Systematic Review and Meta-Analysis

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The effect of magnesium sulfate on surgical field during endoscopic sinus surgery

A meta-analysis of randomized controlled trials

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Abstract

Introduction: The benefits of magnesium sulfate for surgical field during endoscopic sinus surgery remain controversial. We conduct a systematic review and meta-analysis to explore the influence of magnesium sulfate versus placebo on surgical field during endoscopic sinus surgery.

Methods: We search PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases through November 2018 for randomized controlled trials (RCTs) assessing the effect of magnesium sulfate versus placebo on surgical field during endoscopic sinus surgery. This meta-analysis is performed using the random-effect model.

Results: Four RCTs and 404 patients are included in the meta-analysis. Overall, compared with control group endoscopic sinus surgery, magnesium sulfate has remarkably positive impact on surgical field scores (MD=−1.76; 95% CI=−2.33 to −1.18; $P<.00001$), and intraoperative blood loss (MD=−89.09; 95% CI=−163.20 to −14.97; $P=.02$), but shows no markedly effect on surgery duration (MD=−7.08; 95% CI=−21.38 to 7.22; $P=.33$), fentanyl (MD=−0.64; 95% CI=−1.97 to 0.70; $P=.35$), and vecuronium (MD=−3.64; 95% CI=−10.99 to 3.70; $P=.33$).

Conclusions: Magnesium sulfate exerts positive impact on surgical field and blood loss reduction for endoscopic sinus surgery.

Abbreviations: ASA = American Society of Anesthesiologists, CI = confidence interval, RCTs = randomized controlled trials, SMD = standard mean difference.

Keywords: endoscopic sinus surgery, magnesium sulfate, meta-analysis, randomized controlled trials, surgical field

1. Introduction

Endoscopic sinus surgery has emerged as a well-established procedure for the treatment of sinonasal diseases, and often suffers from the difficulty in controlling bleeding.[1–3] A small amount of bleeding has a negative impact on confined area of visibility during endoscopic sinus surgery, and subsequently the surgery is difficult to perform and the risk of complications may be increased.[4–6] Controlled hypotension enables us to produce a relatively bloodless surgical field and facilitates surgical dissection, but hypotensive techniques still have certain disadvantages.[7,8]

Various drugs have been developed to reduce the side effects, and they mainly include beta-blockers, nitroglycerine, sodium nitroprusside, and magnesium sulfate.[9–11] For instance, esmolol is one widely used cardio-selective beta-1 receptor blocker with rapid onset and short duration, but has no significant membrane stabilizing activity at therapeutic dosages.[12] Recently, intravenous magnesium sulfate has been found to be a satisfactory agent to achieve controlled hypotension and the clean surgical field for endoscopic sinus surgery via vasodilatation by inhibiting angiotensin converting enzyme activity as well as myocardial depression.[13]

However, the benefit of magnesium sulfate versus placebo for the surgical field during endoscopic sinus surgery has not been well established. Recently, several studies on the topic have been published, and the results have been conflicting.[12,14,15] With accumulating evidence, we therefore perform a systematic review and meta-analysis of RCTs to explore the efficacy of magnesium sulfate versus placebo for the surgical field during endoscopic sinus surgery.

2. Materials and methods

Ethical approval and patient consent are not required because this is a systematic review and meta-analysis of previously published studies. The systematic review and meta-analysis are conducted and reported in adherence to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[16]

2.1. Search strategy and study selection

Two investigators have independently searched the following databases (inception to November 2018): PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases. The

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electronic search strategy is conducted using the following keywords

magnesium sulfate, and endoscopic sinus surgery. We also check the reference lists of the screened full-text studies to identify other potentially eligible trials.

The inclusive selection criteria are as follows: population: patients undergoing endoscopic sinus surgery; intervention: magnesium sulfate; comparison: matched placebo; study design: RCT.

2.2. Data extraction and outcome measures

We have extracted the following information: author, number of patients, age, female, body mass index or weight, American Society of Anesthesiologists (ASA) class (1/2) and detail methods in each group etc. Data have been extracted independently by 2 investigators, and discrepancies are resolved by consensus. We also contact the corresponding author to obtain the data when necessary.

