

QUANTITATIVE ASSESSMENT OF RESIDUAL ANTIDEPOLARIZING BLOCK (PART II)

BY

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SUMMARY

An attempt to estimate residual neuromuscular blockade after the administration of anti-depolarizing relaxants to anaesthetized patients is described. A train of four supra-maximal nerve stimuli was applied to the ulnar nerve and the twitch response (mechanical or electrical) was recorded. The frequency of the train used was 2–2.4 Hz with an interval of 10 seconds between the trains. Clinical recovery from the relaxant was assessed by the ability to lift the head. The ratio of the height of the fourth response of the train to that of the first (ratio (c)) gave a good indication of the degree of residual neuromuscular block as indicated by this simple clinical test. As ratio (c) increased muscle power improved. Obvious muscle weakness was associated with values of ratio (c) of less than 0.6.

Two previous papers (Ali, Utting and Gray, 1970, 1971) have described the use of a train of four stimuli as a method of assessing the degree of neuromuscular blockade due to the antidepolarizing muscle relaxants. The four stimuli (at a frequency of 2–2.4 Hz) were of greater strength than that required to produce a maximal muscle response, and were applied to the ulnar nerve at a train frequency of 0.1 Hz, the resultant muscle activity being assessed either mechanically or by the electromyograph.

Before the muscle relaxant was administered each of the four stimuli gave a twitch response (or evoked electromyogram) of equal height: after the relaxant had been given, however, there was a fade in the four responses, the first being the greatest and the fourth the smallest. The results were quantified using three ratios: the height of the first twitch response of the train of four obtained after the relaxant had been given was compared with the control response (ratio (a)), the height of the second twitch response of the train of four was compared with the height of the first response (ratio (b)), and the height of the fourth response of the train of four to the first response (ratio (c)). It was found that there was a good correlation between ratio (a) and ratios (b) and (c); this is significant since the first ratio involves a direct comparison between partially curarized and control responses, whereas the last two are obtained without the necessity of a control response having been first elicited.

This paper presents an attempt to correlate the three ratios with head-lifting ability in the immediate postoperative period. Head-lifting was chosen as a test of muscle power because the test is easily administered immediately after anaesthesia, and because it represents a more sensitive index of muscle weakness than is given by tests of maximal inspiratory and expiratory flows (Johansen, Jorgensen, and Molbech, 1964).

METHODS

Patients.

It was possible to obtain ratios (a), (b) and (c) in only twenty patients: in ten of these muscle twitch was recorded mechanically and in another ten the record was electromyographic. Details of these patients have been recorded elsewhere (Ali, Utting and Gray, 1971) and the results from these patients are recorded in detail later.

In a further twenty patients, however, it was not possible to determine ratio (a): these patients were treated in the same way as the others but control twitch responses before the relaxant was given were not obtained. Results from these patients have, however, been included in figures 2 and 3.

Basic procedure.

No premedication was given. Just before the induction of anaesthesia, the patient, whilst lying

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flat, was asked to lift his head off the pillow and maintain it unsupported for as long as was comfortable or up to a maximum of 50 seconds. This time (in sec) was taken as a control value; it was found, not infrequently, that patients were unable to keep their head clear of the pillow for the maximum period.

Anaesthesia was induced with thiopentone (250–300 mg) and maintained with a mixture of nitrous oxide and oxygen (5/2 l./min) using a circle circuit of the Boyle III type. Halothane 0.5 per cent was added to the inspired mixture by means of a Fluotec vaporizer, whilst attempts were made to obtain, where possible, mechanical or electromyographic recordings to serve as control responses.

