WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 12, 650-666. Research Article ISSN 2277– 7105

# EFFECTS OF INTRAVENOUS MAGNESIUM SULPHATE ON POSTOPERATIVE ANALGESIA IN PATIENTS UNDERGOING MAJOR ABDOMINAL SURGERIES.

**Aabid Hussain Mir(MD)[1], Velayat Nabi Buchh (MD)[1], Farooq Ahmad Ganie(MS,MCh)[2]*, Ajaiz Rasool(MD)[1], Zaffer Iqbal (MD)[1], Abida Yousuf(MD)[1], Rohey Jan (MD)[1]**

Department of Anaesthesiology and Critical Care and Department of Cardio Vascular and Thoracic Surgery Sheri-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir, India.

Article Received on
30 Sept. 2016,
Revised on 20 Oct. 2016,
Accepted on 09 Nov. 2016
DOI: 10.20959/wjpr201612-7401

***Corresponding Author**
**Dr. Farooq Ahmad Ganie**
Department of cardio vascular and thoracic surgery Sheri-Kashmir Institute of Medical Sciences, Soura, Srinagar, Kashmir, india.

## ABSTRACT

**Background and objectives:** Magnesium has potential as antinocciceptive molecule. These effects are primarily based on physiological calcium antagonism,. Our aim of this study was to evaluate the effects of Magnesium sulphate on quality and potency of postoperative analgesia, postoperative analgesic requirements in patients undergoing major abdominal surgeries under general anaesthesia. We also evaluated its effect on haemodynamic parameters, urine output, postoperative nausea, vomiting and shivering.

**KEYWORDS:** postoperative, analgesia, intravenous, magnesium sulphate, pain, intrabdominal, general anaesthesia.

**CONCLUSION** Magnesium improves quality and potency of postoperative analgesia and decreases postoperative analgesic consumption. It also decreases incidence of postoperative shivering, however it has not any significant effect on hemodynamics, urine output, postoperative nausea and vomiting.

## INTRODUCTION

Major abdominal surgeries are usually accompanied by moderate to severe pain after surgery and adequate postoperative pain management is important for early functional recovery. Uncontrolled postoperative pain may activate sympathetic nervous system and thereby

contribute to morbidity and mortality. the voltage-dependent regulation of calcium influx into the cell, and non-competitive antagonism of N-methyl-D-aspartate (NMDA) receptors[1,2,3] Sympathetic activation may increase myocardial oxygen consumption which may be important in the development of myocardial ischemia and infarction.[4,5] Painful surgical incisions involving the upper abdomen result in reflex mediated increase in tone in abdominal muscles during expiration and decrease in diaphragmatic functions. The result is reduced pulmonary compliance, muscle splinting and inability to breathe deeply or cough forcefully and in some cases hypoxia, hypercarbia, retention of secretions, atelectasis and pneumonia. Suprasegmental reflex responses to pain results in increased sympathetic tone, hypothalamic stimulation, increased catecholamine and catabolic hormone secretion and decreased secretion of anabolic hormones. Multimodal analgesia is nowadays practised for the adequate pain relief including oral, intravenous, transdermal analgesics andregional blocks. In this study we will evaluate the effect of supplemental intravenous magnesium sulphate on postoperative analgesia.

Magnesium is the fourth most plentiful cation in our body. It has anti nociceptive effects in animal and human models of pain. It has been mentioned in a systematic review that it may be worthwhile to further study the role of supplemental magnesium in providing perioperative analgesia, because this is a relatively harmless molecule, is not expensive and also because the biological basis for its potential anti nociceptive effect is promising. These effects are primarily based on physiological calcium antagonism, that is voltage-dependent regulation of calcium influx into the cell, and non-competitive antagonism of N-methyl-D-aspartate (NMDA) receptors.[1,2,3] Neurophysiological studies have demonstrated that Mg is a physiological and pharmacological blocker of NMDA receptors in neuronal tissue. As the role of the NMDA receptor in pain perception has become apparent, there is increasing use of Mg for the management of both acute[6] and chronic pain.[7] Magnesium inhibits calcium entry into neuronal cells at a variety of calcium channels including acting as an NMDA antagonist. Mg penetrates the blood brain barrier poorly. Parenterally administered drug has little CNS depressant effects. Its anticonvulsant action in management of pre-eclampsia may be due to cerebral vasodilator action. The property of blocking NMDA receptors have raised a variety of possibilities for the use of magnesium as a neuroprotective agent in a number of forms of neurological injury[8]Magnesium is called “nature’s physiological calcium channel blocker”.[9] Calcium channel blockers have shown antinocciceptive effects in animals.[10,11] and morphine potentiation in patients with chronic pain.[12]. NMDA receptor antagonists can

prevent the induction of central sensitization due to peripheral nociceptive stimulation and abolish the hypersensitivity once it is established.[13]. In vitro data indicate that extracellular magnesium protects cerebellar neurons against the toxicity of the NMDA agonist glutamate.[14].It has been suggested that substances with calcium channel blocking effects and NMDA antagonists could play a role in prevention of pain and treatment of established pain states.[10,13,15]. In clinical trials, magnesium treatment improved symptoms of primary dysmenorrhea [16,] and had a beneficial effect in patients affected by menstrual migraine[17], or headache.[18]

