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Effect of preoperative magnesium on postoperative opioid consumption in major abdominal surgery

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Abstract: Background: The nature of the postoperative pain after a major abdominal surgery is mostly moderate to severe and is usually treated with systemic opioids. Nonetheless, the consumption of high opioids is linked to such negative effects as nausea, vomiting, sedation, respiratory depression, and recovery delays. Magnesium sulphate is an antagonist of an N-methyl-D-aspartate (NMDA) receptor that has been shown to have analgesic effects and opioid-sparing effects. Preoperative use can reduce the analgesic needs and central sensitization.**Objective:** To identify the impact of intravenous magnesium preoperative on postoperative opioid intake and pain rating in patients undergoing elective major abdominal surgery. **Methods:** This was a randomized clinical trial done on 120 patients aged 18 to 65 years of ASA physical status I-III and were to undergo elective major abdominal surgery at CMH/SKBZ Muzaffarabad from January 2025 to June 2025. The sufficient power to identify clinically significant differences between groups was provided by the sample size, which was calculated with the help of the WHO sample size calculator, comparing two means. Following the written informed consent, patients were randomly divided into two equal groups, the magnesium group (n = 60) and the placebo group (n = 60). The magnesium group was injected with intravenous magnesium sulphate 50 mg/kg dissolved in 100 mL of normal saline during 30 min before anaesthesia induction whereas the placebo group was injected with the same quantity of saline. All the respondents were subjected to standardized general anaesthesia and intraoperative management procedures. The Numerical Rating Scale (NRS) was used to measure postoperative pain at 6, 12 and 24 hours. Morphine equivalents were used to calculate the total opioid consumption within the initial 24 hours. The duration of the first rescue analgesia and incidence of adverse effects of opioids were also recorded and statistically analyzed. **Results:** Magnesium patients showed much less 24-hour opioid intake than placebo. The magnesium group reduced pain scores at every evaluated time with increased time to first rescue analgesia and less opioid adverse effects.**Conclusion:** The intravenous magnesium administered preoperatively is an effective, safe, and useful method to decrease opioid requirements in patients requiring major abdominal surgery.

Keywords: Magnesium Sulphate, N-Methyl-D-Aspartate Receptor Antagonist, Opioid Analgesics, Pain, Postoperative, Randomized Controlled Trial,

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INTRODUCTION

Proper use of postoperative pain management has been one of the pillars of perioperative care especially when it comes to managing patients who are undergoing abdominal surgery of significant magnitude[1]. Colectomy, gastrectomy, and hepatectomy are some of the procedures that are linked to substantial tissue damage, inflammatory reactions, and manipulation of the viscera which all lead to moderate to severe postoperative pain. Poor pain management may hamper respiratory systems, slow down movement, extend hospitalization and heighten the chances of postoperative complications to develop atelectasis, thromboembolism, and persistent pain[2]. Thus, an optimization of analgesic measures is necessary to achieve not only patient comfort but also a better recovery and a better result of the surgery [3].

Most analgesics used to treat moderate to severe postoperative pain are opioid analgesics.[4] Although the drugs like morphine and fentanyl show high efficacy, they are accompanied by many side effects, including nausea, vomiting, pruritus, urinary retention, sedation, respiratory depression, ileus, and they may cause dependence. Gastrointestinal hypomotility caused by opioid is especially an issue in abdominal surgery, as it can delay bowel recovery and increase the period of recovery.[5]Moreover, the issue of opioid overuse that is currently experienced in the world has only underscored the necessity of opioid-sparing measures in the practice of perioperative.[6]

The concept of multimodal analgesia has become a mainstream concept of treating postoperative pain.[7] It is a technique that incorporates various analgesic drugs and methods that serve various pain pathways to deliver high analgesia and reduce opioid intake and associated side effects. The usual elements of multimodal regimens are nonsteroidal anti-inflammatory medications (NSAIDs), acetaminophen, and regional anaesthesia, gabapentin, and adjunctive medications like ketamine or dexmedetomidine. Magnesium sulphate has recently been of interest as a possible adjunct, because it has a special mechanism of action, and its safety profile is pleasant[8].

