

Post-operative neuromuscular function of patients receiving non-depolarising muscle relaxants at Universitas Hospital, Bloemfontein, South Africa

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Abstract

Objectives: To determine the number of patients whose non-depolarising muscle relaxation is adequately reversed. To define factors that contribute to reversal **Design:** A cross sectional study. **Setting:** Universitas Hospital recovery room over a 2 month period. **Subjects:** Patients that received non-depolarising muscle relaxants and who gave informed consent. **Outcome measures:** A quantitative train-of-four (TOF) ratio was determined within 5 to 15 minutes after arrival in the recovery room. **Results:** Recovery to TOF >0.9: 57.1% [95% CI 44.8%; 68.9%] patients. Recovery to TOF >0.8: 82.9% [95% CI 72.0%; 90.8%] patients. More patients who received vecuronium recovered to a TOF <0.8 compared with atracurium and cis-atracurium (Fisher's exact test, $p=0.0151$). **Conclusions:** The muscle relaxation of many patients is not fully reversed in the recovery room, despite a long time lapse since the last drug administration, as well as the administration of neostigmine.

Introduction

All muscle relaxants act on the neuromuscular junction, but differ in the mode, duration and blockade intensity. Non-depolarising relaxants competitively occupy the receptor on the motor end plate, which prevents acetylcholine from attaching to receptors. At the end of surgery, muscle relaxation is terminated by either natural decay of the muscle relaxant or reversal with neostigmine, which prevents breakdown of acetylcholine. This leads to the muscle relaxant being displaced from receptor sites by the accumulation acetylcholine. Clinical measures of adequate return of muscle function (e.g. a 5 second head-lift) is still widely used and considered adequate to protect the airways.¹ Other studies have shown that clinical measures are unreliable endpoints, and that a sustained head-lift may correspond to a TOF variation between 0.45 and 0.8.^{2,3} It has also been demonstrated that these

measures underestimate residual relaxation of other muscles such as facial muscles.²

Electrical stimulation of peripheral nerves and the evaluation of the muscle response is now widely used as a better alternative to clinical assessment of recovery from muscle relaxation. Various modes of stimulation are used such as titanic stimulation, post titanic facilitation, double burst stimulation and TOF stimulation. With the TOF, four electrical stimuli are applied to a peripheral nerve at 2 Hz and the height or force of movement after the fourth stimulation is expressed as a ratio compared with the first movement. Often this TOF ratio is also a clinical estimation (adequate surgical relaxation is often defined as the presence of no more than one of the four twitches).⁴ The TOF-Watch®SX is an apparatus that quantifies this ratio by acceleromyography (Force = Mass x Acceleration). Acceleromyography correlates well with mechanomyography, which is also used to measure the force of contraction. Previously, a patient with a TOF value of 0.7 to 0.8 was considered to have adequate return of neuromuscular function. Kopman et al², however, found that volunteers with TOF values < 0.9 had diplopia, and difficulty in tracking moving objects. The authors then considered that a TOF value of 0.9 indicated a "satisfactory" recovery from neuromuscular blockade. A TOF value of <0.8 was also considered to indicate a residual block.⁵

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The aim of this study was to determine post-operative neuromuscular function in patients who received non-depolarising relaxants by using the TOF-Watch®SX apparatus in the recovery room of Universitas Hospital.

Methods

Patients who underwent surgery at the Universitas Hospital, Bloemfontein (September 2002 – December 2002) and received non-depolarising relaxants were included in this cross-sectional study. Patients who would need non-depolarising relaxants were pre-determined and these patients were tested for neuromuscular function post-operatively within 15 minutes after arriving in the recovery room by using the TOF-Watch®SX apparatus. Electrodes were placed over the ulnar nerve and the acceleration sensor was connected to an unrestricted thumb. A patient with a TOF value of 0.9 was considered to have recovered from a neuromuscular block, and a patient with a value of <0.8 to still exhibit residual paralysis. Patient demographics and the dose and type of muscle relaxant received were determined from the relevant patient files and anaesthetic charts. The anaesthetists managing the patients were not alerted about the measurements. Anaesthetic charts were reviewed in the recovery room for the collection of relevant information.

The pilot study included 5 patients who received relaxants plus 5 patients who received no relaxants, who were then tested with the TOF apparatus. The two groups were compared, thus testing the apparatus and customising the researchers to its accuracy. These patients were not included in study analysis. A further seventy patients or guardians gave written informed consent to be included in the main study. The Ethics Committee of the Faculty of Health Sciences, University of the Free State approved the study.