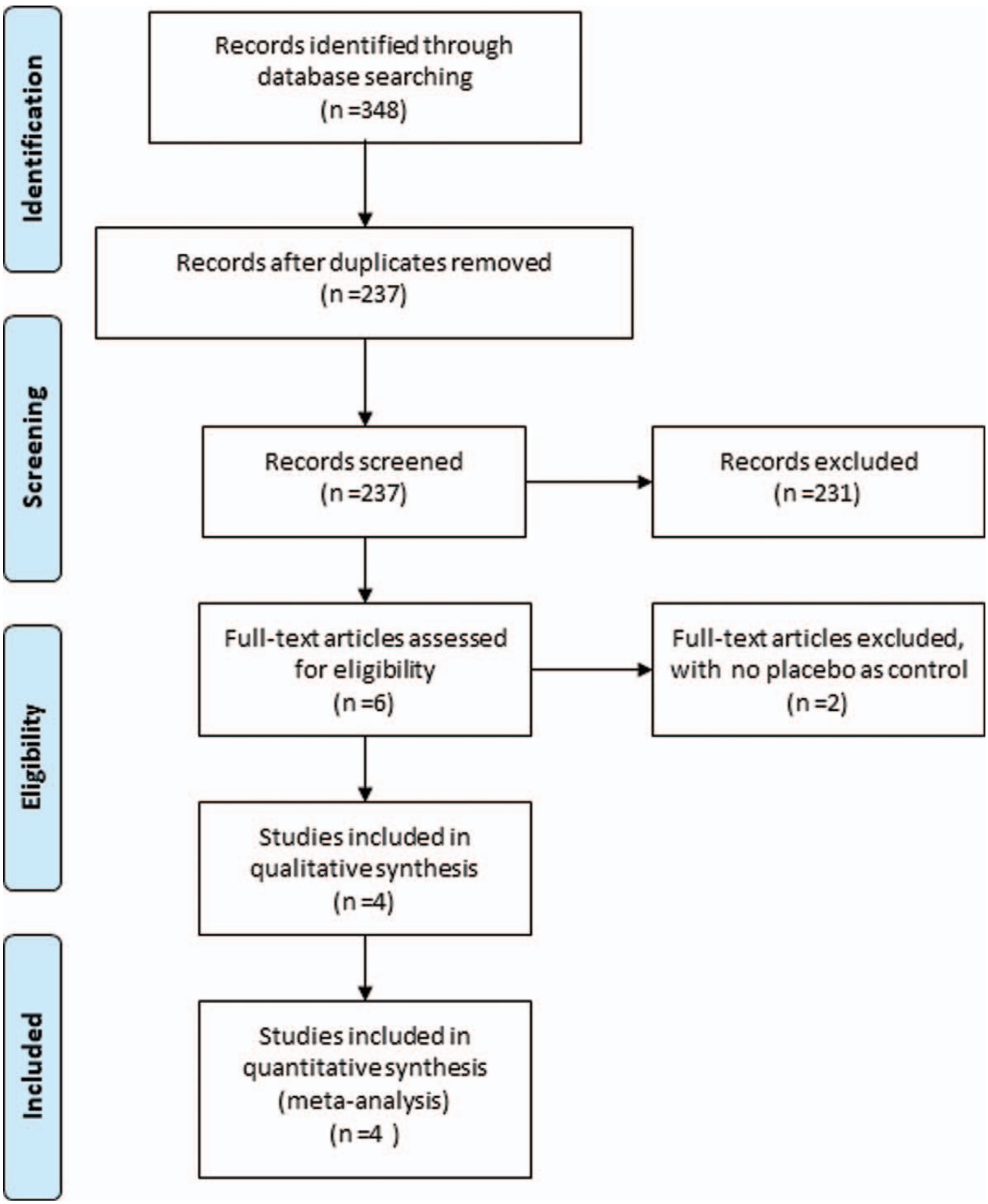

Figure 1. Flow diagram of study searching and selection process.

The primary outcome is surgical field scores. Secondary outcomes include intraoperative blood loss, surgery duration, fentanyl, and vecuronium.