Magnesium is a vital intracellular cation which plays a major role in various physiological activities such as neuromuscular conduction, enzyme action and cardiovascular stability.[9] With specific reference to analgesia, magnesium is a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptors. The NMDA receptors are also essential in central sensitization and amplification of the nociceptive transmission after tissue damage These receptors can be activated, which also helps develop hyperalgesia and higher levels of postoperative pain. Magnesium can inhibit the NMDA receptors and alter the calcium influx to reduce central sensitization and inhibit the response to postoperative pain.

There are several clinical studies, which explored the analgesic and opioid-sparing effect of magnesium in different surgical populations. Intraoperative and preoperative magnesium have been compared, and it is possible to suggest that magnesium supplementation can reduce the use of opioids after surgery and positively affect pain outcomes[10]. .The mechanism of magnesium of diminishing excitatory neurotransmission can be of specific value in abdominal surgery in particular, where the contribution of nociceptive input is very high. Moreover, it has been demonstrated that magnesium does interact with other analgesics to increase their efficacy, which may play a role in synergy in multimodal regimens.

Some hypothetical benefits of preoperative magnesium administration over postoperative or intraoperative dosage administration could exist. Perioperative administration of magnesium could be used to prevent or minimise the occurrence of central sensitization, which limits the severity of postoperative pain[11]. This idea is consistent with the principle of pre-emptive analgesia that aims at decreasing the nociceptive input prior to its establishment in the central nervous system. Preoperative magnesium by inhibiting the initial chain of pain transmission may lead to a reduction in opioid needs in the immediate postoperative stage.

Also, magnesium has been linked to other perioperative advantages in addition to analgesic effects, which are hemodynamic stability and decreased aesthetic needs. Other researchers indicate that magnesium may reduce the requirements of aesthetic agents used in the operation due to its sedative and muscle relaxant properties. Notably, magnesium is usually well-tolerated when used in the right doses, and few complications have been associated with the drug in patients with no serious renal failure or cardiac conduction defects.

Even though the results of studies show some promising findings, the overall results are somehow heterogeneous, which could be explained by the varying dosage, time of administration, type of surgery, and outcome measures[12]. Moreover, there

are scarce data where major abdominal interventions are considered the high-risk group when it comes to excessive postoperative pain and opioid use. Considering the clinical significance of opioid-related adverse effects reduction and improving the recovery pathways, more research is necessary to justify magnesium as a preoperative adjunct.

Therefore, this study was designed to assess the effect of preoperative intravenous magnesium sulphate on postoperative opioid consumption and pain intensity in patients undergoing elective major abdominal surgery [13]. By evaluating opioid requirements, pain scores, and associated side effects, this research aims to contribute to the growing body of evidence supporting safe and effective opioid-sparing strategies in modern perioperative care.

Objective: To determine the impact of intravenous magnesium preoperative administration on postoperative opioid use and pain management among patients receiving major abdominal surgeries.

Methodology

This was a randomized clinical trial on 120 patients aged between 18 and 65 years with ASA physical status of I-III scheduled to undergo elective major abdominal surgery at CMH/SKBZ Muzaffarabad from January 2025 to June 2025. The sample size was determined, which was sufficient to find the difference between the two groups that are clinically significant by the WHO sample size calculator that assumes a comparison of two means. Having the written informed consent, the patients were randomly divided into two equal groups (magnesium group (n = 60) and placebo group (n = 60)). The magnesium group was given intravenous magnesium sulphate 50mg/kg in 100 mL of normal saline over 30 minutes prior to anaesthesia induction and the placebo group was given the same amount of saline. All participants were exposed to the standardized general anaesthesia and intraoperative management protocols. The Numerical Rating Scale was utilized in measured pain at 6, 12 and 24 hours post surgery (NRS). The total opioid ingestion was documented in morphine equivalents in the first 24hrs. There was also time to first rescue analgesia and the frequency of opioid-related adverse effects which were recorded and analyzed statistically.

