Journal of Anesthesia & Clinical Research

Bansal, J Anesth Clin Res 2015, 6:7
DOI: 10.4172/2155-6148.1000547

Review Article Open Access

Magnesium: Emerging Potentials in Anesthesia Practice

Teena Bansal*

Department of Anesthesiology & Critical Care, Pt. B.D. Sharma University of Health Sciences, Rohtak-12400, Haryana, India

***Corresponding author:** Teena Bansal, Assistant Professor, 2/8 FM, Medical Campus, PGIMS, Rohtak-12400, Haryana, India, Tel: +919315839374; E-mail: aggarwalteenu@rediffmail.com

Received date: June 25, 2015, **Accepted date:** July 22, 2015, **Published date:** July 30, 2015

Abstract

Magnesium, a non-competitive blocker of N-methyl-D-aspartate receptor, initially used for management of preeclampsia, arrhythmia and bronchial asthma, is of great importance in anesthesia practice nowadays. It is being used intravenously, intrathecally as well as epidurally for postoperative pain relief. Recently it has gained popularity as an adjuvant in blocks. Anesthetic and analgesic sparing characteristics of magnesium enable anesthesiologists to reduce the dose of anesthetics during surgery and the use of analgesics after surgery.

Keywords: Magnesium; Anaesthesia practice

Introduction

Magnesium plays a critical role in a variety of physiologic processes. Ever since the study of magnesium sulphate in clinical anesthesia beginning in 1996, magnesium has drawn attention in the field of anesthesia and pain medicine [1]. Magnesium is the fourth most important cation in the body and second most important intracellular cation. It is found in abundance within the earth's crust as deposits of magnesite and dolomite. It was first isolated in 1808 by the English chemist Sir Humphrey Davy using electrolysis of a mixture of magnesia and mercury oxide.

Magnesium is of importance in anesthesia practice for several reasons. First, this ion is essential for many biochemical reactions and its deficiency may produce clinically important consequences during anesthesia or in the intensive care unit. Second, the extensive use of magnesium sulphate in obstetric practice requires that anesthesiologists be familiar with the pharmacological action of this drug and its interaction with anesthetic agents. Third, few of its properties may be of value in certain areas of anesthetic practice [2,3]. The physiological role of magnesium is due to its calcium channel blocking properties at smooth muscle, skeletal muscle and conduction system levels. The analgesic properties are due to NMDA receptor blocking action. It is a cost effective widely used drug with multidisciplinary applications [4].

Physiology

In humans, magnesium is distributed principally between bone (53%) and intracellular components of muscle (27%) and soft tissues (19%). One percent of total body magnesium is found in serum and red blood cells. Serum magnesium comprises only approximately 0.3% of total body magnesium, where it is present in three states: ionised (62%), protein bound (33%) mainly to albumin and complexes to anions such as citrate and phosphate. The daily estimated average requirement is 200 mg for females and 250 mg for males. The normal range of magnesium in plasma is 1.4-2.2 meq/L (0.7-1.1 mmol/L) [5].

Available Formulation

The available formulation of magnesium for intramuscular and intravenous use is magnesium sulphate. This drug is available in 2 ml ampule. Each ml contains magnesium sulphate (heptahydrate) 500 mg, which provides 4.06 meq each of magnesium and sulphate and water for injection q.s. The pH is 5.5-7.0. The solution contains no bacteriostatic agent or other preservatives. The molecular formula is $MgSO_4.7H_2O$ and the molecular weight is 246.47.

Effects on Various Systems

By competing with calcium for membrane binding sites and by stimulating calcium sequestration by sarcoplasmic reticulum, magnesium helps to maintain a low resting intracellular free calcium ion concentration which is important in many cellular functions. The electrical properties of membranes and their permeability characteristics are also affected by magnesium. Magnesium has important effects on the cardiovascular system. It affects myocardial contractility by influencing the intracellular calcum concentration and the electrical activity of myocardial cells and the specialized conducting system of the heart by its ability to influence movement of ions such as sodium, potassium and calcium across the sacrolemmal membrane. Magnesium may also affect the vascular smooth muscle tone. Magnesium has a key role in many other important biological processes such as cellular energy metabolism, cell replication and protein synthesis [6].

