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Post-Surgical Analgesic Efficacy of Magnesium Sulphate Versus Lignocaine with Acetaminophen in Asthmatic Patients

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ABSTRACT

Objective: To compare the analgesic efficacy of intravenous Magnesium Sulfate combined with intravenous Acetaminophen versus intravenous Lignocaine with intravenous Acetaminophen when used in asthmatic patients undergoing laparoscopic cholecystectomy.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Anesthesiology, Combined Military Hospital, Rawalpindi Pakistan, from Jan to Jun 2023.

Methodology: The patients were divided into Group-M (n=55) receiving IV MgSO4 and IV Acetaminophen and Group-L (n=55) IV Lignocaine with IV Acetaminophen. Variables measured were per-operative mean heart rate, mean arterial pressure, time to first rescue analgesia, total dose of analgesia required in the next 24 hours post-surgery, and median pain scores at 1-, 3- and 6-hour intervals.

Results: Mean time required to request the first dose of rescue analgesia was 123.76±11.94 minutes for Group-M versus 134.25±6.47 minutes for Group-L (p<0.001). The mean total dose of rescue analgesia required 24 hours post-procedure was 37.09±12.8 mg in Group-M versus 42.00±14.83 mg in Group-L (p=0.066).

Conclusion: We conclude that both intravenous Magnesium Sulfate and intravenous Lignocaine provide satisfactory analgesia with comparable and decreased post-operative pain scores in asthmatic patients.

Keywords: Acetaminophen, Asthma, Cholecystectomy, Lignocaine, Magnesium Sulfate.

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INTRODUCTION

Asthma remains one of the most common respiratory diseases worldwide with 260 million people living with the disease globally in 2019.[1] It is estimated that 1 in 10 school-going children suffers from the spectrum of this disease ranging from mild allergic tendencies to life-threatening bronchospasm.[2] Even with effective therapy, severe respiratory limitation can result in case of environmental factors and stress triggers including surgery and its related surgical stress.[3] Managing an optimized patient with asthma is still a challenge to the anesthetist due to altered lung compliance and modified lung mechanics prone to develop severe bronchospasms activated by multiple factors during surgery.[4] These include the choice of anesthesia given, drugs administered, advanced age, history of smoking, and recent infections like sinusitis.[5]

Laparoscopic cholecystectomy remains the choice surgery for cholelithiasis worldwide and has largely and completely replaced conventional open cholecystectomy except in a few indicated patients.[6] The changes associated with pneumoperitoneum and the effect of general anesthesia on lung mechanics have been known to result in exacerbation in patients completely optimized before surgery.[7] It then becomes imperative to prevent these trigger factors and the release of histamine and other vasoactive agents by selecting appropriate drugs for anesthesia.

Both intravenous Magnesium Sulfate and Lignocaine have been proposed to promote bronchodilation, decreasing the circulating histamine associated with the stress of surgery and having a membrane stabilizing effect promoting improved lung compliance in asthmatic patients.[8] Their recent proposed role as non-opioid analgesics confers them an added advantage in patients where opioids are associated with complications due to the release of histamine and respiratory depression causing considerable morbidity as in asthmatic patients.[9] We aim to compare both these drugs when used in combination with NSAIDs for their analgesic efficacy and whether one is superior to the other.

This study aims to compare the analgesic efficacy of intravenous Magnesium Sulfate combined with

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intravenous Acetaminophen versus intravenous Lignocaine with intravenous Acetaminophen in asthmatic patients undergoing laparoscopic cholecystectomy while preventing the use of opioids in these patients for a better adverse effects profile.

METHODOLOGY

This quasi-experimental study was carried out at the Department of Anesthesiology, Combined Military Hospital, Rawalpindi, Pakistan from June 2023 to December 2023 after approval from the ethical review board (vide letter no 499). A pilot study was carried out in the institute with 20 patients to assess for sample size calculation. The difference between both groups for mean time to first rescue analgesia came out to be 15±2.36 minutes. The sample size was then calculated keeping the confidence interval at 95%, power of test at 80%, keeping the mean difference for time to first rescue analgesia being 15.00±2.36 minutes between both groups with population variance at 1000.[10] The sample size came out to be 70 patients. we included 110 patients in our study. The method of randomization was a non-probability consecutive sample in a lottery method keeping in line with the CONSORT guidelines (Figure).