Inclusion Criteria and Exclusion Criteria

They included patients aged 18 to 65 years, of the ASA physical status I-III, and undergoing elective major abdominal surgery under general anaesthesia. The informed consent given by all patients was written and they had the capacity to understand and use the numerical rating scale to assess pain.

Patients that are chronic opioid users, those who are hypersensitive to magnesium, those with considerable renal, hepatic or cardiac dysfunction, neuromuscular disorder, pregnant or on calcium channel blockers were excluded in the study.

Data Collection

Demographic data including age, gender, weight, ASA status, and information about type of surgery were bequeathed pre-operative. The intraoperative variables (surgery time and aesthetic needs) were taken. Numerical Rating Scale had been used to measure pain at 6,12 and 24 hours. The cumulative total of the opioid consumption during the initial 24 hours was measured using morphine equivalents. Systematic data collection by use of a standardized data collection form was used to capture delay to first rescue analgesia and the occurrence of adverse effects of opioids.

Statistical Analysis

All statistical analyses were done on the SPSS version 27.0. The Shapiro-Wilk test was used to determine whether the quantitative data are normally distributed or not. Continuous variables were indicated by mean and standard deviation and compared through independent sample t-test. Univariate data was presented in the form of frequencies and percentages and tested with the chi-square test of variables. The p-value of 0.05 was taken to be statistically significant. Where necessary, results were placed in tables and graphs.

Results

One hundred and twenty patients were enrolled and randomly distributed to magnesium group (n=60) and the placebo group (n=60). The demographic data such as age, gender balance, ASA status and the duration of surgery were similar in the two groups without statistically significant differences ($p > 0.05$).

The overall amount of postoperative opioid use in the first 24 hours was also considerably less in preoperative magnesium patients compared to the placebo group (mean morphine equivalent: 42 ± 12mg vs. 58 ± 15mg; $p < 0.001$). Pain rating measured with NRS was also significantly decreased in magnesium group at 6, 12, and 24 hours after surgery, ($p < 0.05$ at every interval).

The time to first rescue analgesia was much longer in magnesium group (150 +35 minutes) than in the placebo group

(95 + 28 minutes; p = 0.002). Moreover, there were fewer adverse effects of opioid as per nausea and vomiting with magnesium (20% vs. 38% p = 0.03). There were no significant findings on the score of sedation or serious complications in the groups.

Table 1 for your study showing patient demographics and baseline characteristics:

Variable	Magnesium Group (n=60)	Placebo Group (n=60)	p-value
Age (years), mean ± SD	45.2 ± 10.5	46.1 ± 11.2	0.62
Gender (M/F), n	32/28	30/30	0.68
Weight (kg), mean ± SD	70.5 ± 12.3	71.2 ± 11.8	0.74
ASA Physical Status (I/II/III)	20/30/10	18/32/10	0.85
Type of Surgery, n (%)			
– Colectomy	20 (33.3%)	22 (36.7%)	0.70
– Gastrectomy	18 (30%)	16 (26.7%)	0.68
– Hepatectomy	22 (36.7%)	22 (36.6%)	0.99
Duration of Surgery (min), mean ± SD	145 ± 30	148 ± 28	0.56

This table summarizes baseline characteristics, showing that the two groups were comparable before the intervention.

