Original Article

www.ijrhs.com
ISSN (o):2321–7251

Evaluation of post – operative residual curarization in neurosurgical patients with the use of a neuromuscular monitor Train –Of- Four Guard

Sanesh V. Tuteja [1], Lalita V. Tuteja [2]

1- Senior Resident, Department of Orthopaedics, Dr. DY Patil Medical College and Hospital, Nerul, Navi Mumbai.
2- Professor, Department of Anaesthesia, MGM Medical College and Hospital, Kalamboli, Navi Mumbai

Submission Date: 29-05-2014, Acceptance Date: 12-06-2014, Publication Date: 31-07-2014

How to cite this article:

Vancouver/ICMJE Style

Tuteja SV, Tuteja LV. Evaluation of post – operative residual curarization in neurosurgical patients with the use of a neuromuscular monitor train – Of four guard. Int J Res Health Sci [Internet]. 2014 Jul 31;2(3):776-82. Available from http://www.ijrhs.com/issues.php?val=Volume2&iss=Issue3

Harvard style

Tuteja, S.V., Tuteja, L.V. Evaluation of post – operative residual curarization in neurosurgical patients with the use of a neuromuscular monitor train – Of four guard. *Int J Res Health Sci*. [Online] 2(3). p.776-82 Available from: http://www.ijrhs.com/issues.php?val=Volume2&iss=Issue3

Corresponding Author:
Dr. Sanesh V. Tuteja, DNB(Ortho), MS (Ortho), D.Orth, Senior Resident, Department of Orthopaedics, Dr. DY Patil Medical College and Hospital, Nerul, Navi Mumbai. Email: stuteja@hotmail.com

Abstract:

Rationale: Traditionally, reversal of neuromuscular blocking agent is monitored using clinical criteria that is subjective and vary depending upon the anaesthetist's judgment. There is a need for objective methods of monitoring neuromuscular block. Neuromuscular monitoring permits administration of neuromuscular blockers to obtain optimum muscle relaxation desirable for surgical procedures. **Design:** The study was carried out in tertiary hospital involving 50 patients undergoing elective neurosurgical procedures, receiving atracurium by syringe infusions for maintenance of General Anaesthesia. The patients were randomized into two groups of 25 each, who were be transferred to the recovery room on the basis of clinical criteria and on the basis of Train –of – four (TOF) Guard monitoring at extubation where the TOF ratio was >0.80 as recommended by Eriksson [5] in the year 1988 and Viby Mogensen [6] in the year 1989. **Statistical analysis:** The data was analyzed using the unpaired Students t- test as the Test for Significance and Standard Error of Difference between Two Proportions for comparing the number of patients with post- operative residual curarization in the two study groups. Significance was asserted to 'p' less than 0.05. **Results:** The TOF ratio in the recovery room was significantly lower in Group transferred on the basis of Clinical Monitoring (Group A) **[Mean 0.791 ± 0.144]** compared to Group transferred on the basis TOF Monitoring (GroupB) **[Mean 0.877 ± 0.051]** indicating a high incidence of PORC in Group A. **Conclusion:** Monitoring of TOF ratio perioperatively and adequate antagonization of non-depolarising neuromuscular blockade can prevent PORC and its complications.

Key words: Post Operative Residual Curarization (PORC), Train –Of- Four (TOF) Guard Monitoring, Atracurium

Introduction

Post – operative residual curarization (PORC) is an important cause of postoperative hypoxaemia in the recovery room. Partial paralysis of the respiratory muscles and functional impairment of the muscles of the pharynx and upper oesophagus

can predispose the patients to aspiration and postoperative pulmonary complications [1,2]. Early emergence from anaesthesia after surgery is indicated in neurosurgical patients [3] to permit immediate assessment of the results of surgery, to provide a baseline for continuing postoperative neurological follow up to provide an earlier re-intervention if necessary. The main disadvantage of early awakening is the increased risk of hypoxemia and hypercarbia [3]. Hence monitoring detection and management of PORC becomes very important.

Traditionally, this reversal is monitored in day- to- day anaesthesia using clinical criteria which being subjective, vary depending upon the anaesthetist and his/ her clinical judgment; hence the need for a monitor which will give constant readings is indicated so that it can be used in addition to the clinical criteria. Objective methods of monitoring such as mechanomyography, electromyography or acceleromyography are used, as mentioned by J. Viby Morgensen in the year 2000.