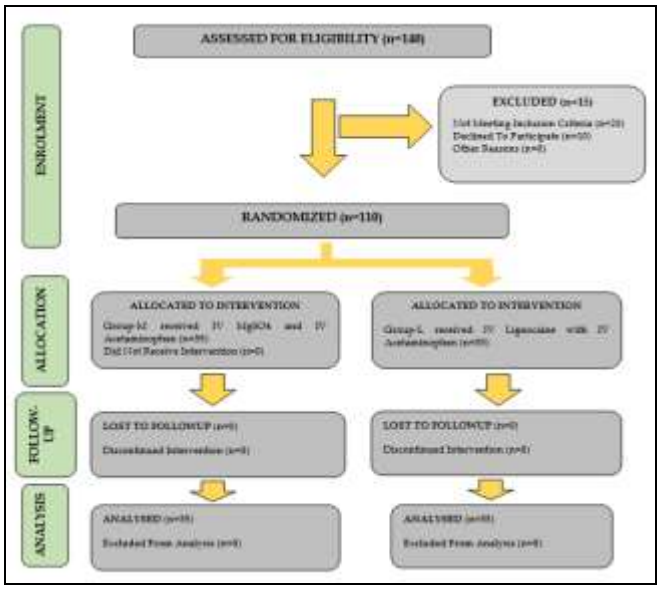


Figure: Phases of the Study

Inclusion Criteria: ASA-I and II patients diagnosed with asthma by spirometry pre- and post-bronchodilator therapy with confirmation of reversibility presenting to the surgical department for elective laparoscopic cholecystectomy compliant and optimized treatment were included in the study.

Exclusion Criteria: Patients with major cardiac or respiratory disease, low ejection fraction, unoptimized for hypertension or diabetes, patients with cholecystitis, patients allergic to Acetaminophen, MgSO4, Lignocaine or Nalbuphine, patients with a history of asthma exacerbation requiring admission in the last 8 weeks, patients on oral or intravenous Steroids for asthma and patients unwilling to be included in the study.

The study method included all patients as per the inclusion criteria furnished. The patients were randomized into Group-M (n=55) receiving IV MgSO4 and IV Acetaminophen and Group-L (n=55) IV Lignocaine with IV Acetaminophen. Once the patients were divided into two groups after randomization, an informed written consent was taken. Standard monitoring including non-invasive blood pressure, heart rate, capnography, and ECG was attached to participants in both groups. Patients in Group-M received intravenous MgSO4 at 50 mg/kg diluted in 100 ml of Normal Saline over 15 minutes with intravenous Acetaminophen 15 mg/kg over 15 minutes before induction of anesthesia followed by an infusion of intravenous Magnesium Sulfate at 25 mg/kg/hr per-operatively. Patients in Group-L received intravenous Lignocaine at a dose of 1.5 mg/kg with intravenous Acetaminophen 15 mg/kg over 15 minutes before the induction of anesthesia followed by an infusion of intravenous Lignocaine at 2 mg/kg/hr per-operatively.

Anesthesia was induced in both groups with IV Propofol 2 mg/kg, and IV Atracurium 0.5 mg/kg with maintenance done with 70% oxygen with Isoflurane at 1.0 MAC. Per-operative variables recorded were mean heart rate (HR) and mean arterial pressure (MAP) between both groups at two intervals of 15 minutes after surgical incision (HR 1 and MAP 1) and 15 minutes before extubation (HR 2 and MAP 2). Patients were extubated after Neostigmine 0.05 mg/kg and Glycopyrrolate 0.01 mg/kg were given for reversal of the neuromuscular block. Intra-operative bradycardia (heart rate <60 beats per minute) and hypotension (mean arterial pressure <60 mmHg) were treated with IV Atropine 0.5 mg stat and IV Phenylephrine 50 mcg stat respectively.[11] Post-operatively, median pain scores were observed in the surgical care unit in both groups at 1, 3, and 6 hours. The time to first rescue analgesia and the total dose of analgesia used in 24 hours were recorded and assessed on the visual analog scale (VAS). Rescue analgesia given was IV

Ketorolac 30 mg in 100 ml Normal Saline over 30 minutes according to VAS scores as described when the score reached above 4.

Primary variables measured were per-operative mean heart rate, mean arterial pressure, time to rescue analgesia, and median pain scores at 1-, 3- and 6-hour intervals. Secondary variables were the incidence of hypotension, respiratory depression, nausea, and vomiting between both groups. Demographic data were statistically described in terms of mean and SD, frequencies, and percentages when appropriate. Independent samples t-test was used to compare statistical means between both groups. Median pain scores were compared using the Mann-Whitney U test. A *p*-value of ≤0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.00.

RESULTS

A total of 110 patients were included in the study, divided into Group-M and Group-L. Mean age of patients in Group-M was 30.36±4.01 years versus 30.38±4.02 years in Group-L (*p*=0.981). The mean weight of patients was 67.82±3.85 kg in Group-M versus 68.13±3.89 kg in Group-L (*p*=0.677) (Table-I).

Table-I: Comparison of Demographic Characteristics Among Groups (n=110)

Variable(s)	Group-M (n=55)	Group-L (n=55)	*p*-value
Mean Age (Years)	30.36±4.01	30.38±4.02	0.981
Mean Weight (Kg)	67.82±3.85	68.13±3.89	0.677

The mean duration of surgery was 129.44±7.21 minutes in Group-M versus 128.91±6.46 minutes in Group-L (*p*=0.687). While observing the primary variables, the mean time required to request the first dose of rescue analgesia was 123.76±11.94 minutes for Group-M versus 134.25±6.47 minutes for Group-L (*p*<0.001). The mean total dose of rescue analgesia required 24 post-procedures due was 3.09±12.8 mg in Group-M versus 42.00±14.83 mg in Group-L (*p*=0.066).