## METHODS

This prospective, double blind placebo controlled randomised study was undertaken over a period from August 2013 to April 2015. Two hundred ASA I and II patients aged between 18 and 65 years undergoing major abdominal surgeries like gastrectomy, pancreatico-duodenectomy, hysterectomy, hysterectomy with salpingo-oophorectomy, hemicolectomy, colectomy, low anterior resection, abdomino-perineal resection & CBD exploration were enrolled into the study. They were explained on the use of visual analogue scale (VAS starting from 0, no pain, to 100, worst pain imaginable) [19,20,21] for evaluation of pain, during the preoperative visit. Patients with allergy to magnesium salts, cardiovascular, hepatic ,or renal dysfunction, atrioventricular conduction disturbance, neuromuscular diseases, opioid or analgesic abuse and patients who were on calcium channel blockers were excluded from the study.Both the patient and the anaesthesiologist were blinded and drugs were prepared by a person not involved in the study. Patients were randomly (sealed envelope method) assigned to one of the two groups, magnesium group (Group M, $n$=100) received 50 mg/kg of magnesium sulphate in 100 ml of isotonic saline over 10 minutes immediately before anaesthesia induction and then 15 mg/kg/hr by continuous i.v. infusion until the end of operation and saline group (Group S, $n$=100) received same volume of isotonic saline till the end of operation.

Pre anaesthetic evaluation was done for all patients and tablet Alprazolam 0.5 mg orally night before surgery was given to all the patients. Patients were advised to remain fasting for at least 8 hours prior to surgery.

Upon arrival in the operating room, standard monitoring including ECG, non-invasive arterial pressure, neuromuscular monitoring, capnography and pulse oximetrywere established. In

addition patients urine output was also monitored. A blood sample for serum Mg levels was obtained while establishing an intravenous access.

Anaesthesia was induced in both the groups with propofol 2mg/kg, morphine 100ug/kg, fentanyl 2ug/kg and atracurium 0.6mg/kg. Following induction, anaesthesia was maintained using oxygen in nitrous oxide along with isoflurane 0.6- 1.2%, with atracurium top ups as indicated by the neuromuscular monitoring (a train of four count of 2 or more). Ventilation was adjusted to maintain normocapnia. Fentanyl 25ug boluses were given intravenously for inadequate analgesia in both the groups. Inadequate analgesia was defined as an increase in mean arterial pressure or heart rate by more than 20% of preanaesthetic values.

Continuous monitoring of the patients was facilitated by multichannel monitors. Base line pulse, blood pressure, ECG, and $SPO_2$ were recorded before inducing the patient. Blood pressure, heart rate, oxygen saturation, capnography, neuromuscular blockade, urine output, electrocardiogram were monitored throughout the surgery.

Hypotension defined as 25% decrease of systolic blood pressure compared with preoperative control levels was treated with following measures:

- Rapid infusion of intravenous fluids.
- Intravenous ephedrine administered in small increments of 6mg and maximum of 30mg. Intravenous atropine was given for bradycardia (heart rate less than 50beats/min).

At the end of surgery neostigmine 60ug/kg and glycopyrollate 10ug/kg was used to reverse the residual neuromuscular block. At the same time magnesium sulphate infusion was terminated and a blood sample sent for magnesium levels. Granisetron 40 ug/kg i.v. was given as an antiemetic. Following extubation the patients were monitored in the post anaesthesia care unit and discharged when a Modified Alderette score[22,23] of >9 was achieved. VAS scores [19,20,21] were evaluated at emergence from anaesthesia and at 30 min, 2, 4, 12, 24, and 48 hours after the surgery. Magnesium levels were also checked 24 hours after surgery. Every patient admitted to PACU was monitored periodically for heart rate, blood pressure, respiratory rate, oxygen saturation and level of pain.[24]

**Recorded.**

Post-operative analgesia was provided by the in charge nurse in the form of 1.5 mg i.v. boluses of morphine with a maximum of 6mg in 4 hours. Analgesic consumption at 30 min

and at 2, 4, 12, 24, and 48 hours after surgery were recorded. In addition, episodes of shivering and postoperative nausea and vomiting (PONV) were monitored and recorded at emergence and throughout the remainder of study period.

The primary outcome of the study was postoperative analgesic consumption and the secondary outcomes monitored were number of episodes of shivering, nausea and vomiting over a period of 48 hours postoperatively.

