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RESEARCH

Postoperative neuromuscular function following non-depolarising muscle blockade in patients at Inkosi Albert Luthuli Central Hospital, Durban

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Background: Residual neuro-muscular blockade after the end of general anaesthesia may occur when non-depolarising muscle relaxant (NDMR) drugs are used. Train-of-four (TOF) stimulation is used to quantify the degree of residual paralysis, with a TOF ratio of less than 0.9 postoperatively associated with increased morbidity in patients. The aim of this study was to survey the degree of residual paralysis in patients in the post-anaesthesia care unit (PACU) at Inkosi Albert Luthuli Central Hospital (IALCH), Durban, over the survey period.
Methods: This cross-sectional observational study was performed over a two-month period at IALCH, assessing the postoperative neuromuscular function of patients who had received NDMR drugs (rocuronium ($n = 64$) or cisatracurium ($n = 6$)) intraoperatively. Muscle function was assessed using acceleromyography and TOF stimulation, utilising a TOF Watch SX device, with function grouped according to previously defined targets as less than a ratio of 0.7, less than a ratio of 0.9 and less than a ratio of 1.0.
Results: Recovery to a TOF ratio of less than 0.7, 0.9 or 1.0 was observed in 5 (7.1%), 20 (28.6%) and 44 (62.9%) of patients respectively.
Conclusions: Although the results obtained compare favourably with other studies in similar patient populations, a considerable subset of patients still arrive in the PACU with inadequate return of neuromuscular function.

Keywords: post-anaesthesia, postoperative residual curarisation, postoperative residual weakness, residual block, residual neuromuscular block, residual paralysis

Introduction

Since the 1940s, muscle relaxants have formed an essential component of general anaesthesia, greatly improving surgical conditions.[1] Associated with the use of these drugs, however, are multiple risks including the risk of incomplete reversal of neuromuscular blockade at the end of surgery. Already as early as 1954 a sixfold increase in mortality was being reported in patients who had received muscular paralysis as part of their anaesthetic.[2]

Clinical measures to assess neuromuscular function have long been used in anaesthesia and include amongst others, the five-second head-lift, tongue protrusion, jaw clench, grip strength and assessment of tidal volume.[3–5] Studies soon showed, however, that despite the ability to perform these clinical tests, significant impairment in muscle function could still persist.[3,4,6] Recent studies have shown clinical measures to be both unreliable and insensitive; however, despite this, many anaesthetists persist in relying on these tests as the sole indicators of recovery from neuromuscular blockade.[7,8]

Using evoked responses as a measure of muscle function was popularised after the development of the train-of-four (TOF) method of neurostimulation in the 1970s.[9] A TOF refers to four supramaximal impulses delivered at 0.5 second intervals which in turn result in four measurable muscle twitches. These twitches can then be assessed either subjectively using visual or tactile methods of assessment, or objectively using various devices. The advantage of the TOF lies in the fact that, as a ratio, baseline measurement of muscular function is not needed in order to interpret the result.[10]

Visual or tactile assessments utilising peripheral nerve stimulation, while often better than clinical methods, still exhibit poor sensitivity for detecting clinically significant levels of residual neuromuscular blockade, with most evaluators unable to discriminate past a TOF ratio of 0.4.[8] This poor sensitivity is exacerbated when assessed by junior or relatively inexperienced anaesthetists.[11] Objective quantitative measures of neuromuscular function have subsequently been developed. These include mechanomyography, which utilises a strain gauge to measure muscular tension; electromyography, which utilises electrodes to measure the compound muscle potential; kinemyography, based on the piezoelectric effect caused by the deformation of a mechanosensor; phonomyography, which measures the low-frequency sounds created by muscle contraction; and acceleromyography, which also utilises a piezoelectric sensor, but this time to measure acceleration produced by the muscle twitch which in turn is directly proportional to the force of muscle contraction.[12,13] Mechanomyography is still considered the gold-standard measurement technique; however, it is complicated and bulky to set up and use in daily practice.[14]

