Journal of Clinical Anesthesia (2015) **27**, 595–601

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Journal of Clinical Anesthesia

Original Contribution

The effect of magnesium sulphate on intubating condition for rapid-sequence intubation: a randomized controlled trial☆,☆☆

Mi-Hyun Kim MD, PhD (Professor)[a], Ah-Young Oh MD, PhD (Professor)[b], Sung-Hee Han MD, PhD (Professor)[b], Jin-Hee Kim MD, PhD (Professor)[b], Jung-Won Hwang MD, PhD (Professor)[b], Young-Tae Jeon MD, PhD (Professor)[b,*]

[a]*Department of Anesthesiology and Pain Medicine, Seoul St Mary's Hospital, Catholic University of Korea, Seoul, South Korea*
[b]*Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea*

Received 13 September 2013; revised 15 June 2015; accepted 9 July 2015

Keywords:
Intratracheal;
Intubation;
Magnesium sulphate;
Neuromuscular block

Abstract

Study objectives: We compared magnesium sulphate with control, ketamine, rocuronium prime, and large-dose rocuronium (0.9 mg/kg) with regard to intubation conditions during rapid-sequence induction.

Design: This is a prospective, randomized, double-blinded study.

Setting: The setting is at an operating room in a university-affiliated hospital.

Patients: One hundred ten patients scheduled for general anesthesia were randomly allocated to the following 5 groups in equal numbers.

Interventions: The control and rocuronium 0.9 groups received rocuronium 0.6 and 0.9 mg/kg, respectively; the ketamine group was given 0.5 mg/kg ketamine 2 minutes before 0.6 mg/kg rocuronium; the rocuronium prime group received 0.06 mg/kg rocuronium 3 minutes before 0.54 mg/kg rocuronium; and the magnesium group received 50 mg/kg magnesium sulphate. Intubation was initiated 50 seconds after the rocuronium injection.

Measurements: Intubating condition (primary outcome), rocuronium onset, rocuronium duration, train-of-four ratio upon intubation, and hemodynamic variables (secondary outcomes) were recorded.

Main results: The excellent intubating condition was more frequent in the magnesium group ($P < .05$). Onset of neuromuscular block was shorter in the magnesium group than in the control, ketamine, and rocuronium prime groups ($P < .05$). No difference in onset time was found between the magnesium and rocuronium 0.9 groups. Block duration was longest in the rocuronium 0.9 group. The train-of-four ratio on intubation was lowest in the rocuronium prime group. The only adverse event was a burning or heat sensation reported by 5 patients in the magnesium group.

ConclusionsMagnesium sulphate pretreatment was most likely to provide excellent intubating condition for rapid-sequence intubation compared with the control, ketamine pretreatment, rocuronium prime, and large-dose rocuronium. However, magnesium sulphate administration is associated with a burning or heat sensation.

1. Introduction

Succinylcholine is the first-choice neuromuscular blocking agent for rapid-sequence intubation [1]. Succinylcholine

☆ Funding: No funding was obtained for this study.
☆☆ Conflict of interest: none.

* Corresponding author at: Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, 166, Gumi-ro, Seongnam-si, Gyeonggi-do, South Korea. Tel.: +82 31 787 7493.
E-mail address: ytjeon@snubh.org (Y.-T. Jeon).

http://dx.doi.org/10.1016/j.jclinane.2015.07.002
0952-8180/

is contraindicated in patients with major burns (beyond 48 hours), major crush injuries (beyond 48 hours), and spinal cord injuries due to the risk of hyperkalemia [2]. Several alternative methods of facilitating neuromuscular block have been introduced to improve intubating condition during rapid-sequence intubation.

Ketamine pretreatment accelerates neuromuscular block by increasing cardiac output and blood pressure and thereby shortening rocuronium circulation time [3]. The priming technique, in which a subparalyzing priming dose of a nondepolarizing muscle relaxant preoccupies nicotinic cholinergic receptors, reduces time for the subsequent paralyzing dose to occupy enough receptors for a significant neuromuscular block [4]. Large-dose rocuronium [1] and magnesium sulphate pretreatment [5] also provide a faster neuromuscular block than does standard dose rocuronium (0.6 mg/kg) alone.

