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Post-Tetanic Count Recovery after Cisatracurium in Elderly Patients

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Abstract

Background: The temporal relationship between recovery of a certain post-tetanic count (PTC) and the recovery of the first twitch (T_1) in the train-of-four (the PTC-T_1 interval), is specific for each neuromuscular blocking drug (NMBD). A previous study reported prolongation of the PTC - T_1 interval in the elderly after rocuronium. The ability to accurately predict the return of T_1 is an important component of PTC monitoring since it may affect clinical decisions about administration versus withholding a maintenance dose of the NMBD. This study was designed to evaluate PTC recovery from intense cisatracurium-induced NMB in geriatrics and investigate its relationship with T_1.

Methods: After IRB approval, Thirty-two patients who are older than 65yr were recruited and the informed consent signed. After anesthesia induction, neuromuscular monitoring was performed using acceleromyography. Cisatracurium 0.15 mg/kg was administered and tracheal intubation performed when the response to TOF stimulation was abolished. Cycles of post- tetanic stimulation were applied every 6 minutes with TOF monitoring in between. Anesthesia was maintained with propofol infusion and nitrous oxide in oxygen 60:40. Measurements included time to reappearance, and number of PTC, time to T_1, and the number of PTC when T_1 was imminent. The correlation between PTC and T_1 was also studied.

Results: 32 subjects were studied 32. The mean time needed for the first response to post-tetanic stimulation (PTC_1) to appear was 34.4 ± 5.5 minutes and the mean time needed for T_1 to reappear was 45.7 ± 5.8 minutes. The median number of detectable PTC just before or coinciding with T_1 appearance was 9. There was a strong correlation between the number of detectable PTC and time to T_1 appearance (Correlation coefficient 0.929).

Conclusions: There is a consistent temporal relationship between the number of PTC and the time to T_1 recovery after cisatracurium in elderly patients. This may allow more accurate control and predictable recovery from intense cisatracurium-induced block in the elderly.

Introduction

Post-tetanic stimulation (PTS) is a valuable method that can be used to monitor recovery from intense degrees of neuromuscular block (NMB) [1, 2]. A close correlation has been found between the number of detectable post-tetanic responses (post-tetanic count or PTC) and the interval after which the first twitch in the TOF (T_1) is likely to appear (PTC-T_1 interval) [3-5]. This relationship provides the clinician with the ability to predict the remaining time for the block to recover from the intense block phase, and is specific for each neuromuscular blocking drug (NMBD) [6]. It has been demonstrated, however, that advanced age is associated with prolongation of the PTC-T_1 interval after rocuronium [7]. The effect of aging on the PTC-T_1 interval has not been studied, however, after cisatracurium. Although recovery from intermediate degrees of NMB after cisatracurium had been previously investigated [8], it is important to study recovery from the more intense phase that occur before the detection of T_1. Some delicate surgical interventions require maintenance of the intense block for long periods which necessitates clinical decisions about administering or withholding a NMBD dose to be accurately made. The PTC-T_1 relationship after cisatracurium has been previously established in young adults [6], but has not been investigated in the elderly yet. The goal of this study was to investigate the recovery from intense cisatracurium-induced NMB in elderly patients and to evaluate the temporal relationship between the PTC and T_1.

Methods

The study protocol was approved by our institutional review board. All study subjects were chosen from patients scheduled to have elective surgical procedures requiring muscle relaxation and tracheal intubation. After obtaining written informed consents, Thirty-two, ASA Physical Status I & II patients, whose ages were ≥ 65 years, were included in this study. Patients who had any history of neuromuscular disorders, intake of medications that may affect neuromuscular functions, history of renal, hepatic, or neurologic disorders, or a body mass index greater than 30 were excluded from the study. In all patients, anesthesia was induced with propofol 1.5-2.0 mg/kg IV and fentanyl 1.0μg/kg and maintained with a propofol infusion 100-200 mcg/kg/min and 60% nitrous oxide in oxygen. Body temperature was monitored with an esophageal probe and kept within a narrow range (36-37°C) by using forced warm air. After intravenous induction, acceleromyographic neuromuscular monitoring was started by using the TOF-Watch monitor. Stabilization of the responses was initially performed by applying a short 50 Hz tetanus for 5 seconds before applying repeated 1 Hz single twitch stimulations to the ulnar nerve at the wrist. After twitch stabilization and equipment calibration,

