




Original Article

Effect of Intravenous Magnesium Sulphate versus Ketamine as Pre-emptive Analgesia on Haemodynamic Parameters and Post-Operative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy under General Anaesthesia: A Randomized Control Trial

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ABSTRACT

Background and Aims: Pain being a complex and subjective experience is known to have been poorly managed in clinical settings. Pre-emptive analgesia has been defined as an anti-nociceptive treatment that prevents establishment of altered central processing of afferent input from injuries. The current study was done to assess the pre-emptive analgesic efficacy of intravenous Ketamine and Magnesium Sulphate in patients who underwent laparoscopic cholecystectomy. The study aimed to compare the analgesic effect of Ketamine and Magnesium Sulphate over a period of 24 hours, time for first rescue analgesia requirement and total requirement of rescue analgesia in 24 hrs. Haemodynamic parameters like heart rate, systolic, diastolic and mean arterial pressure and side effects like sedation, hallucination and PONV were also compared.

Material and Methods: In this randomized controlled trial, 60 participants aged 18–65 years undergoing laparoscopic cholecystectomy were randomized to either the Ketamine or Magnesium Sulphate group. Analgesic effect, first rescue analgesia and total requirement of rescue analgesia were compared for 24 hours after surgery. Haemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were also monitored intra-operatively till 24 hours post extubation.

Results: DBP and MAP were significantly higher in the Ketamine group in the 8th hour post extubation with a p value 0.028 for DBP and p value 0.022 for MAP. Pain was significantly higher in the Magnesium Sulphate group in the 4th hour post extubation (p value <0.001) whereas in the 24th hour it was significantly higher in the Ketamine group (p value 0.0020). Requirement of rescue analgesia (p value 0.018) and time of first rescue analgesia (p value 0.012) was significantly higher in Magnesium Sulphate group.

Conclusion: Ketamine given pre-emptively 10 minutes before the incision significantly decreases post-operative pain as compared to Magnesium Sulphate in patients undergoing laparoscopic cholecystectomy.

Keywords: Ketamine; Magnesium Sulphate; Pre-emptive analgesia; Laparoscopic cholecystectomy.

INTRODUCTION

Pain is a complex experience and is poorly managed in the clinical settings. Effective postoperative pain management improves patient satisfaction and reduces morbidity.^[1]

Pre-emptive analgesia can be stated as administering analgesic before giving a painful stimulus to prevent or diminish the intensity of pain. It has been suggested to result in enhanced pain control, decreased analgesic consumption and patient satisfaction.

NMDA receptor blockers like Ketamine and Magnesium Sulphate, help in decreasing the post-operative pain and analgesia demand when given both post-operatively and pre-emptively. [2]

The current study was done to compare the pre-emptive analgesic efficacy of Ketamine and Magnesium Sulphate.

MATERIAL AND METHODS

“In this randomized controlled double blinded trial, 60 participants aged 18–65 years undergoing laparoscopic cholecystectomy were randomized to either the Ketamine or Magnesium Sulphate group. Patients of American Society of Anaesthesiology score (ASA) 1 and 2 and patients undergoing laparoscopic cholecystectomy using four ports were included in the study. Patients with any systemic co-morbidity including uncontrolled hypertension and diabetes, heart block, renal impairment (serum creatinine greater than the institutional reference range), hepatic impairment (transaminases greater than double the institutional reference values), psychiatric disorders like Schizophrenia and Mania, patient on any addictive drug or history of allergy to any drug used in the trial, pregnancy and lactation, Glaucoma, raised intracranial pressure and duration of surgery more than 90 minutes were excluded from the study. The study was done after obtaining Institutional Ethical Committee Clearance (SMIMS/IEC/2022-108) and written informed consent from the patient. The study was registered with Clinical Trial Registry India (CTRI/2022/12/048059). The study was conducted over a period of 18 months from 14.12.22 to 14.06.24.

Once the patients were shifted to the preoperative area, their vital parameters were recorded which would serve as base line parameters. The patients were then divided into two groups; Group 1 and Group 2. Group 1 received Ketamine and Group 2 received Magnesium Sulphate. Drugs were allotted based on random number table. Patients were taught how to report pain intensity on the Numerical Rating Scale (NRS); point 0 represents no pain and 10 represent the worst imaginable pain.