Plasma concentration (mmol/L)	Clinical effects
0.7-1.0	Normal range
3.0-5.0	ECG changes
4.0-5.0	Areflexia
6.0-7.0	Respiratory arrest
10.0-12.5	Cardiac arrest

Table 1: Adverse effects of Magnesium at different concentrations.

The normal range of Magnesium in plasma is 0.7-1.1 mmol/L. The adverse effects appear at different ranges (Table 1).

Mechanism of Action

Magnesium is a noncompetitive blocker of N-methyl-D-aspartate (NMDA) receptor with antinociceptive effects. It is also a physiological calcium antagonist at different voltage gated channels which may be important in the mechanism of antinociception [7,8]. Magnesium is not a primary analgesic itself, it enhances the analgesic actions of more established analgesics as an adjuvant agent.

The role of magnesium for perioperative analgesia has been investigated by many authors during general anesthesia as well as spinal anesthesia. Magnesium sulphate has been reported to be effective in perioperative pain treatment and in blunting somatic, autonomic and endocrine reflexes provoked by noxious stimuli [9,10]. Usual regimens of magnesium sulphate administration were a loading dose of 30-50 mg/kg followed by 6-20 mg/kg/h (continuous infusion) till the end of surgery. However, a single dose of magnesium without maintenance infusion was also effective for postoperative analgesia in some reports. Various studies have shown a beneficial effect on postoperative pain outcomes with a variety of magnesium pretreatments ranging from intravenous single boluses to intravenous infusions.

Role of Magnesium in Anesthesia

- Postoperative pain relief
- To obtund hypertensive response to intubation
- In pheochromocytoma
- In obstetrics and obstetric anaesthesia
- In cardiac anaesthesia
- In management of shivering
- Muscle Relaxation

Postoperative pain relief

Magnesium has been used intravenously, intrathecally as well as epidurally for pain relief. Recently it has gained popularity as adjuvant in blocks.

Role during general anaesthesia: Ryu et al. reported that administration of magnesium sulphate 50 mg/kg immediately before surgery followed by 15 mg/kg/h continuous infusion intraoperatively till the end of surgery in gynaecology patients receiving propofol-remifentanil TIVA significantly decreased the requirements of neuroblocking agent during surgery and decreased the analgesic consumption after surgery. Also patients receiving magnesium displayed less postoperative nausea vomiting and shivering [11]. Similar observations have been made by Lee et al. [12]. Koinig et al. in a study reported that perioperative administration of intravenous magnesium sulphate reduces intraoperative as well as postoperative analgesic requirement [13].

Kiran et al. studied the efficacy of single dose of intravenous magnesium sulphate to reduce postoperative pain in patients undergoing inguinal surgery under general anesthesia. Patients of magnesium group received single dose of magnesium sulphate 50 mg/kg in 250 ml of normal saline infused over 30 minutes preoperatively and concluded that administration of intravenous magnesium sulphate significantly reduces postoperative pain [14].

Limitations as an analgesic: However, some studies have concluded that magnesium sulphate has limited or no effect. Ko et al. and Paech et al. reported that perioperative iv magnesium administration did not reduce postoperative pain and analgesic consumption in patients undergoing abdominal hysterectomy and caesarean delivery respectively [15,16]. Tramer et al. also observed that the pretreatment of magnesium sulphate in patients undergoing ambulatory ilioinguinal hernia repair or varicose vein operations had no effect on postoperative analgesia [17].

