

## Prolonged relaxant effects of vecuronium in patients with deliberate hypermagnesemia: time for caution in cesarean section

AKIKO YOSHIDA<sup>1</sup>, YOSUKE ITOH<sup>1</sup>, KEI NAGAYA<sup>1</sup>, KAZUYA TAKINO<sup>1</sup>, JUN-ICHI SUGAWARA<sup>2</sup>, TAKASHI MURAKAMI<sup>2</sup>, KUNIHIRO OKAMURA<sup>2</sup>, and MASAHIKO TAKAHASHI<sup>3</sup>

<sup>1</sup>Department of Anesthesiology, Tohoku University Hospital, Sendai, Japan

<sup>2</sup>Department of Obstetrics and Gynecology, Tohoku University Hospital, Sendai, Japan

<sup>3</sup>Department of Dental Anesthesia and Pain Management, Tohoku University Hospital, 4-1 Seiryō-machi, Aoba-ku, Sendai 980-8575, Japan

### Abstract

We present two cases showing significantly prolonged action of vecuronium from magnesium treatment after general anesthesia for urgent cesarean section. The serum magnesium levels were maintained at a therapeutic range for severe eclampsia in one patient (5.6 mg·dl<sup>-1</sup>) and for tocolysis in another with placenta previa totalis (6.9 mg·dl<sup>-1</sup>). The obstetrics-specific emergency in each patient led us to proceed with general anesthesia but using reduced-dose vecuronium, which failed to prevent prolongation of the neuromuscular block. As a result, the patients received prolonged mechanical ventilation. Our cases underscore the need for anesthesiologists as well as obstetricians to be aware of the prolongation of the action of nondepolarizing muscle relaxants as a result of magnesium treatment.

**Key words** Eclampsia · Placenta previa · Tocolysis · Spinal anesthesia · Obstetrics

### Introduction

The impending approval of the Ministry of Health, Labour and Welfare for the use of magnesium sulfate (MgSO<sub>4</sub>) as a tocolytic in addition to its use as an antieclamptic will lead Japanese anesthesiologists to more-frequent encounters with obstetric patients with deliberate hypermagnesemia. The choice of anesthetic techniques for such patients remains controversial, especially in cases of cesarean section because these can involve both magnesium-specific and obstetrics-specific issues. It has been recognized that the action of nondepolarizing muscle relaxants is significantly prolonged in the presence of therapeutic serum levels of magnesium [1]. For cesarean section, therefore, anesthesiologists may prefer spinal or epidural anesthesia in hypermagnesemic parturients, whereas coexisting ob-

stetric conditions such as eclampsia or placenta previa occasionally require them to use general anesthesia even though it includes the risk of prolonged neuromuscular block when nondepolarizing relaxants are used. We present two such cases in which Mg-induced prolongation of vecuronium action necessitated continuous artificial ventilation after general anesthesia for cesarean section in patients with deliberate hypermagnesemia, including an eclamptic parturient with acute coagulation abnormalities and threatened premature delivery with placenta previa totalis.

### Case report

#### Case 1

A 36-year-old woman (163 cm, 66 kg) with severe eclampsia was referred to us at 34 weeks gestation for urgent cesarean section because she had developed an acute coagulation abnormality. MgSO<sub>4</sub> to prevent convulsions and hydralazine to control hypertension had been infused intravenously (IV). The most recent laboratory data obtained at the time of the decision of cesarean section showed hemoglobin 17.1 g·dl<sup>-1</sup>, hematocrit 52.4%, platelet count 110 × 10<sup>3</sup>·μl<sup>-1</sup>, fibrinogen 24 mg·dl<sup>-1</sup>, fibrinogen degeneration products 33 μg·dl<sup>-1</sup>, and antithrombin III 70%. The hepatorenal biochemical markers remained within normal ranges and the plasma concentration of magnesium was 5.6 mg·dl<sup>-1</sup>. After review of the preoperative information, a decision was made to proceed with general anesthesia due to concern about possible hemorrhage in the spinal canal that is associated with neuraxial anesthesia.