The use of intermediate duration neuromuscular blocking drugs in modern anaesthesia practice has not eliminated the problem of PORC as evidenced by E Tobin and colleagues [4] in which 65% of patients had a Train- of- four (TOF) ratio of ≤ 0.70 at extubation.

This study evaluates a neuromuscular monitor TOF GUARD NMT (ORGANON TEKNIKANN) was used to judge the adequacy of recovery and as recommended by Eriksson [5] and Viby Mogensen [6], a TOF ratio of ≥0.80 was used to study the incidence of the residual neuromuscular blockade while comparing clinical criteria, following use of atracurium infusions for neurosurgical procedures.

Material and Methods

The study was carried out in a tertiary institution with well established neurosurgical and anesthesia set up. The Institutional Ethics committee approval and written informed consent was obtained
This is a randomized prospective study involving 50 patients undergoing elective neurosurgical procedures, receiving atracurium by syringe infusions for maintenance of general anaesthesia.

Inclusion Criteria

1. Males and females above the age of 18 years, undergoing elective neurosurgical procedures.
2. Patients expected to resume spontaneous breathing after surgery.

Exclusion criteria

1. Age under 18 years.
2. Patients suffering from major hepatic, renal, respiratory and cardiovascular disorders.
3. Patients suffering from diseases of neuromuscular transmission like myasthenia gravis.
4. Patients taking drugs altering neuromuscular transmission like magnesium suphate, calcium channel blockers, aminoglycosides, furosemide, phenytoin etc.
5. Patients expected to require ventilator support post operatively.

Study Design:

The patients were divided into two groups. Group A consist of 25 patients who were transferred to the recovery room on the basis of clinical criteria. Group B consist of 25 patients who were transferred to the recovery room on the basis of TOF Guard monitoring at extubation where the TOF ratio was >0.80 as recommended by Eriksson [5] in the year 1988 and Viby Mogensen [6] in the year 1989.

Technique of anaesthesia:

All the patients received anticholinergic premedication with atropine. Analgesia was achieved with fentanyl. Maintenance of anaesthesia was carried out with nitrous oxide and oxygen with propofol syringe infusion at the rate of 4-6 mg/kg/hr and muscle relaxation was maintained with a continuous infusion of atracurium. The decision to administer additional boluses of relaxant, the timing of stopping of infusion of relaxant, administration of neostigmine and timing of extubation were all performed solely at the discretion of the anaesthesiologist caring for the patient, according to the established clinical criteria.

All patients were reversed with neostigmine 0.05mg/kg and Glycopyrolate 0.2 mg and extubated prior to shifting to the recovery room.

In Group A, the patients were transferred to the recovery room on the basis of clinical criteria whereas in Group B the patients were transferred to the recovery room on the basis of TOF Guard monitoring at extubation where the TOF ratio was >0.80 as recommended by Eriksson [5] in the year 1988 and Viby Mogensen [6] in the year 1989.

On arrival to the recovery room, an assessment of residual neuromuscular blockade, was made by accleromyography, using TOF GUARD INMT (Manufacturer: ORGANON TEKIKANN NV, Model: Ty TOF Guard, Year of Manufacture: 1997, Made in Belgium) and clinically. Care was taken to

obtain the readings from the normal limb if the opposite limb was paretic due to the disease process or as a result of surgery.

The hand and forearm of the patient was mobilized in a splint. The temperature of the recording site as detected by the TOF GUARD was recorded. The ulnar nerve was stimulated supramaximally with train – of – four square pulses of 0.2 milliseconds duration, delivered at a frequency of 2Hz for two seconds, repeated every 15 seconds. The force of contraction of adductor pollicis was measured accleromyographically and the TOF ratio is measured using the formula:-

TOF ratio = force of fourth twitch / force of first twitch.

Expressed as a percentage.

TOF stimuli were applied until a stable assessment could be made, which usually took less than two minutes. If the TOF ratio was less than 0.80, then repeated TOF stimuli were applied every minute until the ratio was more than 0.80, which indicates adequate recovery of neuromuscular function and monitoring was terminated. If the TOF ratios were less than 0.80 even after one hour of monitoring in the recovery room, additional dosage of neostigmine was given to completely antagonize the block and the patient was monitored till the TOF ratio was more than 0.80.