The normal range of magnesium in plasma is 1.4-2.2 meq/L. Hypomagnesimia can occur frequently after surgeries such as abdominal, orthopaedic and cardiac surgery as well as after minor surgeries [13,18]. Tramer et al. hypothesized that magnesium substitution was beneficial as an analgesic only in patients who had hypomagnesimia [17]. Thus decrease in pain intensity was not due to a direct analgesic effect of magnesium but rather to the prevention of hypomagnesemia and thus prevention of subsequent NMDA activation. Patients undergoing major surgery without magnesium supplementation were shown to be at risk of developing hypomagnesimia in the first 24 postoperative hours [19]. The decrease was probably due to the large loss of fluids and fluid movement between body compartments. Magnesium is a non-competitive blocker of NMDA receptor. It was observed that in magnesium free solutions, the excitatory amino acids L-glutamate and L-aspartate opened the NMDA cation channels and in the presence of magnesium, the probability of opening of the channel was reduced [20]. Thus, substitution of Magnesium in surgical patients at risk of developing hypomagnesimia should prevent hypomagnesimia related opening of the NMDA receptors. An inverse relationship between the severity of pain and serum magnesium levels has been observed in women during labour and in patients with different medical conditions such as myocardium infarction or pancreatitis. Hence the control of perioperative serum magnesium levels and the prevention of hypomagnesemia should be given priority [21].

Role during spinal anesthesia: Recent studies suggest the role of magnesium sulphate as an adjuvant to local anesthetics in spinal anesthesia in different doses. First prospective human study evaluating whether intrathecal magnesium could prolong spinal opioid analgesia was carried out by Buvanendran et al. Fifty two patients requesting analgesia for labour were randomized to receive either intrathecal fentanyl 25 μg plus saline or fentanyl 25 μg plus magnesium sulphate 50 mg as part of a combined spinal-epidural technique. Significant prolongation in the median duration of analgesia (75 min) in the magnesium plus fentanyl group was observed compared with the fentanyl alone group (60 min) without increased adverse effects [22]. Ozalevli et al. in a study to investigate the effect of adding 50 mg intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anesthesia in patients undergoing lower extremity surgery concluded that magnesium sulphate significantly delayed the onset of sensory and motor blockade but also prolonged the period of analgesia without additional side effects [23]. Jaiswal et al. evaluated and compared the effect of addition of two different doses i.e. either 50 mg or 100 mg of intrathecal magnesium sulphate to bupivacaine on the quality of spinal anesthesia in patients undergoing lower limb orthopedic surgery. A significant increase in the duration of analgesia and anesthesia was observed when magnesium sulphate was added to intrathecal bupivacaine with no increased incidence of side effects rather decreased the incidence of shivering significantly. Moreover, it appeared that analgesia seemed to have dose related linear relationship with magnesium sulphate [24].

In addition Iv magnesium sulphate infusion during spinal anesthesia was reported to improve postoperative analgesia and to reduce cumulative consumption of analgesics after total hip replacement arthroplasty [25]. Similar results have been observed by Agrawal et al. [26]. Postoperative iv magnesium sulphate infusion also increased the time to analgesic need and reduced the total consumption of analgesics after spinal anaesthesia [27].

A study observed the effect of intravenous infusion vs intrathecal magnesium sulphate during spinal anesthesia in patients undergoing total hip arthroplasty surgery. The authors suggested that both iv infusion and intrathecal injection of magnesium sulphate improved postoperative analgesia. In addition iv infusion of magnesium sulphate led to relative hypotension and decreased blood loss [28].

Role during epidural anaesthesia: Arcioni et al. observed that intrathecal and epidural magnesium sulphate potentiated and prolonged motor block. These authors concluded that in patients undergoing orthopaedic surgery, supplementation of spinal anesthesia with combined intrathecal and epidural magnesium sulphate significantly reduced patients' postoperative analgesic requirements. Magnesium blunts NMDA channels in a voltage dependent way and produces a dramatic reduction of NMDA induced currents [29]. Magnesium sulphate as an adjuvant to epidural bupivacaine prolonged the duration of analgesia [30,31].