The drugs were prepared in identical looking 100ml normal saline bottles as follows:

- Ketamine -0.5mg/kg body weight in 100 ml normal saline
- Magnesium Sulphate -30mg/kg body weight in 100ml normal saline
- The final solution was colourless and transparent.

Once the patient was wheeled in the OT, his/her vitals were recorded, which served as pre induction parameters. A standardized anaesthesia technique was used for all patients. After intubation the vitals like HR, SBP, DBP, MAP were checked again, the study drug was then infused over 10 minutes before incision. All this was done by an OT technician not involved in the process of anaesthesia and surgery in operating room [OR]. The haemodynamic parameters were recorded immediately after study drug was infused followed by 5 mins, 15mins, 30 mins and 60 mins after the drug infusion.

After the end of the surgery, the patient was extubated, and parameters were recorded.

NRS for post-operative pain was recorded at 0, 30 mins, 1 hour, 2 hours, 4 hours, 6 hours, 8 hours, 12 hours, and 24 hours.

Rescue analgesia i.e. Tramadol 100mg in 100 ml NS was given to the patient if the NRS score was greater than 5.

Side effects like sedation, post-operative nausea and vomiting were also monitored over a period of 24 hours.

The data was tabulated and analysed using Microsoft Excel and SPSS (statistical package for social sciences)-21 software version. Different statistical aggregates like mean and median were used to analyse numerical variables. Appropriate statistical methods were used to determine the significance of differences between various data. Frequency distribution was used in case of categorical variables (nominal and ordinal). The categorical data was analysed using χ^2 and Fisher Exact test. A p value <0.05 was considered significant.”

RESULTS

“Data of 60 patients were analyzed. Socio-demographic parameters of the participants including age, gender, ASA classification, co-morbidities were analysed and were comparable between the two groups. Intra-operative haemodynamic parameters like oxygen saturation, respiratory rate, HR, SBP, DBP, MAP were all comparable between the two groups It was also seen that more number of rescue analgesia were required for the Magnesium Sulphate group.

Post-operative nausea and vomiting. Ramsay Sedation score and hallucination are all comparable between the two groups.”

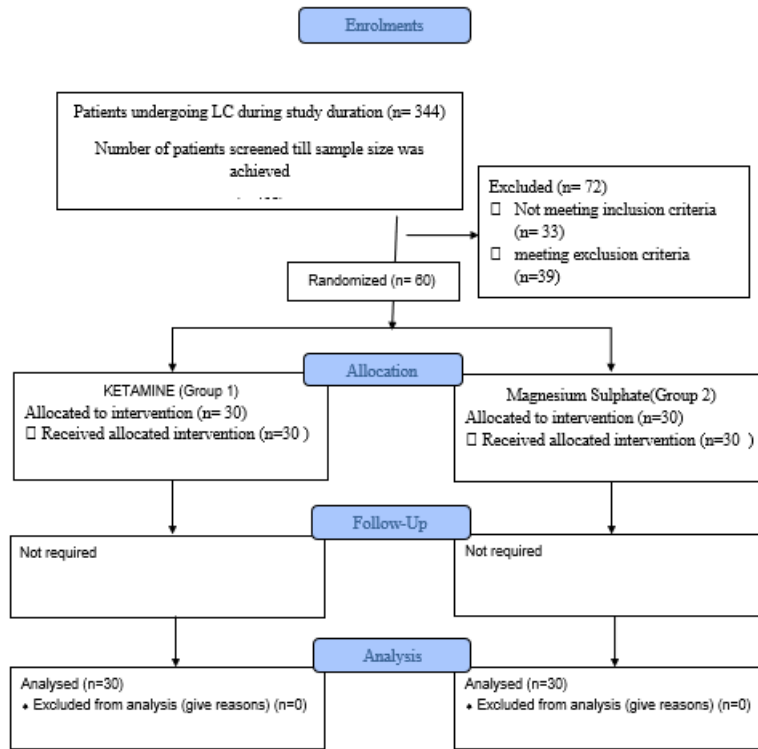


Figure 1: Consort Diagram

DBP and MAP were significantly higher in the Ketamine group in the 8th hour post extubation (p value 0.028) (p value 0.022).