After control responses had been obtained or the attempt to obtain them had been abandoned because of shortage of time one of three relaxants was given (tubocurarine 0.66 mg/kg, pancuronium 0.1 mg/kg or alcuronium 0.28 mg/kg). Intubation of the trachea was performed as soon as practicable and IPPV was established; anaesthesia was continued with a mixture of nitrous oxide and oxygen, no other analgesic agent or volatile adjuvant being employed. At the end of the operation (37–178 min after the relaxant had been administered) a mixture of atropine 1.2 mg and neostigmine 5 mg was given to reverse the neuromuscular block, and the administration of nitrous oxide was discontinued. The appearance of reaction to the endotracheal tube and of spontaneous respiration was noted, as was movement of the limbs, etc. After the endotracheal tube had been removed the patient was asked to open his eyes, protrude his tongue and cough. Later he was asked to lift his head off the pillow and keep it elevated for as long as possible. Head-lifting was assessed at 5-min intervals and, at the same time, the muscle twitch or electromyographic response to intermittently applied trains of four stimuli was recorded. Monitoring was continued for 5–30 min after the administration of neostigmine, the time available depending on the circumstances in the recovery room.

Nerve stimulation and muscle recording.

The ulnar nerve was stimulated at the elbow using 25-gauge needle electrodes. Square wave stimuli of duration 0.3 msec and of intensity 10–

20 per cent greater than that required to produce maximal muscle twitch response were delivered from a Grass stimulator (S8) by way of a Grass stimulus isolation unit (SIU478). The pattern of nerve stimulation was planned in such a way that single stimuli at a frequency of 0.3 Hz were delivered first to obtain a maximal response. The stimulus intensity was then increased by 10–20 per cent and trains of four stimuli were used at a frequency of 2 Hz (or 2.4 Hz when the electromyographic recordings were taken).

It was planned to obtain a control trace after the thiopentone had been administered, but before the muscle relaxant was given. In cases in which it was not possible to obtain a control before the muscle relaxant was given, or in cases in which the needle electrodes came out, a maximal response to the train of four stimuli was sought in the curarized patient and after it had been obtained the stimulus intensity was increased marginally.

Mechanical twitch response was recorded using the force of the thumb adduction as measured by an Ether (UF1) tensile compressive transducer assembled in the form of a hand grip (Ali, 1970). An electromyographic record was obtained (in ten patients) from the belly of the first dorsal interosseous muscle of the hand: a Medelec Ms5 electromyograph was used, the (triggered) sweeps being photographed with a polaroid camera.

RESULTS

There was invariably complete ablation of the mechanical or electrical muscle twitch response for a period of at least 3–5 min after the administration of the relaxant. Before attempted reversal of the neuromuscular block with neostigmine, however, some spontaneous recovery of the mechanical or electrical twitch response to the train of four stimuli was usually observed. At this stage the response to the first stimulus of the train reappeared first and usually afforded the only evidence of muscle activity, although occasionally a smaller second response was recorded. After neostigmine had been given the rate of recovery of the twitch responses to the train of four stimuli was, of course, markedly increased (figs. 4 and 5).

Correlation of ratios with head-lifting.

Figures 1, 2 and 3 show the relationship between the duration of voluntary head-lifting

