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Magnesium Sulfate: A Versatile Anesthetic Adjuvant

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Abstract

Magnesium sulfate has long been used to prevent seizures in parturients with preeclampsia. Additionally, it has been used in patients with status asthmaticus or Torsades de pointes arrhythmia. Recently, numerous clinical studies reported that magnesium sulfate may improve postoperative analgesia, neuromuscular relaxation, post anesthetic shivering, sore throat, back pain after surgery. If used appropriately, magnesium sulfate can be advantageous for patients recovering from surgery.

Keywords: Magnesium Sulfate; Postoperative Analgesia; Post Anesthetic Shivering.

Introduction

Magnesium sulfate has not been familiar to anesthesiologists until recently. However, magnesium plays a critical role in a variety of physiological processes of the human body. Recently, it has drawn much attention in the field of anesthesiology [1,2], resulting in numerous publications of clinical studies [3,6], review articles, and meta-analyses [7-12]. In this review article, clinical efficacies of magnesium sulfate are described.

Pharmacology and Physiology

As the 4th most common cation, magnesium plays a variety of key roles in the physiological processes of the human body [13]. The normal plasma concentration range of magnesium is around 0.7–1.3 mmol/L (1.4-2.6 mEq/L). Unless patient's renal function is compromised, hyper magnesemia is rare in clinical settings. Hypo magnesemia, on the other hand, is common in perioperative situations because magnesium, supplied through diet, is easily lost by enema, bleeding, and transfusion [13,14]. Magnesium depletion often occurs in patients just before surgery, which peaks immediately after surgery [13]. From a physiological perspective, magnesium is a noncompetitive N-methyl-d-aspartate (NMDA) receptor antagonist and a calcium channel blocker.

Magnesium sulfate-a drug with high therapeutic index—is a safe drug. Magnesium toxicity occurs when the level goes above 4 mM/L, which begins with a loss of deep tendon reflex and drowsiness [13]. When the level further increases, respiratory arrest (> 6 mM/L) or cardiac arrest (> 8 mM/L) may develop [16]. Calcium administration, supportive care with ventilatory/circulatory support and/or excretion of magnesium (loop diuretics or hemodialysis) may be used to treat magnesium toxicity.

Post operative Analgesia

Adequate treatment of pain after surgery is important not only for the recovery from surgical operation but also for the prevention of chronic postsurgical pain [17]. Since magnesium sulfate was studied in surgical patients for the first time in 1996 [18], numerous clinical studies have been reported regarding its analgesia potentiation in surgical patients. Most previous studies suggest that perioperative intravenous administration of magnesium sulfate potentiates analgesia after surgery [9,10]. The usual dosage regimen of magnesium sulfate was as follows: a loading dose of 30–50 mg/kg followed by a maintenance dose of 6-20 mg/kg/h (continuous infusion), until the end of surgery [11]. Even a single bolus dose of magnesium sulfate without the maintenance dose was previously reported to provide effective postoperative analgesia [19].

In terms of potentiation of postoperative analgesia, magnesium sulfate may decrease not only opioid consumption after surgery, but also improve pain scores as well [20]. Decreased opioid consumption after surgery can be associated with less postoperative complications, such as nausea and vomiting [6,21]. Sometimes, magnesium sulfate decreased the requirement for anesthetics during surgery. Ryu et al. [22] made a comparison between magnesium sulfate and remifentanil as an agent for hypotensive anesthesia in patients undergoing middle ear surgery. Both drugs showed adequate level of controlled hypotension; however, the magnesium group showed more favorable postoperative courses with better analgesia.

In addition, sevoflurane was less required in the magnesium group, showing a sevoflurane-sparing effect of magnesium sulfate. The analgesia-potentiating effect of magnesium stabilized blood pressure and heart rate during recovery from anesthesia [22]. It is also conceivable that the use of magnesium sulfate during surgery may mitigate remifentanil-induced hyperalgesia in patients recovering from remifentanil-based anesthesia [23].

The usefulness of magnesium was also reported for postoperative analgesia in patients undergoing spinal anesthesia.

Intravenous administration of magnesium sulfate improved postoperative analgesia in patients undergoing total hip replacement arthroplasty under spinal anesthesia [6]. A small dose of magnesium sulfate added to intrathecal administration of local anesthetic extended the duration of spinal anesthesia and improved postoperative analgesia [4,24-26]. Moreover, only postoperative intravenous administration of magnesium sulfate increased the time to analgesic need and the total consumption of analgesics after spinal anesthesia [6,27]. Unlike intrathecal magnesium sulfate administration, there are limited data on the effectiveness of epidural administration. Arcioni et al. [24] reported that combined intrathecal and epidural administration of magnesium sulfate reduced postoperative analgesic requirements. When mixed with local anesthetics, magnesium also showed beneficial effects in intravenous regional anesthesia (Bier block).

