Archives of Anesthesiology and Critical Care (Autumn 2022); 8(4): 310-317.

Available online at http://aacc.tums.ac.ir

Research Article

Comparison of Analgesic Effects of Intravenous and Intraperitoneal Magnesium Sulphate in Laparoscopic Cholecystectomy: A Prospective Randomized Controlled Study

*Ankit Kansal[1], Dinesh Kataria[2], Shankey Garg[3], Swati Taneja[4], Shalvi Mahajan[3]**

[1]*Department of Anesthesia, ESIC Model Hospital, Ludhiana, India.*

[2]*Department of Anesthesia and Critical Care, Fortis hospital , Mohali, India.*

[3]*Department of Anesthesia and Critical Care, PGIEMR, Chandigarh, India.*

[4]*Department of Anesthesia and Critical Care, GMCH-32, Chandigarh, India.*

ARTICLE INFO

Article history:
Received 20 January 2022
Revised 19 February 2022
Accepted 06 March 2022

Keywords:
Analgesia;
Intravenous;
Intraperitoneal;
Laparoscopic cholecystectomy;
Magnesium sulphate

ABSTRACT

Background: Postsurgical pain following laparoscopic cholecystectomy is often associated with delayed recovery and discharge from the hospital. Magnesium sulphate as an adjuvant has shown a potential role as an anti-analgesic drug perioperatively. However, the data on the effectiveness and safety of magnesium sulphate delivered via two distinct routes (intravenous and intraperitoneal) for postoperative pain management is scant.

Methods: This prospective randomized controlled trial was conducted on 80 adult patients. Group A (n=40) received 30ml intravenous magnesium sulphate(50mg/kg) and 30ml 0.25% bupivacaine intraperitoneal infiltration. Group B (n=40) received 30ml intraperitoneal infiltration of magnesium sulphate(50mg/kg) along with 0.25% bupivacaine and 30ml intravenous 0.9% normal saline infusion. Postoperative pain-free duration, pain scores (visual analog score), need of rescue analgesia, intraoperative hemodynamics and postoperative complications were noted.

Results: The Visual analogue scores at 1,2,4 and 6 postoperative hours were 1.75±0.78, 1.33±0.66, 0.60±0.50, 0.45±0.55 in Group B and 2.13±0.61, 1.65±0.62, 1.28±0.88, 0.73±0.51 in Group A respectively (P-value-0.02,0.03,0.00 and 0.02). The time of the first request for rescue analgesia in Group A was 37.09± 5.54 and in Group B 52.00±4.30 (P value-0.00). Mean heart rate, systolic and diastolic blood pressure were significantly lower in Group A compared to Group B (P-value<0.05). Extubation and emergence time was significantly higher in group A compared to Group B (P-value -0.00). The Abbreviated mental test (AMT)-4 cognition scores were similar in both groups while Alert, Voice, Pain and Unresponsive (AVPU) sedation score was higher at the first postoperative hour in Group A (1.30± 0.46) compared to Group B (1.10 ± 0.30) (P value- 0.026).

Conclusion: Intraperitoneal magnesium is a safe and efficient means of controlling postoperative pain. Additionally, it decreases the time required for emergence and extubation as compared to intravenous delivery. Intravenous magnesium has better hemodynamic control in perioperative period.

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: drshalvimahajan@gmail.com

Laparoscopic cholecystectomy is commonly performed as ambulatory surgery. Postoperative pain following laparoscopic cholecystectomy has a variable course with potentially harmful effects. The most intense pain was seen on the day of surgery and pain subsequently declines over 3-4 days [1]. Opioids form the basis of perioperative pain management. However, they have several unwanted side effects. Thus, the notion of multimodal analgesia was proposed for laparoscopic cholecystectomy more than two decades ago in order to facilitate quick recovery and early departure from the hospital [2-4]. The combination of opioids with non-opioids in multimodal analgesia provides additive or synergistic analgesic action along with less opioid-related side effects.

Several non-opioid antinociceptive drugs are nonsteroidal anti-inflammatory drugs (NSAIDs), NMDA antagonists (ketamine, magnesium sulphate), local anesthetic agents (lignocaine), gabapentenoids, Alfa-2 agonists (dexmedetomidine) along with the central neuraxial block, regional blocks, and surgical wound infiltration form pillars of multimodal analgesia [5-6]. Currently, Paracetamol and other NSAIDs administration is a well-accepted concept [7]. Local anesthetic agents when administered intraperitoneally have been found to decrease postsurgical pain following laparoscopic cholecystectomy [8].