**STATISTICAL ANALYSIS**

The study was a randomised double blind study to compare the two groups of matched patients in term of different variables under study. The repeated measurement analysis within groups was employed to compare the two groups. Also, the continuous variables were analysed with independent t-test and Wilcoxon-Mann Whitney U- test which belongs to the parametric and non-parametric categories of tests. Also, the categorical variables were analysed with chi-square test. The required sample size is 100 for each group for the study, for 80% power of study and for moderate effect size. All the results were discussed on 5% level of significance i.e, P-value less than 0.05 was considered significant.

**RESULTS**

VAS scores were lower at 0 min, 30 min, 1 hour, 2 hours, 4 hours, 12 hours, 24 hours, 48 hours in magnesium group than saline group but scores were statistically significant p-value< 0.05 at 0 min, 2, 4, 12 and 24 hours and statistically insignificant at 30 minutes and 48 hours (p-value>0.05). The 48 hour mean VAS score was lower in Magnesium group than Saline group. Comparing the two groups for 48 hours postoperatively analgesic consumption is lower in magnesium group than saline group at 30 minutes, 1 hour, 2 hours, 4 hours, 12 hours, 24 hours and 48 hours,however at 0 minutes postoperatively none of the patients received analgesia. Consumption of analgesia is statistically significant at 2 hours (p-value<0.05) and statistically non-significant at other intervals of time.Number of rescue analgesic doses was lesser in the magnesium group than the saline (control) group with 152 total doses given for saline group patients and 72 doses given to magnesium group patients with mean dose of 0.8±0.577 in magnesium group and 1.5±1.295 in saline group. Analgesic consumption was lower in saline group and was statistically significant with p-value< 0.05.

There was no significant difference between the two groups regarding hemodynamic parametres, $spO_2$, urine output and postoperative nausea vomiting. Shivering was seen in 4

patient in Group M and 24 patients in Group S which was significant which depicts administration of magnesium decreases incidence of postoperative shivering.Delayed extubation or prolonged neuromuscular blockade was not seen in any of patients.

No significant difference was found between the two groups in terms of age, gender, weight or anaesthetic time (Table 1).Hemodynamic variables were recorded at induction, 30 minutes, 1 hour, 1.5, 2, 3, 4, 12, 24 and 48 hours. There was no significant difference in haemodynamic variables (heart rate, systolic and diastolic blood pressure) during the intra- or postoperative period (Figs 1, 2 and 3). Overall perioperative (induction to 48 hours postoperatively) mean HR±SE in magnesium group was 82.696 ±1.161 and saline group was 80.012 ± 1.161 with p-value of 0.109 ( statistically insignificant).Overall perioperative (induction to 48 hours postoperatively) mean SBP ±SE in magnesium group was 119.028±1.068 and saline group was 116.008±1.068with p-value of >0.05( statistically insignificant) and overall perioperative (induction to 48 hours postoperatively) mean DBP ±SE in magnesium group was 77.360±0.456 and saline group was 79.80±0.456with p-value of >0.05 ( statistically insignificant).

A non-significant difference (p> 0.05) was observed with respect to intra- and post-operative urine output in between the two groups. Urine output from induction to 12 hours in two groups was comparable with overall mean± SE in magnesium group 255.00± 7.579 and saline group 244.92± 7.579(Fig 4).

Evaluation of pain by using Standard VAS revealed lower VAS scores in the magnesium group(mean VAS=19.029±1.008) than saline group( mean VAS= 27.600±1.008) at all intervals of time starting from 0 hours postoperatively to 48 hours postoperatively. VAS scores were lower at 0 min, 30 min, 1 hour, 2 hours, 4 hours, 12 hours, 24 hours, 48 hours in magnesium group than saline group but scores were statistically significant p-value< 0.05 at 0 min, 2, 4, 12 and 24 hours and statistically insignificant at 30 minutes and 48 hours (p-value>0.05)(Table 2). Number of rescue analgesic doses was less in the magnesium group than the saline (control) group with 152 total doses given for saline group patients and 72 doses given to magnesium group patients with mean dose of 0.8±0.577 in magnesium group and 1.5±1.295 in saline group. Analgesic consumption was lower in saline group and was statistically significant with p-value<0.05(Table 2). Comparing the two groups postoperative analgesic consumption is lower in magnesium group than saline group at all intervals of time except at 0 min where none of the patients received analgesia. Consumption of analgesia is

statistically significant at 2 hours (p-value<0.05) and statistically non-significant at other intervals of time.(Table 3 & Fig5) Serum magnesium levels were comparable in both the groups at start of surgery and 24 hours postoperatively but were increased in magnesium group in immediate postoperative period which is statistically significant (p-value<0.05)(Fig 6). A total of 28 patients from magnesium group and 36 from saline group received additional 25 ug of Fentanyl i.v.intraoperativelywhich was comparable in both groups and statistically non-significant (p-value>0.05).

