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Anesthesiology
67:806-808, 1987

Neuromuscular Interaction of Magnesium with Succinylcholine-vecuronium Sequence in the Eclamptic Parturient

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Succinylcholine-vecuronium sequence has been safely used to provide neuromuscular blockade in parturients undergoing cesarean section under general anesthesia.¹ Succinylcholine provides a rapid onset of profound muscular relaxation that facilitates tracheal intubation, while the nondepolarizing relaxants, such as vecuronium, can be used to maintain muscular relaxation.²

We found that eclamptic parturients receiving magnesium treatment demonstrate the interaction of magnesium with both succinylcholine and vecuronium neuromuscular blockade. We also compared the neuromuscular response to that achieved when the same doses of succinylcholine and vecuronium were used in a control group of noneclamptic parturients having no magnesium therapy.

MATERIALS AND METHODS

The neuromuscular blockade of succinylcholine-vecuronium sequence was investigated in six eclamptic parturients, aged 25-32 yr, undergoing cesarean section at 34-40 weeks gestation. Preoperatively, all the

eclamptic parturients were given 4 gm of magnesium sulphate iv, to be followed by an infusion at a rate of 2 gm · h⁻¹. The serum level of magnesium at the time of cesarean section ranged from 4.1-6.0 mEq/L. The neuromuscular blockade was compared to that achieved in a control group of six noneclamptic parturients, aged 23-37 yr, undergoing elective repeat cesarean section at 37-40 weeks gestation.

Neuromuscular blockade was investigated by a Datex Relaxograph® monitor. The ulnar nerve was stimulated supramaximally at the wrist every 20 s, and the electromyographic response was displayed. The monitor uses the train-of-four principle at a stimulus rate of 2 Hz, and features an automatic search for the supramaximal current level.

All patients were premedicated with im glycopyrrolate 0.2 mg. After patients were breathing oxygen, anesthesia was induced with thiopental 3 mg · kg⁻¹ iv. Succinylcholine 1.5 mg · kg⁻¹ was then injected iv, and its neuromuscular effect was monitored. When complete neuromuscular blockade was achieved, the trachea was intubated, and anesthesia was maintained with nitrous oxide:oxygen (2:1) supplemented by 100 µg fentanyl iv following delivery of the baby.

When 75% recovery of succinylcholine block was reached, a bolus of vecuronium 25 µg · kg⁻¹ was injected and its neuromuscular blockade was monitored. At 75% recovery of the twitch response, incremental doses of 12.5 µg · kg⁻¹ of vecuronium were injected to maintain relaxation throughout surgery. The neuromuscular blockade achieved by the initial bolus of vecuronium, and the number of incremental doses re-

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Received from the Department of Anesthesiology, American University of Beirut, Beirut, Lebanon. Accepted for publication May 19, 1987.

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Key words: Anesthesia: obstetric. Ions: magnesium. Neuromuscular relaxants: succinylcholine; vecuronium.

quired to maintain relaxation, were compared in the two groups. At the end of surgery, residual neuromuscular blockade was antagonized whenever the ratio of the fourth to the first evoked response (T_4/T_1 ratio) was <0.75 , by a mixture of neostigmine $0.025 \text{ mg} \cdot \text{kg}^{-1}$ and atropine $0.01 \text{ mg} \cdot \text{kg}^{-1}$.

All data were expressed as mean \pm SD. One-sided t test was used to compare the mean values in the two groups. $P < 0.05$ was considered significant.