Magnesium sulphate, a non-competitive NMDA antagonist, has been proven in animal and human pain models to have antinociceptive properties.4 Various authors have employed magnesium sulphate as a component of multimodal analgesia to control perioperative pain after laparoscopic cholecystectomy through different routes, including intravenous and intraperitoneal [9-12]. However, we were unable to locate any study comparing magnesium sulphate analgesic and hemodynamic effects via intravenous and intraperitoneal routes. Thus, the study was planned to assess the effectiveness and safety of magnesium sulphate in relieving postoperative pain via two distinct routes, intravenous and intraperitoneal. Primary objective of the study was to compare perioperative analgesic efficacy of magnesium sulphate administered by two different routes. Secondary objective was assessment of hemodynamics parameters and the adverse side effects of magnesium sulphate if any in either group.

Methods

After institutional ethics committee approval, a prospective, randomized, double-blinded study was conducted in the department of anaesthesia and intensive care between August 2018 and September 2019.

Study Participants: The research enrolled 80 patients aged 18 to 65 years with an ASA I or II status who were scheduled for laparoscopic cholecystectomy. Written informed consent was obtained from all patients before the enrollment in the study. Patients with coronary heart disease, deranged renal or hepatic function, pregnancy, obesity, history of drug allergy to magnesium, psychiatric disorder, cognitive disorder, peripheral neuropathy such as diabetic neuropathy, moderate to severe painful condition unrelated to the surgery, chronic alcoholism, already on calcium channel blockers, beta-blockers or taking magnesium were excluded from the study. Intraoperatively, complicated laparoscopic cholecystectomies converted to open cholecystectomy were also excluded.

A complete pre-anesthetic evaluation was carried out. All those patients who agreed to participate in the study were educated about the visual analog scale (VAS) for pain assessment. In addition, Preoperative cognition status was assessed using a basic test of cognition i.e. AMT-4 score. The patients were kept nil per oral for 6 hours before surgery and premedication of alprazolam 0.25 mg tablet and tablet ranitidine 150mg was given 2 hours before surgery according to institutional protocol.

Randomization and Blinding

Patients were randomized using a computer-generated random number table. Opaque sealed envelope technique was used for concealment and subsequently, envelopes were opened just before shifting the patient inside operation theatre. The anesthesia resident (who collected data), operating surgeon, and the patient all were blinded to the administered study drug. Two coded syringes were prepared and labeled by a senior anesthetist, along with a date. Eighty patients who were randomly assigned to one of two groups:

Group A: Received intravenous magnesium sulphate and intraperitoneal 0.25% bupivacaine.

Group B: Received intraperitoneal magnesium sulphate with 0.25% bupivacaine and intravenous 0.9% saline.

Study Drug Preparation

Two 50ml syringes were loaded for each patient and were labeled as intravenous and intraperitoneal depending upon the group allocation.

For group A: One syringe contained 30ml of magnesium sulphate according to 50mg/kg up to a maximum of 2g for intravenous administration and the other syringe contained 30ml of 0.25% bupivacaine for intraperitoneal administration (maximum allowable dose of bupivacaine- 2mg/kg).

For the group B: One syringe was filled with 30ml of the solution containing magnesium sulphate according to 50mg/kg (maximum-2g) along 0.25% bupivacaine (maximum allowable dose of bupivacaine- 2mg/kg) for intraperitoneal administration and the other syringe was filled with 30 ml of 0.9% saline for intravenous administration. The contents of the syringe were disclosed to the investigator only after the conclusion of data collection.

