Clinical, electrical and mechanical correlations during recovery from neuromuscular blockade with vecuronium

J. Y. Dupuis MD, R. Martin MD FRCPC,
J. P. Tétrault MD FRCPC

In order to determine correlations between electromyographic (EMG), mecanomyographic (MMG) and clinical criteria of adequate recovery from neuromuscular blockade with vecuronium, seven young healthy conscious volunteers were given subparalysing doses of vecuronium. During recovery from neuromuscular blockade, vital capacity, negative inspiratory pressure, peak expiratory flow rate and five-second head lift were assessed. Neuromuscular monitoring included the evoked EMG response of the adductor digiti minimi and the simultaneous evoked MMG response of the adductor pollicis on the same side. We found that all subjects maintained head lift for five seconds at EMG T_4/T_1 of 0.70, and they achieved normal respiratory tests at EMG T_4/T_1 of 0.90. The MMG T_4/T_1 needed for the subjects to perform normal respiratory tests was found to be 0.50, at which time six of the seven subjects were able to perform adequately the head lift test.

La corrélation entre l'électromyographie (EMG), la mécanomyographie (MMG) et des critères cliniques de récupération adéquate suite à l'administration de doses sous-paralytiques de vécuronium a été étudiée chez sept jeunes volontaires sains. Pendant la phase de récupération du bloc neuromusculaire, la capacité vitale, la force inspiratoire, le débit expiratoire de pointe et la capacité de maintien de la tête soulevée pour cinq

secondes ont été évalués. Le monitoring neuromusculaire comprenait au niveau d'un même membre supérieur un EMG de l'adductor digiti minimi et un MMG de l'adductor pollicis. En ce qui a trait à l'EMG, tous les sujets ont réussi l'épreuve du maintien de la tête soulevée pour cinq secondes lorsque le rapport T_4/T_1 était de 0,70 et les tests de fonction respiratoire se sont avérés dans les limites normales lorsque le rapport T_4/T_1 était revenu à 0,90. Quant au MMG, six des sept sujets ont réussi le test du maintien de la tête soulevée pour cinq secondes lorsque le rapport T_4/T_1 était de 0,50, alors que tous les tests de fonction respiratoire étaient revenus à la normale à ce moment-là.

The evoked mechanical (MMG) and electrical (EMG) responses of muscular activity are two methods currently used to provide measurement of muscle relaxation during and after anaesthesia.¹⁻³ While the MMG responses of the adductor pollicis have been extensively studied and compared with clinical criteria of recovery from neuromuscular blockade in the presence of d-tubocurarine,⁴⁻⁸ similar comparisons have not been performed using EMG responses of the adductor digiti minimi muscle⁹ and MMG responses of the adductor pollicis, in the presence of vecuronium.

In the presence of d-tubocurarine, a MMG train-of-four (T_4/T_1) value of 0.70 is known to correlate with full recovery of respiratory function in partially curarized conscious volunteers,⁷ and with acceptable criteria for extubation in anaesthetized patients.^{6,8} This T_4/T_1 value and its clinical correlations are currently applied to the other nondepolarizing muscle relaxants, but no controlled studies have been done to support the assumption that the peripheral manifestations of neuromuscular blockade and their correlation with respiratory function are the same for all nondepolarizing muscle relaxants.

This study was designed to determine the EMG and MMG T_4/T_1 values compatible with full recovery of

Key words

MEASUREMENT TECHNIQUES: electromyography, neuromuscular blockade, respiratory function;
MONITORING: neuromuscular function;
NEUROMUSCULAR RELAXANTS: vecuronium;
measurement of response.

From the Department of Anaesthesia, University of Sherbrooke, C.H.U.S., Sherbrooke, Quebec.

Address correspondence to: Dr. R. Martin, Department of Anaesthesia, Centre Hospitalier Universitaire de Sherbrooke, 3001, 12th Avenue North, Fleurimont (Quebec), J1H 5N4.

respiratory function in healthy conscious volunteers during recovery from a vecuronium-induced neuromuscular blockade.