Quantitative neuromuscular monitoring has become widely available in many centres, with acceleromyography favoured over alternative methods due to its reproducibility, sensitivity and ease of use in a clinical context.[8] Several studies have shown the benefit of intraoperative use of acceleromyography in significantly reducing the incidence of postoperative residual curarisation but, despite this, it is still often not routinely applied in the clinical setting.[15–17]

It has long been recognised that residual neuromuscular blockade may adversely affect the patient's outcomes in the postoperative period.[18] Various studies have measured both the physiological and clinical sequelae of postoperative residual curarisation, and these findings have been incorporated into recommended anaesthetic practice over the years.[2,10,19–23] With the advent of neuromuscular monitors and the increased use of TOF monitoring to assess degree of neuromuscular blockade, a TOF ratio greater than 0.7 was recommended in order to minimise postoperative morbidity and mortality associated with the use of NDMR drugs.[9] This number was based on the studies of Ali et al. published in 1975, who correlated TOF ratios to measurements of respiratory reserve, namely, vital capacity, negative inspiratory force and peak expiratory flow rate.[18] More recently, in the mid-1990s it began to emerge that even relatively high levels of motor recovery (TOF 0.7–0.9) were still associated with significant negative objective outcomes such as impaired inspiratory function, decreased hypoxic drive, increased incidence of bronchial obstruction, decreased oesophageal sphincter tone, functional impairment of pharyngeal muscles, increased episodes of aspirations and delayed discharge from the recovery room.[8,10,24–26] Furthermore, TOF ratios of less than 0.9 are strongly associated with unpleasant subjective experiences for the patient including diplopia, difficulty speaking, difficulty swallowing, unsteady gait and sensations of fatigue and muscle weakness.[8,10,24–26] These newer studies have resulted in a recovery to a TOF of 0.9 or greater prior to extubation becoming widely adopted as a standard of anaesthetic practice following non-depolarising neuromuscular blockade.[5,10,21,27] Furthermore, recent studies have illustrated a small degree of overestimation of the TOF ratio when utilising acceleromyography. This has raised the possibility that in clinical practice TOF ratios of 1.0 should be targeted to ensure an effective TOF ratio greater than 0.9 when utilising acceleromyographic-based monitoring equipment such as the TOF-Watch®.[28,29]

The reported incidence of postoperative residual curarisation varies widely with published studies reporting an incidence as low as 3% in some centres,[30] while other studies have reported incidences as high as 88% in other centres.[3,31] This large variance may be partly due to the differing methodology applied by the studies, as well as different criteria used to define postoperative residual curarisation. A recent meta-analysis estimates that around 40% of patients arrive in the post-anaesthesia care unit postoperatively with a TOF of less than 0.9, and around 12% with a TOF of less than 0.7.[27]

Unfortunately there is little information available regarding the incidence of residual neuromuscular blockade following surgery in the South African context. A study of 70 patients at Universitas Hospital in Bloemfontein published in 2004 reported only 57.1% of their subjects recovering to a TOF > 0.9, suggesting the possibility that other hospitals in South Africa may also demonstrate a similar poor level of postoperative muscular recovery in their patients too.[22] Importantly, however, since then the routine non-depolarising muscle relaxant drugs used have changed with the widespread adoption of rocuronium into daily practice, as well as the decrease in the use of older drugs such as vecuronium and atracurium. This emphasises the need for further studies to help clarify the current extent of the problem in the South African context.

Methodology

Overview

The study is designed as a prospective non-randomised cross-sectional study of the degree of neuromuscular function of eligible patients, as defined by a TOF ratio, presenting at Inkosi Albert Luthuli Central Hospital over a defined two-month period, November 1, 2015 to December 31, 2015. Ethical approval to conduct the study was granted by the Biomedical Research Ethics Administration of the University of KwaZulu-Natal (Reference: BE057/14).