Results

The patients' ages ranged from 5 to 79 years (median 38.5 years); 26 (37.1%) were male and 44 female (62.9%). More than half (54.3%) the patients were white, 42.9% were black and 2.9% were coloured.

According to the current standard TOF value of 0.9, 57.1% [95% CI 44.8%; 68.9%] of the patients had recovered from the neuromuscular block. Many more patients (82.9% [95% CI 72.0%; 90.8%]) had recovered when judged by a TOF standard of 0.8.

The comparison of the TOF value with respect to age, operation time, and the time lapse from last relaxant dosage until the TOF value was determined, is given in Table I. No significant differences were found when age, gender or race was looked at in relation to neuromuscular recovery.

Table I Comparison of the TOF value with respect to age, operation time, and the time lapse from last dosage until the TOF was determined (n=70). There were no significant differences between recovery groups for these parameters.

	<0.8 (n=12)		≥0.8-0.9 (n=18)		≥0.9 (n=40)	
	Median	Range	Median	Range	Median	Range
Age (years)	41.5	18-71	28.5	17-73	45.5	5-79
Operation time (hour:min)	1:20	0:25-2:00	1:05	0:23-5:00	1:27	0:30-3:40
Time lapse (hour:min)	1:22	0:35-2:20	1:13	0:35-5:40	1:16	0:10-2:45

The patients received one of three non-depolarising relaxants, namely vecuronium (24 patients), atracurium (37 patients), and cis-atracurium (9 patients). Significant differences (Fisher's exact test, $p=0.0151$) between type of relaxant and recovery were found (Table II). According to the 0.9 TOF value, 58.3% vecuronium patients, 59.5% atracurium patients, and 44.4% cis-atracurium patients had recovered. Atracurium patients had the best recovery when the TOF value of 0.8 is accepted. However, if values less than 0.8 are considered, significantly fewer patients recovered when vecuronium was administered.

Table II. The patients' TOF value in the recovery room when compared with type of agent administered (n=70)

	n	<0.8	0.8-0.9	0.9
Vecuronium	24	8 (33.3%)	2 (8.3%)	14 (58.3%)
Atracurium	37	4 (10.8%)	11 (29.7%)	22 (59.5%)
cis-Atracurium	9	0 (0%)	5 (55.6%)	4 (44.4%)

The time of last dose muscle relaxant to TOF measurement [median(minimum-maximum)] in hours:minutes for different muscle relaxants was 1:25 (0:35-2:45) for vecuronium, 1:00(0:10-4:45) for atracurium, and 1:30(0:59-5:40) for cis-atracurium. This time was significantly shorter in the atracurium group compared with the other relaxants ($p=0.0119$, Kruskal-Wallis test).

Four vecuronium patients (16.7%), 9 atracurium patients (24.3%), and 6 cis-atracurium patients (67%) received a follow-up dose. Total doses [median (minimum-maximum)] for vecuronium, atracurium, and cis-atracurium, respectively were 6.5 mg(3-12 mg), 30 mg (1-50 mg), and 10 mg (5-26 mg). The pooled initial relaxant dosages ranged from 1 mg to 50 mg (median 10 mg) with the follow-up dosages ranging from 1 mg to 10 mg (median 3 mg). Post-operatively, the neuromuscular blockade was reversed with a mixture of atropine/glycopyrolate and neostigmine in 64 patients (91.4%). Of the patients who did not receive neostigmine, 4 had vecuronium and one each atracurium and cis-atracurium.

Discussion

This study intended to measure the results of routine practices at Universitas Hospital for the study period. Quantitative TOF measurements were used and the strict TOF recovery criterium (TOF >0.9) was compared with less strict criteria (<0.8 and ≥0.8-0.9). The values were chosen in the light of recent clinical findings that patients with TOF <0.9 still experienced clinical paralysis, manifested by diplopia and difficulty to track movement.² In Kopman's study it was also concluded that it is impossible to

give reliable TOF break-points at which signs and symptoms will be present. This may lead us to conclude that a TOF >0.9 should be the safe value to aim for. Whether such a high level of recovery is necessary is debatable, since the patient will usually recover rapidly, even if the TOF is <0.8.⁵ Since some patients however have prolonged residual block, they have to be observed closely.

