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Comparison of Post-Operative Pain Relief in patients receiving Non-Steroidal Anti-Inflammatory Drug, Weak Opioids with and Without Magnesium Sulphate in patients undergoing Open Abdominal Surgery

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Abstract: Background: Postoperative pain following open abdominal surgery remains a major concern and is associated with delayed recovery and increased morbidity. Multimodal analgesia has been advocated to improve pain control while reducing opioid-related adverse effects. Magnesium sulphate, due to its NMDA receptor antagonistic action, has emerged as a potential adjunct in pain management; however, evidence comparing its additive benefit remains limited.**Objectives:** To compare postoperative pain relief in patients receiving non-steroidal anti-inflammatory drugs (NSAIDs) and weak opioids with and without magnesium sulphate undergoing open abdominal surgery.**Study Design & Setting**: Randomized controlled trial conducted at the Department of Anaesthesia, Dow Hospital, Karachi 20 January 2025 to 20 April 2025.**Methodology:** A total of 110 patients aged 18–65 years undergoing open abdominal surgery were randomly allocated into two groups. Group A received intravenous ibuprofen, tramadol, and magnesium sulphate, while Group B received ibuprofen and tramadol only. Pain was assessed using the Visual Analog Scale (VAS) at multiple time intervals up to 24 hours postoperatively. Requirement of rescue analgesia and overall pain relief were also recorded. Data were analyzed using SPSS version 26.**Results:** Mean pain scores were significantly lower in Group A at all time points ($p < 0.05$). The requirement of rescue analgesia was also reduced in Group A, with statistically significant differences observed at 6, 12, and 24 hours. Effective pain relief was achieved in 85.5% of patients in Group A compared to 67.3% in Group B ($p = 0.028$).**Conclusion:** The addition of magnesium sulphate to NSAIDs and weak opioids provided superior postoperative analgesia and reduced analgesic requirements.

Keywords: Magnesium sulphate, Multimodal analgesia, NSAIDs, Open abdominal surgery, Postoperative pain, Tramadol

INTRODUCTION

Major abdominal surgery involves diverse procedures and requires tailored pain management strategies based on both patient and surgical factors. Effective

postoperative analgesia is crucial, as poorly managed pain is linked to increased morbidity, delayed recovery, and a lower quality of life. Inadequate pain relief can also lead to long-term problems, including opioid dependence and chronic post-surgical pain.1,2 Traditionally, opioids have been the primary treatment for postoperative pain. However, concerns over opioid-related risks—such as addiction and respiratory depression—have led to the development of alternative, multimodal pain management strategies.3 These strategies, which combine pharmacological and non-pharmacological approaches, aim to reduce pain intensity while minimizing opioid use and side effects.4,5

Multimodal analgesia has been shown to reduce pain, opioid-related side effects, and recovery time. It also promotes early mobilization and self-care, making it a key component of Enhanced Recovery After Surgery (ERAS) protocols, which emphasize opioid-sparing strategies.6 In a survey from a developing country, 11% of IVRA (intravenous regional anesthesia) anesthesiologists reported supplementing lidocaine with other agents, including NSAIDs, opioids, muscle relaxants, clonidine, and magnesium sulphate. Evidence supports the use of NSAIDs, especially ketorolac, in IVRA for improved postoperative pain control.7,8

Despite magnesium sulphate's potential as an adjunct for pain management, there is a lack of research comparing NSAIDs and weak opioids with and without magnesium in open abdominal surgery patients.9 Our pilot study (unpublished data) was conducted to explore the potential benefit of adding magnesium sulphate to NSAIDs and weak opioids in patients undergoing open abdominal surgery. A total of 60 patients were included, with 30 patients allocated to receive NSAIDs, weak opioids, and magnesium sulphate, and 30 patients receiving NSAIDs and weak opioids alone. The mean age in the NSAID, weak opioid, and magnesium group was 34.3 ± 8.61 years, while in the NSAID and weak opioid group it was 34.93 ± 8.5 years. Both groups were predominantly female, comprising 63.3% in the magnesium group and 60% in the non-magnesium group. These baseline characteristics indicated that both groups were comparable in terms of demographic distribution prior to intervention. Preliminary results indicate that magnesium supplementation provides superior postoperative pain relief, with 86.66% of patients in the NSAID, weak opioid, and magnesium group reporting effective pain control, compared to 66.67% in the NSAID and weak opioid group.