Methods

The protocol was approved by our Hospital Ethics Committee, and seven healthy volunteers (three women and four men), aged 24 to 34, signed an informed consent to participate in the study. The subjects, who were residents in anaesthesia, did not receive premedication. An intravenous catheter and routine monitoring including continuous electrocardiogram, indirect blood pressure measurement, end-tidal CO_2 and pulse oximetry were installed in each subject in a semi-recumbent position. To ensure the comfort of the subjects and to maintain good stability of the MMG baseline monitoring of the adductor pollicis muscle during ulnar nerve stimulation, regional blocks of the medial cutaneous nerve of the forearm and of the cubital nerve on the same side were performed at the axillary level with 10 ml of carbonated lidocaine one per cent plus epinephrine 1/400,000.

A neuromuscular transmission monitor Datex NMT 221 was used to produce supramaximal train-of-four stimulation (range 40 to 50 MA) 2 Hz, of the ulnar nerve at the wrist every 20 sec, and to record the evoked EMG response of the adductor digiti minimi muscle. The simultaneous evoked MMG response of the adductor pollicis on the same side was measured using a force-displacement transducer, Grass FT-10, connected to a polygraph. A stabilization period of about five minutes was respected for EMG and MMG T_4/T_1 responses.

Before the administration of vecuronium, the subjects were instructed in the tests to be performed. They were also acquainted with the different pieces of equipment to be used, including the nose clip and the mouthpiece. The following variables were continuously measured: oxygen saturation with a pulse oximeter Datex 251; end-tidal CO_2 with a capnograph Datex 254; tidal volume and respiratory frequency with a spirometer, Ohio 5400. Intermittently, at the various levels of muscle relaxation to be studied, the subjects were asked to lift their head for five seconds. Thereafter, the following respiratory variables were measured: vital capacity with a Vitalograph spirometer (model R, of Vitalograph Limited, Ireland), peak expiratory flow rate with an Assess Peak Flow Meter (Healthscan Inc., U.S.A.), inspiratory pressure with a calibrated water column manometer. The values of the EMG and MMG twitch responses T_1/T_c were recorded at the times of respiratory tests.

After measuring control values of the above variables, an initial intravenous bolus of vecuronium ($0.01 \text{ mg} \cdot \text{kg}^{-1}$), was administered, followed by either a bolus, $0.005 \text{ mg} \cdot \text{kg}^{-1}$, and/or a continuous infusion titrated to

achieve a stable state of neuromuscular blockade at a level of EMG T_4/T_1 of 0.50 ± 1 per cent. The measurements of the variables were then made twice, with the highest values being recorded. The measurements were repeated at each 0.10 ± 1 per cent increase in the EMG T_4/T_1 during spontaneous recovery until a value of 1.00 was achieved. Each studied level of muscle relaxation was kept stable by infusion of vecuronium in order to allow enough time to perform the clinical tests.

For statistical analysis, comparisons with control values were made with an analysis of variance for repeated measures, using the Dunnett's test. A value of $P < 0.05$ was considered significant. Comparisons between the MMG and EMG evoked muscle responses were made with simple linear regression.

Results

All volunteers, except one, experienced a pleasant sedative sensation after the administration of the first bolus of vecuronium, and five of them felt that this sensation persisted for as long as 30 to 60 minutes after the end of the experiment. Weakness of the eyelids with diplopia, followed by moderate weakness of the facial muscles and of the masseter were the first manifestations of motor blockade in all cases. Difficulty in swallowing appeared afterwards. One subject complained of chest tightness at the maximum depression of neuromuscular function (MMG T_4/T_1 of 0.50), while none of the others complained of dyspnoea at any time. In all subjects, respiratory rate, tidal volume, end-tidal CO_2 and oxygen saturation remained unchanged during the whole experiment.

All subjects, except one, could sustain head lift for five seconds at EMG T_4/T_1 of 0.50. That subject succeeded in performing the test only when the EMG T_4/T_1 attained 0.70.

Figure 1 shows the variations in peak expiratory flow rate, inspiratory pressure and vital capacity, according to the different level of muscle relaxation as measured with the EMG monitor. All values returned within control values when the EMG T_4/T_1 was 0.90, with a corresponding value of EMG T_1/T_c of $0.83 (\pm 0.07)$. Figure 2 shows the variations in the same respiratory variables, in relation to the MMG T_4/T_1 values recorded at the time of clinical testing. All variables returned to control values when the MMG T_4/T_1 was higher than 0.50, with a corresponding value of MMG T_1/T_c of $0.90 (\pm 0.10)$. The relation between the EMG T_4/T_1 and the MMG T_4/T_1 is expressed by the following linear regression equation: $y = 1.033x - 20.605$; $r = 0.78$ (Figure 3).