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repeated supramaximal TOF stimulation were applied every 15s. All responses were displayed on a monitor and recorded for later analysis. The TOF-Watch temperature probe was taped to the thenar muscles to ensure that the hand temperature is maintained within a close range (32-33°C) throughout the study period. Cisatracurium 0.15 mg/kg (3 x ED_{95}) was then intravenously administered over 5 sec. When the TOF responses were completely ablated, tracheal intubation was performed and the response to PTS was evaluated every 6 minutes. The PTS cycle consisted of 15 pre-tetanic 1 Hz single twitches followed by 50 Hz tetanic stimulation for 5 seconds followed by a 3 seconds pause after which 15 post-tetanic 1Hz stimuli were applied. This cycle was repeated every 6 minutes with TOF monitoring in between the cycles until T_1 was detected which constituted the end point for our study. The following parameters were measured:

1- Time from cisatracurium administration until the appearance of the first detectable response (or responses) to PTS and the number of these responses (PTC)

2- Time from cisatracurium administration until reappearance of T_1

3- Time from the different post-tetanic responses obtained to T_1 (PTC-T_1 interval)

4- PTC immediately before (or coinciding with) the return of T_1.

Statistical analysis

All statistical analyses were performed using SPSS® software version 11.0.1 (SPSS, Chicago, IL). Statistical significance was accepted at $P < 0.05$. The nonlinear regression plot was created using Sigmaplot 2001 software version 7.0.1 (SPSS).

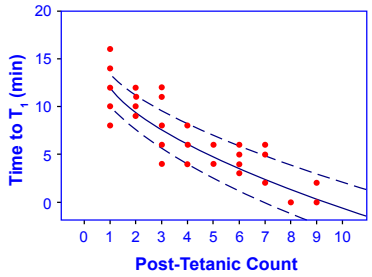

Figure1: Relationship between the post tetanic count (PTC) and time to first response to train-of-four stimulation (T1) during neuromuscular blockade caused by cisatracurium in elderly adults. The predicted mean curve (solid line) and the 95% confidence limits (hashed lines) are shown. Note that overlap may obscure some data points.

Age		73.7 ± 6.3
Gender	Males	15
	Females	17
Height (cm)		166.2 ± 9.4
Weight (kg)		79.1 ± 7.7
ASA	1	8
	2	24

Table1: Demographic data (expressed in mean ± SD).

Recovery index	Time (min)
PTC_1 (N= 22)	34.4 ± 5.5
PTC_2 (N=4) PTC_3 (N=5) PTC_4 (N=11) PTC_5 (N=9)	39.8 ± 6.3
PTC_6 (N=13) PTC_7 (N=9) PTC_8 (N=3) PTC_9 (N=7)	44.4 ± 6.6
T_1	45.7 ± 5.8
PTC_1-T_1	11.2 ± 1.1

Table 2: Recovery of the Post-tetanic count (PTC) and the first response in the Train-of-four (T1) after cisatracurium 0.15 mg/kg in elderly patients.

a	17.5248
b	-5.7259
SE of estimate	1.6320
Correlation coefficient	0.929

Table 3: Nonlinear regression indices.

A nonlinear relationship between PTC and time to T_1 has been previously established (1). Time to T_1 has been described by a near-linear decrease with the square root of PTC. This is expressed as: $t = a + b\sqrt{PTC}$, where t= the interval between a given PTC and first detection of T_1, a = a constant (intercept), and b = the regression coefficient (slope) of the near-linear relationship. The validity of this equation was tested for cisatracurium in the dose given. To create the correlation curve, the pooled data were plotted separately and the nonlinear least squares regression line was drawn with 95% confidence intervals. Pearson correlation coefficient was also calculated.

Results

A total of thirty-two subjects were studied. Ages ranged between 66-89 yrs (mean 73.7). The demographic characteristics are shown in (Table1).

Since PTS was applied every 6 minutes, it was impossible to obtain the time to a PTC of 1 in all subjects. Time from cisatracurium administration to PTC_1 was only calculated on those subjects in whom the cycle coincided with its appearance (22 patients). The first detectable response to PTS was with a count of 2 or 3 in nine subjects and with a count of 4 in one patient. The mean time from cisatracurium administration to PTC_1 was 34.4 ± 5.5 min. and the mean time to T_1 was 45.7 ± 5.8 min. The mean PTC_1-T_1 duration was 11.2 ± 2.1 min. and the median was 10.33 min. In thirty one patients T_1 was elicited ≥ 10 min after the appearance of PTC_1. The number of PTC immediately before the appearance of T_1 ranged from 8-9 responses (mode value: 9). This count was only detected in nine subjects in whom the timing of the cycle coincided with this level of recovery and not in all subjects. (Table 2) summarizes the times from cisatracurium administration to the different recovery indices.

