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Original Article

Anaesthesia Section

Analgesic Effects of Intravenous Paracetamol versus Intravenous Magnesium Sulphate in Patients undergoing Major Abdominal and Upper Limb Surgeries under General Anaesthesia: A Randomised Clinical Study

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ABSTRACT

Introduction: Effective postoperative pain management is essential for patient recovery and satisfaction. Intravenous (i.v.) paracetamol and magnesium sulfate are two options that have shown promise in reducing pain and opioid use.

Aim: To compare the efficacy of intraoperative i.v. magnesium sulfate versus i.v. paracetamol on postoperative analgesic requirements in major surgeries under general anaesthesia.

Materials and Methods: This prospective randomised clinical study was conducted in the Department of Trauma and Emergency at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India, and included 100 patients classified as American Society of Anaesthesiologists (ASA) grade I and II. The patients were assigned to two groups: Group P received 20 mg/kg i.v. paracetamol, and Group M received 20 mg/kg i.v. magnesium sulfate in 100 mL of normal saline. Written consent was obtained from all the participants. Baseline parameters were monitored and a standardised general anaesthesia protocol was followed. Postoperatively, pain was assessed using the Visual Analog Scale (VAS) and analgesic requirements and adverse effects were recorded. Statistical analysis was conducted using the t-test via GraphPad Prism (Dotmatics, GraphPad Software, San Diego, California).

Results: A comparison of pain scores revealed similar levels immediately after surgery (Group P: 7.1, Group M: 7.2) and at six hours postsurgery (Group P: 2.1, Group M: 2.0). At 12 hours, Group M reported higher pain (6.8) compared to Group P (6.2), but pain levels were comparable at 18 hours (Group P: 3.0, Group M: 3.1). There was no significant difference in the number of rescue analgesia injections used (Group P: 2.0, Group M: 1.9, p-value=0.348). Diclofenac consumption was higher in Group P (300 mg) compared to Group M (290 mg, p-value=0.00526). The time to the first rescue analgesic was longer in Group M (5.2 hours) compared to Group P (4.6 hours, p-value=0.023). Adverse effects such as nausea, vomiting, sedation and respiratory depression were similar between groups, with no significant differences.

Conclusion: The i.v. paracetamol and magnesium sulfate provided comparable postoperative pain relief. Group P had lower pain levels at 12 hours, while Group M required less diclofenac and had a longer time to the first rescue analgesic. Adverse effects were similar, making both drugs effective options for pain management.

Keywords: Opioid, Pre-emptive, Rescue analgesia, Visual analogue scale

INTRODUCTION

Postoperative pain management is an important aspect of patient recovery following surgeries. Poor pain control not only causes discomfort but also delays mobilisation and prolongs hospital stays. Opioids remain a primary treatment option [1], but their side-effects necessitate alternative strategies. Non Steroidal Anti-Inflammatory Drugs (NSAIDs) and acetaminophen, commonly used as antipyretics, can serve as adjuncts or substitutes for opioids in postoperative pain management [1]. Pain, recognised as the fifth vital sign, must be effectively controlled to prevent complications, reduce mortality rates and lower hospital costs [1-3]. A broad range of analgesic options exists, including parenteral and oral NSAIDs, sublingual and i.v. opioids, N-methyl-D-aspartate (NMDA) receptor antagonists, local anaesthetics for neuraxial administration, peripheral nerve blocks, wound infiltration, intraperitoneal installations and systemic Gamma-aminobutyric acid (GABA) analogues [4,5]. Magnesium (Mg), the body's fourth most abundant cation, plays a role in numerous enzymatic processes, with its analgesic effects likely mediated through calcium channel and NMDA receptor inhibition [4,5]. Meanwhile, paracetamol (acetaminophen) is widely used for its antipyretic and analgesic properties, acting via COX inhibition and serotonergic pain modulation, though its narrow therapeutic index requires cautious use [6,7].

