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Original contribution

Antagonism of profound cisatracurium and rocuronium block: the role of objective assessment of neuromuscular function☆

Aaron F. Kopman MD [a,*], David J. Kopman MD [b,1], Jennifer Ng MD [a], Lee M. Zank MD [a]

[a]*Department of Anesthesiology, New York Medical College, Valhalla, NY, USA*
[b]*Department of Anesthesiology, New York-Presbyterian Hospital, New York City, NY, USA*

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Abstract

Study Objective: The purpose of this study is to determine the incidence of significant (train-of-four [TOF] ratio <0.70), but clinically undetectable (TOF ratio >0.40), residual neuromuscular block after neostigmine antagonism of profound cisatracurium (CIS) or rocuronium (ROC) block.

Design: Prospective, randomized, open-label study.

Setting: University hospital.

Patients: Forty ASA physical status I and II undergoing elective surgical procedures.

Interventions: Anesthesia was induced with propofol 1.5 to 2.5 mg/kg IV plus fentanyl 2 to 4 μg/kg and maintained with N_2O/desflurane plus narcotic supplementation. The electromyographic response of the adductor pollicis was recorded. Train-of-four stimulation was given every 20 seconds. Twitch height (T1) and TOF fade ratio were continuously recorded. In group 1 (n = 20), neuromuscular block was induced with CIS 0.10 mg/kg, and T1 was maintained at 5% of control by a constant infusion of CIS until the end of surgery. One minute after the termination of the infusion, neostigmine 0.05 mg/kg was administered. T1 and TOF values were monitored continuously for the next 20 minutes. Group 2 (n = 20) is identical to group 1 except that the initial drug was ROC 0.60 mg/kg, and paralysis was maintained with an infusion of ROC.

Measurements and Main Results: There were no significant differences in the recovery patterns of CIS vs ROC. The duration (bolus to end of infusion) in both groups averaged 2.7 hours, and the mean cumulative dose of relaxant approximated 4 × the ED_{95}. T1 at the time of reversal was 6% (4%-10%) of control. Mean TOF ratios at 10, 15, and 20 minutes were 0.55, 0.71, and 0.0.81, respectively. Return to a TOF ratio >0.40 was always achieved in 15 minutes or less. However, at 20 minutes postreversal, 5 of 40 subjects had TOF ratios <0.70 and only 11 individuals had recovered to a TOF ratio of 0.90 or greater.

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* Corresponding author. Department of Anesthesiology, St Vincent's Hospital Manhattan, New York City, NY 10011, USA. Tel.: +1 212 604 2636; fax: +1 212 604 2637.

E-mail addresses: akopman@svcmcny.org (A.F. Kopman).

[1] At the time the study was performed, David Kopman was a research assistant in the Department of Anesthesiology at Saint Vincent's Hospital Manhattan.

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Conclusions: Most clinicians cannot detect tactile fade once the TOF ratio exceeds 0.40. When reversing profound block, an objective monitor of neuromuscular function is required if the extent of residual block is to be assessed with any confidence.

1. Introduction

Prompted by a series of reports that documented residual neuromuscular weakness of clinical significance continues to occur with unacceptable frequency in Post-Anesthesia Care Units (PACU) [1-4], Eriksson [5] in a recent editorial in *Anesthesiology* suggested that ". . . it is time to . . . introduce objective neuromuscular monitoring [measurements of the train-of-four (TOF) ratio in real time] in all operating rooms, not just those occupied by researchers and aficionados of muscle relaxants. Objective neuromuscular monitoring . . . should . . . be used whenever a nondepolarizing neuromuscular blocking agent is administered." We recently expressed some reservations with Eriksson's proposal [6]. We thought that his suggestion could be interpreted to imply that administration of an intermediate acting relaxant guided only by subjective estimation of the TOF represented substandard care, and that knowledgeable and appropriate management of relaxants was not possible without quantitative monitoring equipment. On the basis of our own data, we respectfully disagreed. Fifty-eight of 60 patients (reversed at an average TOF count of 2) achieved a TOF ratio of 0.70 or greater within 15 minutes of antagonism of either cisatracurium (CIS) or rocuronium (ROC).