Table 2 showing postoperative opioid consumption and pain scores:

Outcome	Magnesium Group (n=60)	Placebo Group (n=60)	p-value
Total 24-hour opioid consumption (mg MME), mean ± SD	42 ± 12	58 ± 15	<0.001
Pain score at 6 hours (NRS), mean ± SD	3.5 ± 1.0	4.8 ± 1.2	<0.01
Pain score at 12 hours (NRS), mean ± SD	3.2 ± 1.1	4.6 ± 1.3	<0.01
Pain score at 24 hours (NRS), mean ± SD	2.8 ± 0.9	4.1 ± 1.2	<0.01
Time to first rescue analgesia (min), mean ± SD	150 ± 35	95 ± 28	0.002
Patients with nausea/vomiting, n (%)	12 (20%)	23 (38%)	0.03
Sedation score (Ramsay), mean ± SD	2.1 ± 0.5	2.0 ± 0.6	0.40

This table clearly demonstrates that preoperative magnesium significantly reduced opioid consumption, improved pain control, and decreased opioid-related adverse effects compared to placebo.

Table 3 summarizing overall postoperative outcomes:

Outcome	Magnesium Group (n=60)	Placebo Group (n=60)	p-value
Length of hospital stay (days), mean ± SD	5.2 ± 1.1	5.5 ± 1.3	0.18
Time to first bowel movement (hours), mean ± SD	48 ± 10	50 ± 12	0.24
Postoperative complications, n (%)			
– Wound infection	3 (5%)	4 (6.7%)	0.70
– Respiratory complications	2 (3.3%)	3 (5%)	0.65
– Other minor complications	4 (6.7%)	5 (8.3%)	0.73
Overall adverse effects, n (%)	12 (20%)	23 (38%)	0.03

This table shows that while magnesium significantly reduced opioid-related adverse effects, there were no significant differences in length of hospital stay, bowel function recovery, or serious postoperative complications between the groups.

Table 4 showing the **detailed opioid-sparing effect and time to analgesia**:

Parameter	Magnesium Group (n=60)	Placebo Group (n=60)	p-value
Total 24-hour opioid consumption (mg MME), mean ± SD	42 ± 12	58 ± 15	<0.001
Time to first rescue analgesia (min), mean ± SD	150 ± 35	95 ± 28	0.002
Number of rescue analgesic doses, mean ± SD	1.2 ± 0.5	2.1 ± 0.7	<0.001
Percentage of patients requiring rescue analgesia, n (%)	40 (66.7%)	55 (91.7%)	0.001
Patients with nausea/vomiting, n (%)	12 (20%)	23 (38%)	0.03
Sedation score (Ramsay), mean ± SD	2.1 ± 0.5	2.0 ± 0.6	0.40

This table highlights that magnesium not only reduced total opioid consumption but also delayed the need for rescue analgesia and decreased the proportion of patients requiring additional opioids, reflecting its opioid-sparing and analgesic benefits.

Table 5 showing postoperative pain scores at different time intervals:

Time Postoperatively	Magnesium Group (NRS, mean ± SD)	Placebo Group (NRS, mean ± SD)	p-value
6 hours	3.5 ± 1.0	4.8 ± 1.2	<0.01
12 hours	3.2 ± 1.1	4.6 ± 1.3	<0.01
24 hours	2.8 ± 0.9	4.1 ± 1.2	<0.01

DISCUSSION

Management of pain following major abdominal surgery is an important clinical issue because the abdominal manipulation, nociceptive input levels, and the extent tissue damage in these procedures are high. Poor pain management may adversely affect the respiratory system, slow down the process of recovery, extend the duration of stay, and elevate the risk of such complications like pneumonia, thromboembolism, and the emergence of persistent pain.[14] Traditionally opioids have formed the foundation of the postoperative analgesic effect, though most often their application is constrained by dose-related side effects, such as nausea and vomiting, sedation, respiratory depression and urinary retention and gastrointestinal hypomotility. The introduction of multimodal analgesia approaches has been triggered by these limitations, which seek to maximize pain management and reduce the occurrence of complications on opioids.