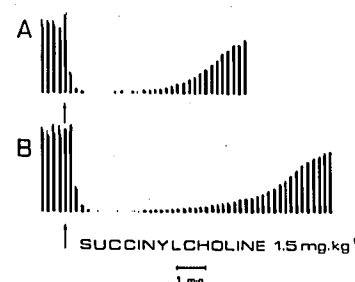
RESULTS

Prior to injection of succinylcholine, the baseline twitch and train-of-four responses were normal in both the control and the eclamptic parturients. The iv injection of succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ in the eclamptic parturients produced complete neuromuscular blockade after $75.0 \pm 13.8 \text{ s}$. Recovery of neuromuscular transmission reached 75% after $8.3 \pm 2.6 \text{ min}$ after injection of the muscle relaxant (fig. 1A). In the control noneclamptic parturients, complete neuromuscular blockade was achieved after $71.7 \pm 14.7 \text{ s}$. Recovery of neuromuscular transmission reached 75% after $9.5 \pm 2.5 \text{ min}$ (fig. 1B). There was no significant difference between the two groups in the onset time of succinylcholine block or recovery time (*i.e.*, time from 25 to 75% recovery of control twitch height) ($P > 0.05$). In both groups, succinylcholine neuromuscular blockade was depolarizing in nature, as evidenced by T_4/T_1 ratio, which ranged between 0.90 and 1.0.

At 75% recovery from succinylcholine blockade, vecuronium $25 \mu\text{g} \cdot \text{kg}^{-1}$ was injected in the two groups of parturients. In all the eclamptic parturients, this dose of vecuronium produced 100% neuromuscular blockade; recovery of the twitch response reached 75% after $34.5 \pm 7.2 \text{ min}$ (fig. 2A), when no or only one additional dose (mean 0.67 ± 0.45) of $12.5 \mu\text{g} \cdot \text{kg}^{-1}$ vecuronium was required to maintain relaxation until the end of surgery. In the control group, $25 \mu\text{g} \cdot \text{kg}^{-1}$ of vecuronium did not result in complete neuromuscular blockade in any parturient, but only produced 25–85% (mean $42.5 \pm 22.9\%$) depression of the twitch response, which recovered rapidly after $9.2 \pm 3.9 \text{ min}$ (Fig. 2B); subsequent injections of three to five (mean 4.0 ± 0.6) incremental doses of $12.5 \mu\text{g} \cdot \text{kg}^{-1}$ were required to maintain relaxation. There was a significant difference between the two groups in the degree and duration of neuromuscular blockade achieved by the initial dose of vecuronium, and in the number of incremental doses required to maintain relaxation ($P < 0.05$).

In both groups, surgery lasted for 55–75 min. At the termination of surgery, spontaneous recovery of neuromuscular transmission was observed, as evidenced by T_4/T_1 ratio above 0.75 in two eclamptic parturients

FIG. 1. Electromyographic tracing comparing the neuromuscular blockade achieved by succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ in an eclamptic parturient (A), to that achieved in a control patient (B).



and in three noneclamptic parturients. Residual neuromuscular blockade, as evidenced by T_4/T_1 ratio less than 0.75, was observed in four eclamptic parturients and three parturients of the control group. Residual blockade could be completely antagonized in both groups, as evidenced by T_4/T_1 ratio above 0.90, by a mixture of neostigmine $0.025 \text{ mg} \cdot \text{kg}^{-1}$ and atropine $0.01 \text{ mg} \cdot \text{kg}^{-1}$ iv.

DISCUSSION

Magnesium sulphate is widely used for management of the eclamptic parturient. At the neuromuscular junction, magnesium decreases the presynaptic release of acetylcholine, reduces the sensitivity of the postjunctional membrane to the liberated acetylcholine, and decreases the excitability of the muscle fiber membrane.^{3,4} Such neuromuscular effects of magnesium are expected to potentiate the nondepolarizing block, and to antagonize the depolarizing block of succinylcholine.⁵ However, magnesium supposedly potentiates the neuromuscular blockade of both succinylcholine and d-tubocurarine in the isolated rat phrenic nerve-diaphragm preparation;⁶ the action of succinylcholine is potentiated by a factor of 1.9, while that of d-tubocurarine is potentiated by a factor of 4.1. Further *in vivo* experimental investigations using the cat and rabbit have shown that other nondepolarizing relaxants, whether long-acting, such as pancuronium, or intermediate-acting, such as vecuronium, are also potentiated by magnesium; the ED_{50} of pancuronium⁷ and vecuronium⁸ is linearly and inversely related to the serum concentration of magnesium.