Role in blocks: In addition to central location of NMDA receptors, these receptors have been identified peripherally. El Shamaa et al. observed that the admixture of magnesium sulphate to local anesthetic bupivavaine during femoral nerve block provided a profound prolongation of duration of both sensory and motor block, in addition to a significant decrease in postoperative pain scores and total dose of rescue analgesia with a longer bearable pain periods in the first postoperative day [32]. Magnesium affects peripheral nerves as it interferes with release of neurotransmitters at the synaptic cleft or potentiates local anaesthetic action [2]. Hassan et al. evaluated the effect of magnesium sulphate as an adjuvant in potentiating the analgesic effect of bupivacaine in paravertebral block in modified radical mastectomy and concluded that adding magnesium sulphate to bupivacaine resulted in more efficient analgesia with opioid-sparing and decreased postoperative nausea and vomiting in first postoperative 24 hours [33]. Goyal et al. concluded that administration of a small dose of magnesium only in the axillary sheath during brachial plexus analgesia resulted in prolonged time of postopearive pain relief with reduction of postoperative analgesia requirement without any major side effects [34].

To obtund hypertensive response to intubation

Magnesiium has been highlighted on its efficacy to attenuate cardiovascular responses associated with tracheal intubation [35,36]. Laryngoscopy and tracheal intubation cause release of endogenous catecholamines, increasing both blood pressure and heart rate with possible sequelae such as intracranial bleeding and myocardial ischemia. Magnesium can attribute to stabilization of cardiovascular parameters and prevent hypertension at intubation. This effect can be especially valuable in the context of the hypertensive diseases of pregnancy. James et al. studied post intubation catecholamine levels and impact of intubation on heart rate and blood pressure in a randomized controlled trial of intravenous magnesium 60 mg/kg vs 0.9% saline administered preintubation. Noradrenaline levels were significantly higher in the control group compared to those receiving magnesium and this increased level persisted for 5 minutes post intubation. Heart rate increased slightly on administration of magnesium but then remained stable throughout intubation. The control group showed significant increase in heart rate and blood pressure [37].

In pheochromocytoma

Magnesium has a marked antiadrenergic property. In addition to this, its vasodilator and antiarrythmic effect have led to the use of magnesium during surgery for pheochromocytoma [5].

Role in obstetrics and obstetric anesthesia

Magnesium has an increasing role in the treatment of the parturient with important implications for the obstetric anesthetist. Magnesium has been used to treat acute hypertensive crisis especially in the context of pheochromocytoma management and treatment of pregnancy related hypertension. It is now well established in the management of severe preeclampsia and prevention/treatment of eclamptic seizures, where it is considered as standard therapy. It prevents or controls convulsions by blocking neuromuscular transmission and decreasing the release of acetylcholine at the motor nerve terminals. Its antihypertensive action is due to its calcium channel blocking action. The use of magnesium for neuroprotection of preterm fetus, preventing disabling cerebral palsy in the newborn, will undoubtedly continue to increase [38]. It is used to treat premature labour. It has beneficial effects on both maternal and uteroplacental hemodynamics in preeclampsia [5].

As an adjunct to general anesthesia, Lee and Kwon in their study observed that intravenous administration of magnesium 45 mg/kg before induction of anesthesia, led to greater hemodynamic stability and lower bispectral index implying less risk of awareness [39]. However, pretreatment with magnesium sulphate did not lower serum cardiac troponin I values in moderate preeclampsia undergoing elective caesarean section using spinal anesthesia [40].

Role in cardiac anesthesia

The areas of particular relevance to anesthesiologist are arrhythmia and cardiac surgery. It is a valuable anti-arrhythmic agent. It is successfully used in the treatment of ventricular arrhythmias associated with acute myocardial infarction, long QT syndrome and digitalis toxicity [5]. There is high risk of magnesium depletion during CABG surgery with CPB. This hypomagnesemia precipitates both cardiac arrhythmias and vasoconstriction of either coronary arteries or the used mammary graft which in turn aggravates arrhythmias. Magnesium supplementation can stabilize the myocardial cell membrane and provide some cardioprotective effect against arrhythmias [41]. During on pump CABG surgery, the combined administration of magnesium and lidocaine as a bolus dose starting after intubation followed by continuous infusion reduced the incidence of reperfusion VF by 62% and post-CPB ventricular arrhythmias by 70%. Magnesium supplementation stabilized the myocardial cell membrane and provided cardioprotective effect against ventricular arrhythmias [42]. Magnesium administration before, during surgically induced myocardial ischemia, and at the time of myocardial reperfusion appears to improve post-ischemic myocardial recovery but if given after myocardial reperfusion has begun, it does not produce beneficial effect [43].