These findings suggest that magnesium could be a valuable addition to multimodal analgesia for open abdominal surgery. This study fills a critical gap in the literature, offering new insights into magnesium's role in pain management and informing future protocols for improving postoperative outcomes. To compare the post-operative pain relief in patients receiving non-steroidal anti-inflammatory drugs, weak opioids with and without magnesium sulphate in patients undergoing open abdominal surgery.

MATERIALS AND METHODS

This study was conducted in the Department of Anaesthesia at the Dow Hospital, Karachi from 20 January 2025 to 20 April 2025 after approval of the synopsis from CPSP. The sample size was calculated using the WHO sample size calculator. The parameters used included a frequency of pain relief in the NSAID, weak opioid, and $MgSO_4$ group of 86.66% (pilot data collected data) and a frequency of pain relief in the NSAID and weak opioid group of 66.67%. The power of the test (1-β) was 80%, and the level of significance (α) was 5%. The estimated sample size was 110, with 70 patients in each group. A non-probability consecutive sampling technique was used. Patients aged 18–65 years of either gender who were undergoing open abdominal surgery irrespective of reason were included in the study. Immunocompromised patients, patients with renal impairment or chronic liver disease, those undergoing emergency surgery, and patients with ASA > III were excluded. All patients admitted for open abdominal surgery in the surgical ward who fulfilled the inclusion criteria were enrolled in the study. Before enrollment, all risks and benefits of the study were explained to the patient or attendant (if the patient was unable to give consent), and written informed consent was taken. After obtaining consent, baseline demographic variables such as age and gender, along with clinical details including hypertension, diabetes mellitus, smoking status, ASA status, and indication of surgery, were recorded on a predesigned proforma.

All patients undergoing open abdominal surgery were randomly divided into two groups using an opaque sealed envelope technique. Patients in group A received intravenous ibuprofen 400 mg, tramadol 2 mg/kg, and magnesium sulphate 20 mg/kg, while patients in group B received intravenous ibuprofen 400 mg and tramadol 2 mg/kg. In both groups, the medications were administered preoperatively just before induction, diluted in 100 ml normal saline infusion. After completion of infusion, patients were shifted to the operation theatre, where anaesthesia was administered by an anesthesiologist. Standard monitoring, including pulse oximetry, noninvasive blood pressure, and electrocardiography, was applied along with a respiratory gas monitor to assess end-tidal carbon dioxide and minimum alveolar concentration (MAC) of the anaesthetic agent. A neuromuscular monitor with an acceleromyograph was also attached to monitor the depth of neuromuscular blockade. Vital signs were recorded

every minute for the first five minutes after intubation and then every 15 minutes thereafter. Ringer's lactate infusion was started, and induction was carried out using intravenous propofol (2 mg/kg) and vecuronium bromide (0.1 mg/kg) to facilitate intubation. Intubation was performed when the train-of-four (TOF) count reached zero. Anaesthesia was maintained using 50% nitrous oxide and sevoflurane to maintain a MAC between 0.7 and 1.0. Additional doses of vecuronium bromide (0.01 mg/kg) were administered whenever the TOF count exceeded 2. A combination therapy of dexamethasone 4 mg intravenously at induction and ondansetron 4 mg intravenously at the end of surgery was administered to prevent postoperative nausea and vomiting. Injection diclofenac 75 mg intravenously was added to the intravenous fluids before the end of surgery for postoperative analgesia. At the end of surgery, inhalational anaesthetics were discontinued, and neuromuscular blockade was reversed using neostigmine 0.05 mg/kg with glycopyrrolate 0.008 mg/kg intravenously when the TOF ratio exceeded 25%. Patients were extubated when they were fully conscious, had stable vital parameters, and achieved a TOF ratio greater than 90%. In the postoperative period, patients were followed for 24 hours and were assessed for 24-hour postoperative Visual Analog Scale (VAS) score and 24-hour postoperative analgesic consumption. Rescue analgesia was provided when the VAS score was greater than 3 in the form of intravenous or intramuscular diclofenac 75 mg or oral paracetamol 500 mg. Based on pain score and consumption of rescue analgesia, pain relief was labelled as defined in the operational definition. The final outcome was assessed after 24 hours post-surgery. All study variables, including age, gender, diabetes, hypertension, smoking status, reason for surgery, ASA class, duration of surgery, and pain relief, were recorded on a predesigned proforma.