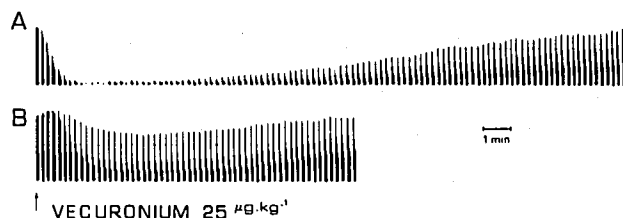


FIG. 2. Electromyographic tracing comparing the neuromuscular blockade achieved by vecuronium $25 \mu\text{g} \cdot \text{kg}^{-1}$ in an eclamptic parturient (A), to that achieved in a control patient (B).

Our report, in contrast with the observations on the isolated rat phrenic nerve-diaphragm preparation,⁶ shows that the neuromuscular blockade of succinylcholine is not potentiated in the eclamptic patients having magnesium therapy. The onset, degree, and duration of succinylcholine blockade were not significantly different between the eclamptic and the control patients. The discrepancy between magnesium-succinylcholine interaction in the isolated rat phrenic-nerve diaphragm preparation and that observed in our patients may be related to species variation.⁹ In all our patients, whether eclamptic or noneclamptic, succinylcholine resulted in a depolarizing neuromuscular blockade, as evidenced by T_4/T_1 ratio which ranged between 0.9 and 1.0. In the rat, succinylcholine only causes partial depolarization of the endplate from -90 mV to -65 mV, which is not enough to cause depolarizing blockade.¹⁰ The discrepancy may also be attributed to the absence of plasma cholinesterase in the isolated preparation, and, hence, magnesium-succinylcholine interaction represents only their direct neuromuscular effects. In man, succinylcholine is rapidly hydrolyzed by the plasma cholinesterase, which plays the predominant role in controlling the concentration and, consequently, the degree and duration of succinylcholine neuromuscular blockade.¹¹ Magnesium does not impair, and may even increase, the plasma cholinesterase activity.¹² Thus, in the eclamptic parturient having magnesium therapy, a single dose of succinylcholine can be safely used to facilitate tracheal intubation without fear of delayed onset of relaxation or unduly prolonged paralysis.¹³ These findings may not apply when repeated doses¹⁴ or infusions of succinylcholine are used. Under these conditions, phase II block can develop and, similar to nondepolarizing block, it may be potentiated by magnesium therapy.

Similar to previous experimental investigations,⁸ the present report confirms that the nondepolarizing neuromuscular blockade of vecuronium is markedly potentiated by therapeutic serum levels of magnesium, which has no clinical effect on both the twitch or the train-of-four responses. Such marked potentiation can be attributed to the ability of magnesium to reduce the output of acetylcholine from the nerve terminals and decrease the sensitivity of the postjunctional membrane to the chemical transmitter.^{3,4} In all eclamptic parturients, vecuronium $25 \mu\text{g} \cdot \text{kg}^{-1}$ produced complete and prolonged neuromuscular blockade, while injection of the same dose in the control noneclamptic parturients only resulted in partial and short-lasting blockade. Such magnesium-vecuronium interaction can explain the markedly prolonged neuromuscular blockade which has been reported following the use of the normal doses of vecuronium in the eclamptic parturient having magnesium therapy.¹⁵ Despite such magnesium-vecuronium

potentiation, careful titration of the dose of vecuronium in our eclamptic patients resulted in a controlled neuromuscular blockade which recovered spontaneously, or could be readily antagonized by neostigmine at the end of surgery.

In conclusion, in the eclamptic parturients having magnesium therapy, succinylcholine produces a clinically normal response and, hence, can be safely used to provide a rapid, profound, and short-lasting neuromuscular blockade that facilitates tracheal intubation. Neuromuscular blockade can be maintained by the intermediate-acting relaxant vecuronium. Similar to other nondepolarizing relaxants, vecuronium blockade is potentiated by magnesium therapy, and, hence, its dose must be reduced and carefully titrated by a nerve stimulator in order to ensure timely recovery of neuromuscular transmission at the termination of surgery.

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