After obtaining verbal informed consent in the operating theater, anesthesia was induced using the rapid-sequence technique with thiopental 250 mg and succinylcholine 40 mg IV, followed by tracheal intubation and maintained with nitrous oxide 60% in oxygen

Address correspondence to: M. Takahashi

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and IV vecuronium 3 mg. A female infant weighing 1660 g was born with normal activities within a few minutes after the intubation. Subsequently, pentazocine 30 mg and droperidol 5 mg were administered IV. Train-of-four (TOF) monitoring on the left wrist was started after the delivery because we had not suspected that the interaction of Mg and vecuronium at a dose of 0.05 mg/kg would result in such a severe prolongation. Although the obstetricians found abruptio placentae, the surgical procedure was uneventfully completed in 23 min and nitrous oxide was discontinued. Surgical blood loss was 350 g. At 45 min after giving vecuronium, insufficient breathing was recognized with 20% recovery in the TOF ratio. The following IV administration of atropine 1 mg and neostigmine 2 mg reversed it to 90%, and the patient became fully responsive under adequate spontaneous respiration. The tracheal tube was removed and the patient was transferred to the postanesthetic recovery room. Fifteen minutes later, she started to complain of dyspnea with shallow and frequent breathing. Pressure-support ventilation via a face mask was immediately applied, and the TOF ratio was confirmed to be as low as 40% together with visible fade of muscle twitches. Prolongation of the vecuronium action due to hypermagnesemia was strongly suspected. After obtaining verbal informed consent, she was given propofol 80 mg and fentanyl 0.2 mg IV followed by tracheal intubation and transferred to the Intensive Care Unit (ICU). Her plasma concentration of magnesium was 4.5 mg·dl<sup>-1</sup> upon transfer to the ICU. Mechanical ventilation was continued under sedoanalgesia using IV infusion of propofol and fentanyl. Her TOF ratio, which had fallen below 30% on admission, recovered in the ICU to over 90% during the following 5 h. The sedoanalgesia was discontinued and the trachea was extubated after confirming adequate breathing and the conscious level. No sequelae were observed, and she was discharged from the ICU on the next morning and from the hospital 2 weeks later.

### Case 2

A 35-year-old woman (151 cm, 51 kg) at 33 weeks gestation was referred to us for urgent cesarean hysterectomy because of failure of tocolysis in pregnancy together with myoma uteri and placenta previa totalis. Continuous IV MgSO<sub>4</sub> had kept her plasma concentration of magnesium at 5–6 mg·dl<sup>-1</sup> but failed to prevent untoward uterine contraction. Laboratory examination obtained immediately before the decision for cesarean section had shown a plasma serum magnesium level of 6.9 mg·dl<sup>-1</sup> and mild anemia (hemoglobin 10.4 g·dl<sup>-1</sup>, hematocrit 34.2%) without coagulation abnormalities. Slightly increased liver transaminases (alanine aminotransferase 75 U·l<sup>-1</sup>, aspartate aminotransferase

48 U·l<sup>-1</sup>) had also been identified. Concern for uncontrollable hemorrhaging during the procedure led us to proceed with general anesthesia despite the fact that we had strongly suspected the possibility of a need for prolonged artificial ventilation after surgery based on our experience in case 1.

Verbal informed consent for general anesthesia and the risk of prolonged mechanical ventilation due to the magnesium-enhanced action of vecuronium was obtained from the patient upon transfer to the operating theater. Anesthesia was induced using the rapid-sequence technique with thiopental 250 mg and succinylcholine 40 mg IV, followed by tracheal intubation. The TOF monitoring on the left wrist was started simultaneously with the thiopental injection. Her lungs were mechanically ventilated with 60% nitrous oxide in oxygen. On the appearance of a 30% recovery of the first-twitch response to TOF stimulation at 5 min after giving succinylcholine, vecuronium 2.5 mg was given IV. A male infant weighing 1480 g with Apgar score of 2 at 1 min was born within a few minutes after the intubation. His critical condition prompted pediatricians to initiate immediate resuscitation including tracheal intubation, followed by intensive care in the Neonatal ICU. Fentanyl 0.2 mg was given IV to the mother after delivery. The surgical procedure, including a simple hysterectomy, was completed in 36 min. Surgical blood loss amounting to 1140 g was treated with an infusion of crystalloid fluid with no adverse hemodynamic changes. Upon confirming the absence of the TOF response at 70 min after giving vecuronium, magnesium-induced prolongation of vecuronium action was diagnosed and the patient was transferred to the ICU with continuing mechanical ventilation. Thirty minutes later, she showed slight head movement and frowned while the TOF response remained at 3. Continuous IV infusion of propofol and fentanyl was started. The plasma concentration of magnesium was 4.8 mg·dl<sup>-1</sup> at this point. Her TOF ratio remained as low as 30% at 2 h after the vecuronium injection but recovered to 95% during the following 3 h. Subsequently, the sedoanalgesia was discontinued and the tracheal tube was removed after confirming adequate spontaneous respiration and consciousness. No sequelae were observed, and she was discharged from the ICU the next morning and from the hospital 10 days later. Her baby required transient respiratory support and was discharged from the hospital 3 weeks later.