Discussion

In this study, when measuring the evoked EMG response of the adductor digiti minimi in the presence of partial

FIGURE 1 Changes from control in mean $\pm$ SD of peak expiratory flow rate, vital capacity and inspiratory pressure at different evoked EMG train-of-four responses of the adductor digiti minimi. * $P < 0.005$ and ** $P < 0.01$ when compared with control.

neuromuscular blockade with vecuronium, we found that an EMG T_4/T_1 value of 0.90 must be attained for healthy conscious volunteers to achieve normal respiratory function tests. When measuring the evoked MMG response of the adductor pollicis in the same situation, an MMG T_4/T_1 value of 0.50 was necessary to perform the same respiratory function tests.

The linear regression equation defining the relationship between the EMG and MMG T_4/T_1 values in presence of

FIGURE 2 Changes from control in mean $\pm$ SD of peak expiratory flow rate, vital capacity and inspiratory pressure at different evoked MMG train-of-four responses of the adductor pollicis. * $P < 0.005$ when compared with control.

vecuronium, shows that the evoked MMG response of the adductor pollicis lags behind the evoked EMG response of the adductor digiti minimi by about 20 per cent. Authors of previous studies^{2,3} found a similar equation for atracurium given to anesthetized patients, and accepting a MMG T_4/T_1 of 0.70 as a reliable sign of recovery,⁷ they deduced that an EMG T_4/T_1 of 0.90 should be attained

FIGURE 3 Mean $\pm$ SD MMG T_4/T_1 values in relation to EMG T_4/T_1 values, and regression line of simultaneous monitoring of the evoked MMG responses of the adductor pollicis and evoked EMG responses of the adductor digiti minimi.

before considering adequate recovery of neuromuscular function in anesthetized patients. The clinical correlations found in our study now confirm that conclusion. Data obtained with electrodes over thenar or hypothenar (in the present study) aspects of the hand for EMG are considered to be similar by many authors,³ but this question is beyond the scope of this investigation.

On a theoretical basis, according to the linear regression equation, an MMG T_4/T_1 of 0.70 should correlate with full recovery of respiratory function. However, when the values of the different variables were matched to the MMG T_4/T_1 values recorded at the time of the functional tests, we found that all respiratory tests had returned to normal when the MMG T_4/T_1 was 0.50. This low value of T_4/T_1 correlating with normal respiratory function has previously been suggested in a study using atracurium, where the authors based their conclusion on the fact that none of the patients with a MMG T_4/T_1 of 0.50 showed signs of residual muscle relaxation in the three hours following their transfer to recovery room.¹⁰ Another recent study done with atracurium showed that an EMG $T_4/T_1 > 0.60$ is consistent with normal respiratory function.¹¹ Therefore, all recent studies suggest that T_4/T_1 values lower than 0.70 correlate with adequate recovery of respiration in the presence of intermediate-acting muscle relaxants.

The reason for a lower MMG T_4/T_1 correlation with normal respiratory function in presence of vecuronium compared with d-tubocurarine⁷ is not clear. It may simply be due to the different settings of the investigation. It may also be because different nondepolarizing muscle relaxants have different sparing effect on respiration, so that monitoring of the peripheral evoked response of a muscle (the adductor pollicis) does not indicate the same information about respiratory muscles when different muscle

relaxants are used. This is accepted when depolarizing and nondepolarizing muscle relaxants are compared.¹² Previous comparisons between d-tubocurarine, gallamine and toxiferine, suggested a different sparing effect of respiration for those relaxants, but the authors were careful in their conclusions. They felt that the difference between the various nondepolarizing relaxants was due to the fact that maximal muscle relaxation was not the same for each muscle relaxant.¹²

