

Pretreatment with magnesium sulphate is associated with less succinylcholine-induced fasciculation and subsequent tracheal intubation-induced hemodynamic changes than precurarization with vecuronium during rapid sequence induction

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Abstract : Although it has side effects, succinylcholine is still widely used in rapid sequence induction. The aim of the present study is to evaluate the effects of pretreatment with magnesium and precurarization of vecuronium on succinylcholine-induced fasciculation and subsequent tracheal intubation-induced hemodynamic changes during rapid sequence induction. Fifty-five patients were allocated to three groups by a blinded randomization : Group M received saline 100 ml with magnesium 40 mg·kg⁻¹ for 5 min at 6.5 min before induction and subsequently administered saline 1-2 ml at 1.5 min before induction ; Group V received saline 100 ml for 5 min at 6.5 min before induction and subsequently administered vecuronium 0.02 mg·kg⁻¹ at 1.5 min before induction ; Group C received saline 100 ml for 5 min at 6.5 min before induction and then saline 1-2 ml at 1.5 min before induction. Fasciculation scores and mean percent changes of heart rate, systolic blood pressure and rate pressure product between baseline and after induction were significantly lower in group M than those in group C and group V. Pretreatment with magnesium is more effective to limit succinylcholine-induced fasciculation and subsequent tracheal intubation-induced hemodynamic changes in rapid sequence induction compared with vecuronium pretreatment, although magnesium does not prevent the elevation of serum potassium concentration after induction.

Key words : Rapid sequence induction ; magnesium ; vecuronium ; succinylcholine ; fasciculation.

INTRODUCTION

Succinylcholine (SCC) widely used in rapid sequence induction has side effects around induction ; increases in serum potassium concentration, fasciculation and life-threatening arrhythmia (1-6). Precurarization with nondepolarizing muscle relaxant is commonly used to limit these SCC-induced side effects (2, 3, 7-9) except for arrhythmia. However, this could cause partial paralysis, partial

paralysis-induced discomfort (2) or delays of onset of SCC (1).

On the other hand, magnesium sulphate (MgSO₄) has precurarization-effects that reduce SCC-induced fasciculation (1, 4-6, 10) and increases in serum potassium concentration (5, 10) without the delay of onset (5) and prolongation (1, 5) of SCC-induced effects. Furthermore, MgSO₄ prior to tracheal intubation decreases the hemodynamic response (11). It has antiarrhythmic effects (12) and produces vasodilation by direct action on the blood vessels (12) and by interfering with vasoconstricting substances (12, 13). Therefore, it theoretically must prevent SCC-induced side effects and the hemodynamic response to tracheal intubation.

However, it causes unpleasant warm sensation for conscious patients by rapidly (14) or slowly (2 min) injection (4), although it suppresses hypertension induced by intubation in hypertensive proteinuric pregnant patients (14). MgSO₄ administered between administration of sedatives and SCC to avoid unpleasant sensation does not suppress hypertension and increases in heart rate (HR) induced by rapid sequence induction (1).

We, therefore, hypothesize that pretreatment with very slow injection (5 min) of MgSO₄ suppresses SCC-induced fasciculation and subsequent

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hemodynamic responses to tracheal intubation more than precurarization with vecuronium bromide (VB) during rapid sequence of anesthesia.

METHODS

The present study was approved by the ethical committee of our institution for human investigation, and written informed consent was obtained from 55 ASA physical status I and II patients scheduled for surgery under general anesthesia with tracheal intubation. Patients were excluded if they were pregnant, had neuromuscular disease or had a contraindication to SCC. Patients administered with calcium channel or β -blocking agents were also excluded. All patients received hydroxyzine 25-50 mg and atropine sulphate 0.5 mg intramuscularly 1 hour before induction. Standard monitoring was used, including NIBP, ECG and pulse oximetry.