Clinical assessment of recovery was made in all patients who were sufficiently awake and co-operative. The patient's responses were recorded as normal (+) or weak (-). The clinical tests that suggest adequate neuromuscular recovery are:-

1. Sustained head lift for 5 seconds
2. Sustained leg lift for 5 seconds
3. Sustained hand – grip for 5 seconds

Patients who were able to perform one of these tests were considered to have achieved adequate clinical recovery (ARC `+`) and those who were not able to perform even one of these tests were considered not to have achieved adequate clinical recovery (ARC `-`)

The incidence of PORC in each of the groups was assessed evident as a TOF ratio of less than 0.80 in the recovery room. Also, the following variable were noted for stastical analysis:

- Duration of anaesthesia (interval between induction to stopping of infusion of the relaxant) (min)
- Interval between stopping the infusion and administration of neostigmine (min)
- Interval between extubation and first TOF ratio measurement in the recovery room (min)
- First stable TOF in the recovery room.

Statistical analysis: The data was analyzed using Standard Error of Difference between Two Means using the unpaired Students t- test as the Test for Significance and Standard Error of Difference between Two Proportions for comparing the number of patients with post- operative residual curarization in the two study groups. Significance is asserted to 'p' less than 0.05.

Results:

Although 28% **(p0.0043)** of patients in Group A showed PORC on TOF Guard monitoring, none of these patients showed any signs of inadequate clinical recovery as judged by clinical criteria.

The patients were all administered oxygen by mask and the monitoring was continued by the attending anaesthesiologist both by clinical criteria and TOF Guard monitoring for any evidence of PORC in the post operative period. None of the patients were administered supplementary doses of neostigmine and none of them required ventilatory support. There was no correlation between the duration of anaesthesia and the TOF ratio in the recovery room. Also, there was no correlation between the duration of surgery and the TOF ratio in the recovery room.

There was no significant correlation between the Interval between stopping of infusion of relaxant & neostigmine administration and TOF ratio in the recovery room.

Discussion

The use of short acting Neuromuscular blockers and perioperative monitoring has been found to be helpful in reducing the incidence of PORC [1,2]. This study describes the use and advantage of neuromuscular junction monitoring in clinical settings using atracurium infusions for maintenance of anaesthesia in neurosurgical patients.

TRAIN- OF- FOUR STIMULATION (TOF)

Four supramaximal stimuli are given every 0.5 seconds (4 Hz). When used continuously each set of stimuli normally repeated every 10th of 12th second. Each stimulus causes the muscle to contract and fade in the response provides the basis for evaluation. That is dividing the amplitude of the 4th response by the amplitude of the 1st response

provides the TOF ratio. With a partial non-depolarizing block TOF ratio decreases. With a partial depolarizing block there is no fade. If fade is present, it indicates development of Phase II block.

Advantages

1. Degree of block directly can be read from the TOF response even when preoperative value is lacking.
2. Less Painful
3. Generally does not affect the degree of neuromuscular block.

Acceleromyography

Based on Newton's 2nd law, "Force equals mass times acceleration", if mass is constant acceleration is directly proportional to force.

It uses piezoelectric ceramic wafers with electrodes on both the sides. Exposure of the electrode to the force generates an electrical voltage proportional to acceleration of thumb in response to nerve stimulation.

The TOF Guard used in the present study works on this principle and is a compact, microprocessor controlled, solid state battery powered system. It can deliver TOF measurements, Post Tetanic Count and Train-of-Four ratio and Double Burst Stimulation. It can be programmed for use in intensive Care Unit, to monitor long term relaxation and delivering of TOF every 5 minutes. The data can be stored and played back from a memory card.

The present study is undertaken to evaluate the usefulness of tactile assessment of the response of adductor pollicis to supramaximal train –of- four stimulation of the ulnar nerve at wrist at the end of anaesthesia, at extubation and recovery room to prevent the occurrence of residual curarization.

Perioperative monitoring of neuromuscular function using a peripheral nerve stimulator was not used in this study since one of the aim of the study was to determine whether clinically used tests to assess recovery of neuromuscular function can be applied to neurosurgical patients and to mimic routine clinical practice of anaesthesia as far as possible. Many studies have shown that perioperative monitoring of neuromuscular function by a peripheral nerve reduces the incidence but does not eliminate the problem of PORC [7,8]. It has been shown by Mortensen CR et al [9] that perioperative monitoring of neuromuscular transmission by acceleromyography can prevent residual neuromuscular blockade.