A close correlation was found between the number of detectable PTC and the time needed for T_1 to be elicited (correlation coefficient 0.929). (Table 3) summarizes the regression indices reflecting this close relationship.

The pooled data from all subjects were plotted and the equation mentioned earlier in the methods section was used to create the temporal relationship curve between PTC and T_1. The recovery curve fitted the previously published model.

Discussion

PTS is the only available nerve stimulation pattern that can be used to monitor neuromuscular recovery during an intense NMB [2]. Although it is a well established method of nerve stimulation, the reproducibility of its results when used in elderly patients had never received much attention. In order to test the reliability of PTS when used in the elderly, Baykara et al. [7] compared recovery from intense rocuronium-induced NMB in both young adults and elderly patients [7]. The authors found that although there was a definite PTC/T_1 relationship in both age groups, the duration between PTC_1 and T_1

was longer in the elderly than in young adults (22.3 min versus 14.8 min). This difference in the predicted time of T_1 reappearance should be considered when using PTC monitoring in elderly patients. Failure to do so will deprive the method of one of its main advantages which is the ability to predict the onset of TOF recovery and the clinical consequences that may be associated with this recovery. Our results showed that there was a significant PTC/T_1 correlation in elderly patients recovering from intense cisatracurium- induced NMB. Our results and those of Baykara et al. [7] validate using PTC monitoring to monitor recovery from an intense NMB in older patients since both studies confirmed the existence of a close relationship between PTC and T_1. The difference between our results and those from the Baykara's study is that the PTC_1- T_1 interval in our study was similar to that obtained from our earlier study in which young adults were investigated [6]. The clinical implication of our findings is that during recovery from intense cisatracurium- induced NMB, the predicted time of T_1 reappearance in relation to PTC_1 is the same regardless of the patient's age which allows accurate quantification of block intensity and timely intervention when needed. The most likely explanation for the difference between our results from those reported with rocuronium is probably related to the different distribution and elimination pathways for each drug [9]. Whereas rocuronium is dependent on hepatic and renal elimination that may be impaired in the elderly, cisatracurium is mainly eliminated by Hoffman degradation which is not expected to be much affected in advanced age [10,11].

The PTC and the temporal relationship between the count and T_1 provide valuable information to the anesthesiologist and their monitoring is recommended when diaphragmatic immobility is indicated. Diaphragmatic movements can result in hiccups, bucking, or coughing which may have grave consequences during delicate surgical interventions like laser ophthalmic surgery, neurosurgical procedures, and endoscopic thoracic surgery. It has been recommended to keep the PTC below 5 in order to prevent significant diaphragmatic recovery [12]. Since the diaphragm recovers much faster than any other skeletal muscles, the anesthesiologist should not wait for the adductor pollicis first response to TOF stimulation to appear before administering a maintenance dose of the NMBD [13]. The depth of NMB can be maintained by titrating NMBD administration when the PTC has recovered to 5 rather than waiting for T_1 to appear by which time the diaphragm could have recovered to 25% of the control values and coughing or bucking may be imminent if not already occurring [12]. On the other hand, at the end of surgery, the anesthesiologist can predict the recovery time for T_1 and accordingly plan the time of reversal drug administration. From our data, intense cisatracurium-induced NMB in elderly subjects was associated with the same predictable recovery profile and the same temporal relationship between the different recovery indices as compared with younger subjects. The results from our study, however, should not be extrapolated to other NMBDs. Further research is needed to establish the PTC/T_1 relationship when other NMBDs are used in elderly population and document any deviation from the expected early recovery profile in younger adults. In contrast to the significant affects that aging may have on the pharmacokinetics of NMBDs, no evidence exists that old age may be associated with any changes in the pharmacodynamic response [14-16].

In summary**,** The consistent temporal relationship between PTC and TOF is preserved in geriatric patients. Further research is needed to examine the PTC/TOF relationship in the elderly during recovery from intense NMB induced by other NMBDs.

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