Both oral and i.v. paracetamol have shown effectiveness, with recent studies evaluating i.v. administration [8-10]. Similarly, i.v. magnesium sulfate has demonstrated opioid-sparing effects and improved postoperative pain control in various surgical procedures [8-10]. While some studies favour i.v. paracetamol over magnesium sulfate for perioperative analgesia [4], others report reduced 24-hour rescue analgesia with preoperative i.v. magnesium sulfate in caesarean sections without significant adverse effects [11].

Thus, this study aimed to evaluate the analgesic efficacy of i.v. paracetamol versus i.v. magnesium sulfate in major abdominal and upper limb surgeries under general anaesthesia. By addressing this gap, the findings could help optimise postoperative pain management reduce reliance on opioids, and refine anaesthetic practices in high-pain surgical procedures.

MATERIALS AND METHODS

This prospective interventional randomised double-blinded clinical study was conducted in the Department of Trauma and Emergency

at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India from November 2024 to January 2025. Ethical approval was granted by the Institutional Ethical Committee (IEC) via letter no. 30/IEC/IGIMS/2021 prior to commencement, and the study was registered with CTRI (CTRI/2024/11/076902).

Inclusion criteria: Patients scheduled for lower abdominal and upper limb surgeries under general anaesthesia, patients classified as ASA grade I and II and patients aged between 18 and 65 years were included in the study.

Exclusion criteria: Patient refusal for general anaesthesia, patient refusal to enrol in the study, patients with cardiovascular disease, renal failure, hepatic dysfunction and chronic pulmonary disease, obesity (BMI ≥30 kg/m²), bleeding disorders (platelet count <50,000/mm³), and a history of allergy or sensitivity to any of the study drugs were excluded from the study.

Sample size: The sample size was calculated based on a previous study by Santhi Sree M and Usha Rani A [4]. The sample size was determined using the formula: $n=(Z\alpha+Z\beta)^2 (\sigma_1^2+\sigma_2^2)/d^2$

where,

σ1=Standard deviation of Group 1;

σ2=Standard deviation of Group 2;

d=expected mean difference

α=Type I error (5%)

β=Type II error (10%)

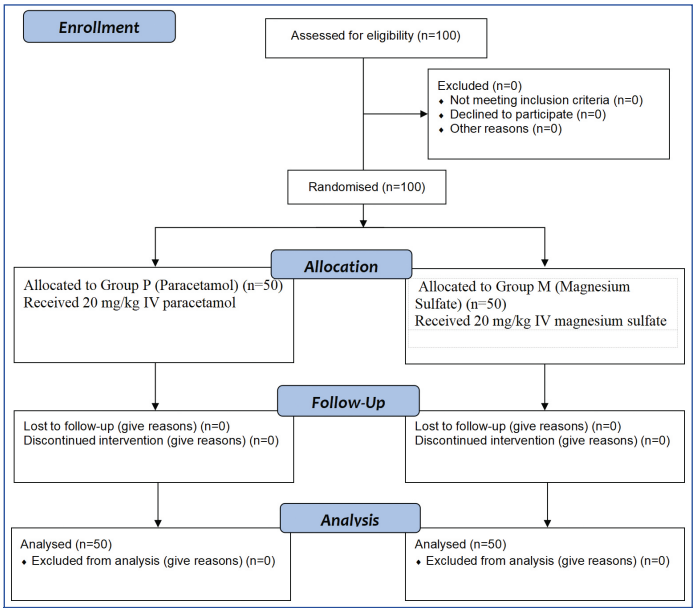
Power of study=90%

Data loss=10%

Sample size, n=50/group

Study Procedure

The study included 100 patients with ASA grades I and II [12], who were randomly assigned into two groups of 50 using computer-generated randomisation. Group P received 20 mg/kg of paracetamol in 100 mL via i.v. infusion over 10 minutes, administered immediately after intubation and before surgery. Group M received 20 mg/kg of magnesium sulfate in 100 mL of normal saline over 10 minutes, also administered immediately after intubation and before surgery. The 20 mg/kg dose of i.v. paracetamol and i.v. magnesium sulfate aligns with clinical standards, ensuring effective analgesia while minimising side-effects [Table/Fig-1] [13,14].