Management of shivering

Magnesium sulphate is found to be effective in management of postoperative shivering after general anesthesia as well as spinal anesthesia [44,45]. Elsonbaty et al. found magnesium sulphate to be an effective way for the control of shivering and suggested that it could replace meperidine for treatment of shivering during spinal anesthesia with low incidence of side effects. Antishivering effect may be due to blocking of NMDA receptors leading to a decrease in norepinephrine and 5 HT as both of these have role in thermoregulatory control. Magnesium sulphate is an attractive choice for shivering control because hypomagnesemia is observed during induced hypothermia [45]. Ibrahim et al. further observed that following spinal anesthesia prophylactic magnesium sulphate infusion lowered the incidence of shivering [46].

Muscle relaxation

Magnesium potentiates the action of non-depolarizing neuromuscular blockers by inhibiting the release of acetylcholine from motor nerve terminal. It also decreases the sensitivity of postjunctional membrane and reduces the excitability of nerve fibre. As a result reduced doses of non-depolarizing muscle relaxants are recommended when magnesium sulphate used [2].

There are diverse clinical implications of potentiation of muscle relaxation by magnesium sulphate. First of all, it can be used as an adjuvant to tracheal intubation. Kim et al. observed that magnesium sulphate, when combined with rocuronium priming, improved rapid-requence intubating conditions compared with either magnesium sulphate or priming used alone [47]. Due to the effect of drug or disease, sometimes patient exhibits resistance to non-depolarizing muscle relaxants. Magnesium can be used effectively in these cases. Kim et al. reported that valproic acid decreases rocuronium duration resulting in increase in its requirement, but this increase was attenuated by administration of magnesium [48]. Children with cerebral palsy also show resistance to non-depolarizing muscle relaxants. Rocuronium requirement was significantly decreased in these patients on administration of magnesium [49]. In addition, pretreatment with magnesium sulphate is associated with less fasciculation induced by succinylcholine.

Role of Magnesium in Critical Care

Magnesium deficiency has been found in 65% adults and 30% neonates in intensive care units as compared to 11% in general hospital inpatients. It is used in the treatment of respiratory failure, neonatal pulmonary hypertension and tetanus [5].

Many factors contribute to magnesium deficiency in critically ill patients. These factors include impaired GI absorption, nasogastric suction, poor content of magnesium in feeding formulae or TPN solution, administration of drugs like diuretics, aminoglycosides, amphotericin-B which cause renal wasting of magnesium [50].

Hypomagnesemia is associated with increased mortality in critical care patients more so in patients with sepsis, diabetes and other electrolyte abnormalities.

Mortality

Safavi et al. observed a higher mortality rate in hypomagnesemic patients as compared to normomagnesemic patients (55% vs 35%) [51]. Limaye et al. observed that mortality rate in hypomagnesemic group was 57% which was significantly higher as compared to 31% in the normomagnesemic group. The higher mortality rates in hypomagnesemic patients was explained by greater incidence of electrolyte abnormalities especially hypokalemia and cardiac arrhythmias and a strong association of hypomagnesemia with sepsis and septic shock. The need and duration for ventilator support was significantly higher in the hypomagnesemic patients [52].

Sepsis and diabetes

Hypomagnesemia is associated with increased release of endothelin and proinflammatory cytokines and leads to sepsis. There is a strong relationship between hypomagnesemia and insulin resistance. Magnesium supplementation leads to decreased requirement of insulin.