Anesthesia Protocol

On arrival of the patient in the operation theatre, routine intra-operative monitoring (pulse oximetry, non-invasive

blood pressure and 5-lead ECG) were established. Neuromuscular monitoring was attached. A balanced salt solution was started intravenously @2ml/kg/hour and palonosetron 75mcg was administered. Fentanyl (2mcg per kg body weight) was administered intravenously. Anesthesia induction was done with propofol (titrated to loss of response to verbal commands). After confirming bag and mask ventilation, injection rocuronium (0.6 mg/kg) given and the trachea was intubated with suitable sized endotracheal tube, once the Train of four (TOF) score was zero. Anesthesia was maintained with oxygen/ air/isoflurane with target minimum alveolar concentration (MAC) 1-1.2. End-tidal carbondioxide (ETCO2) was kept between 35–40 mmHg by adjusting minute ventilation. After intubation, 30ml intravenous study solution was injected @150ml/hour before trocar placement.

After induction of anesthesia and infusion of intravenous study solution, pneumoperitoneum was created by a surgeon with carbondioxide insufflation to maintain intra-abdominal pressure between 12 and 14 mmHg throughout the surgical procedure. Then, 30ml of intraperitoneal study solution was instilled by the surgeon before starting surgical dissection.

After the creation of pneumoperitoneum and intraperitoneal drug instillation, the patient was positioned in reverse Trendelenburg position with the operating table tilted to the left to optimize the laparoscopic view for the surgeon.

The analgesia was maintained with intravenous fentanyl (0.5mg/kg) intraoperatively whenever there was a 20% rise in the baseline blood pressure or heart rate. The neuromuscular block was checked every 5 minutes to keep a TOF score of 2. Paracetamol 1gram intravenous was administered to all patients at the time of removal of the gall bladder. Anesthesia was discontinued at the time of skin suturing. Once a TOF score was 4, the residual effect of a neuromuscular blocking agent was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg) and with spontaneous adequate respiratory efforts, the trachea was extubated. Patients were transferred to the postoperative care area once fully awake and respond to vocal commands.

After shifting the patient to a recovery room, the time was taken as zero minutes. Inj. Tramadol 50 mg intravenously was given once the patient has VAS greater than 3 or a request for analgesia was made. Time of administration of the first dose of rescue analgesia and total analgesic requirement in the postoperative period was recorded.

Outcome measure- The following measures were assessed and recorded:

1.Mean VAS score during first six hours post-operatively.

2.The time to first analgesic administration in post operative period

3.Blood pressure and heart rate, measured in pre-op (baseline), before induction, after intubation, before pneumoperitoneum, every 10 minutes after pneumoperitoneum till extubation, after extubation, before shifting from operating room and every 30 minutes thereafter in the post-operative recovery ward.

4.Extubation time was defined as the time from discontinuation of isoflurane till extubation.

5.Time of emergence was defined as time to first response to a simple verbal command following discontinuation of isoflurane (eye-opening, tongue protrusion).

6.The occurrence of any adverse events, including bradypnea (respiratory rate (RR) <8bpm), desaturation SpO2 reaching 90% or less, sedation, hypotension (MAP less than 55 mmHg or less than 20% of baseline), bradycardia (heart rate less than 50/min or less than 20%of baseline), nausea, and vomiting.

7.The patient's cognition and sedation were checked preoperatively and at first, second and fourth postoperative hours using AMT-4 score and AVPU score respectively.

Statistical analysis

The data was put into an MS EXCEL spreadsheet and analyzed with the Statistical Package for Social Sciences (SPSS) 21.0. Continuous variables were reported as mean, SD, and median, whereas categorical variables were provided as number and percentage. The Kolmogorov-Smirnov test was used to determine if the data was normal. Non-parametric tests were performed if normality was refused. When the data sets were not normally distributed, the unpaired t-test/Mann-Whitney Test was used to compare quantitative variables between the two groups. The Chi-Square test/exact Fisher's test was used to compare qualitative variables. A statistically significant P-value of 0.05 was used.

Sample size calculation

The sample size was calculated by using the study done by Rania M. Ali as a template, Cohen's effect size was used to calculate the sample size of two samples with a continuous outcome variable using the analgesic consumption/ patient (mg) parameter [13]. A sample size of 80 (40 in each group) was required to detect an effect size of .99 with 80% power of the study and a two-sided alpha error of 5%.

Results

Total 80 patients participated in the study after enrollment and were analyzed (Figure1).

Baseline demographic variables and surgical factors were identical in two groups (Table1).

