

Comparison between the Clinical Assessment, Peripheral Nerve Stimulation (PNS), and Acceleromyography (AMG) to Reverse Neuromuscular Blockade

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ABSTRACT:

BACKGROUND:

Traditionally, most of anesthesiologists in Iraq evaluate the degree of neuromuscular blockade during and after anesthesia using clinical criteria alone, which are inaccurate to assess adequate recovery from neuromuscular block (NMB) which is essential for the patient to have full control of pharyngeal and respiratory muscles. Fade cannot be detected reliably with a peripheral nerve stimulator (PNS) at a TOF ratio > 0.4. The time gap between losses of visual fade by using a PNS until objective TOF ratio has returned to > 0.90 can be considered "the potentially unsafe period of recovery."

OBJECTIVE:

To compare between assessment of subjective clinical, subjective TOF by peripheral nerve stimulation (PNS), and objective TOF by acceleromyography (AMG) before reversal of neuromuscular blockade

PATIENT AND METHOD:

A prospective clinical trial of one hundred females who underwent caesarian section under general anesthesia. Standard anesthesia was conducted for all patients. Giving of neuromuscular reversal was decided by the anesthesia care providers depending on clinical criteria, at that time, TOF measured by 2 ways, 1st: counting the twitches visually (principal of PNS), and 2nd: the device showing the TOF reading objectively (principal of AMG).

RESULT:

Comparisons between subjective criteria and objective AMG T4/T1 ratios revealed no statistical significance ($P > 0.05$) in all comparisons (except that with the moving limb and lift the head). The association and consistency of subjective criteria and visual PNS was insignificant differences in all comparisons. There was wide discrepancy between objective reading and the visual PNS.

CONCLUSION:

The moving limbs and sustained lift head 5 seconds clinical criteria were correlated to TOF. Other criteria (protruding tongue, respiratory effort, and swallowing reflex) were not correlated to TOF. Objective AMG more sensitive to detect the fourth twitch than the subjective PNS.

KEY WORDS: train of four (TOF), peripheral nerve stimulator (PNS).

INTRODUCTION:

Muscle relaxants have been used in clinical settings for almost 60 years. Still, neuromuscular blocking agents are associated with a significant incidence of postoperative residual effects in the operating room (OR). Monitoring the effect of neuromuscular blocking agents helps to ensure appropriate intraoperative use and effective antagonism of these agents. However, for many years, clinical criteria alone (e.g. 5 seconds head

lift, eye opening and tongue protruding in response to verbal commands, presence of partial efforts of breathing, and other skeletal movements, and grip strength) were used to determine the degree of block and the adequacy of recovery. ⁽¹⁾

Clinical signs alone are not an adequate and sensitive means of detecting residual block. ⁽²⁾ When the TOF ratio is greater than 0.6, most patients are able to sustain head lift for three seconds or more, but this does not ensure normal muscle strength. ⁽³⁾ Thus, it is essential to monitor neuromuscular recovery following the administration of neuromuscular blocking drugs. ⁽²⁾

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Clinicians monitor the evoked responses objectively or subjectively.⁽⁴⁾

The most popular method of (subjective) neuromuscular fade in response to TOF stimulation is visual and/or tactile assessment.⁽⁵⁾

These subjective means should be augmented by objective assessment tools (e.g., mechanic or electromyographic), especially in patients at risk for postoperative residual paralysis.⁽⁶⁾ One of objective monitoring is AMG. The objective monitor can display the percent change of the evoked response from baseline, and the calculated TOF ratio.⁽⁷⁾

The combination of clinical evaluation along with neuromuscular monitoring should be used.⁽⁸⁾

Although Ali and colleagues originally suggested that a recovery of the TOF ratio to 0.7 was necessary to protect the airway after tracheal extubation, it is now accepted that a ratio of 0.9 is necessary in this respect.^(9, 10, 11) Residual paralysis associated with a significant risk to patient recovery.⁽¹²⁾ The depth of neuromuscular block at the time of administration of anticholinesterases has an influence on their effect. There is a marked increase in the time to recovery of the TOF ratio to 0.7 if neostigmine is administered at T1, 10–20% after pancuronium, vecuronium,⁽¹³⁾ or rocuronium.⁽¹⁴⁾ It was initially recommended that antagonism of neuromuscular block with an anticholinesterase should not be attempted until two twitches of the train-of-four (TOF) twitch response are detectable, otherwise it will be ineffective.⁽¹⁵⁾ Therefore, doses up to 0.07 mg/kg add little; in addition, the agent must be injected only when sufficient spontaneous recovery is observed in order to attain a TOF ratio = 0.9 within a reasonable time, i.e., 10–15 min following neostigmine. In fact, it is recommended to wait until there are 4 visible twitches following TOF stimulation before administering neostigmine.^(16,17)