Population and study sample

The population from which the sample was drawn were patients who had recently arrived in the PACU (within 15 minutes of arrival), and had received intraoperative non-depolarising neuromuscular blocking agents. The anaesthetist was not notified that testing of neuromuscular function was to be performed in the PACU. Only patients who had been extubated were included in the study. Furthermore the study included only patients who had given prior informed consent. A convenience sampling strategy was utilised.

Technical information

Upon arrival at the PACU, eligible patients were evaluated within 15 minutes using a TOF-Watch SX® accelerometer-equipped neurostimulator (Schering-Plough Corp, Kenilworth, NJ, USA). The device was applied according to manufacturer recommendations. The ulnar nerve was stimulated with TOF stimulation (4 pulses 0.2 ms in duration, at a frequency of 2 Hz), with a supra-maximal stimulation being applied. Subsequent muscle twitches from the adductor pollicis were recorded. Results were recorded as a TOF value between 0 and 1 as displayed on the device. Data were collected by the principal researcher and stored on a password-protected Excel® (Microsoft Corp, Redmond, WA, USA) spreadsheet file.

Statistics

Data were grouped into three groups. The first group included all patients with a TOF ratio less than 1. The second group, a subset of the first, included all patients with a TOF ratio less than 0.9. The final group, a subset of the second, included all patients with a TOF ratio less than 0.7. Data were entered into SPSS® version 21 (Statistical Packages for the Social Sciences; IBM Corp, Armonk, NY, USA) for analysis. A p-value < 0.05 was considered as statistically significant. A descriptive statistical analysis of the data (means, standard deviations, ranges, frequencies and percentages, etc.) was initially conducted prior to conducting Fisher's exact test to test any associations between categorical variables.

Results

A total of 70 patients met the inclusion criteria and were evaluated. Among the 70 patients, 44 (62.9%) had a TOF ratio less than 1.0, 20 (28.6%) had a TOF ratio less than 0.9, and 5 (7.1%) had a TOF ratio less than 0.7, within 15 minutes of arrival at the PACU. The mean TOF ratio measured was 0.91 + –0.12 (95% CI 0.88; 0.94).

Thirty-eight (54.3%) of the patients were male and 32 (45.7%) were female. The TOF ratio differences between male and females were not significant for the less than 0.7 (p = 1.00), less than 0.9 (p = 0.940) or less than 1.0 (p = 0.423) cut-offs. The patients' ages ranged from 13 to 86 years old, with a mean age of 46.76 years; 7 (10%) of patients were greater or equal to 65 years old. The difference between TOF ratios between patients older than or equal to, or those younger than 65 years old was not significant for either the less than 0.7 (p = 0.419), less than 0.9 (p = 1.00) or less than 1.0 (p = 1.00) cut-offs.

Table 1: Patient characteristics

TOF ratio	Total	< 0.7	< 0.9	< 1.0
Number	70	5 (7.1%)	20 (28.6%)	44 (62.9%)
Age	46.76 ± 16.98	50.4 ± 12.62	49.85 ± 11.97	47.32 ± 15.73
Sex (M/F)	38/32	3/2	11/9	26/18

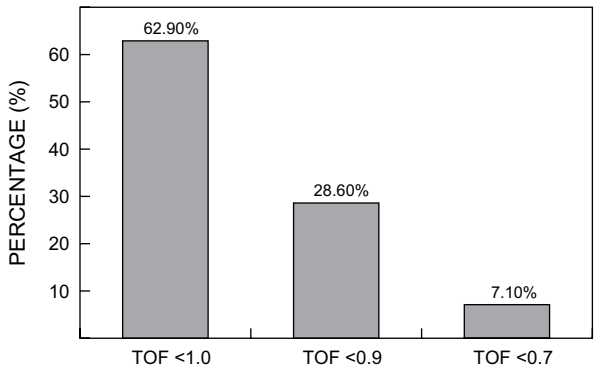

Figure 1: Percentage of subjects with residual paralysis.

Three patients did not receive neostigmine as a reversal agent for their non-depolarising muscle block. Of these, one patient had a TOF ratio less than 1.0, and none had a TOF ratio less than 0.9.