Comparing postoperative PONV and hypotension, these effects were comparable in two groups and statistically non-significant (p-value >0.05). Shivering was lesser in Magnesium group as compared to Saline group and was statistically significant (p-value<0.05) (Table 4)

**Table 1.Table 1 Patient characteristics and anaesthetic time. N=100 for each group. Values shown as mean± standard deviation.**

| Variable | Magnesium group | Saline group | p-value |
|---|---|---|---|
| Age | 46.64±11.365 | 42.80±11.754 | 0.2461 |
| Male/female | 60/40 | 52/48 | 0.569 |
| Weight | 64.92 ± 6.614 | 67.00±9.452 | O.3718 |
| ASA I/II | 60/40 | 64/36 | 0.771 |
| Anaesthetic time | 153.80 ± 33.332 | 156.00± 32.146 | 0.813 |

**Table 2.Mean VAS scores in two groups.**

| Mean VAS Score ± SD at various intervals postoperatively | Magnesium group (n=100) | Saline group (n=100) | p-value |
|---|---|---|---|
| 0 hours | 12±9.574 | 20±10.00 | 0.006* |
| 30 mins | 16±9.129 | 22±9.574 | 0.28 |
| 2 hours | 22.40±14.224 | 34.40±13.868 | 0.004* |
| 3 hours | | | |
| 4 hours | 22.40±14.342 | 32.80±12.082 | 0.004* |
| 12 hours | 21.60±8.00 | 30.40±16.197 | 0.019* |
| 24 hours | 19.20±12.884 | 29.20±14.411 | 0.013* |
| 48 hours | 19.60±7.348 | 24.40±9.609 | 0.053 |
| Overall mean VAS± SE | 19.029±1.008 | 27.600± 1.008 | <0.001* |
| Total number of rescue analgesic doses | 72 | 152 | 0.014 |

SD= standard deviation, SE= standard error, *= Statistically significant

**Table 3.Comparison of the analgesic consumption by number of patients in two groups at different intervals of time.**

| Analgesic consumption at different intervals | Number of patients receiving analgesia in Magnesium group | Number of patients receiving analgesia in Saline group | Total number of patients receiving analgesia in both groups | p-value |
|---|---|---|---|---|
| 0 hours | 0 | 0 | 0 | 0 |
| 1 hours | 0 (0%) | 4(100%) | 4(100%) | 0.312 |
| 2 hour | 28(35%) | 52(65%) | 80(100%) | 0.083 |
| 4hours | 24 (40%) | 36(60%) | 60(100%) | 0.355 |
| 12 hours | 8(20%) | 32(80%) | 40(100%) | 0.034 |
| 24 hours | 20(45.5%) | 24(54.5%) | 44(100%) | 0.733 |
| 48 hours | 0 | 8 (100%) | 8 (100%) | 0.149 |

**Table 4 . Comparison of number of patients having postoperative nausea vomiting, hypotension and shivering in two groups.**

| | Magnesium group(n=100) | Saline group (n=100) | p-value |
|---|---|---|---|
| PONV | 16 | 20 | 0.713 |
| Shivering | 4 | 24 | 0.042 |
| Hypotension | 12 | 8 | 0.645 |

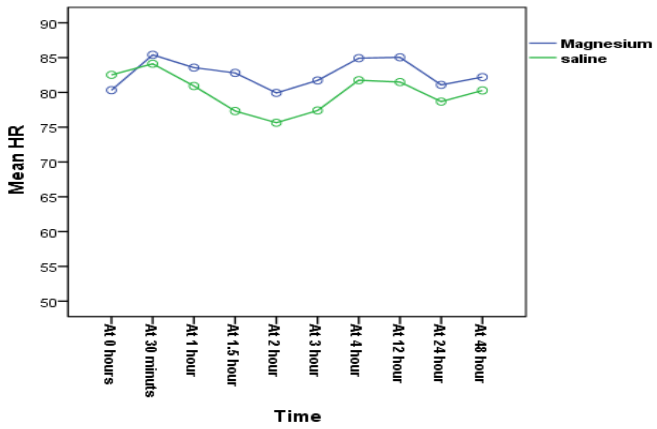


**Fig 1.Line diagram showing mean heart rate in two groups at various intervals of time. No significant difference was found between two groups during perioperative period.**

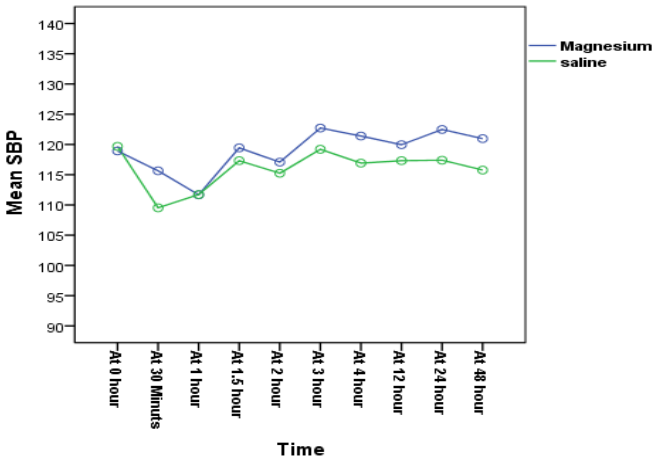


**Fig 2.Line diagram showing mean systolic blood pressure in two groups at various intervals of time. No significant difference was found between two groups during perioperative period.**