No studies have compared intubating conditions among these methods. Therefore, we compared magnesium sulphate with control, ketamine, priming, and large-dose rocuronium (0.9 mg/kg) with regard to intubating condition (primary outcome) during rapid-sequence intubation. We hypothesized that magnesium sulphate would provide an excellent intubating condition due to its profound acceleration of rocuronium onset [5]. Onset and duration of rocuronium, train-of-four (TOF) ratio at the time of intubation, and cardiovascular changes after rapid-sequence intubation (secondary outcomes) were also compared.

2. Materials and methods

This double-blind randomized controlled trial received approval from the Institutional Review Board of Seoul National University Bundang Hospital (institutional review board no. B-1102-121-005) and was registered at ClinicalTrials.gov (ID, NCT01479751). Written informed consent was obtained from all participants. Patients (age, 18-65 years; body mass index, 18.5-24.9 kg/m^2) with American Society of Anesthesiologists physical status of I-II and Mallampati class of I-II, who were scheduled for an elective operation under general anesthesia in Seoul National University Bundang Hospital were enrolled in the study. Exclusion criteria were renal, hepatic, cardiovascular, or neuromuscular disease; breast-feeding; pregnancy; anticipated difficult airway; and medications that influence neuromuscular transmission such as antiepileptics, corticosteroids, furosemide, and aminoglycosides [2].

After establishing pulse oximetry, electrocardiogram, and noninvasive blood pressure monitoring, 110 patients were randomly allocated into 1 of 5 parallel groups (control, ketamine, priming, rocuronium 0.9, and magnesium groups) in equal numbers, using a computer-generated random sequence (Research Randomizer program, version 3.0; http://www.randomizer.org) prepared by a research assistant who was not involved in the study. The group allocation was concealed in sealed opaque envelopes that were numbered consecutively. The envelopes were opened sequentially upon patients' (consent obtained) arrival at the operating room by an anesthetist who subsequently prepared the study drugs and labeled them as "1st," "2nd," "3rd," and "4th" study drug, respectively, designating the order of the drug injections (Table 1). The anesthetist who prepared the study drugs did not participate in the other process of the study and was unaware of the study objectives and outcome measures. The drugs were administered intravenously in the following sequence (Table 1) by a trained nurse who was not involved in this trial and was unaware of the treatment allocation. Magnesium sulphate (50 mg/kg) or the same volume of 0.9% saline (the other groups) was infused over 10 minutes. Neuromuscular monitoring was performed in agreement with the clinical research consensus [6] using TOF-Watch SX (Organon, Ltd, Dublin, Ireland). Two pediatric surface electrodes were affixed 3 cm apart over the ulnar nerve on the side of the wrist without either an intravenous catheter or a blood pressure cuff. The hand and forearm were immobilized. A hand adapter (Organon) was placed on the thumb. After a midazolam (0.05 mg/kg) injection, calibration (using implanted mode 2) and stable twitches (<5% deviation, for 2 minutes) were confirmed. Then, TOF stimulations (2 Hz, square wave, 200-μs stimulus duration) were continued every 15 seconds. Subsequently, a priming dose of rocuronium (0.06 mg/kg, rocuronium prime group) or the same volume of 0.9% saline (the other groups) was given. One minute later, 0.5 mg/kg ketamine (ketamine group) or the same volume of 0.9% saline (the other groups) was administered. Two minutes later, 2 mg/kg propofol, 1 μg/kg remifentanil, and rocuronium (control, ketamine, and magnesium groups, 0.6 mg/kg; rocuronium prime group, 0.54 mg/kg; rocuronium 0.9 group, 0.9 mg/kg; diluted to a total volume of 10 mL with 0.9% saline; total injection time, 5 seconds) were injected in rapid succession. The laryngoscopy was commenced 50 seconds from the start of rocuronium administration with an attempt to complete intubation within 20 seconds. A skilled staff anesthetist who was blind to the group assignments performed the intubation and graded the intubation condition. If successful intubation was not carried out within 30 seconds (ie, 70 seconds after the start of rocuronium injection), the attempt was recorded as a failure. Intubating condition (Table 2) [6]; Cormack-Lehane grade [7]; time from start of rocuronium injection (0.54, 0.6, or 0.9 mg/kg), until TOF count reached 0 (onset of rocuronium) and time until TOF count recovered to 2 (duration of rocuronium); and TOF ratio at the time point of intubation were recorded. Mean arterial pressure and heart rate were measured at baseline; after anesthetic induction (before intubation); immediately after intubation; and at 1, 2, 3, 4, and 5 minutes after intubation.

3. Sample size and statistics

Based on pilot data of 7 patients in each group, a ≥50% increase in the incidence of excellent intubating condition in