More patients recovered to a TOF ratio of less than 0.9 that had received rocuronium than had received cisatracurium although this result was not statistically significant (Fisher's exact test, $p = 0.051$) (see Table I). There was no statistically significant difference between rocuronium and cisatracurium when using a TOF ratio of 0.7 as a cut-off (Fisher's exact test, $p = 0.37$) (see Figure 1).

Discussion

Non-depolarising muscle relaxants are an indispensable part of general anaesthesia. It has long been known that with the use of NDMR drugs comes the potential for residual neuromuscular blockade after the end of anaesthesia and subsequently an increase in postoperative morbidity and mortality. Clinical methods such as the five-second head lift are commonly used to ascertain muscle function at the end of surgery; however, these methods have been shown to be insensitive and inferior to quantitative methods, most notably quantitative TOF ratio measurement. Furthermore, decreased incidence of postoperative residual curarisation has been demonstrated in units that have applied routine use of quantitative TOF ratio measurement as part of their unit protocols when using non-depolarising muscle relaxants.[30,32] Despite this evidence, however, many anaesthetists still do not routinely use methods other than clinical indicators to ascertain muscle function at the end of surgery.

A TOF ratio value of greater or equal to 0.9 is currently widely recommended as the minimum acceptable TOF ratio prior to extubation.[5,10,20,27] TOF ratio cut-offs of 0.7 and 0.9 were used in this study to align with previously recommended minimum acceptable values and to allow for easy comparison between practices at the study centre and other centres where similar studies have been performed.[18,24–26] A further cut-off of TOF ratio values less than 1.0 was included after recent studies demonstrated a tendency for overestimation of the TOF ratio by acceleromyographic-based neuromuscular stimulators such as the TOF-Watch SX®.[26, 28] The cut-off value of 1.0 was suggested to compensate for this tendency and ensure an effective TOF ratio of 0.9.

The incidence at the study centre of 28.6% of patients arriving in the PACU with a TOF ratio of less than 0.9, and 7.1% with a TOF ratio of less than 0.7 compared favourably with a recent meta-analysis that published estimates of around 40% and 12% respectively.[27] A similar South African study in 2004 of 70 subjects at Universitas Hospital in Bloemfontein demonstrated a higher incidence of residual neuromuscular block with 42.9% of their patients arriving in PACU with a TOF ratio of less than 0.9 and 17.1% with a TOF ratio of less than 0.7.[22] The reason for the variance is beyond the scope of this study but may reflect multiple potential factors such as marked increased use of newer non-depolarising muscle relaxants with an altered pharmacokinetic profile, such as rocuronium, since the earlier study was performed. Other potential factors include a difference in the spectrum of surgical procedures performed at the various centres, as well as varying levels of experience amongst the anaesthetic practitioners involved. When utilising the newly proposed cut-off value of less than 1.0, in order to ensure an effective clinical TOF ratio greater than 0.9, the percentage of subjects classified as having inadequate return of muscle function increases to a sizeable 62.9% of patients. It must be noted, however, that the use of this value as a cut-off is still not widely accepted and has yet to be verified in studies as having a direct clinical correlation.

Various studies have found conflicting results as to whether a significant difference can be found in TOF ratios when analysed according to age and gender.[6,22,33,34] When reviewing the data according to demographics, there were no significant differences between TOF ratios when grouped according to age or sex, although comparison is made difficult by the small sample sizes involved.

The validity of comparisons between the types of muscle relaxants and TOF ratios observed were also hampered by only a small sample of 6 (8.6%) patients in the study having received cisatracurium. The small sample recruited perhaps reflects a bias on behalf of the anaesthetic practitioners at the study centre towards the use of rocuronium, as choice of anaesthetic technique was left entirely to the practitioner's discretion. A tendency for slightly improved muscle function after rocuronium was, however, observed when using a value of 0.9 as the cut-off ($p = 0.051$).