Patients were randomly assigned to following three groups : Group M (n = 18) received saline 100 ml with MgSO_4 40 $\text{mg}\cdot\text{kg}^{-1}$ (1) for 5 min at 6 min 30 sec before induction and subsequently administered saline 1-2 ml at 90 sec before induction ; Group V (n = 19) received saline 100 ml for 5 min at 6 min 30 sec before induction and subsequently administered VB 0.02 $\text{mg}\cdot\text{kg}^{-1}$ at 90 sec before induction ; Group C (n = 18) received saline 100 ml for 5 min at 6 min 30 sec before induction and then saline 1-2 ml at 90 sec before induction. The study solution was prepared in advance by an independent investigator who was not involved in the data collection. In our preliminary study, VB 0.02 $\text{mg}\cdot\text{kg}^{-1}$ induced 90%, 90% and 100% reduction of twitch responses (n = 3) at 90 sec after the pretreatment of VB. Therefore, we chose the dosage of VB at 0.02 $\text{mg}\cdot\text{kg}^{-1}$ and 90 sec as the waiting time. Also, in our preliminary study, it took about 4 min (246.3 ± 65.2 sec [200-360] ; n = 11) to induce the most attenuation of twitch responses by the slowly injection of MgSO_4 40 $\text{mg}\cdot\text{kg}^{-1}$.

Patients were preoxygenated via face mask and were asked for their subjective feeling (no unpleasant, mild unpleasant, severe unpleasant) during receiving pretreatment drugs and until before loss of consciousness. Anesthesia was induced with propofol 2 $\text{mg}\cdot\text{kg}^{-1}$ and SCC 1.5 $\text{mg}\cdot\text{kg}^{-1}$ was injected at 5 sec after the injection of propofol. After SCC-induced fasciculation finished at the toe, trachea was intubated. After induction of anesthesia, patients were ventilated (tidal volume : 6-10 mL kg^{-1} ; respiratory frequency : 6-10 times min^{-1}) to adjust

at normocapnia (end-tidal carbon dioxide at 35-45 mmHg) at FiO_2 0.3.

Arterial blood samples (1 ml) were obtained via the femoral artery before the study and 2 min after an administration of SCC. The serum concentration of ionized potassium and ionized magnesium were measured by ion-selective electrode analysis (Stat Profile M, NOVA Biomedical Corporation, Waltham, MA, USA).

Blood pressure and HR were recorded before induction and every 1 min for the first 10 min after induction. The Rate pressure product (RPP? systolic blood pressure (SBP) \times HR) was calculated every time point.

The degree of muscle fasciculation after administration of SCC was recorded on a scale of 0 to 3 : no fasciculations = 0 ; mild, fine fasciculations of the eyes, neck, face, or fingers without limb movement = 1 ; moderate fasciculations occurring at more than two sites or obvious limb movement = 2 ; vigorous or severe, sustained, and widespread fasciculations = 3 (15).

Intubating conditions (excellent, good or poor) were recorded by the blinded anesthetist (S.K) performing tracheal intubation and this assessment was followed by the previous literature (16).

Values are expressed as mean \pm SD unless otherwise specified. The patient characteristics were analyzed using a one-way analysis of variance and Kruskal-Wallis test. Fasciculation scores, intubation conditions and the measurement variables were analyzed by Kruskal-Wallis test. The measurement variables were analyzed by Mann-Whitney U-test between the groups with Bonferroni's correction. Comparisons between baseline and peak of SBP, mean arterial pressure (MAP), HR and RPP were analyzed by Wilcoxon signed rank test. Comparisons of baselines of HR, SBP, RPP and MAP among three groups were analyzed by one-way ANOVA. $P < 0.05$ was considered as significant unless otherwise specified.

RESULTS

Patient characteristics were similar among the three groups (Table 1). There were no patients who had unpleasant sensation induced by pretreatment drugs.

Fasciculation scores were observed higher in Group C ($P = 0.0004$) and Group V ($P = 0.004$) than in Group M (Table 2). Fasciculation score 2 and 3 occurred in 11.1% of Group M, while those occurred in 72.3% of Group C and in 47.4% of Group V.

Table 1
Patient characteristics

	Group C (n = 18)	Group M (n = 18)	Group V (n = 19)
Age (yr)	52.8 ± 14.1	49.4 ± 14.3	44.3 ± 15.1
Height (cm)	159.9 ± 7.8	158.1 ± 6.3	158.8 ± 7.6
Weight (kg)	60.5 ± 9.4	56.6 ± 8.2	56.8 ± 10.8
BMI (kg·m ⁻²)	23.7 ± 3.4	22.6 ± 2.5	22.4 ± 3.0
Gender (M/F)	6/12	6/12	3/16
ASA status (I/II)	8/10	9/9	15/4

Values are presented as mean ± SD or absolute number.
There were no statistical differences among three groups.
BMI = body mass index.