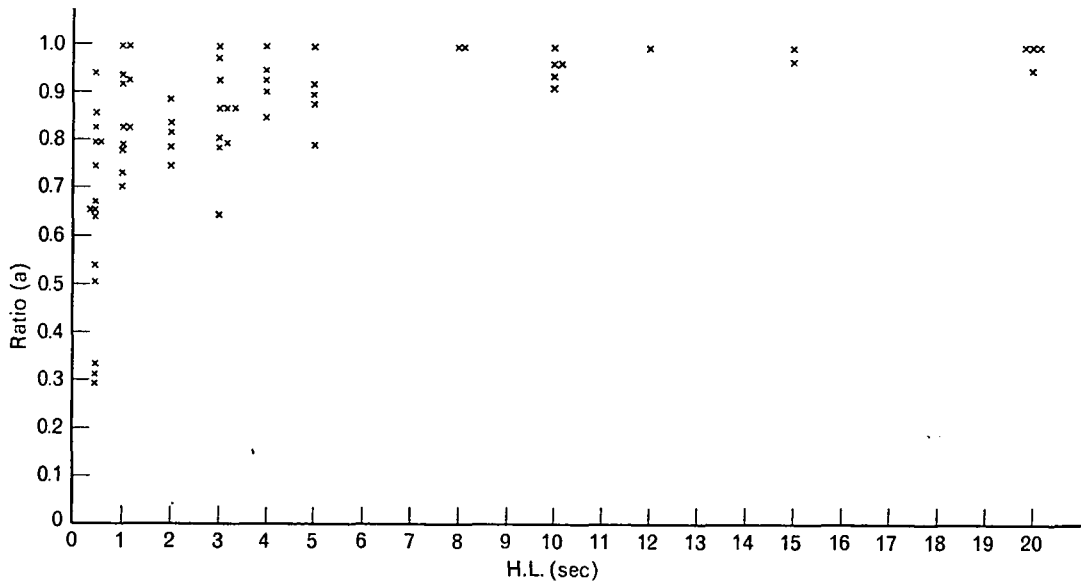


FIG. 1

The relationship between ratio (a) (height of first twitch response in train of four to control twitch response before curarization) and the duration of voluntary head-lifting after attempted reversal of antidepolarizing muscle block with neostigmine. Note that when ratio (a) was between 0.9 and 1.0 one patient could not lift his head whilst another could do so for 20 sec. (H.L. = head lifting.)

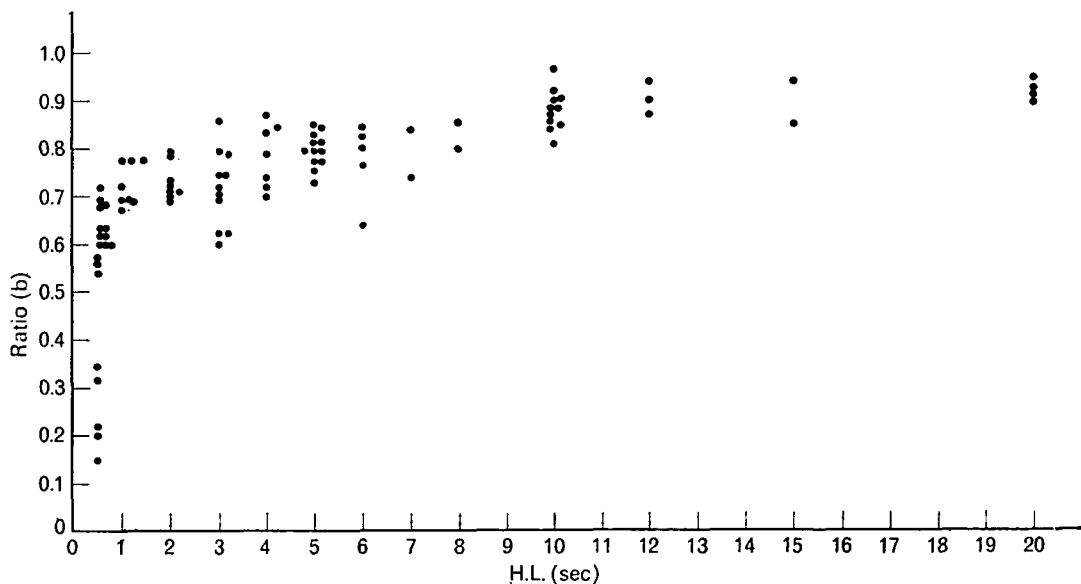


FIG. 2

The relationship between ratio (b) (height of second twitch response of train of four to first twitch response) and the duration of voluntary head-lifting after attempting reversal of antidepolarizing muscle block with neostigmine. Note that when ratio (b) was between 0.7 and 0.8 one patient could not lift his head whilst others could do so for 5 sec.