### Discussion

Magnesium ions, taking the place of calcium, suppress neurotransmitter release at the nerve endings including that of acetylcholine at the motor endplate. It is well

established that magnesium in the range of therapeutic serum concentrations (5–8 mg·dl<sup>-1</sup>) prolongs the action of nondepolarizing muscle relaxants, although it does not, at least clinically, affect that of succinylcholine [1]. Therefore, options in general anesthesia for cesarean section include rapid-sequence induction with succinylcholine and maintenance, when needed, with reduced-dose vecuronium [2], mivacurium [3], or succinylcholine infusion [4] in hypermagnesemic patients. However, the magnitude and duration of the magnesium-relaxant interaction vary among individuals [3,5], so that these practices cannot eliminate the risk of residual relaxant effects in all patients, as described in the present report. Because neither a history of neuromuscular disease nor the use of other relevant agents was indicated, magnesium-vecuronium interaction most likely explains the present episodes. As a result, the events per se indicate that the vecuronium doses of approximately 0.05 mg·kg<sup>-1</sup> that we used were too large for both patients. However, precise titration of relaxants is often difficult and is not always possible in every medical condition.

Apart from the growing contention regarding the choice between general and neuraxial anesthesia for cesarean section in parturients with eclampsia or placenta previa [6–8], threatened coagulopathy or hemodynamic catastrophe often compel anesthesiologists to proceed with urgent general anesthesia even for hypermagnesemic patients, despite being aware that the use of nondepolarizing muscle relaxants could result in prolonged neuromuscular blockade. The potentiation of nondepolarizing relaxants by magnesium may be reversed by using cholinesterase inhibitors or calcium. However, these do not seem to be optimal choices because of their transient effects as we experienced recurarization in case 1. A reasonable alternative includes continuous management of the airway and breathing until the relaxants are metabolized or excreted. In the present clinical practice, artificial ventilation per se can be applied with minimal risk. Without adequately informed consent, however, prolonged mechanical ventilation after surgery could alarm patients and families. Although our patients and families consented to the postoperative therapy, we do not think that it was appropriate to have obtained verbal

informed consent for the specific treatments in the operating theater. After the experience of these two cases, the anesthesiologists and obstetricians in our institution concurred that, when patients are treated with MgSO<sub>4</sub>, they be informed of the possibility of delayed extubation and necessity of being admitted to the ICU after general anesthesia when the decision for cesarean section is made, whether it is elective or urgent.

The official approval of parenteral MgSO<sub>4</sub> as a tocolytic can be expected to greatly increase the use of this agent in obstetric practice and to result in greater numbers of patients with deliberate hypermagnesemia who require cesarean section. In such situations, our cases underscore the need for anesthesiologists as well as obstetricians to be aware of the prolongation of the action of nondepolarizing muscle relaxants by magnesium treatment and, when general anesthesia with these relaxants is chosen, the possible need for postoperative respiratory support.

## References

1. James MFM (1998) Magnesium in obstetric anesthesia. *Int J Obstet Anesth* 7:115–123
2. Baraka A, Yazigi A (1987) Neuromuscular interaction of magnesium with succinylcholine-vecuronium sequence in the eclamptic parturient. *Anesthesiology* 67:806–808
3. Hodgson RE, Rout CC, Rocke DA, Louw NJ (1998) Mivacurium for cesarean section in hypertensive parturients receiving magnesium sulfate therapy. *Int J Obstet Anesth* 7:12–17
4. Crawford JS, Lewis M, Davies P (1985) Maternal and neonatal response related to the volatile agent used to maintain anaesthesia at cesarean section. *Br J Anaesth* 57:482–487
5. Kwan W, Lee C, Chen B (1996) A noninvasive method in the differential diagnosis of magnesium-induced protracted neuromuscular block in a severely eclamptic patient. *J Clin Anesth* 8:392–397
6. Howell P (1998) Spinal anesthesia in severe preeclampsia: time for reappraisal or time for caution? (Editorial). *Int J Obstet Anesth* 7:217–219
7. Aya AGM, Mangin R, Vialles NV, Ferrer JM, Robert C, Ripart J, de La Coussaye JE (2003) Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy patients: a prospective Cohort comparison. *Anesth Analg* 97:867–872
8. Lipman S, Carvalho B, Brock-Utne J (2005) The demise of general anesthesia in obstetrics revisited: prescription for a cure (Editorial). *Int J Obstet Anesth* 14:2–4