Residual Neuromuscular Blockade: A Comparison of Double Burst Stimulation and Train-of-Four

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ABSTRACT:

Introduction:*Monitoring of neuromuscular blockade helps to detect the depth of neuromuscular blockade and adequacy of recovery of neuromuscular function following injection of an anticholinesterase drug.*

Methodology:*This study was conducted after getting institutional approval. One hundred and forty patients belonging to ASA-PS I & II were included in this study. Patients were monitored with three electrode electrocardiogram monitoring, pulse oximetry, nasopharyngeal temperature and non invasive blood pressure.*

Results:*Although the 'p' value between duration of anaesthesia and TOF and DBS equal is highly significant (p<0.001), the corresponding `r value is not very strong.*

Conclusion:*Absence of fade on DBS correlates better with clinical recovery of neuromuscular blockade, than absence of fade on TOF stimulation.*

Key words:*Neuromuscular, Monitoring, Double burst stimulation, train of four*

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-4994.2015.00029.3

INTRODUCTION

Neuromuscular monitoring is commonly used during the use of non-depolarizing muscle relaxants in anaesthesia. Monitoring of neuromuscular blockade helps to detect the depth of neuromuscular blockade and adequacy of recovery of neuromuscular function following injection of an anticholinesterase drug[1].

Neuromuscular monitoring is recommended in patients with altered pharmacokinetics and pharmaco-dynamics, prolonged surgeries, where infusion of non-depolarizing relaxant is used and where complete recovery of neuromuscular function is mandatory as in patients with severe pulmonary disease[2]

The train-of-four (TOF) stimulation is the most common mode of peripheral nerve stimulation used during general anaesthesia[3]. Recently, a new mode of peripheral nerve stimulation - Double Burst Stimulation (DBS) has been developed to detect any residual neuromuscular blockade and adequacy of reversal from neuromuscular blockade. It is claimed that DBS is more sensitive than TOF to detect residual neuromuscular blockade[4].

METHODOLOGY

This study was conducted after getting institutional approval. One hundred and forty patients belonging to ASA-PS I & II were included in this study. Patients of either sex between the age of 15 – 60 years, undergoing elective surgical procedures under general anesthesia with endotracheal intubation and controlled ventilation were studied. Surgeries of duration 60 – 180 minutes were included in the study. Patients whose trachea were to remain intubated, those in whom the neuro muscular blockade was not to be reversed at the end of surgery, whom and hypothermic patients and those with neuro muscular, liver and renal diseases were excluded from the study.

All patients were premedcated with oral diazepam (0.1 – 0.2 mg/kg) in the previous night and in the morning of surgery, pethidine (1mg/Kg) or morphine (0.1 mg/Kg) and promethazine (0.5 mg/Kg) intramuscularly 60 – 90 minutes before anesthesia.

Patients were monitored with three electrode electrocardiogram monitoring, pulse oximetry, nasopharyngeal temperature and non invasive blood pressure. Neuro muscular transmission was not monitored during anesthesia until following reversal of the neuromuscular blockade. Patients were included with thiopentone sodium intravenously, intubated under muscle relaxation with an appropriate sized cuffed endotracheal tube. General anesthesia was maintained with oxygen, nitrous oxide, halothane, and muscle relaxation provided throughout surgery with I.V pancuronium. Analgesia was provided with either I>V. morphine or I>V pethidine according to the concerned anesthesiologist discretion. The last dose of pancuronium was administered at 45 minute before reversal of neuro muscular blockade and the time when this was give noted. Towards the end of surgery all anesthetics were cut off. A peripheral nerve stimulator having both TOF and DBS mode was attached over the patients ulnar nerve at the wrist. The time of adminstartion of neostigmine and the dose of neostigmine were all judged by concerned anesthesiologist. Neuro muscular blockade was

reversed with neostignmine and atropine. The time at which neostigmine was administered noted.

Following neostigmine administration, TOF stimulation was given with 50mA every 30 seconds. The TOF was visually evaluated. At this moment the clinical recovery of the patient was evaluated by noting the patient's ability to open eyes, mouth, and grip the examiner's hand.

Co: No clinical sign present
C+: One sign present
C++: Two signs present
C+++: Three signs present

Whether the patient's trachea was extubated or not, was also noted.