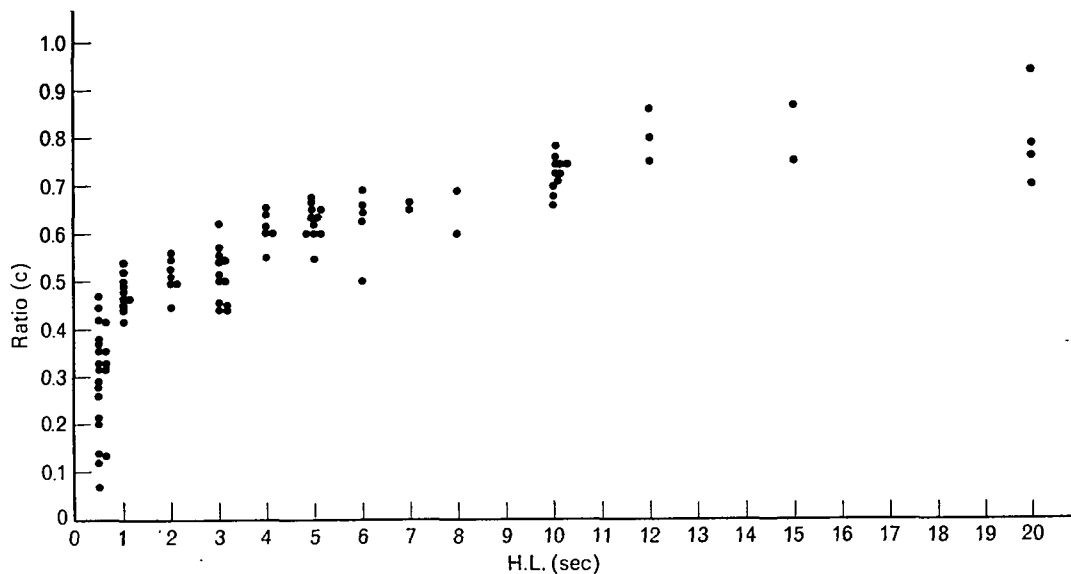


FIG. 3

The relationship between ratio (c) (height of fourth twitch response of train of four to first twitch response) and the duration of voluntary head-lifting after attempting reversal of anti-depolarizing muscle block with neostigmine. Note that when the ratio (c) is 0.6 or more all the patients were able to lift the head for at least 3 sec.

and ratios (a), (b) and (c) respectively. In these figures data from all the forty patients in the trial are presented.

Inspection of figure 1 shows that ratio (a) is not a sensitive test of recovery of muscle power as judged by head-raising. Thus it can be seen that even when (a) had returned almost to unity one patient was still unable to lift his head off the pillow, but another patient was able to sustain head-raising for 20 sec. Ratio (b), on the other hand, is a more sensitive index of recovery of muscle power (fig. 2). Nevertheless it provides a poor discrimination between those whose muscle power, judged by head-raising ability, has substantially returned, and those in whom it is still quite inadequate. Thus values of ratio (b) between 0.7 and 0.8 were found in one patient who was unable to lift his head off the pillow at all, and in other patients who were able to sustain head-raising for 5 sec.

As would be expected, ratio (c) provided the most sensitive index of return of muscle power as indicated by the head-raising test. Inspection of figure 3 reveals that no patient with a value of ratio (c) less than 0.4 was able to lift his head off the pillow, and all patients with a value of ratio

(c) greater than 0.6 were able to lift the head for a period of 3 sec or more.

Table I gives details of those patients in whom it was possible to determine all three ratios (i.e., those in whom an adequate control trace was obtained after thiopentone had been given but before the relaxant had been administered). Of the twenty patients, numbers 1-7 and 13-15 inclusive were investigated using an evoked mechanical twitch response and numbers 8-12 and 16-20 inclusive were investigated using evoked action potentials recorded on the electromyograph. There is reason to believe that the results obtained from these two methods are fundamentally similar (Ali, Utting and Gray, 1970).

The table shows that despite the fact that three different anti-depolarizing muscle relaxants were used (tubocurarine 1-12; pancuronium 13-16; alcuronium 17-20) and despite the fact that the range of dosage of these drugs was wide, increase in the value of the three ratios (a), (b) and (c) ran *pari passu* with the recovery of muscle power as estimated by the head-lifting test. It is also evident that ratio (c) gave the most sensitive index of return of muscle power.

The control values for the duration of head-

TABLE I

A summary of the data obtained from monitoring the evoked mechanical twitch response (force of thumb adduction) 1-7 and 13-15, and the evoked electromyogram from the belly of the first dorsal interosseous muscle of the hand (8-12 and 16-20).