Pain relief was labelled if the patient did not complain of moderate to severe pain (VAS >3) and did not require rescue analgesia. Rescue analgesia was given if VAS was >3. Diabetes mellitus was defined as a patient with a known history of DM and on oral hypoglycemic agents or insulin for at least the last six months. Hypertension was defined as a patient with a known history of HTN and on anti-hypertensive medication for at least six months. A smoker was defined as a person who had smoked ≥100 cigarettes in their lifetime and had smoked in the last one month. An ex-smoker was defined as an individual who had smoked more than 100 cigarettes in their lifetime but had not smoked in the past 28 days; according to international standards, a person was considered an ex-smoker if they had been completely smoke-free for at least one month (28 days).

Data were analyzed using SPSS version 26.0. Qualitative variables such as gender, diabetes mellitus, hypertension, smoking status, reason for surgery, ASA class, and pain relief were presented as frequency and percentage. Quantitative variables such as age and duration of surgery were expressed as mean ± standard deviation or median with interquartile range based on the normality of data. The Shapiro–Wilk test was applied to assess normality. Pain relief was compared between the two groups using the Chi-square test or Fisher's exact test at a 5% level of significance. Effect modifiers, including age, gender, diabetes, hypertension, smoking status, reason for surgery, ASA class, and duration of procedure, were controlled through stratification. Post-stratification, the Chi-square test or Fisher's exact test was applied, and a p-value <0.05 was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics were comparable between the two groups. The mean age in Group A was 34.6 ± 8.2 years and in Group B was 35.1 ± 8.5 years, showing no statistically significant difference ($p = 0.742$). The gender distribution was also similar, with females constituting 63.6% in Group A and 60.0% in Group B ($p = 0.689$). The mean duration of surgery did not differ significantly between the groups (92.5 ± 18.4 minutes in Group A vs 95.2 ± 17.9 minutes in Group B, $p = 0.418$). Likewise, the frequencies of hypertension, diabetes mellitus, smoking status, and ASA class were comparable between both groups with no statistically significant differences ($p > 0.05$), as given in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics of Patients (n = 110)

Variable	Group A (NSAID + Weak Opioid + $MgSO_4$) (n=55)	Group B (NSAID + Weak Opioid) (n=55)	p-value
Age (years)	34.6 ± 8.2	35.1 ± 8.5	0.742
Gender			
Male	20 (36.4%)	22 (40.0%)	0.689
Female	35 (63.6%)	33 (60.0%)	
Duration of Surgery (mins)	92.5 ± 18.4	95.2 ± 17.9	0.418
Hypertension (Yes)	14 (25.5%)	16 (29.1%)	0.672

Diabetes Mellitus (Yes)	12 (21.8%)	11 (20.0%)	0.812
Smoking Status			
Smoker	10 (18.2%)	12 (21.8%)	0.755
Non-Smoker	30 (54.5%)	28 (50.9%)	
Ex-Smoker	15 (27.3%)	15 (27.3%)	
ASA Class			
I	18 (32.7%)	17 (30.9%)	0.834
II	25 (45.5%)	27 (49.1%)	
III	12 (21.8%)	11 (20.0%)	

The comparison of postoperative pain scores (VAS) at different time points demonstrated significantly lower pain scores in Group A compared to Group B. Immediately after surgery, the mean VAS score was 2.8 ± 1.1 in Group A versus 3.6 ± 1.3 in Group B ($p = 0.001$). At 6 hours, the scores were 3.1 ± 1.2 and 4.2 ± 1.4 respectively ($p < 0.001$). Similarly, at 12 hours and 24 hours, Group A continued to show significantly lower pain scores compared to Group B ($p = 0.002$ and $p = 0.003$, respectively), as given in Table 2.