2.3. Quality assessment in individual studies

Methodological quality of the included studies is independently evaluated using the modified Jadad scale.[17] There are 3 items for Jadad scale: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score≤2 is considered to be of low quality. If the Jadad score≥3, the study is thought to be of high quality.[18]

2.4. Statistical analysis

We estimate the mean difference (MD) with 95% confidence interval (CI) for continuous outcomes (surgical field scores, intraoperative blood loss, surgery duration, fentanyl, and vecuronium). A random-effects model is used regardless of heterogeneity. Heterogeneity is reported using the I^2 statistic, and $I^2 > 50\%$ indicates significant heterogeneity.[19] Whenever significant heterogeneity is present, we search for potential sources of heterogeneity via omitting 1 study in turn for the meta-analysis or performing subgroup analysis. All statistical analyses are performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

3. Results

3.1. Literature search, study characteristics, and quality assessment

A detailed flowchart of the search and selection results is shown in Fig. 1. Three hundred forty-eight potentially relevant articles are identified initially. Finally, 4 RCTs that meet our inclusion criteria are included in the meta-analysis.[12–15]

The baseline characteristics of the 4 eligible RCTs in the meta-analysis are summarized in Table 1. The 4 studies are published between 2006 and 2017, and sample sizes range from 20 to 294 with a total of 404. Magnesium sulfate is administered by 40 mg/kg intravenously as a bolus over 10 minutes before induction of anesthesia, followed by 9 to 30 mg/kg/h through infusion.

Among the 4 studies included here, 2 studies report surgical field scores,[12,14] 3 studies report intraoperative blood loss,[12,14,15] 3 studies report surgery duration,[12,13,15] 2 studies report fentanyl and vecuronium.[14,15] Jadad scores of the four included studies vary from 3 to 5, and all 4 studies are considered to be high-quality ones according to quality assessment.

3.2. Primary outcome: surgical field scores

This outcome data is analyzed with the random-effects model, and compared to control group for endoscopic sinus surgery, magnesium sulfate results in significantly surgical field scores (MD = −1.76; 95% CI = −2.33 to −1.18; $P < .00001$) with significant heterogeneity among the studies ($I^2 = 77\%$, heterogeneity $P = .04$) (Fig. 2).

3.3. Sensitivity analysis

Significant heterogeneity is observed among the included studies for surgical field scores, but there are just 2 RCTs, and it is not available to perform sensitivity analysis via omitting 1 study in turn.

Table 1

Characteristics of included studies.

NO.	Author	Magnesium sulfate group						Control group						Jada scores
		Number	Age (years)	Female (n)	Body mass index (kg/m^2) or weight (kg)	ASA class (1/2)	Methods	Number	Age (years)	Female (n)	Body mass index (kg/m^2) or weight (kg)	ASA class (1/2)	Methods	
1	Elsersy 2017	146	36±7	66	31±3 kg/m^2	—	A magnesium infusion of 30mg/kg in the first hour followed by 9 mg/kg/h until the end of the surgical procedure	148	36±8	67	31±3 kg/m^2	—	Matched placebo	5
2	Jangra 2016	10	36.4±9.7	3	64.6±12.0 kg	10/0	Magnesium sulfate 40 mg/kg intravenously as a bolus over 10 min before induction of anesthesia, followed by 15–30 mg/kg/h through infusion	10	31.9±9.0	4	54.8±11.5 kg	9/1	Matched placebo	4
3	Aravindan 2016	15	33.73±10.47	7	23.42±4.42 kg/m^2	13/2	40 mg/kg bolus in a volume of 5 ml followed by 15-mg/(kg.h) infusion (total volume of 10 mL/h)	15	34.87±12.15	7	22.33±2.89 kg/m^2	10/5	matched placebo	3
4	Elsharnouby 2006	30	29.2	14	72.1±11.3 kg	—	Magnesium sulfate 40 mg/ kg, administered as a slow i.v. bolus over a 10 min period before the induction of anaesthesia, and 15 mg/kg/h by continuous i.v. infusion during the operation	30	39.1	11	74.7±10.6 kg	—	Matched placebo	4

ASA = American Society of Anesthesiologists.