Patient No.	Dose (mg/kg)	Relaxant-neostigmine interval (min)	Ratios at 5-minute intervals after reversal with neostigmine 5 mg, with corresponding values for head-lifting (sec)																			
			5				10				15				20				25-30			
			(a)	(b)	(c)	HL	(a)	(b)	(c)	HL	(a)	(b)	(c)	HL	(a)	(b)	(c)	HL	(a)	(b)	(c)	HL
1(T)	0.72	50	0.8	0.6	0.5	3	0.8	0.6	0.5	3												
2(T)	0.71	74	0.9	0.7	0.6	4																
3(T)	0.80	75	0.9	0.7	0.5	1	1.0	0.8	0.5	1	1.0	0.8	0.6	3	1.0	0.8	0.6	4				
4(T)	0.64	78	0.8	0.7	0.5	2	0.9	0.8	0.6	4												
5(T)	0.73	95					0.7	0.5	0.2	0	0.9	0.8	0.5	1	1.0	0.8	0.6	3				
6(T)	0.85	138	0.8	0.7	0.5	2	0.9	0.8	0.6	5												
7(T)	0.55	60	0.9	0.7	0.5	3	1.0	0.8	0.6	5	1.0	0.8	0.7	8								
8(T)	0.87	37	0.5	0.5	0.3	0	0.7	0.6	0.4	0					0.7	0.7	0.5	1	0.8	0.7	0.5	1
9(T)	0.53	43	0.8	0.7	0.4	0	0.8	0.8	0.5	1					0.9	0.9	0.6	3	1.0	0.8	0.7	10
10(T)	0.61	47	0.8	0.6	0.3	0	0.9	0.8	0.5	3					0.9	0.8	0.7	10	1.0	0.9	0.8	20
11(T)	0.58	70	0.8	0.7	0.4	3	0.8	0.7	0.6	5					1.0	0.9	0.8	12				
12(T)	0.63	134	0.9	0.8	0.5	3					1.0	0.9	0.8	20								
13(P)	0.09	40					0.9	0.7	0.5	2												
14(P)	0.10	53					0.7	0.6	0.3	0	0.8	0.6	0.4	1	0.9	0.6	0.5	1				
15(P)	0.09	73	0.9	0.9	0.6	5	1.0	0.9	0.7	10	1.0	0.9	0.7	10								
16(P)	0.11	77	0.8	0.6	0.3	0	0.9	0.7	0.5	2					0.9	0.8	0.6	4				
17(A)	0.23	38	0.7	0.7	0.4	1	0.8	0.8	0.5	2					0.9	0.9	0.6	4				
18(A)	0.40	60	0.6	0.3	0.1	0									0.7	0.6	0.3	0				
19(A)	0.24	80	0.9	0.9	0.7	10	1.0	0.9	0.9	15	1.0	1.0	0.9	20								
20(A)	0.24	178	0.4	0.2	0.1	0					0.7	0.6	0.4	0	0.9	0.7	0.5	3	1.0	0.9	0.8	15

There were ten males and ten females. Tubocurarine was given to patients 1-12, pancuronium to patients 13-16 and alcuronium to patients 17-20. Reversal of antidepolarizing neuromuscular block was attempted with neostigmine after variable periods of time from the administration of the initial dose of the relaxant. Ratios (a), (b) and (c) are represented at 5-min interval after neostigmine had been given with corresponding values for head-lifting (in seconds) (details in text).

HL=head lifting; T=tubocurarine; P=pancuronium; A=alcuronium.

there was obvious muscular weakness, the eyelids drooped, there was tracheal tug, and the patient could only just raise his head off the pillow. Five minutes later ratio (a) was 0.9, ratio (b) 0.8 and ratio (c) 0.6: at this stage the patient could lift his head off the pillow for 5 seconds and clinical recovery appeared to be good, there was no drooping of the eyelids and tracheal tug had disappeared.

Figure 5 illustrates one of the electromyographic recordings: this was obtained from a 23-year-old male weighing 65 kg (table I, patient 10). Tubocurarine (0.61 mg/kg) was administered. Reversal of the neuromuscular block using neostigmine 5 mg, preceded by atropine 1.2 mg was attempted 47 min after the relaxant had been given. The subsequent increase in the three ratios studied is clearly shown.