The ability to sustain a normal head lift against gravity is a more sensitive index of recovery of neuromuscular blockade than a normal train-of-four.¹³ The results of our study might appear to contradict that concept. However, it is important to recall that the sensitivity of the head-lift test was originally established with the use of a strain gauge dynamometer allowing a precise measurement of the strength of the neck muscles involved in head lift.⁴ In our study, such a specific measurement was not done. It was a clinical assessment in a semi-recumbent position. Therefore, the only conclusion that can be drawn from our results is that the clinical assessment of head lift in partially curarized patients can be misleading, just as the tactile assessment of the TOF response of the adductor pollicis.¹⁴

We cannot explain the pleasant sedative effect described by six of the seven subjects. It began before evidence of onset of neuromuscular blockade at EMG and MMG and lasted many minutes after complete recovery from neuromuscular blockade. There is no mention of such effect in previous studies in conscious volunteers. However, pancuronium is known to reduce halothane requirement in man.¹⁵ We can only speculate that vecuronium, which has a similar molecular structure, could have a central effect.

We conclude that during neuromuscular blockade with vecuronium in young healthy patients the EMG evoked response of the adductor digiti minimi correlates with recovery of normal respiratory function when the T_4/T_1 is 0.90. The MMG evoked response of the adductor pollicis has a similar clinical correlation when the T_4/T_1 is 0.50. Our conclusions have two implications. First, as more research on muscle relaxants is done with the EMG Datex NMT 221, efforts should be made by the authors to use a T_4/T_1 value of 0.90 in the analysis of their variables. This would allow correlations with clinical tests or with previous data obtained from MMG monitoring. Secondly, the possibility of a different sparing effect of respiration among the various nondepolarizing relaxants should be explored. This could help to explain some of the different effects observed between the intermediate-acting muscle relaxants, vecuronium and atracurium, and the long-acting ones, such as d-tubocurarine.

References

- 1 Ali HH, Savarese JJ. Monitoring of neuromuscular function. *Anesthesiology* 1976; 45: 216–48.
- 2 Kopman AF. The relationship of evoked electromyographic and mechanical responses following atracurium in humans. *Anesthesiology* 1985; 63: 208–11.
- 3 Weber S, Muravchick S. Electrical and mechanical train-of-four responses during depolarizing and nondepolarizing neuromuscular blockade. *Anesth Analg* 1986; 65: 771–6.
- 4 Johansen SH, Jorgensen M, Molbech S. Effect of tubocurarine on respiratory and nonrespiratory muscle power in man. *J Appl Physiol* 1964; 19: 990–4.
- 5 Walts LF, Levin N, Dillon JB. Assessment of recovery from curare. *JAMA* 1970; 213: 1894–6.
- 6 Ali HH, Kitz RJ. Evaluation of recovery from nondepolarizing neuromuscular block, using a digital neuromuscular transmission analyzer: preliminary report. *Anesth Analg* 1973; 52: 740–4.
- 7 Ali HH, Wilson RS, Savarese JJ, Kitz RJ. The effect of tubocurarine on indirectly elicited train-of-four muscle response and respiratory measurements in humans. *Br J Anaesth* 1975; 47: 570–4.
- 8 Brand JB, Cullen DJ, Wilson NE, Ali HH. Spontaneous recovery from nondepolarizing neuromuscular blockade: correlation between clinical and evoked response. *Anesth Analg* 1977; 56: 55–8.
- 9 Ali HH. Monitoring neuromuscular function. *Anesthesiology* 1986; 64: 532.
- 10 Jones RM, Pearce AC, Williams JP. Recovery characteristics following antagonism of atracurium with neostigmine or edrophonium. *Br J Anaesth* 1984; 56: 453–7.
- 11 Sharpe MJ, Lam AM, Nicholas JF, Chung DC, Merchant R, Alyafi W. Correlation between integrated evoked EMG and respiratory function following atracurium administration. *Can J Anaesth* 1987; 34: S77–8.
- 12 Foldes FF, Monte AP, Brunn HM, Wolfson B. Studies with muscle relaxants in unanesthetized subjects. *Anesthesiology* 1961; 22: 230–6.
- 13 Miller RD. Antagonism of neuromuscular blockade. *Anesthesiology* 1976; 44: 318–29.
- 14 Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jorgensen B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology* 1985; 63: 440–3.
- 15 Forbes AR, Cohen NH, Eger EI. Pancuronium reduces halothane requirement in man. *Anesth Analg* 1979; 58: 497–9.