$DBS_{3,3}$ was given only when there was absence of fade of TOF. If fade was present on DBS, the stimulation was given every 30 seconds, till there was no fade (DBS D2/D1=1). The time at which fade disappeared was noted. At this context the clinical status of the patient was again noted by evaluating the patient's ability to open eyes, mouth and grip the examiner's hand. The patient's trachea was extubated or not was also noted.

RESULTS

We studied a total number of 140 patients (n = 140). In all the patients TOF and DBS were compared. The different durations and clinical status when TOF and DBS were equal were also evaluated.

Table1: Demographic data

Age in years (mean)	40.3
Weight in Kgs (mean)	50.5

The different observations, standard deviations (SD) and standard error of mean (SEM) are given in the table below Table2:

Table: 2

Observation (Duration)	Mean (min)	Standard deviation (min)	Standard error of mean (min)
Anaesthesia(DA)	146.14	28.11	2.38
Last dose of pancuronium to neostigmine (DLPN)	54.74	6.83	0.58
Neostigmine to TOF equal (DTOF)	4.42	2.73	0.23
TOF equal to DBS equal (DoBs)	4.72	2.89	0.24
Neostigmine to DBS equal (DNDBS)	9.15	4.75	0.40

All the patients had fade on DBS when the TOF ratio was 1. The time from TOF equal to DBS equal varied from 1 to 15 minutes with a mean of 4.72 minutes.
The relationship between TOF and DBS equal and trachea extubated are shown in table 3.

Table 3

Mode	Number of patients extubated	Percentage
TOF Equal	12	8.5
DBS Equal	95	67.85

As can be seen from the table the percentage of patientsextubated when DBS was equal was very high when compared to when only TOF was equal (67.85% vs. 8.5%).
The relationship between clinical sign of recovery, TOF and DBS equal andextubation are shown in the Table 4

Table 4

Clinical status	TOF Equal DBS fade				TOF and DBS Equal			
	No of patients	ok	No of Patients extubated	%	No of patients	%	No of Patients extubated	%
Co	51	36.4	0	0	24	17.1	1	4.16
C+	6	4.3	0	0	4	2.86	0	0
C++	7	5	0	0	6	4.3	2	33.33
C+++	76	54.3	12	15.5	106	75.7	92	86.8

It was also seen that 36.4% of patients who had TOF equal had no clinical sign of recovery whereas only 17% of patients who had DBS equal had no sign of clinical recovery. Only one out of the 24 patients

who had no clinical sign of recovery when DBS was equal was extubated because the anaesthesiologists were also relying on other signs like tidal volume, coughing, etc, for extubation. Another important observation of this study is that only 76 patients out of 140 had all the 3 clinical signs present when TOF was equal whereas 106 out of 140 patients had all the 3 clinical signs present when DBS was equal. Again out of the 76 patients who had all the 3 clinical signs and TOF equal, only 12 were extubatedwhereas 95 patients out of 106 who had all the three clinical signs present and DBS equal were extubated.

Correlation analysis was done between duration of anaesthesia and time when TOF was equal, and duration of anaesthesia and time when DBS was equal. It was found that there was a linear correlation between the duration of anaesthesia and recovery from neuromuscular blockade as revealed by TOF and DBS monitoring (Table 5).

Table5

Correlation between duration of anesthesia and recovery from neuromuscular		
Mode	**`r' value**	**`p' value**
TOF	0.50	<0.001 (VHS*)
DBS	0.60	<0.001 (VHS*)

VHS = Very Highly Significant

No correlation was found between the duration from the last dose of pancuronium and the recovery after reversal with intravenous neostigmine (Table 6).

Table 6

Correlation between the duration from last dose of pancuronium and the		
Mode	**`r' value**	**`p' value**
TOF	0.065	>0.05 (NS*)
DBS	0.12	>0.05 (NS*)

NS = Not Significant

The linear correlation between the duration of anaesthesia and recovery as revealed by TOF stimulation has been clearly depicted in the. Sixty-four values were above the regression line, 4 values on the line and 72 below the line with a value of 0.50.

The linear correlation between the duration of anaesthesia and time of recovery on DBS stimulation has been shown. Sixty-five values were above the line and 75 below the line with a `r value of 0.60. Although the 'p' value between duration of anaesthesia and TOF and DBS equal is highly significant ($p<0.001$), the corresponding `r value is not very strong.