Traditionally, most of anesthesiologists in Iraq evaluate the degree of neuromuscular blockade during and after anesthesia using clinical criteria alone. This study to compare the decision to administer neostigmine depending on clinical criteria with the subjective TOF by PNS and objective TOF by AMG.

PATIENT AND METHOD:

This is a prospective randomized clinical trial carried out in the Baghdad teaching hospital / medical city complex during a period of two months from the first of march to the 31th of April/ 2012. It involved 100 pregnant ladies aged 18-35 years all of ASA I and II were scaduled for

emergency or elective caesarian section surgeries under general anesthesia.

Any patient with history of neuromuscular, hepatic, or renal disease, body mass index more than 30%, anticipated difficult ventilation or endotracheal intubation, and receiving drugs known to interfere with neuromuscular transmission were excluded from the study.

Standard anesthesia were conducted for all patient, induction was done by thiopental 4-6 mg/kg (anesthetizing dose), succinylecoline 1.5 mg/kg, followed by tracheal intubation. Anesthesia was maintained using 1% halothane in oxygen, atracurium 0.4 mg/kg, and intermittent positive pressure ventilation. ECG, SpO₂, and blood pressure monitoring were maintained. Intraoperative analgesia was provided with intravenous fentanyl in dose of 50 microgram after delivery of baby.

The TOF–watch (Organon, Inc., Dublin, Ireland) device connected to patient, using the ulnar nerve for monitoring, the electrodes are best applied at the volar side of the wrist, the distal electrode was placed about 1 cm proximal to the point at which the proximal flexion crease of the wrist crosses the radial side of the tendon of carpiunlaris muscle.

The proximal electrode preferably was placed 2 to 5 cm proximal to the distal electrode. The piezoelectric ceramic wafer, an acceleration transducer was taped distal to the distal interphalangeal joint of the thumb, and the target arm immobilized with a splint in a position allowing free movement of the thumb.

When the surgical procedure was completed, anesthesiologist assessed the adequacy of neuromuscular reversal using standard clinical criteria like 5 seconds head lift, eye opening and tongue protruding in response to verbal commands, presence of partial efforts of breathing, and other skeletal movements . The anesthesia care providers decided that the patient was ready for giving the reversal of neuromuscular when more than three criteria occurred, at this time TOF ratios were measured using acceleromyography. Two consecutive TOF measurements (separated by 15 s) were obtained, and the average of the 2 values was recorded. If measurements differed by more than 10%, additional TOF measurements were obtained (up to 4 TOF values), and the closest 2 ratios were averaged. TOF measured by 2 ways, 1st: counting the twitches visually (principal of PNS), and 2nd: the device showing the TOF reading objectively (principal of AMG). The clinical criteria, clinical TOF, and device TOF were recorded in already

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prepared data collecting sheet. The data statistically analyzed and P- value less than the 0.05 considered being statistically significant.

RESULTS:

There were 100 female patients enrolled in this study who underwent caesarian section procedure, The mean age of patients was 30.5 ± 5.2 year and the range was(22-38), the mean weight was 73.8 ± 7.3 kg while the mean duration of surgery was 33.3 ± 12 minute.

Regarding the clinical subjective assessment, it had been found that 81 % of the patients had swallowing movement , 73 % protrude their tongue , 90% showed breathing effort and 85% developed moving of limb and lift their head for five second.

Regarding the subjective PNS TOF, it had been found that the anesthesiologists had noticed 3 thumb twitching in (32 %) of patients , three twitches and fade one in (18 %) of patients while four twitches had been noticed in the rest(50%) of the patients.

Regarding the objective TOF, the T4\T1 ratio was categorized into four categories, the reading in 30% of the patients was less than or equal

(30%), the second category (31-40%) were the reading in 31% of the patients, 19% of the patients were recorded a ratio within the third category (41-50%) and finally 20% of the patients were having a ratio more than 50%.