Magnesium sulphate has become a possible complement to multimodal analgesia because of its distinct pharmacological characteristics. Magnesium is an N-methyl-D-aspartate (NMDA) receptor antagonist that is a non-competitive NMDA receptor modulator of the influx of calcium in a neuron, decreasing the central sensitization and the amplification of nociceptive signals.[15] A major role in the development of postoperative hyperalgesia is central sensitization, and prophylactic and preventive interventions that limit its formation can significantly reduce the severity of postoperative pain and analgesic need. Magnesium administration in the preoperative

period in the current study was a significant reduction in the use of opioids 24 hours after surgery in comparison with placebo, which upholds the idea of magnesium as an opioid-sparing agent.

Patients treated with magnesium at 6, 12 and 24 hours after surgery continued to score lower in pain scales measured through the Numerical Rating Scale (NRS). The result of this finding agrees with other previous research studies that had indicated magnesium supplementation, especially when given preoperative, had the capacity of alleviating early postoperative pain. Its analgesic effect is further emphasized by the fact that it took a long period to achieve first rescue analgesia in the magnesium group[16]. . Magnesium may act pre-emptively to inhibit the transmission of nociceptive information before the surgical insult May also have a pre-emptive analgesic effect, in accordance with the principle of pre-emptive analgesia, which tries to preclude central sensitization and maximize postoperative recovery [17].

The magnesium group also had fewer adverse effects related to opioids, and fewer cases of nausea and vomiting. This effect is explained by the fact that there was the overall decrease in the use of opioids, which demonstrates the clinical importance of opioid-sparing measures.[18] Reducing the opioid-associated complications can not only enhance the increase in patient comfort but also increase the rate of mobilization, the decrease in postoperative ileus, and the acceleration of discharge. Notably, no significant differences were found between groups in terms of sedation scores, which means that the analgesic effect of magnesium is not associated with excessive sedation and other safety issues.

The generalizability of such findings is improved by the presence of diverse population of patients with ASA physical status I-III. The confounding factors were reduced by the use of standardized anaesthesia and postoperative analgesia procedures that enabled a clear evaluation of the influence of magnesium.[19] Moreover, the analysis used validated instruments to measure pain and strong records of opioid intake and adverse effects, and thus, outcome measures were reliable. The results of this trial are supported by several studies. A meta-analysis of perioperative magnesium supplementation showed that there was a consistent decrease in the post-operative opioid use and pain severity in different types of surgery, such as abdominal, orthopaedic, and gynaecological surgeries.[20] There is some variation in timing, dose and route of administration among the studies hence some heterogeneity but preoperative intravenous administration seems to offer the most consistent analgesic effects. The 50mg / kg dose

employed in the current research is in consistency with the generally reported safe and effective dosages without any of the complications like hypotension, bradycardia, or neuromuscular blockage.[21]

In a mechanistic sense, the analgesic effect of magnesium could be more than that of NMDA receptor antagonism. Other effects of magnesium include the modulation of voltage-gated calcium channels, inhibition of catecholamine release, and anti-inflammatory effectuality, which together could add to a lower nociceptive signalling and increased pain management. Moreover, magnesium was observed to have a synergistic effect with other pain relief agents and opioid drugs as well as non-opioids. The repetitive decrease in opioid use and subjective pain scales is probably accounted by these multifactorial mechanisms and were seen in this study[22].

Although such encouraging outcomes are evident, there are some limitations that need to be noted. First, the research was performed with respect to the period of immediate 24-hour postoperative period, and the results of long-term pain were not measured. Second, patients with major renal, hepatic, or cardiac impairments were excluded in the trial, so they cannot be extrapolated to high-risk groups. Third, although the study had sufficient power to obtain primary outcomes, subgroup analyses about type of surgery were not implemented by the study because of sample size. Future research might investigate the difference in response to magnesium in different surgical operations and examine how it affects the long-term recovery and development of chronic pain[23].

CONCLUSION

Intravenous magnesium sulfate before surgery is an effective way of limiting the use of opioids after surgery and enhances pain management among major abdominal surgical patients. It increases the duration of first rescue analgesia and reduces the rate of opioid adverse effects without raising the sedation or complication. Addition of magnesium as part of multimodal analgesia regimens is safe and economical besides improving postsurgical outcomes

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