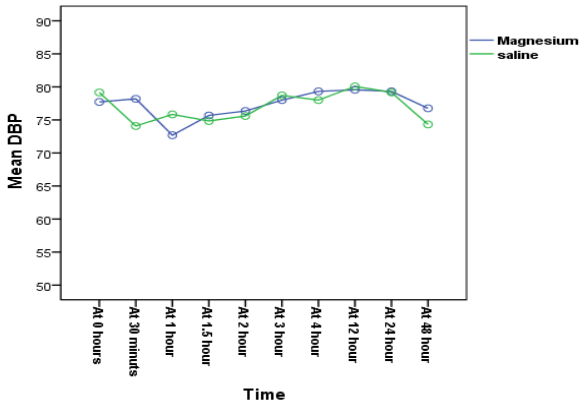


**Fig 3.Line diagram showing mean diastolic blood pressure in two groups at various intervals of time. No significant difference was found between two groups during perioperative period.**

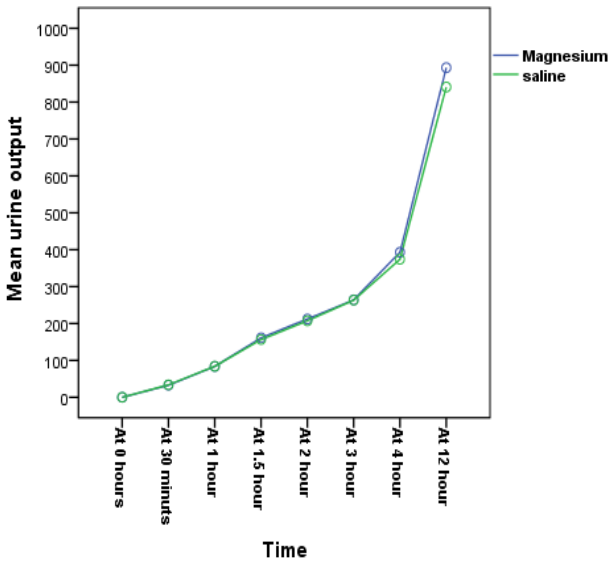


**Fig 4.Line diagram showing mean urine output in two groups at various intervals of time. No significant difference was found between two groups during perioperative period.**

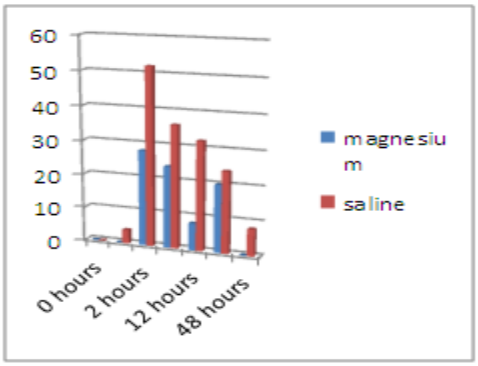


**Fig 5.Bar charts showing number of patients receiving analgesia postoperatively in two groups.**

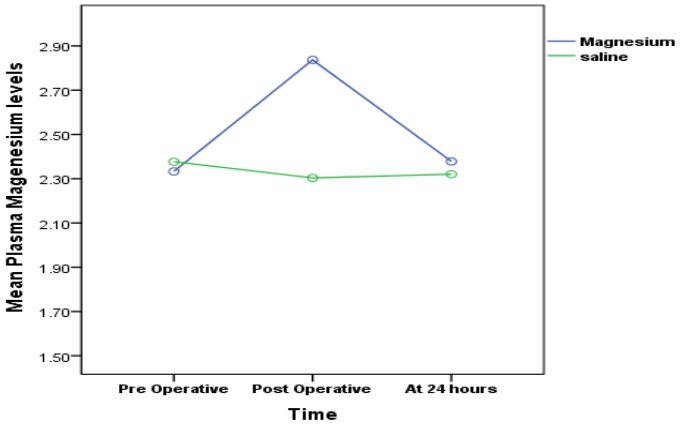


**Fig 6.Line diagram showing serum magnesium levels (mg/dl) preoperatively, immediate postoperatively and 24 hours postoperatively. Serum magnesium levels within normal levels at all intervals of study in both the groups.**

## DISCUSSION

Two main results emerged from this clinical study. First, magnesium had a beneficial effect on postoperative pain intensity and second analgesic requirements in postoperative period decreased in magnesium group. Secondarily, magnesium group displayed less postoperative shivering.