DISCUSSION

The recovery from neuromuscular blockade following reversal with intravenous neostigmine is usually evaluated clinically by the patients ability to open eyes and mouth, protrude tongue, lift the head and legs and grip the examiner's hand on verbal command. Movement of the reservoir bag and measurement of tidal volume have all been used to access the adequacy of recovery from neuromuscular blockade. From these we presume that the patient's neuromuscular function has returned to normal. But this clinical assessment may not always be reliable and in many patients clinical signs may be absent even when the recovery from the neuromuscular blockade is complete. In other situations the patient may have clinically recovered but may have subclinical neuromuscular blockade. To overcome these drawbacks monitoring of neuromuscular function with a peripheral nerve stimulator is always recommended. Monitoring the neuromuscular blockade is especially recommended in situations where the patient has altered pharmacokinetics, altered pharmacodynamics, in cases where continuous infusion of nondepolarizing relaxant is used and when the patient has other organ dysfunction like severe pulmonary disease where complete documented recovery from neuromuscular blockade is necessary. Train-of-four was the mode of peripheral nerve stimulation widely used so far to evaluate the adequacy of recovery. A TOF ratio of 0.7 or more was supposed to mean an almost complete recovery. A TOF ratio of 1 was supposed to denote complete recovery from neuromuscular blockade. Due to the difficulty in clinically (manually or visually)evaluating the fade on TOF, DBS was introduced. In our study of 140 patients we found that all the patients had fade on DBS when TOF was equal (ratio of 1). Several authors have convincingly demonstrated that even when the TOF ratio is 1, DBS showed fade[5,6,7]. They concluded that DBS is more reliable than TOF stimulation in detecting residual neuromuscular blockade. In our study, the duration from TOF equal (ratio 1) to DBS equal (no fade) ranged from 1 to 15 min, with a mean of 4.72 min. This fade on DBS when there is absence of fade on TOF may be clinically significant, especially in patients with severe pulmonary disease or other severe coexisting systemic illness. Clinical significance of the residual blockade is revealed in this study by the fact that the concerned anaesthesiologists who were extubating the trachea on clinical judgement alone could extubate only 12 out of 140 (8.5%) patients when TOF was equal as against 95 (67.85%) when DBS was equal. As the concerned anaesthesiologists were not aware of the status of the neuromuscular recovery as revealed by the TOF and DBS, there were 45 patients who were not extubated even when DBS was equal. This is because the concerned anaesthesiologistsextubated the patients' trachea following assessment of clinical signs of recovery. These signs may have been absent because of the patients being drowsy and sedated due to excessive opioids, halothane or other sedatives.

Also, most of these patients not extubated when there was no fade on DBS, were extubated within

a couple of minutes of DBS becoming equal. We of course did not note the time between absence of fade on DBS and extubation.

As seen in table 4, more number of patients had all the clinical signs of recovery when DBS was equal than when TOF was equal (106 Vs 76). Also when three clinical sign were present and there was absence of fade to TOF and DBS, more number of tracheas were extubated on the DBS equal group than the TOF equal group (96/106) Vs 12/76).

From this it is clear that DBS is more reliable than TOF in assessing complete recovery from neuromuscular blockade. A study by Uede et a1[7] comparing the efficacy of TOF and DBS with clinical signs to detect the residual neuromuscular blockade also revealed that absence of fade on DBS correlated with clinical signs more than the absence of fade in TOF situation.

Another important finding is the relation between the duration of anaesthesia and time required for the complete recovery of neuromuscular function after giving intravenous neostigmine. There is a linear correlation between duration of anaesthesia and absence of fade in TOF and DBS after intravenous neostigmine. This study showed that 25% recovery from neuromuscular blockade was dependent on duration of anaesthesia when TOF was used as a criteria for recovery where as 36% recovery from neuromuscular blockade was dependent on duration of anaesthesia when DBS was used as a criteria for recovery from neuromuscular blockade. The greater the duration of anaesthesia, the greater is the total dose of relaxant used, the greater the blockade which has to be reversed.

CONCLUSION

Duration of anaesthesia has definite correlation with reversal of neuromuscular blockade; the more the duration of anaesthesia, the greater the residual block following reversal with I.V. neostigmine. DBS is more helpful than TOF in detecting residual neuromuscular blockade

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