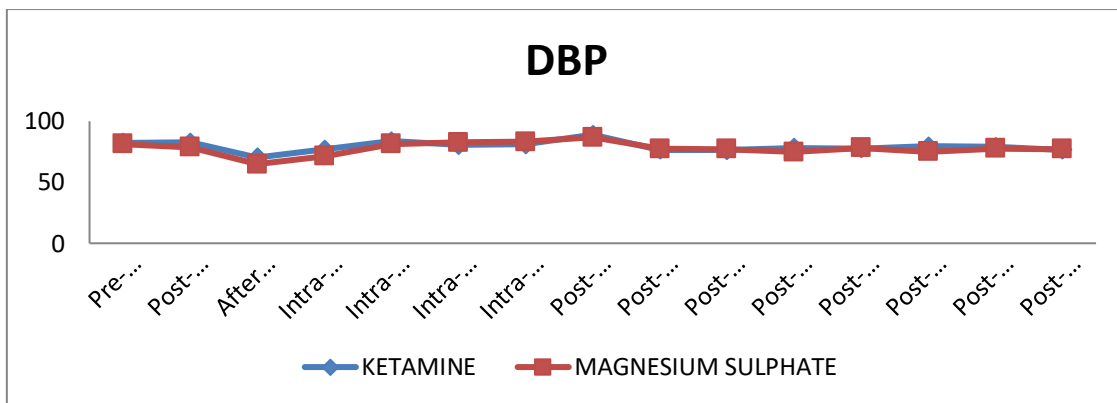


Fig 2: Comparison of Diastolic Blood Pressure among groups

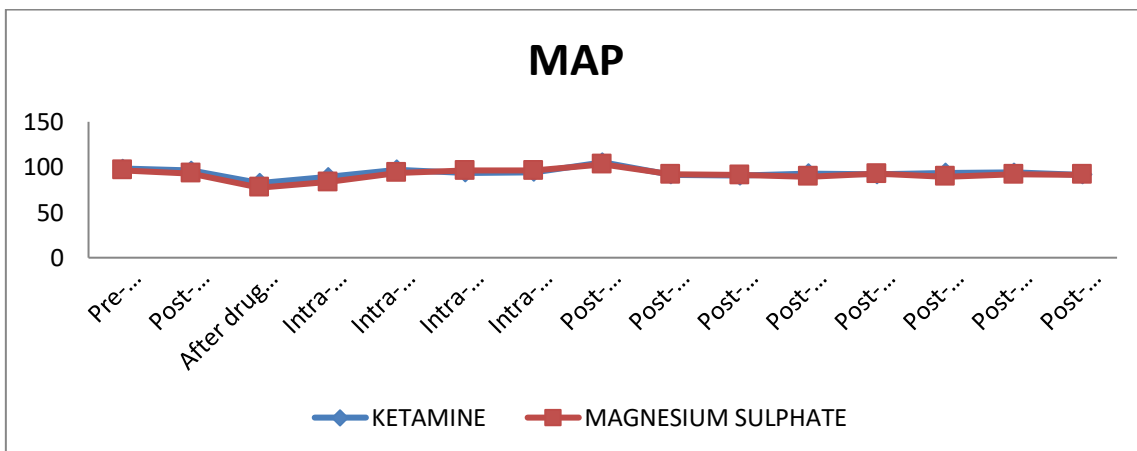


Figure 3: Comparison of Mean Arterial Pressure among groups

Pain was significantly higher in the Magnesium Sulphate group in the 4th hour post extubation (p value <0.001) whereas in the 24th hour it was significantly higher in the ketamine group (p value 0.0020)

Table 1: Comparison of Numerical Rating Scale (NRS) for post-operative pain among groups

Numerical Pain Rating Scale	KETAMINE		MAGNESIUM SULPHATE		Unpaired t test P value
	Mean	SD	Mean	SD	
Immediately After extubation	0.47	0.93	0.87	1.25	0.167
After 30 min	1.07	1.17	1.20	1.15	0.659
After 1hr	1.33	1.21	1.73	1.53	0.266
After 2hrs	2.67	1.37	2.87	1.28	0.562
After 4hrs	3.27	1.41	4.67	1.51	0.000
After 8hrs	3.27	1.55	2.93	1.53	0.406
After 12hrs	3.07	1.36	2.87	1.45	0.585
After 24hrs	3.10	0.99	2.40	1.24	0.020

Requirement of rescue analgesia was significantly higher in Magnesium Sulphate group (p value 0.018) as compared to Ketamine group.