Table 2: Comparison of Pain Scores (VAS) at Different Time Points Between Groups

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Immediately after surgery	2.8 ± 1.1	3.6 ± 1.3	0.001
6 hours after surgery	3.1 ± 1.2	4.2 ± 1.4	<0.001
12 hours after surgery	2.6 ± 1.0	3.5 ± 1.2	0.002
24 hours after surgery	2.1 ± 0.9	2.9 ± 1.1	0.003

The requirement of rescue analgesia was lower in Group A compared to Group B at all observed time points. Immediately after surgery, 18.2% of patients in Group A required rescue analgesia compared to 32.7% in Group B, although this difference was not statistically significant ($p = 0.084$). However, at 6 hours, 12 hours, and 24 hours, the requirement was significantly lower in Group A compared to Group B ($p = 0.012$, $p = 0.041$, and $p = 0.038$, respectively), as given in Table 3.

Table 3: Requirement of Rescue Analgesia at Different Time Points

Time Point	Group A (Yes) n (%)	Group B (Yes) n (%)	p-value
Immediately after surgery	10 (18.2%)	18 (32.7%)	0.084
6 hours after surgery	15 (27.3%)	28 (50.9%)	0.012
12 hours after surgery	12 (21.8%)	22 (40.0%)	0.041
24 hours after surgery	8 (14.5%)	17 (30.9%)	0.038

The overall pain relief outcome at 24 hours showed that a significantly higher proportion of patients in Group A achieved effective pain relief (85.5%) compared to Group B (67.3%), with this difference being statistically significant ($p = 0.028$), as given in Table 4.

Table 4: Overall Pain Relief Outcome at 24 Hours

Pain Relief	Group A (n=55)	Group B (n=55)	p-value
Effective	47 (85.5%)	37 (67.3%)	0.028
Not Effective	8 (14.5%)	18 (32.7%)	

Stratification analysis revealed that effective pain relief was generally higher in Group A across different subgroups. In patients aged ≤35 years, effective pain relief was significantly higher in Group A compared to Group B (87.5% vs 68.8%, $p = 0.041$), while in patients aged >35 years, the difference was not statistically significant ($p = 0.089$). Similar trends were observed across gender categories, although differences were not statistically significant. Among non-diabetic patients, effective pain relief was significantly higher in Group A (88.4% vs 68.2%, $p = 0.021$), whereas no significant difference was observed among diabetic patients ($p = 0.512$). In patients without hypertension, Group A showed significantly better pain relief ($p = 0.034$), while no significant difference was found in hypertensive patients ($p = 0.338$), as given in Table 5.

Table 5: Stratification of Pain Relief with Respect to Selected Variables

Variable	Category	Group A Effective n (%)	Group B Effective n (%)	p-value
Age	≤35 years	28 (87.5%)	22 (68.8%)	0.041
	>35 years	19 (82.6%)	15 (65.2%)	0.089
Gender	Male	17 (85.0%)	14 (63.6%)	0.078
	Female	30 (85.7%)	23 (69.7%)	0.062
Diabetes	Yes	9 (75.0%)	7 (63.6%)	0.512
	No	38 (88.4%)	30 (68.2%)	0.021
Hypertension	Yes	11 (78.6%)	10 (62.5%)	0.338
	No	36 (87.8%)	27 (69.2%)	0.034

DISCUSSION

Postoperative pain following open abdominal surgery remains a significant clinical concern, as inadequate pain control is associated with delayed recovery, increased morbidity, and prolonged hospital stay.10 Non-steroidal anti-inflammatory drugs (NSAIDs) and weak opioids are commonly used components of such regimens. Recently, magnesium sulphate has gained attention due to its NMDA receptor antagonistic properties, which may enhance analgesic efficacy.11,12 However, limited evidence exists comparing the effectiveness of NSAIDs and weak opioids with and without magnesium sulphate in patients undergoing open abdominal surgery.