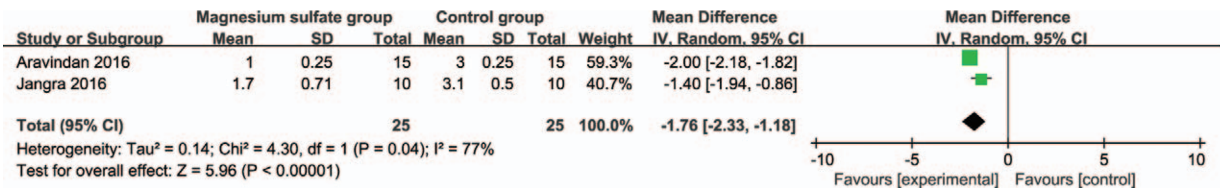

Figure 2. Forest plot for the meta-analysis of surgical field scores.

3.4. Secondary outcomes

In comparison with control group for endoscopic sinus surgery, magnesium sulfate is associated with remarkably decreased intraoperative blood loss (MD = −89.09; 95% CI = −163.20 to −14.97; P = .02; Fig. 3), but has no obvious effect on surgery duration (MD = −7.08; 95% CI = −21.38 to 7.22; P = 0.33; Fig. 4), fentanyl (MD = −0.64; 95% CI = −1.97 to 0.70; P = .35; Fig. 5), and vecuronium (MD = −3.64; 95% CI = −10.99 to 3.70; P = .33; Fig. 6).

4. Discussion

Magnesium sulfate is a well-established vasodilator by increasing the synthesis of prostacyclin and inhibiting angiotensin converting enzyme activity, and has neuroprotective effect during

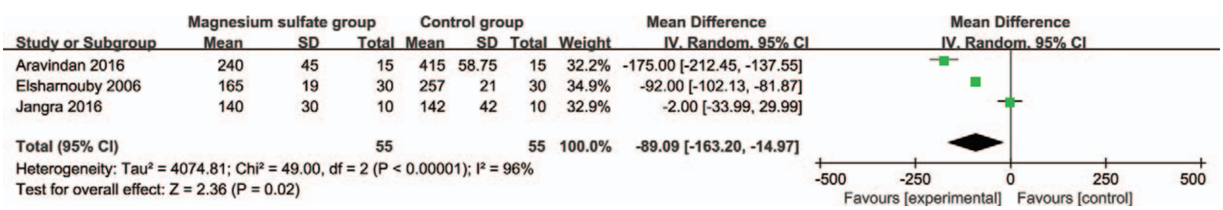

Figure 3. Forest plot for the meta-analysis of intraoperative blood loss (mL).

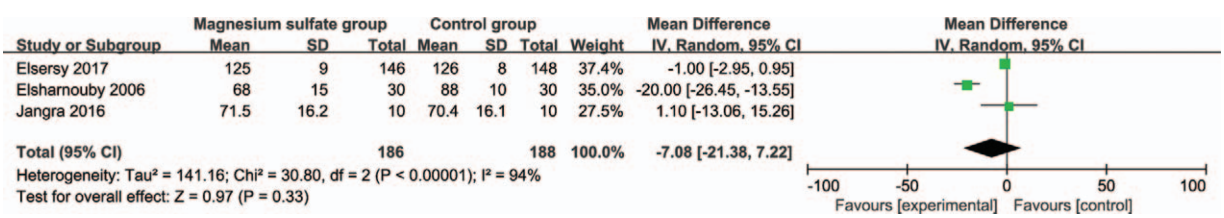

Figure 4. Forest plot for the meta-analysis of surgery duration (min).

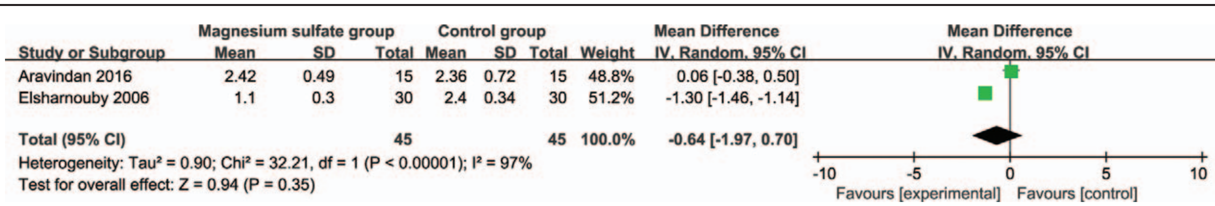

Figure 5. Forest plot for the meta-analysis of fentanyl.