[Table/Fig-1]: CONSORT 2010 flow diagram.

Written informed consent for both study participation and anaesthesia was obtained from each patient before surgery.

Upon arrival in the operating room, an 18G i.v. cannula was inserted, and patients were connected to monitors to record baseline parameters, including Heart Rate (HR), Non Invasive Blood Pressure (NIBP), Respiratory Rate (RR), peripheral Oxygen Saturation (SpO_2), and Electrocardiogram (ECG), which were continuously monitored throughout the procedure. All patients followed a standardised general anaesthesia protocol involving endotracheal intubation and controlled ventilation. Preanaesthetic evaluations were completed, and necessary baseline investigations were conducted.

Fifteen minutes before surgery, i.v. cannulation was performed, and patients were premedicated with i.v. injections of glycopyrrolate 0.2 mg, ondansetron 4 mg, fentanyl 1 mcg/kg, and midazolam 0.02 mg/kg, administered slowly. After three minutes of preoxygenation with eight liters of oxygen, induction was performed with i.v. propofol 2 mg/kg, followed by endotracheal intubation using suxamethonium 1.5 mg/kg and a suitable-sized oral cuffed endotracheal tube.

Anaesthesia was maintained with a mixture of oxygen (33%), nitrous oxide (66%), the muscle relaxant vecuronium at 0.1 mg/kg, and isoflurane (0.2-1.2%). Intermittent Positive Pressure Ventilation (IPPV) was administered using a circle absorption system connected to the anaesthesia workstation, set at 14 breaths per minute and a tidal volume of 8 ml/kg. End-Tidal Carbon Dioxide ($ETCO_2$) was maintained between 30 and 35 mm Hg (millimeters of mercury). The i.v. fluids were administered intraoperatively based on the 4-2-1 formula [15].

Patients received either paracetamol or magnesium sulfate according to the randomisation. Ringer's lactate and dextrose normal saline were used for intraoperative fluid management. Vital parameters, including pulse rate, SpO_2, and systolic and diastolic blood pressure, were recorded at induction, intubation, and every 15 minutes during surgery. In all cases, the duration of surgery exceeded 90 minutes. Postoperatively, the neuromuscular blockade was reversed with neostigmine at 50 µg/kg and glycopyrrolate at 10 µg/kg. Vital signs were monitored during the recovery phase. Patients were transferred to the postoperative ward after ensuring they were conscious and had intact reflexes. They were monitored for six hours postoperatively for analgesia, haemodynamics and temperature.

Pain was assessed every six hours using the VAS [16]. The time to the onset of rescue analgesia was noted and i.v. diclofenac sodium was administered if the VAS score was ≥4. In the VAS scale, 0 indicates no pain, while 10 represents the worst imaginable pain. The first report of pain (VAS >4) in the postoperative period was recorded, and 75 mg/kg of i.v. diclofenac aqueous was administered as a rescue analgesic. Adverse effects, such as nausea, vomiting, sedation and respiratory depression, were observed and managed symptomatically. SpO_2 below 95% was addressed with oxygen supplementation and respiratory support if necessary [16].

STATISTICAL ANALYSIS

The results were compiled, a master chart was created, and the data were statistically analysed. Statistical analysis of the obtained data was performed using a t-test with GraphPad Prism by Dotmatics (GraphPad Software, San Diego, California). The sample size was determined to maintain the power of the study at 90%.