Table 2: Comparison of rescue analgesia requirement among the groups

Variables		KETAMINE		MAGNESIUM SULPHATE		Chisquare test P value
		N	%	N	%	
Rescue analgesia	Yes	8	26.7%	17	56.7%	0.018
	No	22	73.3%	13	43.3%	

The patients in the Magnesium Sulphate group demanded for rescue analgesia earlier compared to the patients in the Ketamine group. The difference in the mean value was statistically significant for the time of first rescue analgesia (p value 0.012).

Table 3: Comparison of time for first rescue analgesia among groups

Variables	KETAMINE		MAGNESIUM SULPHATE		Unpaired t test P value
	Mean	SD	Mean	SD	
Time of first rescue analgesia (hours) (among those who received)	6.5	2.25	4.15	1.90	0.012

DISCUSSION

“Pain is the most unpleasant sensation for a person to experience. [3] Many protocols have been formulated and followed for better post-operative pain control but they come with many side effects. The search for an ideal analgesic with fewer side effects has led us to pre-emptive analgesics. Pre-emptive analgesics are known to be an “anti-nociceptive treatment” [4] which is administered to the patient before a noxious stimulus is given.

Among the many drugs used for pre-emptive analgesia, Ketamine and Magnesium Sulphate have garnered attention for their cost effectiveness and mechanism of action. [4] Due to their antagonist action on the NMDA receptor, they both have analgesic property. Keeping in mind, the different sites of action of the two drugs in the NMDA receptor they both can be compared regarding the analgesia they produce in the post-operative period. [1]

Also keeping in mind, the contrary effects the drugs have on the haemodynamic parameters when administered intravenously, they can be compared regarding the haemodynamic stability they provide intraoperatively as well as post-operatively.

Few studies comparing these two drugs as a pre-emptive analgesic were available in Internet database like PubMed and hence were reviewed.

The current study found that Ketamine is better than Magnesium Sulphate as a pre-emptive analgesic. The study also found out that the haemodynamic parameters, socio-demographic parameters, oxygen saturation and respiratory rate between the two were comparable.

The findings of the current study were in line with Helmy et al^[2] who compared pre-emptive analgesic effect of low dose Ketamine with Magnesium Sulphate and placebo on expectant mothers posted for caesarean section under General Anaesthesia. They used Visual Analogue Score to assess the pain post-operatively and found that there was a significantly low pain score in Ketamine group as compared to Magnesium Sulphate and placebo. They also found that number of post-operative analgesic requirement, was significantly lower in Ketamine group when compared with the Magnesium Sulphate group. Time for the requirement of first analgesia was also later than the time required by Magnesium Sulphate.

Singh et al^[5] concluded in his study that the values of post-operative haemodynamic parameters were highest in the group receiving placebo followed by the group which received higher dose of Ketamine (1mg/kg) than the other groups receiving 0.5mg/kg, 0.25mg/kg. This finding was similar to the current study as the group receiving Ketamine (0.5mg/kg) had elevated post-operative haemodynamic parameters as compared to the Magnesium Sulphate group. They found that VAS score at rest was less than 3 and equal in all four groups receiving different doses of Ketamine. They inferred that irrespective of any sub-anaesthetic dose of Ketamine, pain relief was comparable. It was similar to the current study where the NRS score in the Ketamine group was comparatively less. They also found that Ketamine group (1mg/kg) had 10% incidence of hallucination but other groups receiving lesser doses had none which was also similar to the current study. The findings of the current study were also in line with study conducted by **Mwase et al**^[6] who found that Ketamine had reduced cumulative analgesic requirement in 24 hours post-surgery.”

CONCLUSION

The current study was done to compare the pre-emptive analgesic effect of Ketamine (0.5mg/kg) and Magnesium Sulphate (30mg/kg) in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

The study concluded that

1. The patients in Magnesium Sulphate group complained of significantly more pain from 4th hour onwards in the post-operative period.
2. After 24 hours it was the Ketamine group patients who were in more pain compared to their counterparts. However, the pain experienced by patients in both the groups remained less.
3. The demand for first rescue analgesia was significantly earlier in the Magnesium Sulphate group. The total requirement of rescue analgesia was also significantly higher in the Magnesium Sulphate group.
4. Haemodynamic parameters (Heart rate, Systolic and Diastolic Blood Pressure, Mean Arterial Pressure, SpO₂), Ramsay Sedation Score, hallucination and post-operative nausea and vomiting were not significantly different among the patients receiving either of the two drugs.

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