Post-operative pain scores assessed on the visual analog scale showed median pain scores 1 hour post-surgery at 3.00 (IQR=1.00) in Group-M versus 2.00 (IQR=1.00) in Group-L (*p*=0.353). The same scores assessed at 3 hours were 3.00 (IQR=0.00) in Group-M versus 3.00 (IQR=1.00) in Group-L (*p*<0.001). The final assessment of pain scores at 6 hours showed median pain scores of 3.00 (IQR=0.00) in Group-M versus 3.00 (IQR=1.00) in Group-L (*p*=0.154) (Table-II).

Table-II: Comparison of Operative Parameters Between Both Groups (n=110)

Variable(s)	Group-M (n=55)	Group-L (n=55)	*p*-value
Duration of Surgery (Minutes)	129.44±7.21	128.91±6.46	0.687
Mean Time to First Dose Rescue Analgesia (Minutes)	123.76±11.94	134.25±6.47	<0.001
Total Dose of Analgesia Used In 24 Hours (Mg)	37.09±12.8	42.00±14.83	0.066
Median Postoperative Pain Scores on VAS			
1 Hour Post-Surgery	3.00 (IQR=1.00)	2.00 (IQR=1.00)	0.353
3 Hours Post-Surgery	3.00 (IQR=0.00)	3.00 (IQR=1.00)	<0.001
6 Hours Post-Surgery	3.00 (IQR=0.00)	3.00 (IQR=1.00)	0.154

DISCUSSION

The findings of our study concluded that the mean time required to request first rescue analgesia when pain scores reached >4 was more for the Lignocaine group than the Magnesium Sulfate group. This study was carried out in our institute to look for alternatives to opioids as analgesics in individuals suspected to have complications due to their co-morbidities. Asthma is one of the most common respiratory co-morbid along with chronic obstructive pulmonary disease (COPD) presenting in the pre-anesthesia clinic for surgical fitness.[12] The bronchospasm, mucous plugging, and respiratory distress associated with asthma are triggered per-operatively by many factors, the most common being drugs administered with muscle relaxants and opioids being the major drug groups.[13] Other causes include hypoxia, inadequate depth of anesthesia, underlying infection, and specifically pneumoperitoneum with CO2 affecting the lung mechanics in case of laparoscopic cholecystectomy.[3] It would then be advantageous to look for alternative drug classes associated with minimal or no histamine release, broncho dilatory effects, and membrane stabilizing effects while being satisfactory analgesics either alone or in combination with other safe drugs for asthmatics. This would result in between post-operative recovery and early discharge time resulting in excellent patient compliance and satisfaction.

Our study concluded that the mean time required to request first rescue analgesia when pain scores reached >4 was more for the Lignocaine group than the Magnesium Sulfate group, however, on a clinical basis, even though the results were statistically significant, they were clinically not substantial to recommend one drug over the other. The clinical comparability seen in our study was in line with studies done by Jain *et al.*,[14] and M Toleska *et al.*[15] Both these studies concluded comparable results for both

drugs when assessed clinically with no difference in the analgesic efficacy of Lignocaine and Magnesium. Our study added intravenous Acetaminophen as an adjunct so that may have been a factor in the slightly more profound effect seen in one of the groups. Further studies are needed on how intravenous Acetaminophen may affect the efficacy of these non-opioid drugs. Moreover, in conjunction with the first rescue dose, the total amount of supportive analgesia required in the first 24 hours after surgery was comparable between both groups with no advantage of one drug over the other when used in combination with IV Acetaminophen. The same was reported in studies by Eftekhariyazdi *et al.*,[16] and Toleska *et al*.[17]

Our study also showed comparable results in median pain scores assessed post-surgery. The scores were in the ranges of none to mild pain experienced by the patients and score assessment was done at 1-,3- and 6- hours post-surgery. The results showed an excellent post-operative analgesic effect of both drugs. It is postulated that both drugs act as an analgesic by several mechanisms, but indirect sympathetic inhibition remains the dominant effect resulting in analgesia as well as anxiolysis. Results done to assess pain scores by JiJo *et al.*,[18] and N Jain *et al.*,[14] were in line with the results of our study as well.

There has been renewed interest in our local demographic area to use non-opioid analgesics for pain control in surgeries where extreme pain is not an issue. Data research is still scarce on the subject but studies have been done on the analgesic efficacy of Magnesium and Lignocaine by Azam *et al.*,[19] and also assessing their response to blunt stress by Khalid *et al*.[20] All these studies prove the good role of these agents as adjuvants analgesics and sympatholytic. The study recommends the use of intravenous Magnesium Sulfate and intravenous Lignocaine as good analgesics and adjuvants to NSAIDs in asthmatic patients.

CONCLUSION

We conclude that both intravenous Magnesium Sulfate and intravenous Lignocaine provide satisfactory analgesia with comparable and decreased post-operative pain scores in asthmatic patients.

Conflict of Interest: None.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SH & GS: Data acquisition, data analysis, critical review, approval of the final version to be published.

MAH & SH: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

NIZ & MAS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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