Heart rate, systolic blood pressure, diastolic blood pressure and oxygen saturation ($SpO_2$%) by pulse oximetry were recorded at various intervals in perioperative period starting from baseline, 30 minutes, 1 hour, 1.5hours, 2 hours, 3 hours, 4 hours, 12 hours, 24 hours, and 48 hours post operatively. Magnesium causes a dose-dependent negative inotropiceffect, and in humans, haemodynamic studies have shownthat it has a peripheral (predominantly arteriolar) vasodilatoryeffect. But in the present study the twogroups when compared with reference to mean heart rate, mean systolic blood pressure and mean diastolic blood pressure at various intervals post-operatively, the difference was found to be statistically insignificant (p value > 0.05). No patient in both groups developed bradycardia (heart rate < 60/min), however three patients in magnesium group and two patients in saline group developed hypotension in perioperative period and were given ephedrine 6mg i.v. according to study protocol to normalize arterial pressure. None of the patients had a $SpO_2$ value of < 95% on pulse oximetry.In concordance with our study Tramer Martin R et al[7] also observed non-significant association in the haemodynamic parameters between the two groups. Our study was also in concordance with Hwang JY, Na HS, Jeon YT, Ro YJ, Kim CS, Do SH[25] andHala El-Kerdawy[26] who also found a non-significant association in the hemodynamic parameters between the two groups.

On comparing the VAS scores between the two groups at various intervals a statistically significant difference was found between magnesium versus saline group. Evaluation of pain by using Standard VAS revealed lower VAS scores in the magnesium group(mean VAS=19.029±1.008) than saline group( mean VAS= 27.600±1.008) at all intervals of time starting from 0 hours postoperatively to 48 hours postoperatively. VAS scores were lower at 0 min, 30 min, 1 hour, 2 hours, 4 hours, 12 hours, 24 hours, 48 hours in magnesium group than saline group but scores were statistically significant p-value< 0.05 at 0 min, 2, 4, 12 and 24 hours and statistically insignificant at 30 minutes and 48 hours (p-value>0.05). Overall VAS score difference between magnesium and saline group was statistically significant (p-value<0.05).Our results were in concordance with Hwang JY, Na HS, Jeon YT, Ro YJ, Kim

CS, Do SH[25], J.-H. Ryu., M.-H. Kang, K.-S.Park and S.-H.Do[27],Essam M Manaa and Ama F Alhabib[28],Apan A, Buyukkocak U, Ozcan S, Sari E, Basar H.[29],Kara H, Sahin N, Ulusan V, Aydogdu T.[30], Steinlechner B, Dworschak M, Birkenberg B, et al.[31], Levaux CH, Bonhomme V, Dewandre PY, et al.[32] who also observed significant difference in VAS score between the two groups with lower VAS scores in magnesium group.

The mean number of rescue analgesia doses in magnesium group and Saline group were 0.8± 0.5774, 1.5± 1.295 respectively. In magnesium group overall consumption of analgesics was lower than the saline (control) group with 152 total doses given for saline group patients and 72 doses given to magnesium group patients. Analgesic consumption was lower in saline group and was statistically significant with p-value= 0.014.Comparing the two groups postoperative analgesic consumption is lower in magnesium group than saline group at all intervals of time except at 0 min where none of the patients received analgesia. Consumption of analgesia is statistically significant at 2 hours (p-value<0.05) and statistically non-significant at other intervals of time.The results of our study correlate with Ryu J H et al[30] who observed that intravenous magnesium sulphate administration during TIVA improved the quality of postoperative analgesia. Tramer Martin R et al[7] also observed reduction in analgesic requirements in magnesium group. Hwang J Y[25] et al also observed that i.v. infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia and decreases analgesic consumption.

Herbert Koinig MD, Thomas Wallner MD, Peter Marhofer MD, HaraldAndel MD, Klaus Horauf MD, Nikolaus Mayer MD [33] also concluded that during the intraoperative and postoperative periods, patients in magnesium group required significantly less fentanyl than those in control group and hence i.v. magnesium sulphate administration reduces intraoperative and postoperative analgesic requirements compared with isotonic sodium chloride administration.

Apan A, Buyukkocak U, Ozcan S, Sari E, Basar H. conducted a study on 50 ASA I and II patients undergoing spinal anaesthesia to study effect of $MgSO_4$ infusion on anaesthetic consumption and analgesic requirements and they also concluded that magnesium sulphate infusion may be used as an adjunct for reducing analgesic consumption after spinal anaesthesia.[29]

T. O. Seyhan, M. Tugrul, M. O. Sungur, S. Kayacan, L. Telci, K. Pembec and K. Akpir (2005)conducted a study on 80 women allocated in 4 groups to compare the effects of three different dose regimens of magnesium on intraoperative propofol and atracurium requirement and postoperative morphine consumption in patients undergoing gynaecological surgery. Postoperative analgesia was achieved using PCA and morphine. They also concluded that magnesium infusion leads to significant reductions in intraoperative propofol, atracurium and postoperative morphine consumption.[34]