Neuromuscular blockade was reversed by the administration of neostigmine in the majority of patients in the study (95.7%), with all but three of the patients having received the drug. Interestingly, however, this did not significantly reduce the prevalence of postoperative residual partial paralysis as is evidenced in the results. This provides further motivation for the routine use of quantitative neuromuscular monitoring when using non-depolarising muscle relaxants as administration of neostigmine reversal alone cannot be relied upon to ensure the absence of residual paralysis.

Residual neuromuscular blockade may be the result of many different factors alone or in combination. High doses of non-

depolarising muscle relaxants, repeat doses or infusions, the use of long-acting agents, as well as reversal agent choice, dosing and timing of administration can all contribute to increasing the risk of residual neuromuscular blockade. Further factors such as interacting agents (including residual volatile anaesthetic drugs), hypoxia, hypercarbia, acidosis, liver or renal impairment, hypothermia and age and weight of the patient can all increase this risk even further.[5,14] The purpose of this study was to reflect purely on the number of patients with impaired muscle function postoperatively after receiving non-depolarising muscle relaxants. In doing so it did not attempt to comment on the causes of any impaired muscle function, as these may be both complex and numerous, and are beyond the scope of the study. Furthermore, morbidity and mortality associated with postoperative residual curarisation occurs independent of the causative factor involved, and as such any residual impairment noted in the PACU post-extubation should be a cause for concern.

What is most notable after reviewing the results of this study is that still, after many years of various authors repeatedly emphasising the issue of residual curarisation, and numerous recommendations for the routine use of quantitative TOF ratio measurements when using non-depolarising muscle relaxants, a significant proportion of patients in the study unit are still arriving in the PACU with impaired muscle function.[8,11,18,26,30,32]

This indicates that a renewed emphasis needs to be placed on educating anaesthetic practitioners about the problem of postoperative residual curarisation, as well as ensuring the availability of quantitative neuromuscular monitors in all surgical hospitals with the ultimate aim of incorporating objective neuromuscular monitoring as part of routine evidence-based practice.

