Magnesium Sulfate Plus Lidocaine Reduces Propofol Injection Pain: A Double-blind, Randomized Study

Jiehao Sun, MD; Riyong Zhou, MD; Wendong Lin, MD; Jiahao Zhou, MD; and Weijan Wang, MD

Department of Anesthesiology, 1st Affiliated Hospital, Wenzhou Medical University, Wenzhou, China

ABSTRACT

Purpose: Propofol injection can cause distressing pain, and no method can inhibit it completely. Neither lidocaine nor magnesium sulfate ($MgSO_4$) was sufficient to prevent pain from the injection of propofol. This prospective, double-blind, placebo-controlled study was designed to investigate the efficacy of the $MgSO_4$ plus lidocaine on suppressing propofol injection pain.

Methods: Three hundred women received 300 mg $MgSO_4$ (Group M), 40 mg lidocaine (Group L), or 300 mg $MgSO_4$ plus 40 mg lidocaine (Group M+L). This was followed by administration of 50 mg propofol. Pain scores, behavior-related responses, and diameter of the vein were recorded following the injection of propofol.

Findings: Patients in Group M + L had lower pain scores. Patients' behavior-related responses in Group M + L were also better compared with the other groups. There were no differences in pain scores between Group L and Group M. The target vein diameter change in Group M and Group M + L was more obvious than in Group L.

Implications: Administration of 300 mg $MgSO_4$ plus 40 mg lidocaine reduces propofol injection pain very well. No complications were observed in the treatment groups. (*Clin Ther*. 2016;38:31–38)

Key words: injection pain, magnesium sulfate, propofol.

INTRODUCTION

Administration of propofol can provide good quality of anesthesia and rapid recovery. However, the pain associated with propofol injection is immediate and can be profound. It has been reported that injection pain ranges from 28% to 90%, ranking seventh among the 33 major clinical concerns deserving high priority for improvement.[1] Minimizing propofol injection pain is an important clinical goal because it may influence a patient's perception of quality and acceptability of anesthesia. Several measures have been used to reduce the occurrence of propofol injection pain, including the addition of lidocaine with tourniquet; cooling or warming the propofol; diluting the propofol solution; injection of propofol into a large vein; or prior injections of meperidine, metoclopramide, magnesium, thiopental, ketamine, methylene blue, or a β-blocker.[1–7] We have not found a method that suppresses injection pain completely.

Tourniquet causes dilation of veins, and, interestingly, vein size is an important factor in propofol injection pain.[8] A meta-analysis[1] suggested that use of a rubber tourniquet and lidocaine application before propofol injection was most effective to prevent injection pain. Dae et al[9] demonstrated that higher doses of lidocaine can achieve more analgesia, but the incidence of pain can be still as high as 36.8% when a tourniquet combined with 100 mg lidocaine is applied.[1,8]

Most studies have concluded that the intensity of propofol injection pain is positively correlated with the aqueous free propofol concentration in the lipid emulsion.[10] Propofol-long-chain triglycerides (LCT)/medium-chain triglycerides (MCT), which has less aqueous free propofol, was designed as a new chemical agent causing less injection pain than propofol-LCT, and lidocaine is effective for reducing injection pain associated with this agent.[11] However, the incidence of pain can reach 20% when propofol-LCT/MCT with lidocaine[12] is applied.

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Magnesium sulfate ($MgSO_4$), which could act as vasodilator as well as an N-methyl-D-aspartate (NMDA) receptor antagonist, can partially inhibit propofol injection pain,[2] but to our knowledge no prior study concerning the effect of $MgSO_4$ combined with lidocaine on propofol injection pain has been conducted. We aimed to confirm whether $MgSO_4$ plus lidocaine could effectively suppress propofol injection pain.

PATIENTS AND METHODS

The study is registered in the Chinese Clinical Trial Registry (ChiCTR-TRC-14004939) and was approved by the Institutional Research Ethics Committee of the 1st Hospital of Wenzhou Medical University, China (ethical No. 2014-33) on June 10, 2014. Informed written consent was obtained from all patients. The inclusion criterion of the clinical trial was gynecologic cases referred for hysteroscopy examination performed using total intravenous anesthesia. The patients excluded from this trial were those who required antibiotics, who showed evidence of systemic disease that contraindicated participation in the study, who were older than age 45 years or younger than age 20 years, who disagreed with participation in the study, and others not suitable for participation in the trial. The trial is registered at http://www.chictr.org/cn/proj/show.aspx?proj=8788.

Study Design

A randomization code (generated by Excel 2003, Microsoft Corp, Redmond, Washington) was used to assign patients to the 3 groups by Dr. Sun. The allocation sequence was placed in a sealed envelope for each woman, which was opened before each induction of anesthesia. Upon arrival at the waiting room, patients were educated about the Numeric Rating Scale-Visually (NRS-V), for the purpose of becoming familiar with the method of evaluation.

A nurse anesthetist who was not involved in patient assessment prepared the study solution. Group L received 40 mg lidocaine; Group M received 300 mg $MgSO_4$; Group M + L received the mixture of 300 mg $MgSO_4$ and 40 mg lidocaine. All test drugs were diluted into 4-mL solutions using 0.9% normal saline. No premedication was administered before surgery. A 22-gauge cannula was inserted in a vein on the dorsum of the patient's hand 15 to 20 minutes before propofol administration. Standard monitoring that included noninvasive blood pressure, ECG, and pulse oxygen saturation was used when the patients arrived in the operating room. Supplemental oxygen therapy was given by facemask (100% oxygen at a rate of 4 L/min) when required to maintain saturation $>92\%$ throughout the duration of the study.

Outcome Measures

Patients were in the supine position with the arm next to the body at heart level. Before the test, an anesthesiologist measured the diameter of the target vein (a longitudinal image of the forearm vein 2–3 cm proximal to the injection site; that is, the vein on the dorsum of the hand, was acquired in each patient using an ultrasound scanner with a 38-mm 6- to 13-MHz linear probe [EDGE, Fujifilm SonoSite]). Test solutions were maintained at room temperature, and patients were asked if they experienced any discomfort. Then we waited 10 seconds before administering 50 mg propofol-LCT. During the infusion of propofol, the patients were observed and immediately questioned concerning their pain by NRS-V score. At the same time, another anesthesiologist measured the diameter of the same target vein again. The patients' responses to the injection of propofol were assessed with a 4-point scale by an investigator. The score was graded as 0 = no response; 1 = movement at the wrist only; 2 = movement involving the arm only (elbow or shoulder); and 3 = a generalized response or movement in more than one extremity, including reactions such as discomfort and pain. After a pain assessment regarding the propofol injection, the remainder of the calculated (2 mg/kg) propofol dose and sufentanil (5 μg) was administered. The anesthesiologists and patients were unaware of which solution was administered. After the operation, we asked the women whether they remembered the propofol injection pain or not.

Anesthesia was maintained with propofol and remifentanil in 100% oxygen, and respiration was assisted manually as necessary. Any complications such as pain or edema at the injection site were recorded in the recovery room and 24 hours after discharge.

Our primary outcome was the NRS-V score during the infusion of propofol induction. All other outcomes were considered secondary outcomes.