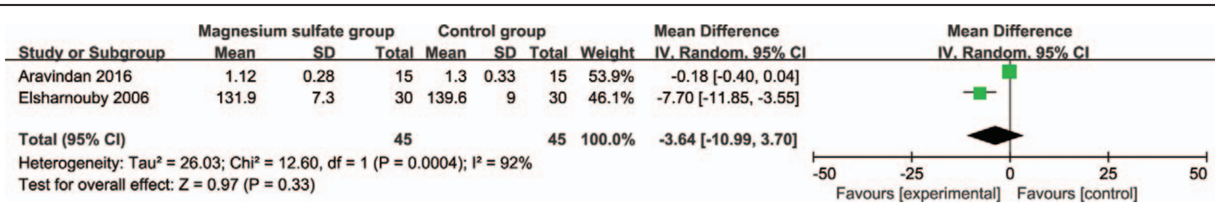

Figure 6. Forest plot for the meta-analysis of vecuronium.

controlled hypotension.[20–23] Magnesium is known as a naturally occurring calcium antagonist and a noncompetitive antagonist of the N-methyl-D-aspartate receptor. Cetylcholine release at the motor endplate is hindered because magnesium competes for calcium channels in the presynaptic nerve terminal.[24–26] Magnesium sulfate has been widely used for controlling blood pressure in preeclampsia, pheochromocytoma and the reduction in blood loss during surgery.[15,20,27]

Successful surgery requires a motionless and clear surgical field, and even minimal bleeding interfering with the visualization of the operative area can lead to increased operative time and complications.[28–30] Previous study reports that magnesium sulfate is capable of reducing arterial pressure, heart rate, blood loss, and duration of sinus surgery.[15] Improved quality of the surgical field is observed after magnesium sulfate application during endoscopic sinus surgery.[12] Our meta-analysis suggests that compared to control group for endoscopic sinus surgery, magnesium sulfate is able to improve surgical field and reduce intraoperative blood loss, but shows no remarkable impact on surgery duration, the dose of fentanyl and vecuronium.

Regarding the sensitivity analysis, there is still significant heterogeneity. However, we cannot perform the sensitivity analysis via omitting one study in turn, because there are just two RCTs for the analysis of surgical field scores. Several reasons may account for this heterogeneity, and they mainly involve different maintenance doses of magnesium sulfate and operation procedures during the surgery. Magnesium sulfate may cause the potential risks such as potentiation of opioids and neuromuscular blockers leading to delayed emergence.[31,32] However, the duration of anesthesia is reduced after the use of magnesium sulfate compared to placebo during endoscopic sinus surgery.[12] In addition, one included RCT reports no episodes of hypotension, arrhythmia or reflex tachycardia during magnesium sulfate infusion, and no patient suffers from rebound hypertension upon discontinuing magnesium sulfate infusion.[15]

There are several potential limitations. First, 4 RCTs are included in this meta-analysis, and 3 of them have a relatively small sample size ($n < 100$) which may result in some overestimation of the treatment effect. Next, significant heterogeneity is observed and it may result from different procedures of surgery and doses of magnesium use. Finally, the meta-analysis of some important index (e.g., pain scores, mean heart rate, and blood pressure) cannot be conducted based on limited data in current RCTs.

5. Conclusions

Magnesium sulfate can provide obviously improved surgical field for endoscopic sinus surgery.

Author contributions

Conceptualization: Yinglong Zhang.
Data curation: Yinglong Zhang.
Formal analysis: Yinglong Zhang.
Methodology: Dongli Hu.
Resources: Wei Liu, Dongli Hu.
Software: Hong Jiang.
Supervision: Wei Liu, Hong Pu.
Visualization: Hong Pu.
Writing – original draft: Hong Jiang.

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