By comparisons among criteria of subjective and the monitoring watch readings of T4\T1 ratio, no statistical significant difference had been found, $P > 0.05$ in all comparisons (except that with the moving limb and lift the head) , there was inconsistency between criteria of subjective and the monitoring watch readings; majority number of cases with positive criteria of subjective still had low T4\T1 ratio , from other point of view there was no significant association between the presence of three of the criteria with the level of T4\T1 ratio, the moving limb or lift the head criterion had been significantly found consistent with the T4\T1 ratio level, it was more frequent with increasing T4\T1 ratio, $P.value = 0.002$, as shown in table (1), from other point of view, by comparison in mean T4\T1 ratio in between those patient who had moving their limb and lifting head the and those who were negative criterion it had been significantly different those with positive criterion had higher ratio than those with negative $P.value = 0.001$, table (2).

Table 1: Comparison of criteria of subjective with T4\T1 ratio.

Criteria of subjective	Monitoring watch reading of T4\T1 ratio				Total	P value
	$\leq 30\%$	31 – 40%	41 – 50%	$> 50\%$		
Swallowing movement	22	27	15	17	81	0.23 ns *
Protruding tongue	21	26	11	15	73	0.39 Ns
Breathing effort	27	25	19	19	90	0.13 Ns
Moving limb or head	16	19	20	30	85	0.002 significant

* ns (not significant)

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Table 2: Comparison of mean T4/T1 ratio among patients with positive and negative moving limb or head criterion.

		Moving limb or head		P.value
		Yes	NO	
Monitoring watch reading of T4/T1 ratio	Mean \pm SD	40.26 \pm 10.7	22.2 \pm 3.9	(0.001)Significant
	No. of patients	85	15	

The association and consistency of subjective criteria and visual PNS was presented by table (3), no significant differences had been found between the criteria of subjective and visual PNS, P < 0.05 in all comparisons.

Table 3: comparison of criteria of subjective with visual PNS.

Criteria of subjective	Visual PNS			Total	P value
	3 twitches	3 twitches and fade fourth	4 twitches		
Swallowing movement	26	17	38	81	0.25
Protruding tongue	21	15	38	74	0.29
Breathing effect	28	20	42	90	0.39
Moving limb or head	27	18	37	82	0.4

By close view to the table (4) a wide discrepancy between monitoring watch reading and the visual PNs observed by anesthesiologists, can be noticed.

Table 4: Comparison of visual PNs and T4/T1 ratio.

		Visual PNS			Total
		3 twitches	3 twitches and fade fourth	4 twitches	
Monitoring (AMM) T4/T1 ratio	\leq 30 %	4	8	18	30
	31 – 40%	10	10	11	31
	41 – 50%	10	0	9	19
	> 50%	8	0	12	20
Total		32	18	50	100

DISCUSSION:

In this study, the reversal had been given when more than three criteria occurred. About 85% of patients have lifted heads 5 seconds before reversed muscle relaxant and about 30 patients of them have TOF >50%. It has been argued that the clinical test is not a sensitive test of residual neuromuscular blockade, since both respiratory and expiratory force can be reduced in patients performing a 5 seconds sustained head lift. (18) However this argument is in contrast to the findings of pavlin et al (19) who suggests that the

ability to sustain head-lift for 5 seconds is associated with sufficient strength to protect against both airway and obstruction and used as a test of sufficient neuromuscular recovery and this agree with this study.

A TOF ratio of 0.7_0.8 is normally taken to reflect sufficient recovery of neuromuscular function (20), and 5 seconds sustained head lift is normally not seen at TOF ratio below 0.55-0.60. (18) Therefore, it was surprising; to find in this study so many patients with low TOF ratios were

able to sustain head lift for 5 seconds. Of 85 patients sustained lift- head 5 seconds, 55 patients had TOF <50%. It is noteworthy that the peripheral temperature in current study generally was low, and there was correlation between the peripheral temperature and TOF ratio. This finding is in accordance with peripheral cooling even at normal core temperature may cause a decrease in measured TOF ratio about 9% for each centigrade.⁽²¹⁾