Figure 1- CONSORT Flow Diagram

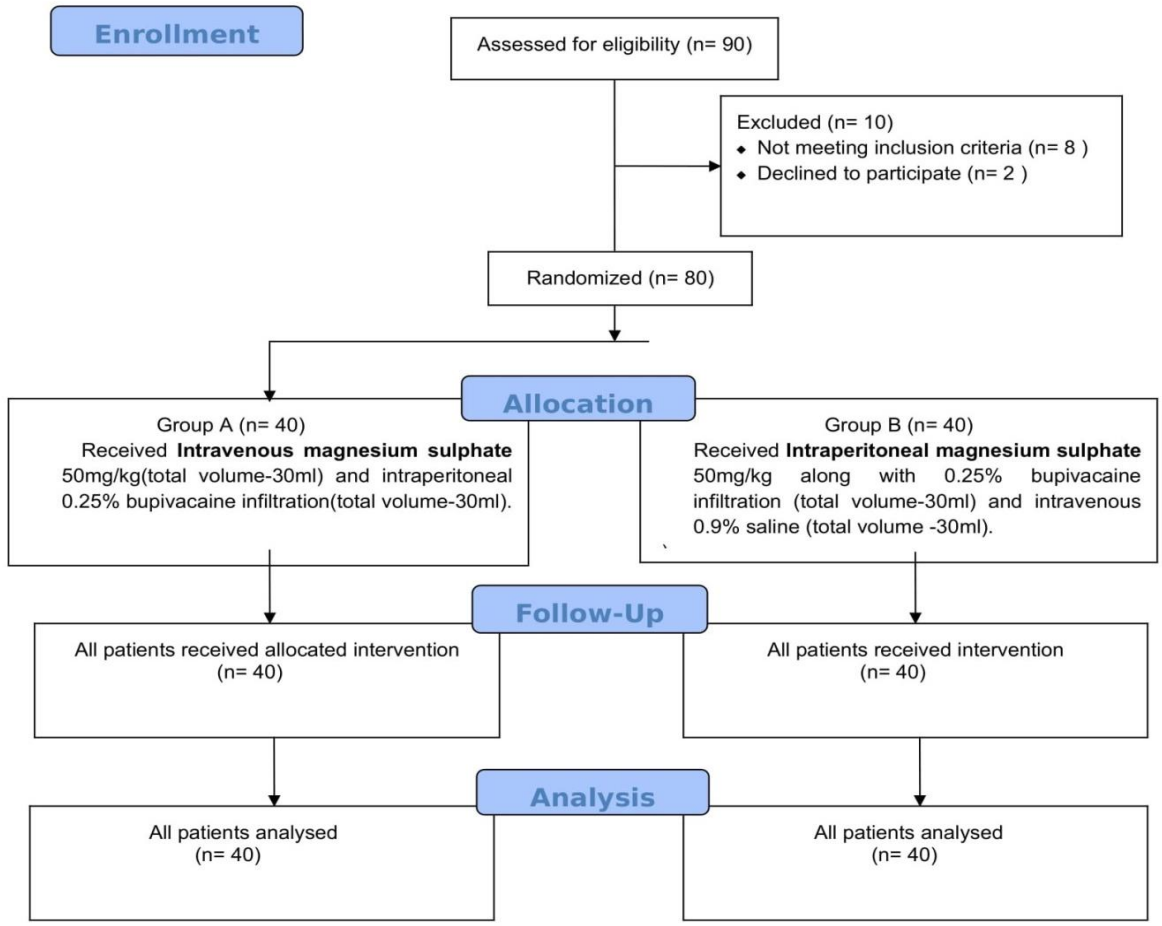


Table 1- Comparison of Base Line Characters and Surgical Factors in Both the Groups

	Group A (mean ± SD)	Group B (mean ± SD)	P value
Age (yrs)	39.13±10.28	40.25±10.90	0.636
Height(cm)	160.05±5.87	161.03±6.77	0.493
Weight(kg)	68.55±11.14	67.30±11.96	0.630
BMI	26.73±3.97	25.84±3.47	0.289
Gender			0.556
Male	6(15%)	8(20%)	
Female	34(85%)	32(80%)	
ASA			0.446
1	28(70%)	31(78%)	
2	12(30%)	9(23%)	
Duration of surgery	48.68±10.32	48.78±14.37	0.972

Pain Parameters

The mean VAS scores were significantly lower in group B than in group A during the first six hours postoperatively (P value <0.03). Total analgesic (fentanyl) requirement intra-operatively in group A was 140.75±24.33 micrograms and in group B was 134.63±1.47 micrograms. Although the mean analgesic requirement in group B was less than group A, it was not statistically significant (P value-0.324). The mean time of the first request for analgesia in group A was 37.09 ± 5.54 minutes and in group B was 52.00±4.3 minutes and was statistically significant (P value-0.000). Postoperative analgesic requirement was significantly lower in group B (6.25±16.75 mg) than in group A (17.50 ± 31.11 mg) (P value-0.04) (Table 2).