The present study demonstrated that the addition of magnesium sulphate to NSAIDs and weak opioids resulted in significantly improved postoperative pain outcomes, as evidenced by lower VAS scores at all-time points (immediate: 2.8±1.1 vs 3.6±1.3, $p = 0.001$; 6 hours: 3.1±1.2 vs 4.2 ± 1.4, $p < 0.001$; 12 hours: 2.6 ± 1.0 vs 3.5 ± 1.2, $p = 0.002$; 24 hours: 2.1 ± 0.9 vs 2.9 ± 1.1, $p = 0.003$), reduced requirement of rescue analgesia at 6, 12, and 24 hours ($p = 0.012$, 0.041, and 0.038, respectively), and a higher proportion of effective pain relief (85.5% vs 67.3%, $p = 0.028$). These findings are consistent with earlier evidence demonstrating the analgesic benefits of magnesium as an adjunct in multimodal analgesia.

Mussrat et al. (2019) reported significantly lower VAS scores in the magnesium group compared to control at 1 hour (2.7 ± 0.43 vs 4.1 ± 0.82, $p < 0.001$) and 6 hours (1.9 ± 0.31 vs 2.3 ± 0.63, $p < 0.001$), along with a prolonged time to first rescue analgesia (105.9 ± 12.7 min vs 67.8 ± 15.3 min, $p < 0.001$).14 Similarly, Tamdogan et al. (2022) demonstrated a significant reduction in postoperative pain scores and opioid consumption with magnesium ($p < 0.05$), while Yazdi et al. (2022) also observed reduced pain intensity after 6 hours and decreased 24-hour morphine consumption in the magnesium group.15,16 These findings strongly align with the present study, particularly regarding lower VAS scores and reduced analgesic requirements, reinforcing the role of magnesium in enhancing postoperative analgesia.

Further supporting evidence was provided by Benevides (2021) and Ersoy et al. (2023), who evaluated multimodal regimens involving NSAIDs and weak opioids. Both studies demonstrated significantly reduced opioid consumption with ibuprofen-based regimens ($p < 0.05$), although VAS scores remained comparable between groups.20,17 In contrast, the current study not only showed reduced analgesic requirement but also significantly lower pain scores, suggesting that the addition of magnesium may provide an incremental benefit beyond NSAID–opioid combinations alone.

Obaid (2025) reported findings closely mirroring the present results, with significantly lower VAS scores and reduced tramadol consumption in the magnesium group (82.1 ± 16.7 mg vs 102.3 ± 18.4 mg, $p < 0.001$), along with prolonged time to rescue analgesia (138.6 ± 31.2 vs 97.4 ± 25.6 min, $p < 0.001$).18 These results are highly comparable to the reduced rescue analgesia requirement observed in the present study, further validating the analgesic efficacy of magnesium sulphate.

On a broader level, Avci et al. (2024) in a systematic evaluation concluded that perioperative magnesium significantly reduced postoperative pain scores and opioid consumption within the first 24 hours which is in strong agreement with the present findings.13 However, Wu et al. (2025), in a meta-analysis, reported some heterogeneity across trials, although an overall trend toward reduced pain and analgesic requirement with NMDA antagonists, including magnesium, was observed.19 This variability may be attributed to differences in surgical procedures, dosing regimens, and study populations.

Overall, the findings of the present study are largely consistent with the majority of existing literature, demonstrating that magnesium sulphate enhances

postoperative pain control and reduces analgesic requirements. Minor variations across studies may reflect methodological differences; however, the cumulative evidence supports the incorporation of magnesium sulphate as an effective adjunct in multimodal analgesia for abdominal surgery.

Study Limitations

This study employed a randomized controlled design, which enhanced the validity of comparisons between the two groups. Standardized anesthesia and analgesia protocols were followed to minimize confounding variables. The use of objective pain assessment tools such as VAS improved the reliability of outcome measurement. Additionally, stratification was performed to control potential effect modifiers. However, the study was conducted at a single center, which may limit the generalizability of findings. The relatively short follow-up duration of 24 hours and absence of long-term pain assessment were additional limitations.

CONCLUSION

The addition of magnesium sulphate to NSAIDs and weak opioids was associated with improved postoperative pain control and reduced need for rescue analgesia. Patients receiving magnesium demonstrated lower pain scores and higher rates of effective pain relief. These findings support the role of magnesium sulphate as a beneficial adjunct in multimodal analgesia for open abdominal surgery.

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Conflict of Interest: No

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