Neurosurgical patients are particularly susceptible to residual curarization mainly because of the difficulty in detecting clinical signs of recovery of neuromuscular function and because antagonization of residual paralysis by anticholinesterases is associated with CNS arousal [10]. The difficulty in detecting signs of adequate clinical recovery may be due to pain, inability to lift the head due to immobilization of neck following cervical spine surgeries, altered level of consciousness and poor Glasgow coma score due to raised intra-cranial pressure, cerebral edema, intra-operative surgical complications and surgeries around the brainstem. Posterior fossa surgeries may be associated with injury or oedema of the vital centres in the brain stem due to extensive brain stem manipulations and difficult tumour resections [11,12], such patients may develop brainstem compression, ischaemia or haematoma and are difficult to wean from anaesthesia. Surgery involving cervical spine may cause oedema of the cord leading to poor attempts at respiration due to involvement of phrenic nerve. These factors, which interfere with assessment of recovery of neuromuscular blockade can be causes of PORC in neurosurgical patients especially when clinical criteria are used for reversal of neuromuscular block.

In our study in the group of patients (Group B) where TOF monitoring was done at extubation, the mean TOF ratio was 0.887 (± 0.051) and the incidence of PORC was 0% when assessed in the recovery room.

Neurosurgical procedures require higher dosage of relaxants and a deeper plane of anaesthesia, which can lead to a high risk of PORC, especially when clinical criteria are being used for reversal of neuromuscular block.

C. Mc Caul and colleagues [4], studied the incidence of PORC following atracurium for ambulatory surgical procedures, and they measured the postoperative first TOF ratio immediately after extubation. This has the advantage that, it will pick up more number of patients with residual blockade, who otherwise would have recovered from the effect of atracurium by the time they were shifted to the recovery room. In this study, the incidence of PORC following atracurium was 65% considering a TOF ratio of more that 0.70 at extubation, to represent adequate recovery.

In the present study, the incidence of PORC, defined as the first stable TOF ratio in the recovery room of less than 0.80, in neurosurgical procedures

following the use of atracurium infusions for muscle relaxation was 28%. This could be explained on the basis that the interval between extubation and TOF ratio measurement (mins) of Group A was 11.48(±1.63) and Group B was 10.96 (±1.71), an average of 11.22 in both the groups. This time interval probably gave more time for recovery of the neuromuscular block and therefore lower incidence of 28% of PORC in our study.

In contrast to the above study, our study in the group of patients (Group B) where TOF monitoring was done at extubation where the mean TOF ratio measured was 0.887 (± 0.051), the incidence of PORC was 0% in the recovery room. These results could be due to monitoring at a TOF ratio of >0.8 at extubation as compared to 0.70 in the above mentioned study.

Brull, Sorin J, in 1997 conducted a study and concluded that where neuromuscular function is not monitored routinely, either intra- or postoperatively, the incidence of residual paralysis in postanesthesia care unit (PACU) remains alarmingly high [13,14]. even short-acting agents such as mivacurium (4%) [15]. Although the use of nerve stimulators has been shown to significantly decrease the incidence of postoperative residual weakness, this complication still occurs [16,17].

In a recently conducted study by Hayes A H and colleagues [18] involving 150 patients undergoing ambulatory surgical procedures, the incidence of PORC, following the use of vecuronium was 64%, following atracurium it was 52% and following rocuronium, 39%. They considered a first stable TOF ratio of 0.80 to represent adequate recovery. The authors attributed such a high incidence of PORC to the fact that a TOF ratio of more than or equal to 0.80 was considered to represent adequate recovery and to a relatively more number of elderly patients in the study. In this study, 68% of the patients were reversed and 41% of patients were monitored with peripheral nerve stimulator. Of the 68% of patients reversed, 49% of them showed evidence of PORC. The incidence of PORC in those not reversed was 60%. Of the 41% of patients who were monitored with PNS, 44% of them showed signs of PORC and the incidence of PORC in those not monitored was 57%. There was no significant difference between the incidence of PORC whether the patients were reversed or not or whether intraoperative monitoring with PNS was used or not.

