0h postoperativno i povećali ukupno zadovoljstvo pacijenata tretmanom.

Zaključak: Preventivna primena kombinacije ketamina i magnezijum-sulfata ima povoljno dejstvo na postoperativni bol posle laparoskopske resekcije tumora debelog creva.

Ključne reči: NMDA-antagonisti, ketamin, magnezijum-sulfat, akutni bol

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