Other electrolyte abnormalities

Hypomagnesemia is commonly associated with other electrolyte abnormalities like hypokalemia, hypophosphatemia, hyponatremia and hypocalcemia. Hypokalemia seen in hypomagnesemic patients is relatively refractory to potassium supplementation until magnesium deficiency is corrected. This is attributed to defective membrane ATPase activity and also because the renal potassium loss is increased in presence of hypomagnesemia. The mechanism of association of hypocalcemia with hypomagnesemia involves defect in synthesis and release of parathyroid hormone as well as the end organ resistance to parathyroid hormone. In addition, magnesium deficiency may directly act on bones to reduce calcium release independent of parathyroid hormone. Hypocalcemia associated with magnesium depletion is also difficult to correct unless magnesium depletion is corrected [52].

Conclusion

Magnesium sulphate, a very old drug having its initial use in preeclampsia, cardiac arrhythmias and bronchial asthma, now has been explored as an anesthetic and analgesic sparing drug in anesthesia practice. There is emerging role of magnesium in critical care patients where it has been shown to decrease mortality in various studies, more so in patients with sepsis and diabetes.

References

1. Tramer MR, Schneider J, Marti RA, Rifat K (1996) Role of magnesium sulfate in postoperative analgesia. Anesthesiology 84: 340-347.
2. James MF (1992) Clinical use of magnesium infusions in anesthesia. Anesth Analg 74: 129-136.
3. James MF (2009) Magnesium: an emerging drug in anaesthesia. Br J Anaesth 103: 465-467.
4. Akhtar MI, Ullah H, Hamid M (2011) Magnesium, a drug of diverse use. J Pak Med Assoc 61: 1220-1225.
5. Fawcett WJ, Haxby EJ, Male DA (1999) Magnesium: physiology and pharmacology. Br J Anaesth 83: 302-320.
6. Swaminathan R (2003) Magnesium metabolism and its disorders. Clin Biochem Rev 24: 47-66.
7. Mayer ML, Westbrook GL, Guthrie PB (1984) Voltage-dependent block by Mg2+ of NMDA responses in spinal cord neurones. Nature 309: 261-263.
8. Iseri LT, French JH (1984) Magnesium: nature's physiologic calcium blocker. Am Heart J 108: 188-193.
9. Kara H, Sahin N, Ulusan V, Aydogdu T (2002) Magnesium infusion reduces perioperative pain. Eur J Anaesthesiol 19: 52-56.