DISCUSSION

It must be remembered that the behaviour of the small muscles of the hand towards antidepolarizing neuromuscular blocking agents may not be quantitatively identical with the behaviour of the other muscles. Nevertheless the results of this investigation showed that there was a good correlation between the value of ratios (b) and (c) (which do not depend on the presence of a control twitch height) and a simple clinical test of recovery. Of the two ratios, of course, ratio (c) gives a more sensitive index for residual neuromuscular block than does ratio (b). Ratio (a), on the other hand, gives a much less valuable correlation with the clinical state of the patient.

The ability to estimate neuromuscular block quantitatively without the need for control response before a relaxant is given is obviously

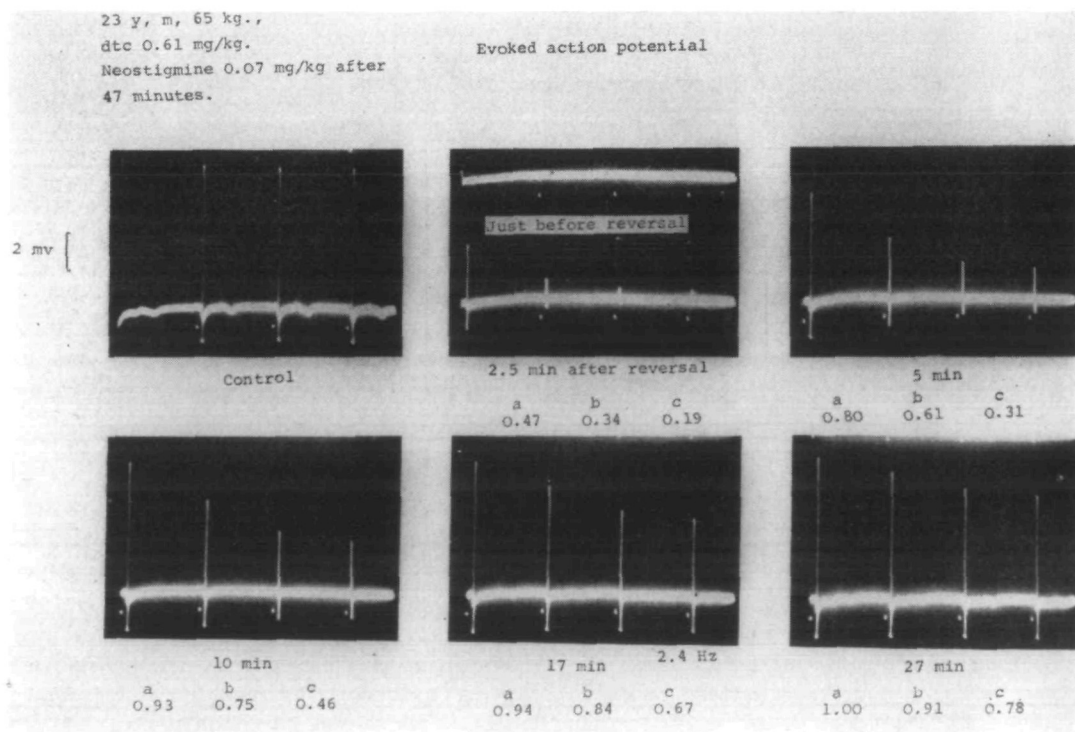


FIG. 5

An evoked electromyogram monitoring reversal of an antidepolarizing neuromuscular block produced by tubocurarine 0.61 mg/kg in a male patient 23 years old and weighing 65 kg (details in the text).

desirable. The presence of a control twitch, moreover, may be misleading. Thus Ali and Nightingale (unpublished), working with human volunteers to whom a small dose of either tubocurarine or pancuronium had been given, found that ratio (a) was sometimes a poor guide to clinical recovery, probably because of technical difficulty in fixing both the stimulating and recording electrodes when measuring the evoked action potential from the belly of the first dorsal interosseous muscle of the hand. In these cases ratios (b) and (c) appeared to be more closely related to the degree of muscle weakness than did ratio (a).