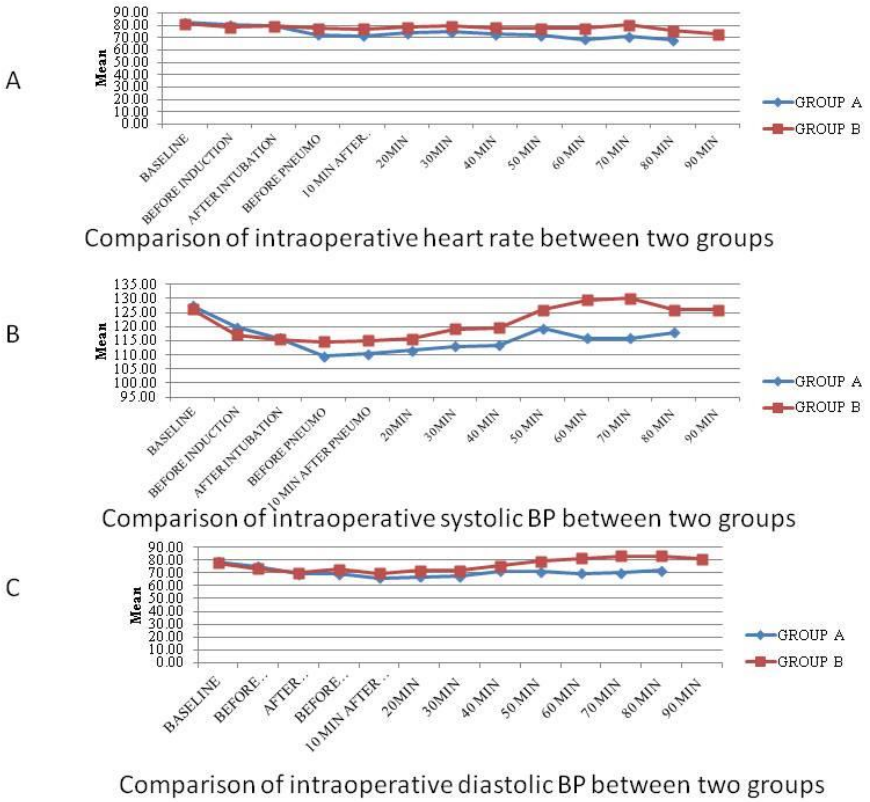
Table 2- Comparison of Pain Score and Analgesic Requirement in Both the Groups

	Group A (mean ± SD)	Group B (mean ± SD)	P value
VAS at 1 hr	2.13± 0.61	1.75± 0.78	0.018
		1.33±	0.04
VAS at 2 hr	1.65± 0.62	0.66	
		0.60 ±	0.36
VAS at 4 hr	1.28 ± 0.88	0.50	
		0.45±	0.04
VAS at 6 hr	0.73± 0.51	0.55	
Time of first request for analgesic	37.09± 5.54	52.00±4.30	0.000
No of analgesic requests in post op			0.119
0	29(73%)	35(88%)	
1	8(20%)	5(13%)	
2	3(8%)	0(0%)	
Total analgesic requirement intra op	140.75± 24.33	134.63± 21.47	0.324