Table 2
Distribution of Fasciculation Scores^a

Score	Group C ^b	Group M ^{c,d}	Group V
0	2 (11.1)	6 (33.3)	1 (5.2)
1	3 (16.7)	10 (55.6)	9 (47.4)
2	3 (16.7)	2 (11.1)	6 (31.6)
3	10 (55.6)	0 (0)	3 (15.8)

Distribution values are given as n (%)

^aSignificant difference among three groups ($P = 0.0003$).

^bNonsignificant difference between Group C and Group V ($P = 0.03$).

^{c,d}Fasciculation Scores were significantly lower in Group M than in Group C ($P = 0.0004$) and Group V ($P = 0.004$).

All hemodynamic parameters were significantly increased by rapid sequence induction in Group C (SBP : $P = 0.001$, MAP : $P = 0.004$, HR : $P = 0.01$, RPP : $P = 0.001$) and Group V (SBP : $P = 0.004$, MAP : $P = 0.002$, HR : $P = 0.0004$, RPP : $P = 0.0005$) (Table 3). In contrast, rapid sequence induction induced significant increases only in MAP in Group M ($P = 0.03$). Also, mean percent changes of HR and RPP in Group M were significantly lower than those in Group V ($P = 0.004$ and $P = 0.01$, respectively).

Serum potassium concentration significantly increased 2 min after administration of SCC comparing with each baseline in Group C ($P = 0.0007$) and Group M ($P = 0.0003$) (Table 4). The increase of serum potassium concentration in Group V was significantly lower than that in Group C ($P = 0.0045$) and Group M ($P = 0.0059$).

Two patients in Group V had good intubation conditions. Every other patient had excellent intubation condition (no significant difference among groups).

DISCUSSION

The present study indicates that the pretreatment of MgSO₄, compared with the precurarization

of VB, decreases SCC-induced fasciculation and tracheal intubation-induced hemodynamic changes during rapid sequence induction. No patients suffered from the prolongation of effects of pretreatment drugs.

The administration of MgSO₄ during rapid sequence induction is effective to decrease SCC-induced fasciculation whenever it is administered, before (4-6) or after (1, 10, 14) administration of sedative drugs. Nondepolarizing muscle relaxants induce the similar effects on SCC-induced fasciculation whenever it is administered (2, 3, 7-9). The present study has shown that the pretreatment of MgSO₄ is superior to the precurarization of one of the nondepolarizing muscle relaxants, VB, to decrease SCC-induced fasciculation.

The administration of MgSO₄ produces vasodilation by direct effects on blood vessels (13) and by indirect effects, including sympathetic blockade and inhibition of release of catecholamine (12). However, the administration of MgSO₄ after giving sedative drugs but before giving SCC does not attenuate tracheal intubation-induced hemodynamic changes, SBP and HR, in rapid sequence induction (1). Therefore, in the present study, the administration of MgSO₄ begins at 6.5 min before administration of SCC to produce the significant effects on the tracheal intubation-induced hemodynamic changes and it takes over 5 min to avoid unpleasant sensation induced by the administration of MgSO₄ (4, 14). In fact, the pretreatment of MgSO₄ did not induce significant changes in SBP, HR and RPP with no unpleasant sensation, and HR and RPP in Group M were significantly lower than those in Group C and Group V. Values of RPP as index of myocardial oxygen consumption (18-20) of more than 20000 have been shown to be associated with angina and myocardial ischemia (20). Furthermore, in patients with preoperative coronary artery disease, RPP should be maintained below 12000 (19) in the period in which