In contrast to the above-mentioned study, our study reports a much lower incidence of 28% of PORC with atracurium infusions. In the present study, it was observed that :-

1. The two groups were similar with respect to age, weight and gender.
2. Although 28% of patients in Group A showed PORC, none of the patients had inadequate clinical recovery on clinical criteria so, there was no need of supplementary doses of neostigmine in any of the two groups. The total dose of neostigmine required for reversal was same in the two groups. Also, the patients with TOF < 0.80 did not require extra neostigmine. But they were monitored by the attending anaesthesialogist.
3. TOF Guard monitoring offered advantages in the neurosurgical patients where maintaining a dense neuromuscular blockade till the end of the surgery becomes mandatory.
4. Neuromuscular monitoring becomes helpful in neurosurgical patients to exclude Residual neuromuscular blockade as one of the cause of delayed awakening.

If one accepts the premise that even a single case of severe undetected respiratory depression and hypoxia especially in the neurosurgical patients in the Post operative Intensive care unit resulting in permanent adverse effect is unacceptable, this problem can be tackled by well trained personal of PACU. Complete reversal of neuromuscular blockade drugs using TOF monitoring is the best prevention. Thus the use of TOF monitoring at extubation was of value and it becomes mandatory to prevent PORC by the use of perioperative monitoring as compared to the clinical criteria in the neurosurgical patients.

PORC is a risk factor for the development of major complications and mortality in the postoperative period. Failure to adequately antagonize medium-duration non-depolarising neuromuscular block is therefore not an acceptable practice in the days of evidence-based medicine.

There is also a need for development of greater awareness regarding the problems of PORC, especially in neurosurgical patients. Competent anaesthesiologist should be available in the recovery room, who can monitor and manage PORC. But the best way to avoid PORC and its complications is by its prevention that can be done by adequate antagonization of nondepolarising neuromuscular

blockade and monitoring of train-of-four ratio perioperatively can lead to prevention of PORC.

Conclusion and Suggestions

1. Neuromuscular monitoring by objective methods is of great value in neurosurgical patients in reducing the incidence of PORC.
2. Perioperative use of neuromuscular monitoring gives the advantage of providing ideal surgical conditions with the added benefit of early emergence from anaesthesia.
3. Post- operative monitoring is a very essential aspect of post operative care to detect and treat early PORC, reducing the incidence of mortality and morbidity.

Source of Funding: ICMR funding Short term Research Studentship

Conflict of Interest: nil

Table No1:

Parameter	Group A		Group B	
	Mean	*SD*	Mean	SD
Age*	39.88	12.36	37.72	15.37
Weight*	58.36	9.58	58.24	11.07
Mean duration of anaesthesia(mins)*	212.20	99.88	234.60	111.92
Mean duration of surgery*	145.40	87.88	162.60	100.43
Interval between stoppage of infusion of relaxant and neostigmine administration (mins)*	17.32	6.45	21	8.53
Interval between extubation and TOF measurement (mins)*	11.48	1.63	10.96	1.71
Total dose of atracurium (mgs)*	107.60	48.65	98.42	38.26
Total dose of neostigmine (mgs)*	2.56	0.30	2.72	0.32
TOF Ratio[#] (p-0.0072)	0.79	0.14	0.87	0.05

#- Statistically significant

***- Statistically not significant**

Acknowledgement

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors/editors/publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

References

1. H Berg, J Viby-mogensen, Roed Mortensen CR, Engbaek J, Skovggard LT: Residual neuromuscular block is a risk factor for postoperative pulmonary complications. Acta Anaesthesiol Scand; 1997; 41: 1095-1103

2. Ali H, Utting, Gray C: Quautitative assessment of residual anti-depolarizing block. Part II. Br J Anaesth, 1971; 43: 478-485.

3. Thomas, K B. Curare: It history and usage. London: Pitman Medical publishing co; 1964.

4. C. McCaul, É. Tobin, J. F. Boylan and A. J. McShane: Atracurium is associated with postoperative residual curarization British Journal of Anaesthesia, 2002; 89; 766-769.

5. Viby Mogensen J, Jensen E; Measurement of acceleration: A new method of monitoring neuromuscular function. Acta Anaesthesiol Scand, 1988; 32; 45.