The main finding is that 57.1% of patients recovered to a TOF of >0.9 and 82.9% patients to a TOF >0.8. Patients

with the latter recovery have been shown to have a low incidence of breathing discomfort, which is present at lower values.⁵ These findings are similar to previous studies that showed that traditional clinical assessment of adequate recovery (such as head lift for 5 seconds) often do not correspond to full neuromuscular recovery.⁶ Usually more subtle minor clinical inadequacies such as diplopia are not used in clinical assessment, but are an indication of insufficient recovery. Under these circumstances patients considered themselves not “remotely” street ready.² It seems logical that routine TOF testing in the recovery room should be done before patients are discharged to wards. Kopman proposed that TOF values should be $>0,9$ and approach 1.² He also found that an adductor pollicis TOF as high as 1 markedly underestimated weakness of neck and jaw muscles. This should caution us not only to rely on peripheral TOF responses, but to evaluate the total patient, since the effects of muscle relaxants vary widely in different muscle groups. Leg- and head lifts were possible in patients with a TOF of 0.6.² The patient may also have other factors such as cold or drugs (eg opioids) present and the evaluation of the TOF should be context-sensitive.

Age, gender and race had no influence on the results, but the three different muscle relaxants that were used, differed significantly in respect of the recovery room TOF values. Vecuronium resulted in most patients exhibiting <0.8 TOF recovery and atracurium resulted in most patients exhibiting >0.8 TOF recovery. The three drugs were very similar in terms of a >0.9 TOF recovery. These findings are not surprising and correspond with the fact that vecuronium in clinically relevant doses is the longest acting drug, whereas atracurium, in clinically relevant doses is the shortest acting. However, in all three groups, the time from the last dose to TOF measurement was longer than previously determined for full recovery.⁷ This period was significantly longer after vecuronium or cis-atracurium administration, compared with atracurium. This suggests that other factors such as concomitant potentiating drugs, temperature or biochemistry might have had a significant influence. These factors were not measured in this study.

Most patients had their muscle relaxants reversed with neostigmine (2.5 to 3 mg). However, this did not guarantee that the TOF recovered to normal levels within 5 to 15 minutes after discharge from the operating room to the recovery room. More patients in the vecuronium group (16.7% as opposed to 11.1% for cis-atracurium and 1.1% for atracurium) did not receive neostigmine. This may have contributed to the results, although the very long periods that lapsed after the last dose of relaxant and the TOF measurements may be expected to reduce the need for reversal. The average total dose matched to the average patient age suggests that the dose range was low rather than high. The total dose may have been underestimated, since anaesthetists were deliberately not reminded to complete the anaesthetic charts meticulously to reduce practice bias.

It is advisable that muscle relaxant dose and recovery be aided by the use of nerve-stimulators.⁷ Since TOF values or reactions were not noted on anaesthetic charts, the incidence of apparatus used for monitoring neuromuscular block reversal could not be evaluated. It is, however, known that it was not used in all cases, and probably not used in the majority of cases. In practice, TOF ratios are often determined by clinical observation of muscle

movement, rather than quantitative measurement. Clinical estimation of the TOF ratio is very useful to determine the minimum relaxant dose. For most kinds of surgery, a dose of non-depolarising muscle relaxant that suppresses the TOF to one or two twitches may indicate sufficient relaxation. On the other hand, if recovery is merely judged by the level of return of the fourth twitch, it is clearly inadequate to guess the TOF ratio by clinical observation. Studies that relate tactile clinical estimation of TOF to residual block have shown that it was no better than clinical judgement of muscle movement to aid either the dose administered or the recovery.⁴ To accurately judge a TOF recovery of >0.9 , quantitative monitoring with a device such as the acceleromyograph or a strain gauge is essential.

Conclusion

Many patients in the study group still had inadequate recovery of neuromuscular function in the recovery room as measured by quantitative TOF ratios using acceleromyography. This was true despite the fact that long periods had lapsed after non-depolarising muscle relaxants (vecuronium, atracurium, and cis-atracurium) were administered, as well as the fact that neostigmine had been administered to reverse muscle relaxation. Since it has been shown that recovery to a TOF $<0,9$ is associated with subtle dysfunction such as diplopia or even breathing difficulties, it is advised that quantitative TOF estimations are done in the recovery room on patients that receive non-depolarising muscle relaxants. Similarly, these patients should only be discharged to the ward with TOF value >0.9 .

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