RESULTS

The demographic data of the two groups, Group P and Group M, were analysed and are presented in [Table/Fig-1]. Both groups consisted of 50 patients each. The gender distribution showed 30 males and 20 females in Group P, and 32 males and 18 females in Group M, with no statistically significant difference between the groups (p-value=0.837) [Table/Fig-2]. The mean age of the patients in Group P was 38.6±9.2 years, while in Group M, it was 39.2±9.8 years, resulting in a p-value of 0.37, indicating no significant age difference between the groups. The mean weight of the patients in Group P was 61.46±8.3 kg, compared to 59.92±9.2 kg in Group M, with a p-value of 0.19, showing no

significant difference in weight between the two groups. Overall, the demographic characteristics were well-matched between Group P and Group M [Table/Fig-2].

Parameters	Group P	Group M	p-value
No. of patients	50	50	-
Male	30	32	0.837
Female	20	18	
Mean age (years)	38.6±9.2	39.2±9.8	0.37
Mean weight (kilograms)	61.46±8.3	59.92±9.2	0.19

[Table/Fig-2]: Demographic data.

The comparison of the VAS scores between Group P and Group M showed similar pain levels immediately after surgery in the recovery room, with Group P scoring 7.1±1.2 and Group M scoring 7.2±1.3. However, at 12 hours after surgery, Group M reported a slightly higher VAS score of 6.8±1.4 compared to 6.2±1.5 in Group P, indicating slightly more pain in Group M. By 18 hours postsurgery, the pain levels were again similar [Table/Fig-3].

Time after surgery	Group P (Mean±SD)	Group M (Mean±SD)
In the recovery room	7.1±1.2	7.2±1.3
6 hours	2.1±0.8	2.0±0.7
12 hours	6.2±1.5	6.8±1.4
18 hours	3.0±1.1	3.1±1.2

[Table/Fig-3]: Comparison of the Visual Analog Scale (VAS) scores in the recovery room and six, 12, and 18 hours after surgery between the groups.

The comparison of the number of rescue analgesia (NSAIDs) used within 24 hours after surgery between Group P and Group M showed no statistically significant difference. Group P required an average of 2±1.34 injections, while Group M required 1.9±1.21 injections, with a p-value of 0.348 [Table/Fig-4].

Group	Group P	Group M	p-value
Number of injections used for rescue analgesia (one injection equals 2 mL, 75 mg/mL)	2±1.34	1.9±1.21	0.348

[Table/Fig-4]: Comparison of the numbers of rescue analgesia {Non-steroidal Anti-Inflammatory Drugs (NSAIDs)} used after surgery in 24 hours.

The outcome measurements over 24 hours postsurgery, where the average pain score (VAS) was similar between the groups. However, diclofenac consumption was significantly higher in Group P (300±12.5 mg) compared to Group M (290±15.8 mg), with a p-value=0.00526, indicating a significant difference. Additionally, Group M had a longer time to first rescue analgesic requirement compared to Group P, with a significant difference (p-value=0.023) [Table/Fig-5].

Outcome measurement	Group P	Group M	p-value
Pain score (VAS)	5.2±1.00	5.4±1.2	0.9
Diclofenac consumption in mg (milligram)	300±12.5	290±15.8	0.00526*
Time to get first rescue analgesic requirement (hours)	4.6±1.2	5.2±1.4	0.023*

[Table/Fig-5]: Outcome measurement in 24 hours between the groups.

The incidence of nausea and vomiting showed no significant difference between the groups. Sedation was reported in 3 (6%) patients in Group P and 2 (4%) patients in Group M, with no significant difference noted. Respiratory depression was observed in 2 (4%) patients in both groups, with a p-value of 0.5, reflecting no significant difference [Table/Fig-6].

	Group P	Group M	p-value
Nausea	6 (12%)	5 (10%)	0.37
Vomiting	4 (8%)	3 (6%)	0.34
Sedation	3 (6%)	2 (4%)	0.41
Respiratory depression	2 (4%)	2 (4%)	0.5

[Table/Fig-6]: Adverse effects.