10. Levaux Ch, Bonhomme V, Dewandre PY, Brichant JF, Hans P (2003) Effect of intra-operative magnesium sulphate on pain relief and patient comfort after major lumbar orthopaedic surgery. Anaesthesia 58: 131-135.
11. Ryu JH, Kang MH, Park KS, Do SH (2008) Effects of magnesium sulphate on intraoperative anaesthetic requirements and postoperative analgesia in gynaecology patients receiving total intravenous anaesthesia. Br J Anaesth 100: 397-403.
12. Lee C, Jang MS, Song YK, Seri O, Moon SY, et al. (2008) The effect of magnesium sulfate on postoperative pain in patients undergoing major abdominal surgery under remifentanil-based anesthesia. Korean J Anesthesiol 55: 286-290.
13. Koinig H, Wallner T, Marhofer P, Andel H, Hörauf K, et al. (1998) Magnesium sulfate reduces intra- and postoperative analgesic requirements. Anesth Analg 87: 206-210.
14. Kiran S, Gupta R, Verma D (2011) Evaluation of a single-dose of intravenous magnesium sulphate for prevention of postoperative pain after inguinal surgery. Indian J Anaesth 55: 31-35.
15. Ko SH, Lim HR, Kim DC, Han YJ, Choe H, et al. (2001) Magnesium sulfate does not reduce postoperative analgesic requirements. Anesthesiology 95: 640-646.
16. Paech MJ, Magann EF, Doherty DA, Verity LJ, Newnham JP (2006) Does magnesium sulfate reduce the short- and long-term requirements for pain relief after caesarean delivery? A double-blind placebo-controlled trial. Am J Obstet Gynecol 194: 1596-1602.
17. Tramèr MR, Glynn CJ (2007) An evaluation of a single dose of magnesium to supplement analgesia after ambulatory surgery: randomized controlled trial. Anesth Analg 104: 1374-1379, table of contents.
18. Do SH (2013) Magnesium: a versatile drug for anesthesiologists. Korean J Anesthesiol 65: 4-8.
19. Sanchez-Capuchino A, McConachie I (1994) Peri-operative effect of major gastrointestinal surgery on serum magnesium. Anaesthesia 49: 912-914.
20. Nowak L, Bregestovski P, Ascher P, Herbet A, Prochiantz A (1984) Magnesium gates glutamate-activated channels in mouse central neurones. Nature 307: 462-465.
21. Weissberg N, Schwartz G, Shemesh O, Brooks BA, Algur N, et al. (1991) Serum and intracellular electrolytes in patients with and without pain. Magnes Res 4: 49-52.
22. Buvanendran A, McCarthy RJ, Kroin JS, Leong W, Perry P, et al. (2002) Intrathecal magnesium prolongs fentanyl analgesia: a prospective, randomized, controlled trial. Anesth Analg 95: 661-666, table of contents.
23. Ozalevli M, Cetin TO, Unlugenc H, Guler T, Isik G (2005) The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anaesthesia. Acta Anaesthesiol Scand 49: 1514-1519.
24. Jaiswal R, Bansal T, Kothari S, Ahlawat G (2013) The effect of adding magnesium sulphate to bupivacaine for spinal anaesthesia: a randomised, double- blind trial in patients undergoing lower limb orthopaedic surgery. Int J Pharm Pharm Sci 5: 179-182.
25. Hwang JY, Na HS, Jeon YT, Ro YJ, Kim CS, et al. (2010) I.V. infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia. Br J Anaesth 104: 89-93.
26. Agrawal A, Agrawal S, Payal YS1 (2014) Effect of continuous magnesium sulfate infusion on spinal block characteristics: A prospective study. Saudi J Anaesth 8: 78-82.
27. Apan A, Buyukkocak U, Ozcan S, Sari E, Basar H (2004) Postoperative magnesium sulphate infusion reduces analgesic requirements in spinal anaesthesia. Eur J Anaesthesiol 21: 766-769.
28. Samir EM, Badawy SS, Hassan AR (2013) Intratheccal vs intravenous magnesium as an adjuvant to bupivacaine spinal anesthesia for total hip arthroplasty. Egyptian Journal of Anaesthesia 29: 395-400.
29. Arcioni R, Palmisani S, Tigano S, Santorsola C, Sauli V, et al. (2007) Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta Anaesthesiol Scand 51: 482-489.
30. Shahi V, Verma AK, Agarwal A, Singh CS (2014) A comparative study of magnesium sulfate vs dexmedetomidine as an adjunct to epidural bupivacaine. J Anaesthesiol Clin Pharmacol 30: 538-542.