It is, of course, true that the train of four stimuli can be used to assess antidepolarizing neuromuscular block before neostigmine has been given. With large doses of relaxant the twitch response is completely ablated but with smaller doses (e.g., tubocurarine 10 mg given to an anaesthetized adult) the process of recovery can be followed throughout.

This paper suggests the need for a clinical nerve stimulator which is capable of delivering short trains of four stimuli at a frequency of 2 Hz which are intermittently repeated at a train frequency of 0.1 Hz. It is hoped to be able to develop a simple apparatus for monitoring the response to the train of four stimuli using largely equipments which are already in the operating theatre or the intensive care unit.

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EVALUATION QUANTITATIVE D'UN
BLOCAGE RESIDUEL ANTIDEPOLARISANT
(SECONDE PARTIE)

SOMMAIRE

Une tentative d'évaluation d'un blocage neuromusculaire résiduel consécutif à l'administration de substances

myorelaxantes non dépolarisantes à des malades subissant une anesthésie, est décrite. Un train de quatre stimuli nerveux supramaximaux a été appliqué au nerf cubital et la réponse par contractions musculaires (mécanique ou électrique) a été enregistrée. La fréquence du train utilisée a été de 2 Hz avec un intervalle libre de 10 sec entre les différents trains. La suppression clinique des effets du myorelaxant a été appréciée par l'aptitude à lever la tête. Le rapport de l'intensité de la quatrième réponse du train par rapport à celle de la première (rapport (c)) a constitué un bon indice du degré de blocage résiduel neuromusculaire, ainsi que le montre ce test clinique simple. La puissance musculaire s'est améliorée parallèlement à l'augmentation du rapport (c). Une faiblesse musculaire évidente accompagnait les valeurs du rapport (c) inférieures à 0,6.

QUANTITATIVE MESSUNG DES
RESTLICHEN ANTIDEPOLARISIERUNGS-
BLOCKS (TEIL II)

ZUSAMMENFASSUNG

Es wird der Versuch beschrieben, in Patienten, denen im anaesthetisierten Zustand nicht-depolarisierende Relaxantien verabreicht wurden, die verbliebene neuromuskuläre Blockade zu messen. Der Nervus Ulnaris wurde hierbei mit vier supramaximalen Nervenstimuli gereizt, und es wurde die Zuckung (mechanisch oder elektrisch) aufgezeichnet. Die Frequenz der einzelnen Stöße betrug 2 Hz und das Intervall zwischen den Stößen 10 Sekunden. Als Kennzeichen für die klinische Erholung wurde die Fähigkeit, den Kopf zu heben, angesehen. Das Verhältnis der Höhe des vierten Ausschlags nach dem Reiz zu der des ersten (Relation (c)) zeigt deutlich das Ausmaß des verbliebenen neuromuskulären Blocks, wie es dieser einfache klinische Test zum Ausdruck brachte. In dem Maße, wie die Relation (c) zunahm, verbesserte sich die Muskelkraft. Eine deutliche Muskelschwäche war vorhanden, wenn die Werte der Relation (c) unter 0,6 lagen.

VALORACION CUANTITATIVA DEL
BLOQUEO ANTIDEPOLARIZANTE
RESIDUAL (PARTE II)

RESUMEN

Es descrito un trabajo para estimar el bloqueo neuromuscular residual después de la administración de relajantes no despolarizantes a pacientes anestesiados. Se aplicó al nervio cubital un tren de cuatro estímulos nerviosos supramaximales y la respuesta de sacudida (mecánica o eléctrica) fue registrada. La frecuencia del tren utilizado fue de 2 Hz con un intervalo de 10 seg. entre los trenes. El restablecimiento clínico de los efectos del relajante fue evaluado por la capacidad para levantar la cabeza. La proporción entre la altura de la cuarta respuesta al tren y la de la primera (proporción (c)) dio una buena indicación del grado de bloqueo neuromuscular residual indicado por esta simple prueba clínica. La potencia muscular mejoró al aumentar la proporción (c). Una debilidad muscular evidente estaba asociada con valores de la proporción (c) de menos de 0,6.