Hemodynamic Parameters

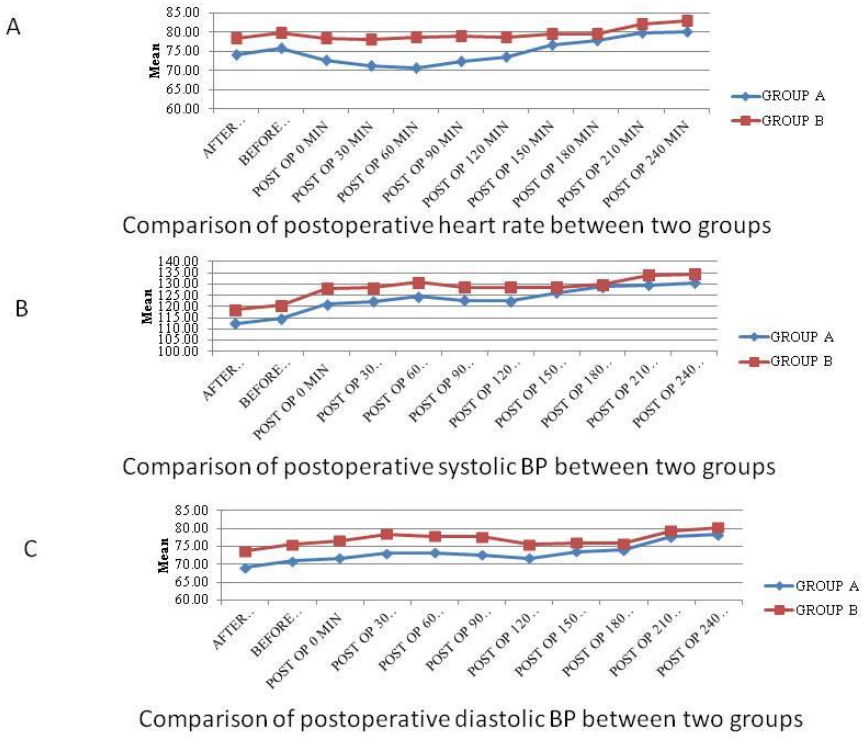
Intraoperatively, mean heart rate, systolic and diastolic blood pressures were comparable in both groups at baseline, before induction and after intubation. However, significantly lower values were recorded in group A compared with group B before pneumoperitoneum, at 10 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes, 60 minutes, 70 minutes after incision ($p<0.05$) (Figure 2).

Figure 2- comparison of intraoperative hemodynamics in both groups



Postoperatively, trends of lower values persisted in group A compared to group B. However, significantly lower values were seen only during the initial 2 hours in the postoperative period with respect to mean heart rate, systolic blood pressure and diastolic blood pressure ($p<0.05$) (Figure 3).

Figure 3- comparison of post operative hemodynamics in both groups



Other Parameters

The mean requirement of the neuromuscular blocking agent in group A was 43.13 ± 6.86 mg and in group B was 41.25 ± 7.05 mg and was comparable in both the groups. Mean extubation time in group A was 16.55 ± 3.13 minutes and in group B was 12.83 ± 3.55 minutes. Mean time of emergence in group A was 13.00 ± 2.41 minutes and in group B was 9.85 ± 2.97 minutes. Mean emergence time and extubation time was significantly higher in group A as compared to group B (P-value <0.04). The incidence of postoperative nausea and vomiting was similar in both groups. AMT-4 cognition score in group A and group B was 4, both pre-operatively and post-operatively. There was no significant difference in the AMT-4 cognition scores of both groups. The mean AVPU sedation score in group A was significantly higher than group B at the first hour. There was no significant difference in the AVPU sedation scores of both groups after the first hour (Table 3).

Table 3- Avpu Sedation Scores in Both the Groups

	Group A (mean ± SD)	Group B (mean ± SD)	P value
Sedation at 1 hr	1.30± 0.46	1.10 ± 0.30	0.026
Sedation at 2 hr	1.00 ± .000	1.00 ± .000	1.000
Sedation at 4 hr	1.00 ± .000	1.00± .000	1.000
Sedation at 6 hr	1.00 ± .000	1.00± .000	1.000

Discussion

Laparoscopic cholecystectomy is one of the most common surgical procedures. JA Lujan et al compared the results of laparoscopic cholecystectomy with open cholecystectomy in the treatment of acute cholecystitis and found that laparoscopic cholecystectomy has low rate of complications, leads to shorter hospital stay, and offers the patient a more comfortable postoperative period than open cholecystectomy [14]. However, intensity of pain felt by patient postoperatively in lap cholecystectomy is higher than in open cholecystectomy [15]. Primary objective of this study was to compare perioperative analgesic efficacy of magnesium sulphate administered by intravenous and intraperitoneal routes. In current study, we found that postoperative VAS score and time

of the first request for rescue analgesia were significantly lower in patients who received intraperitoneal magnesium compared to the intravenous magnesium. However, the amount of intraoperative opioids used was similar in both the groups. Also, hemodynamic parameters were significantly lower intravenous magnesium before creation of pneumoperitoneum, till end of surgery and also in initial 2hours following extubation in postoperative period.