Our comments were not meant to suggest that objective monitoring of the level of neuromuscular block is never indicated. On the contrary, when attempting to antagonize profound nondepolarizing block, we think the opposite is true [7]. Anticholinesterases have a "ceiling" to the extent of the block that can be antagonized. When reversing deep levels of block, the peak effect of the antagonist is followed by a slow plateau phase that represents the balance between diminishing anticholinesterase activity and spontaneous recovery of neuromuscular block [8]. If reversal is initiated at a TOF count of one or less, return to a TOF ratio of 0.40 may be achieved fairly promptly, but further return of neuromuscular function is likely to be slow. Because at a TOF fade ratio of 0.40 to 0.50, subjective (visual or tactile) recognition of fade is not reliable, clinically unacceptable recovery may persist (but be undetectable by convention methods of neuromuscular monitoring) well into the postanesthesia period. The present study was designed to estimate the frequency with which this occurs when antagonism of residual CIS- or ROC-induced neuromuscular block is attempted at a TOF count of one.

2. Materials and methods

Forty ASA physical status I and II adult patients, aged 20 to 70 years, undergoing elective surgical procedures, for which the administration of a muscle relaxant was appropriate, were included in the study. All patients were free from neuromuscular disease and were within 20% of ideal body weight. The protocol was approved by St Vincent's Hospital in Manhattan Human Subject Review Committee, and patient consent was obtained. Anesthesia was induced with propofol 1.5 to 2.5 mg/kg intravenously (IV) plus fentanyl 2 to 4 μg/kg and maintained with N_2O/desflurane plus narcotic supplementation as needed. Ventilation was controlled and end-tidal CO_2 was maintained between 32 and 38 mm Hg.

The indirectly evoked integrated compound action potential of the adductor pollicis muscle to supramaximal stimulation of the ulnar nerve at the wrist was measured and recorded using a Datex 221 NMT monitor (Datex Instrumentarium, Helsinki, Finland). Supramaximal nerve stimulation was achieved using the nerve stimulator incorporated into the Datex unit (pulse width, 100 ms; constant current, 0-70 mA range). The test hand was immobilized, and approximately 200 to 300 g of resting tension was applied to the thumb. After induction of anesthesia and before any muscle relaxants were administered, control twitch height (Tc) and TOF fade ratio (T4/T1) were established after a 5-minute period of baseline stabilization. Train-of-four stimuli were given every 20 seconds during the period of observation, and single twitch depression, indicated by the height of the first TOF twitch/control twitch height (T1/Tc), and TOF fade were continuously recorded. Two randomly selected groups were studied.

In group 1 (CIS, n = 20), CIS 0.10 mg/kg was administered as a rapid intravenous (IV) bolus. When twitch depression was maximal, the patient's trachea was intubated. A CIS infusion (1 μg/kg per minute) was begun as soon as any evoked response returned after the initial drug bolus. If 100% block was not achieved, the infusion was started at the point of peak twitch depression. The infusion was then adjusted to provide approximately 95% twitch depression for the remainder of the case. The duration of all infusions exceeded 90 minutes. When the need for surgical relaxation was over, the infusion was stopped, and 2 minutes later, neostigmine 0.05 mg/kg was administered. Train-of-four values were monitored continuously for the next 20 minutes. Group 2 (ROC, n = 20) is identical to group 1 except that the initial bolus was 0.60 mg/kg and the initial infusion rate was 5 μg/kg per minute.

Twitch height recovery data were normalized to the final measured value of T1. Data were analyzed using appropriate tests, with $P < .05$ considered statistically significant. Continuous objective variables (such as mean TOF ratios