6. J Engbaek, D Ostergaard and J Viby-Mogensen: Double burst stimulation; A new pattern of nerve stimulation to identify residual neuromuscular blockade: British Journal of Anaesthesia 1989: 62: 274-278.

7. Pederson T, J Viby Mogensen, Bang U, Olsen NV, Jensen E, Engbaek J: Does perioperative tactile evaluation of Train of four response influence the frequency of residual neuromuscular blockade. Anesthesiology 1990; 73; 835-839.

8. R Martin, I Bourdna, S Theriault, JP Tetrault, M Pilote RN: Neuromuscular monitoring: Does it make a difference? Can J Anaesth 1996; 46, 6; 585-588.

9. Mortensen CR, Berg H, el-Mahdy A, Viby-Mogensen J: Perioperative monitoring of neuromuscular transmission by acceleromyography prevents residual neuromuscular block following pancuronium. Acta Anaesthesiologica Sandinavia 1995; 39:797.

10. Christie T, Churchill - Davidson H: The St Thomas Hospital nerve stimulator in the diagnosis of prolonged apnoea. Lancet; l; 1958; 76.

11. Fink B: A method of monitoring muscle relaxation by integrated abdominal electromyogram. Anesthesiology 1960; 21: 178-185.

12. Buckett W, Hewitt C, Savage DS: Pancuronium bromide and other steroidal neuromuscular blocking agents containing acetylcholine fragments. J. Med chemisty 1973; 16: 1116-1124.

13. David R Bevan, Charles E smith, Donati F: Postoperative neuromuscular blockade: Comparision between Atracurium, Vecuronium, and pancuronium. Anaesthesiology 1988; 69: 272-276.

14. Brull SJ, Ehrenwerth J, Connelly NR, Silverman DG: Assessment of residual curarization using low-current stimulation. Can J Anaesth 1991; 38:164-8.

15. Bevan DR, Kahwaji R, Ansermino JM, Reimer E, Smith MF, O'Connor GAR, Bevan JC: Residual block after mivacurium with or without edrophonium reversal in adults and children. Anesthesiology 1996; 84:362-7.

16. Shorten GD, Merk H, Sieber T: Perioperative train-of-four monitoring and residual curarization. Can J Anaesth 1995; 42:711-5.

17. Mortensen CR, Berg H, El-Mahdy A, Viby-Mogensen J: Perioperative monitoring of neuromuscular transmission using acceleromyography prevents residual neuromuscular block following pancuronium. Acta Anaesthesiol Scand 1995; 39:797-801.

18. Hayes A H, Mirakhur R K, Breslin D S, Reid J E, McCourt K C: Postoperative residual block after intermediate acting neuromuscular blocking drugs. Anaesthesia 2000; 56: 321-318.

19. Christie T H, churchill-Davidson H C: The St. Thomas nerve stimulator in the diagnosis of prolonged apnoea. Lancet 1: 776, 1958.

20. J. Viby Mogensen, Jorgensen BC, Ording H. Residual curarization in the recovery room. Anesthesiology; 1979; 40; 539-541.

21. C Lennmarken, J B Lofstrom: Partial curarization in the postoperative period. Acta Anaesthesiol scand 1984; 28: 260-262.

22. B N Andersen, J V Madsen, BA Schurizek and B Juhl: Residual curarization: a comparative study of atracurium and pancuronium. Acta Anaesthesiol scand 1988; 32: 79-81.

23. W J Fawcett, A Dash, Francis, J B Liban and J N Cashman: Recovery from neuromuscular blockade: residual curarization following atracurium or vecuronium bolus dosing or infusions. Acta Anaesthesiol scand 1995; 39: 288-293.

24. J Viby-mogensen: Postoperative residual curarization and evidence- based anaesthesia (editorial 1). British journal of anaesthesia 2000; 84:301.

25. Kopman, Aaron F. MD; Yee, Pamela S. BA; Neuman, George G: Relationship of the Train of four fade ratio to clinical signs and symptoms of residual paralysis in Awake volunteers. Anesthesiology 1997; 86: 765-771.

26. Denck NE, Ueda N, Olsen NV, Engback J, Jensen E, Skovgaard LT, Viby-Mogensen J: Manual evalution of residual curarization using DBS;a comparision with train of four. Anesthesiology 1989; 70; 578-581.