Lysakowski C, Dumont L, Czarnetzki C, Martin R. (2007) have done a systematic review of randomized trials on "Magnesium Sulphate as an Adjuvant to Postoperative Analgesia." They concluded magnesium had a beneficial effect on postoperative pain intensity and analgesic requirements which is in accordance with our study.[35]

Essam M Manaaand Ama F Alhabib (2011)conducted a study on 60 adult male and female patients to evaluate the effect of i.v. $MgSO_4$ on the total anaesthetic and analgesic consumption using the clinical parameters in addition to bispectral index and neuromuscular monitoring using train of four. Results showed that total consumption of fentanyl, propofol and rocuronium were significantly less in magnesium group as compared to control group. Recovery time was significantly shorter in magnesium group. Postoperative pain scores as well as total analgesic requirement of morphine was significantly lower in magnesium group compared to control group. They also concluded that magnesium sulphate reduces the total anaesthetic and analgesic requirement as well as postoperative pain.[28]
However, Ko SH, Lim HR, Kim DC, Han YJ, Choe H, Song HS (2001) in their study entitled "magnesium sulfate does not reduce postoperative analgesic requirements" studied whether perioperative intravenous magnesium sulfate infusion affects postoperative pain and results suggested that perioperative intravenous magnesium infusion may not be useful for preventing postoperative pain[36] and their findings were in contrary to our study.

Serum magnesium levels were higher in magnesium group than saline group (p-value<0.05) at 0 hours but were in normal range of serum magnesium levels. There were no side effects associated with hypermagnesemia as serum magnesium levels were in normal range at all intervals. However, preoperative levels and 24 postoperative serum magnesium levels were comparable in both groups (p-value>0.05). Serum magnesium levels of magnesium group returned to preoperative levels within 24 hours after surgery.

In the magnesium group 4patient suffered from shivering during this study, whereas shivering occurred in 24 patients belonging to saline group. The difference among groups was statistically significant (p=0.042). The results of our study correlate with Lysakowski C, Dumont L, Czarnetzki C, Martin R. (2007) who found that perioperative magnesium supplementation prevents postoperative hypomagnesaemia and decreases the incidence of postoperative shivering.[35]

Additional side effects like hypotension, postoperative nausea and vomiting were statistically insignificant between the two groups.

Prolonged neuromuscular blockade or delayed extubation was not seen with any patient in both the groups under study.

## CONCLUSION

Magnesium improves quality and potency of postoperative analgesia and decreases postoperative analgesic consumption. It also decreases incidence of postoperative shivering, however it has not any significant effect on hemodynamics, urine output, postoperative nausea and vomiting.

## REFRENCES

1. Fawcell VY, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth* 1999; 83: 302-20.
2. Billir A, Gulec S, Erkan A, Ozcelik A. Epidural magnesium reduces postoperative analgesic requirement. *Br J Anaesth* 2007; 98: 519-23.
3. Iseri LT, French JH. Magnesium: Nature's physiologic calcium blocker (editorial). *Am Heart J* 1984; 108: 188-94.
4. Liu S, Carpenter RL, Neel JM. Epidural anesthesia and analgesia. Their role in post operative outcome. Anaesthesiology. 1995; 82: 1474.
5. Wu CL, Fleisher LA. Outcomes research in regional anaesthesia and analgesia.2000; 91: 1232.
6. Brill S, Sedgwick PM, Flamann W, et al. Efficacy of intravenous magnesium in neuropathic pain. Br J Anaesth 2002; 89: 711-4.
7. Tramer, Martin R, Schneider. Jurg, Marti, Rene-Andreas, Rifat, Kaplan. Role of Magnesium Sulfate in Postoperative Analgesia. Anesthesiology 1996 Feb; 84(2): 340-7.