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References

1. Griffith HJGE. The use of curare in general anesthesia. Anesthesiology. 1942;3:418–20.
2. Beecher HK, Todd DP. A study of the deaths associated with anesthesia and surgery. Ann Surg. 1954;140(1):2–33.
3. Cammu G, De Witte J, De Veylder J, et al. Postoperative residual paralysis in outpatients versus inpatients. Anesth Analg. 2006;102(2):426–9.
4. Fruergaard K, Viby-Mogensen J, Berg H, et al. Tactile evaluation of the response to double burst stimulation decreases, but does not eliminate, the problem of postoperative residual paralysis. Acta Anaesthesiol Scand. 1998;42(10):1168–74.
5. Kopman AF. Neuromuscular monitoring: old issues, new controversies. J Crit Care. 2009;24(1):11–20.
6. Hayes AH, Mirakhur RK, Breslin DS, et al. Postoperative residual block after intermediate-acting neuromuscular blocking drugs. Anaesthesia 2001;56(4):312–8.
7. Grayling M, Sweeney BP. Recovery from neuromuscular blockade: a survey of practice. Anaesthesia. 2007;62(8):806–9.
8. Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. Anesth Analg. 2010;111(1):129–40.
9. Brand JB, Cullen DJ, Wilson NE, et al. Spontaneous recovery from nondepolarizing neuromuscular blockade: correlation between clinical and evoked responses. Anesth Analg. 1977;56(1):55–8.
10. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. Anesth Analg. 2010;111(1):120–8.
11. Viby-Mogensen J, Jensen NH, Engbaek J, et al. Tactile and visual evaluation of the response to train-of-four nerve stimulation. Anesthesiology. 1985;63(4):440–2.
12. Hemmerling TM, Le N. Brief review: Neuromuscular monitoring: an update for the clinician. Can J Anesthesia/J Can d'Anesthésie. 2007;54(1):58–72.
13. Nauheimer D, Geldner G. [Neuromuscular monitoring: methods and machines]. Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie : AINS. 2008;43(5):374–82; quiz 82.
14. Moi D. Residual neuromuscular blockade. Anaesthesia Tutorial of the Week. 2013;290.
15. Gatke MR, Viby-Mogensen J, Rosenstock C, et al. Postoperative muscle paralysis after rocuronium: less residual block when acceleromyography is used. Acta Anaesthesiol Scand. 2002;46(2):207–13.
16. Mortensen CR, Berg H, El-Mahdy A, et al. Perioperative monitoring of neuromuscular transmission using acceleromyography prevents residual neuromuscular block following pancuronium. Acta Anaesthesiol Scand. 1995;39(6):797–801.
17. Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. Anesthesiology. 2008;109(3):389–98.
18. Ali HH, Wilson RS, Savarese JJ, et al. The effect of tubocurarine on indirectly elicited train-of-four muscle response and respiratory measurements in humans. Brit J Anaesthesia. 1975;47(5):570–4.
19. Brull SJ, Silverman DG. Neuromuscular monitoring and clinical applications: what to do, when, and why? Sem Anesthesia, Perioper Med Pain. 2002;21(2):104–19.
20. Grosse-Sundrup M, Henneman JP, Sandberg WS, et al. Intermediate acting non-depolarizing neuromuscular blocking agents and risk of postoperative respiratory complications: prospective propensity score matched cohort study. BMJ. 2012;345:e6329.
21. Murphy GS. Residual neuromuscular blockade: incidence, assessment, and relevance in the postoperative period. Minerva Anestesiol. 2006;72(3):97–109.
22. Nell WT, Stevenson N, Ridgard T, et al. Postoperative neuromuscular function of patients receiving non-depolarising muscle relaxants at Universitas Hospital, Bloemfontein, South Africa. South Afr J Anaesthesia Analgaesia. 2004;10(1):6–8.
23. Sauer M, Stahn A, Soltesz S, et al. The influence of residual neuromuscular block on the incidence of critical respiratory events. A randomised, prospective, placebo-controlled trial. Eur J Anaesthesiol. 2011;28(12):842–8.
24. Sundman E, Witt H, Olsson R, et al. The incidence and mechanisms of pharyngeal and upper esophageal dysfunction in partially paralyzed humans. Anesthesiology. 2000;92(4):977–84.
25. Eikermann M, Groeben H, Hüsing J, et al. Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. Anesthesiology. 2003;98(6):1333–7.
26. Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. Anesthesiology. 1997;86(4):765–71.
27. Naguib M, Kopman AF, Ensor JE. Neuromuscular monitoring and postoperative residual curarisation: a meta-analysis. Br J Anaesth. 2007;98(3):302–16.
28. Capron F, Alla F, Hottier C, et al. Can acceleromyography detect low levels of residual paralysis?. Anesthesiology. 2004;100(5):1119–24.
29. Kopman AF, Klewicka MM, Neuman GG. The relationship between acceleromyographic train-of-four fade and single twitch depression. Anesthesiology. 2002;96(3):583–7.
30. Baillard C, Clec'h C. Catineau J, et al. Postoperative residual neuromuscular block: a survey of management. Br J Anaesth. 2005;95(5):622–6.
31. Murphy GS, Szokol JW, Marymont JH, et al. residual paralysis at the time of tracheal extubation. Anesth Analg. 2005;100(6):1840–5.
32. Baillard C, Gehan G, Reboul-Marty J, et al. Residual curarization in the recovery room after vecuronium. Br J Anaesth. 2000;84(3):394–5.
33. Almeida MC, Camargo DR, Linhares SF, et al. Evaluation of residual neuromuscular block and late recurarization in the post-anesthetic care unit. Rev Brasileira de Anestesiologia. 2004;54(4):518–31.
34. Tsai CC, Chung HS, Chen PL, et al. Postoperative residual curarization: clinical observation in the post-anesthesia care unit. Chang Gung Med J. 2008;31(4):364–68.

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