DISCUSSION

This study compared pain levels between patients receiving i.v. paracetamol and those receiving i.v. magnesium sulfate postoperatively. It was observed that while both groups reported similar pain levels in the recovery room immediately after surgery (Group P: 7.1, Group M: 7.2), the efficacy of analgesia varied over time. At six hours postsurgery, pain levels had decreased significantly in both groups, with Group P scoring 2.1 and Group M scoring 2.0. However, by 12 hours, Group M experienced slightly higher pain levels (6.8) compared to Group P (6.2), indicating a potential difference in the duration or effectiveness of pain relief between the two treatments. By 18 hours, pain scores were comparable again, with Group P at 3.0 and Group M at 3.1.

The findings of this study align with some existing literature on this topic but also present contrasts in specific outcomes. For instance, the study by Hamed MA and Al-Saeed MA, reported that magnesium sulfate provided better postoperative analgesia and reduced the need for analgesics compared to paracetamol in children post-tonsillectomy. This suggests that magnesium sulfate may offer superior analgesic effects in certain populations or surgical contexts, potentially contrasting with present study results where paracetamol appeared more effective at specific time points [17].

Conversely, Santhi Sree M and Usha Rani A, found that i.v. paracetamol was superior to magnesium sulfate for perioperative analgesia, aligning with present study observation of lower pain scores in Group P at several intervals. This supports the idea that paracetamol might be more effective or have a more consistent analgesic effect in some surgical settings [4]. In contrast, Heydari SM et al., reported that ketamine was superior to both paracetamol and magnesium sulfate for postoperative pain control. While ketamine was not included in present study, this highlights the ongoing debate about the optimal analgesic strategy and suggests that alternative agents might offer more effective pain management compared to magnesium sulfate and paracetamol alone [8].

McKeown A et al., found that preoperative i.v. magnesium sulfate reduced 24-hour rescue analgesia requirements after a caesarean section without serious adverse effects. This supports the potential benefits of magnesium sulfate but also emphasises the need for further research to confirm its efficacy across different surgical procedures and patient populations [11]. Jain N et al., found that the preemptive administration of i.v. paracetamol, lignocaine and magnesium sulfate provides safe, effective and satisfactory analgesia in patients undergoing various abdominal surgeries under general anaesthesia [3], which was in accordance with present study. Kamel W and Shoukry A, investigated magnesium sulfate within multimodal analgesia, noting that the use of magnesium sulfate in a bolus with or without infusion was comparable in controlling intraoperative and postoperative pain [18].

This study compared the efficacy of i.v. paracetamol versus i.v. magnesium sulfate for postoperative pain management over a 24-hour period. The results showed that average pain scores, as measured by the VAS, were similar between the two groups. However, a significant difference was observed in diclofenac consumption, which was notably higher in Group P (300±12.5 mg) compared to Group M (290±15.8 mg), with a p-value of 0.00526. This indicates that Group P required more additional analgesics, which could imply that the initial analgesic effect of paracetamol might be less sustained compared to magnesium sulfate. In addition, the time to the first rescue analgesic requirement was longer in Group M (5.2±1.4 hours) compared to Group P (4.6±1.2 hours), with a p-value of 0.023. This suggests that magnesium sulfate may have a slightly more prolonged effect before additional analgesics are needed.

While this study showed no significant difference in the overall pain scores between paracetamol and magnesium sulfate, the differences in diclofenac consumption and the time to first rescue analgesic suggest varying effects in pain management and duration.

Limitation(s)

This study's limitations include patient variability in the perception of pain, the use of VAS for pain scoring only, a short follow-up duration, and reliance on subjective pain scores, all of which may affect the generalisability and accuracy of the results.

CONCLUSION(S)

In summary, Group P required more additional analgesics, suggesting that the initial analgesic effect of paracetamol may not be as sustained as that of magnesium sulfate. Furthermore, the time to the first rescue analgesic requirement was significantly longer in Group M compared to Group P. This indicates that magnesium sulfate may provide a more prolonged analgesic effect, delaying the need for additional pain relief. The variation in results across different studies underscores the complexity of pain management and the need for tailored approaches based on specific surgical and patient factors. Further research is warranted to explore these differences and optimise analgesic strategies for diverse clinical settings.

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