31. Hasanein R, El-sayed W, Khalil M (2013) The value of epidural magnesium sulfate as an adjuvant to bupivacaine and fentanyl for labor analgesia. Egyptian Journal of Anaesthesia 29: 219-224.
32. ELShamaa HA, Ibrahim M, Eldesuky HI (2014) Magnesium sulfate in femoral nerve block, does postoperative analgesia differ? A comparative study. Egyptian Journal of Anaesthesia 30: 169-173.
33. Hassan ME, Mahran E (2015) Effect of adding magnesium sulphate to bupivacaine on the clinical profile of ultrasound-guided thoracic paravertebral block in patients undergoing modified radical mastectomy. Egyptian Journal of Anaesthesia 31: 23-27.
34. Goyal P, Jaiswal R, Hooda S, Goyal R, Lal J (2008) Role of magnesium sulphate for brachial plexus analgesia. The internet Journal of Anesthesiology 21: 1.
35. Panda NB, Bharti N, Prasad S (2013) Minimal effective dose of magnesium sulfate for attenuation of intubation response in hypertensive patients. J Clin Anesth 25: 92-97.
36. Shin YH, Choi SJ, Jeong HY, Kim MH (2011) Evaluation of dose effects of magnesium sulfate on rocuronium injection pain and hemodynamic changes by laryngoscopy and endotracheal intubation. Korean J Anesthesiol 60: 329-333.
37. James MF, Beer RE, Esser JD (1989) Intravenous magnesium sulfate inhibits catecholamine release associated with tracheal intubation. Anesth Analg 68: 772-776.
38. Dean C, Douglas J (2013) Magnesium and the obstetric anaesthetist. International Journal of Obstetric Anesthesia 22: 52-63.
39. Lee DH, Kwon IC (2009) Magnesium sulphate has beneficial effects as an adjuvant during general anaesthesia for Caesarean section. Br J Anaesth 103: 861-866.
40. Elzayyat NS, Yacoub MH (2014) Effect of preoperative Mg sulfate infusion on serum cardiac troponin (cTn) in moderate preeclamptic undergoing elective cesarean section under spinal anesthesia. Egyptian Journal of Anaesthesia 30: 299-303.
41. Hamid M, Kamal RS, Sami SA, Atiq F, Shafquat A, et al. (2008) Effect of single dose magnesium on arrhythmias in patients undergoing coronary artery bypass surgery. J Pak Med Assoc 58: 22-27.
42. Elnakera AM, Alawady TS (2013) Continuous infusion of magnesium-lidocaine mixture for prevention of ventricular arrhythmias during on-pump coronary artery bypass grafting surgery. Egyptian Journal of Anaesthesia 29: 419-425.
43. Boyd WC, Thomas SJ (2000) Pro: Magnesium should be administered to all coronary artery bypass graft surgery patients undergoing cardiopulmonary bypass. J Cardiothorac Vasc Anesth 14: 339-343.
44. Kizilirmak S, Karakas SE, Akca O, Ozkan T, Yavru A, et al. (1997) Magnesium sulfate stops postanesthetic shivering. Ann N Y Acad Sci 813: 799-806.
45. Elsonbaty M, Elsonbaty A, Saad D (2013) Is this the time for Magnesium sulfate to replace Meperidine as an antishivering agent in spinal anesthesia? Egyptian Journal of Anaesthesia 29: 213-217.
46. Ibrahim IT, Megalla SA, Khalifa OSM, Deen HMSE (2014) Prophylactic vs. Therapeutic magnesium sulfate for shivering during spinal anesthesia. Egyptian Journal of Anaesthesia 30: 31-37.
47. Kim MH, Oh AY, Jeon YT, Hwang JW, Do SH (2012) A randomised controlled trial comparing rocuronium priming, magnesium pre-treatment and a combination of the two methods. Anaesthesia 67: 748-754.
48. Kim MH, Hwang JW, Jeon YT, Do SH (2012) Effects of valproic acid and magnesium sulphate on rocuronium requirement in patients undergoing craniotomy for cerebrovascular surgery. Br J Anaesth 109: 407-412.

49. Na HS, Lee JH, Hwang JY, Ryu JH, Han SH, et al. (2010) Effects of magnesium sulphate on intraoperative neuromuscular blocking agent requirements and postoperative analgesia in children with cerebral palsy. Br J Anaesth 104: 344-350.
50. Dacey MJ (2001) Hypomagnesemic disorders. Crit Care Clin 17: 155-173, viii.
51. Safavi M, Honarmand A (2007) Admission hypomagnesemia--impact on mortality or morbidity in critically ill patients. Middle East J Anaesthesiol 19: 645-660.
52. Limaye CS, Londhey VA, Nadkart MY, Borges NE (2011) Hypomagnesemia in critically ill medical patients. J Assoc Physicians India 59: 19-22.