Many studies and articles state that the subjective clinical criteria are not sufficiently sensitive to assess full recovery, and may associated with postoperative respiratory complications and they just accepted that the TOF ratio threshold allowing complete recovery is closer to 0.9 than 0.7 Debaene *et al.* examined the incidence of residual paralysis (RP) in more than 500 patients who received a single dose of intermediate-duration relaxant; of the 237 patients who had RP more than 60% of them had low degrees of RP with a TOF ratio between 0.7– 0.9. Similar results have been reported by others.⁽²²⁾ Eikermann *et al.*,⁽²³⁾ demonstrated that even slight degrees of RP (TOF ratio > 0.8) may have significant clinical consequences such as impaired inspiratory flow and upper airway obstruction. Therefore extubation at these slight degrees of RP may put the patient at risk. These findings have major consequences for the management, but in fact Eikermann reported, "Despite impaired upper airway function, no jaw thrust was needed, none of the volunteers reported dyspnea and oxygen saturation remained greater than 96% at all times.

Grayling M et al in their study concluded that, clinical tests such as head lift, tidal volume, or hand grip when used as triggers for the administration and antagonism of competitive NMBs have proved to be unreliable and 5 second head lift is the most frequently applied clinical test of residual paralysis used by clinicians⁽²⁴⁾.

In this study 32 patient had been reversed from muscle relaxation with 3 twitches only by peripheral nerve stimulation, while the 4th twitch but available data suggest and TOF ratio were detected by AMG, that is because tactile evaluations may be slightly (but not significantly) more sensitive in detecting residual neuromuscular block than visual assessments.

At a TOF ratio of 0.41 to 0.50, only 37% of inexpert anesthesiologists were able to detect fade visually, compared with 57% who detected fade manually⁽²⁵⁾ so this is the reason for recorded only 3 twitches while the patients

developed clinical criteria of muscle relaxant recovery.

So many studies show that clinicians are unable to reliably exclude residual neuromuscular blockade when using conventional peripheral nerve stimulators because fade is difficult to detect subjectively when TOF ratios are between 0.4 and 0.9.32, however TOF ratios > 0.4 can be measured accurately and displayed numerically using quantitative neuromuscular monitoring.⁽²⁶⁾

In 1985, Viby-Mogensen *et al.*⁽²⁷⁾ measured the ability of anesthesiologists to detect fade using TOF stimulation at varying levels of neuromuscular blockade. Inexpert anesthesiologists in tactile fade detection were able to feel fade only when TOF ratios were > 0.30, the outcomes were better in observers with extensive experience in neuromuscular monitoring, those observers were unable to detect fade 80% of the time when TOF ratios were between 0.51-0.70. Other investigators have confirmed that the majority of evaluators are unable to detect fade when TOF ratios exceed (0.4).^(26, 28, 29)

If the indicator of administering neostigmine is the twitches of TOF and not the clinical criteria, there is controversy about the number of twitches have to be detected to administer the reversal. It was initially recommended that antagonism of neuromuscular block with an anticholinesterase should not be attempted until two twitches of the train-of-four (TOF) twitch response are detectable, otherwise it will be ineffective.⁽¹⁵⁾

According to this statement, all the patients involved in this study were reliable to be given the reversal, whether the TOF measured by PNS or AMG. Another opinion states that the reversal must be injected only when sufficient spontaneous recovery is observed in order to attain a TOF ratio = 0.9 within a reasonable time, i.e., 10-15 min following neostigmine. In fact, it is recommended to wait until there are 4 visible twitches following TOF stimulation before administering neostigmine.^(16,17)

According to this statement, all the patients involved in this study were reliable to be given the reversal if the TOF results of AMG were depended, while according to the PNS the TOF result were in 32 out of 100 patients only 3rd twitch could be detected, and thus they were unreliable to be given the reversal.

The 4th twitch used as Indicator for giving of the neostigmine because it is stated that: "doses up to 0.07 mg/kg add little; in addition, the agent must be injected only when sufficient spontaneous

recovery is observed in order to attain a TOF ratio = 0.9 within a reasonable time, i.e., 10-15 min following neostigmine" ^(16,17). So if it is given before 4th twitch, more time required for full recovery

CONCLUSION:

The moving limbs and sustained lift head 5 seconds clinical criterion were correlated to TOF. Other criteria (protruding tongue, respiratory effort, and swallowing reflex) were not correlated to TOF. Objective AMG more sensitive to detect the fourth twitch than the subjective PNS.

Recommendations:

It is recommended to depend on objective TOF by AMG in the assessment of neuromuscular blockade.

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