8. Meloni BP, Campbell K, Zhu H, et al. In search of clinical neuroprotection after brain ischemia: the case for mild hypothermia (358C) and magnesium. Stroke 2009; 40: 2236–40
9. Iseri LT, French JH: Magnesium nature's physiological calcium blocker (editorial). Amheart J 1984; 108: 188-94.
10. Miranda HF, Bustamante D, Kramer V, Pelissier T, Saavedra H, Paeile C, Fernandez E, Pinardi G:antinocciceptive effects of Ca2+ channel blockers. Eur J Pharmacol1992: 217: 137-41.
11. Wong CH, Dey P, Yarmush J, Wen-hsien W, Zbuzek VK: nifedipine-induced analgesia after epidural injection in rats. AnesthAnalg 1994; 79: 303-6.
12. Santillan R, Maestre JM, Hurle MA, Florez J: Enhancement of opiate analgesia by nimodipine in cancer patients chronically treated with morphine: A preliminary report.Pain1994; 58:129-32.
13. Woolf CJ, Thompson SWN: the induction and maintenance of central sensitization is dependent on NMDA receptor activation: Implications for the treatment of post-injury pain and hypersensitivity states. Pain 1991; 44: 293-9.
14. Cox JA, Lysko PG, Henneberry RC: Excitatory amino acid neurotoxicity at the NMDA receptor in cultured neurons: Role of voltage-dependent magnesium block. Brain Res 1989; 499: 267-72.
15. Dickenson AH: A cure for wind up: NMDA receptor antagonists as potential analgesics. Trends PharmacolSci1990; 11: 307-9.
16. Fontana-Klaiber H, Hogg B. (Therapeutic effects of magnesium in dysmenorrhea).SchweizRundsch Med Prax1990; 79: 491-94.
17. Facchinetti F, Borella P, Sances G, Fioroni L, Nappi RE, Genazzani AR: Oral magnesium successfully relieves premenstrual mood changes. ObstetGynecol1991; 78: 177-81.
18. Peikert A, Wilimzig C, Kohne-Volland R. prophylaxis of migraine with oral magnesium: results from a prospective, multi-center, placebo controlled and double-blind randomised study. Cephalagia1996; 16: 257-63.
19. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain 1986; 27: 117–26.
20. Burckhardt CS, Jones KD. Adult measures of pain: The McGill Pain Questionnaire (MPQ), Rheumatoid Arthritis Pain Scale (RAPS), Short-Form McGill Pain Questionnaire (SF-MPQ), Verbal Descriptive Scale(VDS), Visual Analog Scale (VAS), and West

Haven-Yale Multidisciplinary Pain Inventory (WHYMPI). Arthritis Rheum 2003; 49: S96–104.

21. Ferraz MB, Quaresma MR, Aquino LR, Atra E, Tugwell P, Goldsmith CH. Reliability of pain scales in the assessment of literate and illiterate patients with rheumatoid arthritis. JRheumatol1990; 17: 1022–4.
22. Aldrete JA. The post-anesthesia recovery score revisited. J ClinAnesth1995; 7: 89 –91.
23. Thomas WF, Alex Macario.Thepostanaesthesia care unit. In: Miller RD, ed. Anesthesia,6thEdn. Philadelphia: Churchill Livingstone, 2005; 50: 732-46.
24. American society of anaesthesiologists task force on post anaesthetic care, Pravtice guidelines for postanaesthetic care; A report by ASA task force on postanaesthetic care. Anaesthesiology 2002; 96: 72.
25. Hwang JY, Na HS, Jeon YT, Ro YJ, Kim CS, Do SH. i.v. infusion of MgSO4 during spinal anaesthesia improves postoperative analgesia. Br J Anaesth2010; 104: 89-93.
26. Hala-El-Kerdawy.The effect of combined spinal and epidural magnesium.M.E.JAnesth19(5): 2008.
27. J.-H. Ryu., M.-H. Kang, K.-S.Park and S.-H.Do.Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth2008; 100: 397-403.
28. Manna Essam M, AlhabibAmro F. Effect of magnesium sulphate on the total anaesthetic and analgesic requirements in neurosurgery. J NeurolNeurophysiol2012 s11
29. Apan A, Buyukkocak U, Ozcan S, Sari E, Basar H. postoperative magnesium sulphate infusion reduces analgesic requirements in spinal anaesthesia. Eur J Anaesthesiol 2004 oct; 21(10): 766-9.
30. Ryu JH, Kang MH, Park KS, Do SH. Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenousanaesthesia. Br J Anaesth 2008; 100: 397–403
31. Kara H, Sahin N, Ulusan V, Aydogdu T. Magnesium infusionreduces perioperative pain. Eur J Anaesthesiol 2002; 19: 52– 6.
32. Steinlechner B, Dworschak M, Birkenberg B, et al. Magnesiummoderately decreases remifentanil dosage required for pain management after cardiac surgery. Br J Anaesth 2006; 96: 444 –9.
33. Herbert Koinig MD, Thomas Wallner MD, Peter Marhofer MD, HaraldAndel MD, Klaus Horauf MD, Nikolaus Mayer MD. Magnesium sulphate reduces intra- and post-operative analgesic requirements. AnesthAnalg1998; 87: 206-10.

34. T. O. Seyhan, M. Tugrul, M. O. Sungur, S. Kayacan, L. Telci, K. Pembec1 and K. Akpir. Effects of three different dose regimens of magnesium on propofol requirements, haemodynamic variables and postoperative pain relief in gynaecologicalsurgery. BritishJournal of Anaesthesia 96(2): 247–52.
35. Lysakowski C, Dumont L, Czarnetzki C, Martin R. Magnesium as an Adjuvant to Postoperative Analgesia. A systematic review of randomized trials. AnesthAnalg 2007 Jun; 104(6): 1532-9.
36. Ko SH, Lim HR, Kim DC, Han YJ, Choe H, Song HS. Magnesium sulfate does not reduce postoperative analgesic requirements. Anesthesiology. 2001 Sep; 95(3): 640-6.