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Review

Influence of the perioperative administration of magnesium sulfate on the total dose of anesthetics during general anesthesia. A systematic review and meta-analysis☆

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ABSTRACT

Background: Magnesium sulfate displays numerous characteristics that make it a useful drug in anesthesiology (N-methyl-D-aspartate receptor antagonist, vasodilator, antiarrhythmic, inhibitor of catecholamine release and of acetylcholine in the terminal motor plate). The perioperative use of this drug as an adjuvant capable of decreasing the required dose of anesthetics, has been proposed.
Objectives: To assess the influence of intravenous magnesium sulfate administration during general anesthesia on the overall dose of required anesthetics.
Design: A systematic review of controlled randomized trials and meta-analysis.
Data sources: An electronic bibliography search in MEDLINE and in the Cochrane Database of Controlled trials (CENTRAL) up to 2015.
Study eligibility criteria, participants and interventions: Randomized, double-blind trials relating to general anesthesia in elective surgery using intravenous magnesium sulfate that provide information about the anesthetic requirements in ASA I and II patients.
Results: 20 clinical trials were selected for the qualitative analysis and 19 for the quantitative one. The use of perioperative intravenous magnesium sulfate reduces the requirement of the anesthetic, propofol during induction (−28.52 mg; CI 95% −35.22–1.82; $p < 0.001$) and maintenance (−213.56 mg; CI 95% −322.93, −104.18; $p < 0.001$) of anesthesia. Additionally, magnesium sulfate reduces the requirement of neuromuscular non-despolarizing blocking agents (−2.99 mg; CI 95% -44.47, −1.99; $p < 0.001$) and the intraoperative consumption of fentanile(−53.57 mcg; CI 95% −75.01, −32.12; $p < 0.001$).
Conclusions: We conclude that perioperative magnesium sulfate acts as a coadjuvant drug capable of reducing anesthetic requirements.

Contents

☆ The authors declare no conflict of interest.

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1. Introduction

Anesthetic coadjuvants are a heterogeneous group of drugs that are concomitantly administered with anesthetics in order to increase the effectiveness, improve the delivery and decrease the dosage required of these drugs. Several compounds, such as clonidine, dexmedetomidine, ketamine and magnesium sulfate have been proposed as anesthetic coadjuvants [1,12–16] because of their favorable perioperative effects on the required dose of anesthetics [1–4], intraoperative hemodynamic reactions [5–8] or intra and post-operative analgesia [9–11].

Magnesium is the fourth most abundant ion in the organism and the second in the intracellular medium. It is a cofactor of numerous enzymes that participate in multiple biochemical reactions of energy metabolism and protein synthesis [17,18]. Experimental research has shown a beneficial effect of magnesium administration in a variety of pathological conditions although probably the most documented is the use of magnesium in obstetrics and in cardiology [18–22]. However, the results of some clinical studies are frequently a cause of controversy. In the beginning of the 20th century, magnesium sulfate was proposed as a general anesthetic due to its depressant effects on the central nervous system. However, this point was never demonstrated. Evidence published in the 60s demonstrated that high doses of magnesium did cause central depressant effects, but all of them could be explained by causes different to any possible anesthetic effect of magnesium, such as: peripheral paralysis, narcosis caused by unsuitable ventilation, hypoxia, hypercapnia or circulatory failure [23–24].Finally, in the late 80s, Thompson and colleagues carried out an experiment in rats anesthetized with halothane and concomitantly treated with magnesium [25]. They demonstrated that they were able to achieve a 60% reduction in the minimum alveolar concentration of halothane that could not be attributed to cardiovascular, respiratory or neuromuscular depression. This experiment proved that the anesthetic effect was due to a central action of magnesium [25].

Magnesium sulfate has numerous properties that make it a useful drug in anesthesiology. It has modulatory effects in the hemodynamic responses to stress due to its vasodilatory, antiarrhythmic and catecholamine release inhibitory action [26]. It has anesthetic and analgesic effects due to its actions as an antagonist of N-methyl-D-aspartate (NMDA) receptors in the central nervous system. This effect of magnesium, together with the reduction in the release of catecholamines [26] contribute to reduce the responses to surgery stress. Additionally, magnesium inhibits the motor plate release of acetylcholine [27], thus facilitating the actions of neuromuscular blocking agents (NMBs).

Numerous clinical studies have been carried out on the adjuvancy of magnesium sulfate in the anesthetic protocols of a variety of surgical procedures. We recently performed a meta-analysis to evaluate the influence of magnesium in the pharmacodynamics of neuromuscular blockers (NMB) during general anesthesia [28]. This work proved the beneficial effect of magnesium on various timing parameters of NMB action during anesthesia. To our knowledge, no meta-analysis has ever been performed covering at the same time the intraoperative consumption of anesthetics, hypnotics, opioids and NMBs. Our goal was to evaluate the uselfulness of intravenous magnesium sulfate during general anesthesia to reduce the doses required of anesthetics, hypnotics, opioids and NMBs in ASA I and II patients undergone elective surgery.

2. Methods

We have followed the recommendations established by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement [29].

2.1. Search and information sources

On September 2015 an electronic bibliographic search in MEDLINE that included the words “anesthesia” and “magnesium sulfate” was performed. Also a search was conducted in the Cochrane Database of Controlled trials (CENTRAL) using the search strategy: ((general anesthesia) or (general anesthesia)) and ((magnesium sulfate) or (magnesium sulfate). We did not introduce a time limit for these searches.

2.2. Elegibility criteria. Selection of studies

Two of our investigators, LRR an JSGP, independently reviewed the titles and abstracts of the screening studies. Those relating to general anesthesia in elective surgery using intravenous magnesium sulfate in the immediate preoperative period, or during induction of anesthesia, were selected. We also reviewed the literature provided by each of the papers selected in the pursuit of studies missed in the original search. We selected only double blind random clinical trials that made placebo group comparisons and in which the doses of the intravenous drugs (hypnotic, opioid or NMB) were provided. The following studies were excluded from this meta-analysis: a) those that use magnesium sulfate as part of a therapeutic strategy for other pathologies such as preeclampsia; b) those carried out in critical patients, pregnant women or ASA III (or higher) patients; c)those which were the outcome of an unplanned surgery; d) those that did not report body weight and mean surgical time as a basis for anesthetic dose calculations; and e) studies published in any language other than English or Spanish.

2.3. Data collection process. Data items

Two of us (LRR and JSGdP) reviewed and measured every test by means of the method detailed below and extracted the data for a subsequent analysis. When discrepancies were noticed, these were discussed and resolved by consensus with a third author (JJ).

We prepared a formulary containing the main characteristics of the studies included in the revision, i.e.: author, date, size of the sample, mean weight, mean surgical time, type of surgical procedure, pain intensity according to the surgical procedure, dose and moment of administration of magnesium sulfate (initial bolus dose and continuous perfusion), drugs used for anesthesia (anesthetics, neuromuscular blockers and opioids). Our summary measure is the total administered dose of hypnotics, opioids and neuromuscular blockers during the anesthetic induction and/or maintenance, so it was searched in the