Turan et al. [28] reported that when magnesium sulfate was added to lidocaine for Bier block, the quality of anesthesia and analgesia was improved. However, they also reported that recovery was delayed from Bier block in the magnesium group. The mechanism of pain-reducing effect of magnesium seems to be the attenuating effect on central sensitization via NMDA antagonism [10]. In addition, calcium channel blockade by magnesium may also lead to better postoperative analgesia via augmentation of morphine-induced analgesia [29].

Muscle Relaxation

As a calcium channel blocker, magnesium decreases acetylcholine release at the presynaptic nerve terminals, which diminishes the excitability of muscle fiber and reduces the amplitude of endplate potential, resulting in the potentiation of neuromuscular blockade by nondepolarizing muscle relaxants [30]. Thus, one of the findings from magnesium studies in patients undergoing general anesthesia is that magnesium decreases the requirement for nondepolarizing muscle relaxants [21,31,32] and accelerates the onset of muscle relaxation [33-35].

Although some researchers have focused on the direct effects of magnesium on the neuromuscular blockade, others concluded that magnesium sulfate administration reduced the requirements for nondepolarizing neuromuscular blockers. Administration of magnesium sulfate—while potentiating the effect of muscle relaxants— has not been found to delay the recovery from general anesthesia [21,36,37]. In the operating room, some patients exhibit resistance to nondepolarizing muscle relaxants, which may result from either certain drugs (such as valproic acid) or diseases (such as cerebral palsy) [31,38]. Magnesium sulfate can be used efficaciously in such cases. Moreover, when used during anesthesia induction, magnesium sulfate can prevent cardiovascular responses (hypertension and tachycardia) from endotracheal intubation [39,40]. In addition, when combined with rocuronium priming, magnesium sulfate improved rapid-sequence intubating condition [35].

Magnesium sulfate was also reported to improve tracheal intubation using succinylcholine as it has shown to prevent hyperkalemia and fasciculation induced by succinylcholine [41]. However, it was also reported that the clinical course of malignant hyperthermia induced by succinylcholine was not influenced by magnesium sulfate administration [42]. Recently, intraoperative magnesium sulfate administration showed beneficial to postoperative pulmonary function in patients who underwent video-assisted thoracoscopic surgery [43]. This result seems tobe due to muscle relaxant sparing effect and analgesia potentiating effect of magnesium sulfate [44]. Because postoperative respiratory impairment may result from residual neuromuscular blockade and postoperative pain [45,46] magnesium sulfate use is worth being considered in terms of pulmonary function improvement after surgery.

Miscellaneous Effects

Based on its diverse roles in cellular functions, magnesium sulfate has been suggested to have neuroprotective effects [29]. In the clinical setting, intraoperative use of magnesium sulfate attenuated postoperative neurocognitive impairment [47,48]. Postoperative emergence agitation-related to alteration of cognitive perception-was also reduced in pediatric patients who received magnesium sulfate during adenotonsillectomy [3].

It is also worthy of note that magnesium sulfate has an anti-shivering effect [49]. Shivering is a frequent complication following general anesthesia, and the incidence has been reported to range from 10% to 66% [50]. Due to the undesirable effects of postoperative shivering, such as increased postoperative pain, increased intraocular pressure, interference with monitoring equipment, and increased oxygen consumption [51], it is important to appropriately control postoperative shivering. Kizilirmak et al. [52] reported that an intravenous administration of magnesium sulfate was effective in treating shivering after general anesthesia. Moreover, magnesium sulfate reduced the incidence of shivering after neuraxial blockade when administered intravenously or intrathecally [53,54].

Several studies suggested the effect of magnesium sulfate on postoperative sore throat (POST). Interestingly, various routes of magnesium administration have been shown to effectively control POST. Park et al. [55] described that an intravenous administration of magnesium sulfate appears to be non-inferior to dexamethasone in preventing POST after lumbar spinal surgery in prone position. Magnesium sulfates gargle could also decrease the incidence and severity of POST significantly compared with ketamine gargle [56]. Preoperative administration of oral magnesium lozenge was effective in reducing the incidence and severity of POST in the immediate postoperative period [57].

Since magnesium is an important cofactor of the blood coagulation cascade [58], it also has diverse effects on blood coagulation. Despite some clinical trials that suggested the lack of coagulation effect by magnesium [59,60] several studies have demonstrated an anti-thrombotic effect of magnesium sulfate. Na et al. [31] reported that an intraoperative administration of magnesium sulfate attenuated blood hypercoagulability in

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patients undergoing laparoscopic colorectal cancer surgery [61] and pelviscopic gynecological operations [62]. Because postoperative hypercoagulability could induce thromboembolic complications [63,64], magnesium sulfate administration may be useful for preventing such complications after surgery. Further studies regarding the effects of magnesium sulfate on perioperative blood coagulation are necessary.

Conclusion

Magnesium sulfate has been around for a long time, but only as of recently, its properties have been investigated and found to be useful in the field of anesthesia. If used appropriately, it would enhance smooth recovery and better postoperative outcome for surgical patients.

Conflict of Interest Statement

There is no conflict of interest associated with any of the senior author or other coauthors contributed their efforts in this manuscript.

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