Adequate pain treatment in the postoperative period provides comfort to the patients, speeds up their recovery and allows them to leave the hospital soon. Magnesium sulphate, which may be delivered via a variety of routes, is one of the adjuvant analgesics that have showed promise in lowering postoperative pain. The first clinical trial done by Tramer MR et al, supported that perioperative magnesium sulphate was allied with decreased analgesia, lesser analgesic requirement and improved sleep quality in the post-operative period [7].

O Mentes et al evaluated the role of intravenous magnesium sulphate (50mg/kg) in reducing post-operative pain in laparoscopic cholecystectomy [8]. SK Maharjan et al used a similar dose of magnesium sulphate intraperitoneally i.e. 50mg/kg and demonstrated better the post-operative pain control in laparoscopic cholecystectomy [16]. However, to the best of our knowledge, no study has compared the analgesic effect of magnesium through two different routes i.e. intravenous and intraperitoneal. Therefore, we chose a 50mg/kg dose of magnesium sulphate for both intravenous and intraperitoneal administration in our study and compared analgesic and hemodynamic effects via two different routes.

Intraperitoneal magnesium sulphate, which inhibits both central and peripheral NMDA receptors, reduces post-operative pain more than intravenous magnesium sulphate, which only blocks central receptors. The anti-nociceptive effect of intraperitoneal magnesium sulphate was also observed in a study by SK Maharjan et al, who concluded that combining bupivacaine and magnesium sulphate into the peritoneal cavity at the end of laparoscopic surgery results in better pain control and less analgesic consumption in the first 24 hours compared to the sole bupivacaine group [16].

In our study we found that the heart rate, systolic blood pressure and diastolic blood pressure were significantly lower in patients who received intravenous magnesium as compared to those who received intraperitoneal magnesium. D.Jee et al found that there was a significant association between pneumoperitoneum and stress response due to increase in catecholamines and vasopressin [17]. Dar et al mentioned in their research that intravenous magnesium sulphate attenuates the hemodynamic stress response in laparoscopic abdominal surgeries and provides hemodynamic stability during pneumoperitoneum created for laparoscopic surgery [18-19]. The results of our study are in line with previous research. The decreased the hemodynamic stress response could be due to the anti-adrenergic effects of magnesium sulphate whose intravenous infusion was given before creation of pneumoperitoneum during laparoscopic surgery. Magnesium sulphate inhibits release of catecholamine from peripheral adrenergic terminals and adrenal medulla and also, acts as a direct catecholamine receptor blocker.

Magnesium potentiates neuromuscular block by competing with calcium in presynaptic nerve terminals and inhibits acetylcholine release. We observed that the time of extubation and the time of emergence were significantly higher in patients who received intravenous magnesium as compared to those who received magnesium intraperitoneally. In their study, C. Czarnetzki et al discovered that intravenous magnesium sulphate given 15 minutes before propofol anaesthesia shortened the start time of rocuronium neuromuscular blockade by 35% and prolonged recovery time by roughly 25% [20].

There was no significant difference in the AMT-4 cognition scores of both the group both preoperatively and till 4 hours postoperatively. The mean AVPU sedation score was significantly higher at the first hour in patients who received intravenous magnesium than patients who received magnesium via the intraperitoneal route. There was no significant difference in the AVPU sedation scores of both groups after the first hour. No other adverse effect was seen in both groups.

Limitations: Individuals with ASA I and II were enrolled in the trial. Individuals with heart illness, hepatic or renal pathology, or patients who actually needed stress response attenuation were excluded. It was a single-center research, the results must be titrated for generality and serum magnesium levels were not measured in this investigation.