Table 3
Hemodynamic changes during rapid sequence induction

		Baseline ^c	Peak	Mean percent change (%)
SBP (mmHg)	Group C	140.8 ± 23.7 (105-188)	167.1 ± 26.1* (133-238)	20.6 ± 20.6
	Group M	125.9 ± 19.9 (91-163)	136.2 ± 25.6 (71-173)	8.7 ± 18.2
	Group V	135.0 ± 24.8 (109-189)	156.5 ± 28.7* (110-206)	17.1 ± 17.6
MAP (mmHg)	Group C	99.5 ± 15.0 (77-118)	119.1 ± 18.4* (88-145)	22.5 ± 27.7
	Group M	89.7 ± 15.1 (67-122)	98.8 ± 17.9* (54-128)	11.2 ± 19.6
	Group V	94.7 ± 16.8 (73-129)	110.8 ± 20.4* (79-150)	18.1 ± 17.8
HR (bpm)	Group C	78.6 ± 16.2 (48-111)	89.6 ± 20.5* (56-129)	16.0 ± 28.2
	Group M	83.8 ± 17.6 (53-122)	88.9 ± 16.0 (59-117)	8.0 ± 17.7 ^a
	Group V	72.8 ± 16.4 (42-104)	94.6 ± 16.3* (62-129)	34.2 ± 28.8
RPP	Group C	11161 ± 3509 (6825-19552)	15096 ± 4819* (8896-24897)	42.5 ± 57.0
	Group M	10763 ± 3636 (5936-18910)	12312 ± 3941 (5751-20241)	19.6 ± 38.4 ^b
	Group V	9945 ± 3285 (4494-17955)	14962 ± 4157* (6820-24252)	59.1 ± 47.2

Values are presented as mean ± SD (range).

^{a,b}Mean percent changes of HR and RPP in Group M were significantly lower than those in Group V ($P = 0.004$, $P = 0.01$).

^cThere were no significant difference of baseline of SBP, MAP, HR, RPP among three groups.

* $P < 0.05$ between baseline and peak.

SBP = systolic blood pressure ; MAP = mean arterial pressure ; HR = heart rate ; RPP = rate pressure product.

Table 4
Serum potassium and magnesium concentration before and after rapid sequence induction

		Baseline	2 min after intubation	∅	P value ^a
Serum potassium concentration (mEq L ⁻¹)	Group C	4.14 ± 0.32	4.42 ± 0.57*	0.26 ± 0.30	0.0048
	Group M	4.14 ± 0.40	4.37 ± 0.43*	0.22 ± 0.20	
	Group V	4.06 ± 0.29	4.13 ± 0.29	0.06 ± 0.13 ^b	
Serum magnesium concentration (mEq L ⁻¹)	Group C	1.07 ± 0.08	1.02 ± 0.09	0.01 ± 0.02	0.011
	Group M	1.26 ± 0.31	1.97 ± 0.24*	0.35 ± 0.18 ^c	
	Group V	0.99 ± 0.19	0.98 ± 0.16	0.02 ± 0.01	

Values are presented as mean ± SD.

^a P value means the difference of ∅ among three groups by Kruskal-Wallis analysis.

^bThe increase of serum potassium concentration in Group V was significantly smaller than that in Group C ($P = 0.0045$) and Group M ($P = 0.0059$).

^cThe increase of serum magnesium concentration in Group M was significantly larger than that in Group C ($P = 0.014$) and Group V ($P = 0.014$).

* $P < 0.05$ between baseline and peak.

∅ = the gradient of serum concentration.

intubation is performed because it is one of the highest-risk intervals during anesthesia and operation (19). In the present study, there were no patients (0%) whose RPP achieved over 20000 and eight patients (44%) whose RPP achieved over 12000 in Group M. In contrary, there were three patients (17%) in Group C and two patients (11%) in Group V whose RPP achieved over 20000, and twelve patients (67%) in Group C and sixteen patients (84%) in Group V of which RPP achieved over 12000. This study let us to do further studies of effects of pretreatment of MgSO₄ for patients with preoperative cardiac disease in the future.

It is controversial whether administration of MgSO₄ attenuates an elevation of serum potassium concentration during rapid sequence induction. In the past study, administration of MgSO₄ 40 mg kg⁻¹

over 10 seconds that was followed by administration of thiopentone does not suppress SCC-induced increases in potassium in rapid sequence induction (1). On the other hand, administration of MgSO₄ 60 mg kg⁻¹ over 1 min followed by administration of thiopentone attenuate SCC-induced increases in potassium in rapid sequence induction (12). In the present study, increases in serum potassium concentration in Group M were significant and similar of those in Group C, although MgSO₄ significantly prevents SCC-induced fasciculation. These paradoxical findings could be caused by the inhibition of catecholamine release (12) because an attenuation of β₂ action induces a reduction of intracellular uptake of serum potassium (21, 22).

In conclusion, the present study shows that pretreatment of MgSO₄, not VB, by slowly injection

(5 min) is effective to decrease SCC-induced fasciculation and tracheal intubation-induced hemodynamic changes in rapid sequence induction, although $MgSO_4$, does not prevent the elevation of serum potassium concentration after induction.

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