Conclusion

Magnesium given intraperitoneally is a safe, and more effective in reducing postoperative pain as compared to intravenous route following laparoscopic cholecystectomy. Intraperitoneal magnesium allows patient to be extubated and emerge from surgery sooner compared to the intravenous route. However, better hemodynamic control was seen with intravenous magnesium. None of the group had significant adverse effects. Future multicentric studies are needed with large sample size, cardiac, hepatic and renal disease patients.

References

[1] Michaloliakou C, Chung F, Sharma S. Preoperative multimodal analgesia facilitates recovery after ambulatory laparoscopic cholecystectomy. Anesth

Analg. 1996; 82(1):44-51.
[2] Layzell M. Current interventions and approaches to postoperative pain management. Br J Nurs. 2008; 17(7):414-9.
[3] Wills VL, Hunt DR. Pain after laparoscopic cholecystectomy. Br J Surg. 2000; 87(3):273-84.
[4] Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg. 2001; 167(2):84-96.
[5] Dahl JB, Møiniche S, Kehlet H. Wound infiltration with local anaesthetics for postoperative pain relief. Acta Anaesthesiol Scand. 1994; 38(1):7-14.
[6] Soave PM, Conti G, Costa R, Arcangeli A. Magnesium and anaesthesia. Curr Drug Targets. 2009; 10(8):734-43.
[7] Tramer MR, Schneider J, Marti RA, Rifat K. Role of magnesium sulfate in postoperative analgesia. Anesthesiology: Anesthesiology. 1996; 84(2):340-7.
[8] Mentes O, Harlak A, Yigit T, BALKAN A, Balkan M, Cosar A, et al. Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. Acta Anaesthesiol Scand. 2008; 52(10):1353-9.
[9] Hwang JY, Na HS, Jeon YT, Ro YJ, Kim CS, Do SH. IV infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia. Br J Anaesth. 2010; 104(1):89-93.
[10] Alavi SM, Baharestani B, Farsad BF, Bakhshandeh H, Babaee T, Sdeghpur A, et al. Intraoperative magnesium sulfate can reduce narcotic requirement after coronary bypass surgery. Iranian Heart Journal. 2011;12(1):6-11.
[11] Haryalchi K, Ghanaie MM, Yaghoubi Y, Milani F, Faraji R. An assessment of changes in the magnesium level during gynecological abdominal surgeries. J basic clin reprod sci. 2013;2(2):110-4.
[12] Shah PN, Dhengle Y. Magnesium sulfate for postoperative analgesia after surgery under spinal anesthesia. Acta Anaesthesiol Taiwan. 2016; 54(2):62-4.
[13] Ali RM, Rabie AH, Elshalakany NA, El Gindy TM. Effect of intraperitoneal magnesium sulfate on hemodynamic changes and its analgesic and antiemetic effect in laparoscopic cholecystectomy. Ain-Shams J Anaesthesiol. 2015; 8(2):153-9.
[14] Lujan JA, Parrilla P, Robles R, Marin P, Torralba JA, Garcia-Ayllon J. Laparoscopic cholecystectomy vs open cholecystectomy in the treatment of acute cholecystitis: a prospective study. Arch Surg. 1998; 133(2):173-5.
[15] Ekstein P, Szold A, Sagie B, Werbin N, Klausner JM, Weinbroum AA. Laparoscopic surgery may be associated with severe pain and high analgesia requirements in the immediate postoperative period. Ann Surg. 2006; 243(1):41-6.
[16] Maharjan SK, Shrestha S. Intraperitoneal magnesium sulphate plus bupivacaine for pain relief after laparoscopic cholecystectomy. J Kathmandu Med Coll. 2012; 1(1):21-5.
[17] Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. Br J Anaesth. 2009; 103(4):484-9.
[18] Dar SA, Gupta DD, Deopujari RC, Gomes P. Effect of magnesium sulphate on attenuation of hemodynamic stress responses during laparoscopic abdominal surgeries. J Anesth Clin Res. 2015; 6(590):2.
[19] Paul S, Biswas P, Bhattacharjee DP, Sengupta J. Effects of magnesium sulfate on hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. Anesth Essays Res. 2013; 7(2):228.
[20] Czarnetzki C, Lysakowski C, Elia N, Tramer MR. Time course of rocuronium-induced neuromuscular block after pre-treatment with magnesium sulphate: a randomised study. Acta Anaesthesiol Scand. 2010; 54(3):299-306.