

Original Article**Postoperative residual block in postanesthesia care unit more than two hours after the administration of a single intubating dose of atracurium\***

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**Abstract**

**BACKGROUND:** Residual neuromuscular blockade continues to be a clinical problem after surgical procedures. The purpose of this study was to determine the incidence of residual paralysis in the postanesthesia care unit (PACU) after a single intubating dose of twice of the 95% estimated dose (ED95) of a nondepolarizing muscle relaxant with an intermediate duration of action.

**METHODS:** Two hundred and sixteen patients scheduled for elective surgery under general anaesthesia requiring tracheal intubation were included in the study. They received a single intubating dose of intravenous atracurium (0.5 mg/kg) to facilitate tracheal intubation. At the end of surgery, if train of four (TOF)-ratio was  $\leq 0.9$ , neostigmine 40  $\mu\text{g}/\text{kg}$  intravenously was given. If TOF-ratio was  $\geq 0.9$ , no neostigmine was given. Also, in awake patients with TOF  $> 0.9$ , residual neuromuscular paralysis was evaluated by using clinical tests such as head lift test and tongue depressor test.

**RESULTS:** TOF was less than 0.9 in 48 (22.2%) patients while after 120 minutes, no patients had TOF less than 0.9. Of 33 patients whose operation lasted less than 120 minutes, 4 patients had TOF less than 0.9 at the end of surgery. There was no case of hypoventilation or hypoxia at PACU. The incidence of negative value in clinical tests was high.

**CONCLUSIONS:** Our study gave the impression that more than two hours between the administration of a single intubating dose of an intermediate-acting nondepolarizing muscle relaxant (atracurium) and arrival to the PACU can probably guarantee the lack of a residual paralysis.

**KEYWORDS:** Neuromuscular Blockade, Atracurium, Neostigmine, Neuromuscular Nondepolarizing Agents.

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The clinical significance of the residual neuromuscular blockade in the postanesthesia care unit (PACU) has been identified since about 31 years ago.<sup>1</sup> Throughout the past 15 years, many publications have substantiated that the frequency of partial paralysis correlated with the duration of action of the relaxant agents. The longer the duration of action, the higher the proportion of residual paralysis.<sup>2,3</sup>

In all these researches, residual neuromuscular blockade was described as a train-of-four (TOF) ratio at the adductor pollicis of less than 0.7 or 0.75. This level of recovery was regarded as acceptable level because it was noticed to be the threshold above which volunteers given *d*-tubocurarine were observed to have normal vital capacity and inspiratory force.<sup>4</sup>

In 1996, a TOF ratio of 0.8 was suggested being the cutoff between residual paralysis and

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normal neuromuscular function<sup>5</sup> and was used in two previous investigations.<sup>6,7</sup> This threshold was increased to 0.9 consistent with the latest studies.<sup>8</sup>

For instance, pharyngeal function did not restore to normal after vecuronium administration until an adductor pollicis TOF ratio more than 0.9 was accomplished.<sup>9</sup> When employing this new TOF ratio value as threshold of residual paralysis, the frequency of residual paralysis in the PACU would undoubtedly be more than that observed in the investigations explained before.<sup>1,2</sup>

It is imperative to notice that, in all these investigations, patients received muscle relaxant to facilitate tracheal intubation and also to maintain a satisfactory level of paralysis in accordance with surgical need. When the surgical procedure does not need muscle paralysis, relaxants are given only to facilitate tracheal intubation at a dose commonly equivalent to twice the 95% effective dose at the adductor pollicis (ED<sub>95</sub>).<sup>10,11</sup>

In clinical practice, it seems that if the duration of surgery is lengthy enough, reversal could be overlooked. Therefore, the purposes of the present study that was done in Isfahan University of Medical Sciences during September 2008 till February 2009 were<sup>1</sup> to determine the incidence of residual paralysis subsequent to the administration of a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action (atracurium), and correlate it with duration of surgery in the range of 60 to more than 120 minute; and<sup>2</sup> to compare this incidence when the residual paralysis was defined as a TOF ratio less than 0.9.

## Methods

After obtaining Institutional Ethics Committee approval (University Project Number 388242) and written informed consent from all the patients, two hundred and sixteen ASA I and II consequent patients, aged 18-65 years, scheduled for elective microsurgical surgery of ear and facial plastic surgeries under general anaesthesia requiring tracheal intubation were included in this prospective nonrandomized

observational study that was done in Kashani hospital of Isfahan University throughout September 2008 till February 2009. The approximate duration of surgery was no less than 1 hour.

All these patients received a single intubating dose of intravenous (i.v.) atracurium (0.5 mg/kg)<sup>6</sup> to facilitate tracheal intubation and received no more relaxant subsequently. Patients were excluded from the study if they received a dose of atracurium less than or greater than 0.5 mg/kg, or when additional doses of relaxant were given through the surgical procedure. Also, patients with neuromuscular diseases, preoperative medication that may interfere with neuromuscular transmission, and kidney or liver disease were excluded from the study.

In the operating room, an 18 G intravenous cannula was inserted in an appropriate antecubital vein and Ringer's solution was started, at 10 ml/kg per hour throughout the study period. Monitoring included an automated blood pressure cuff, electrocardiography and pulse oximetry. After preoxygenation, anaesthesia was induced with i.v. thiopental 5 mg/kg, i.v. fentanyl 3 µg/kg and i.v. atracurium 0.5 mg/kg. Patients' lungs were manually ventilated with 100% oxygen before orotracheal intubation was performed.

For neuromuscular monitoring, one arm was fixed in an arm-board and the four ulnar fingers were immobilized. Paediatric electrocardiogram (ECG) surface electrodes were put over the ulnar nerve at the wrist after cleaning and rubbing the skin with an abrasive. Subsequent to induction of anesthesia, the ulnar nerve was stimulated supramaximally every 12 seconds using train-of-four (TOF) nerve stimulation.

Initially, the evoked response from the adductor pollicis muscle was quantified by mechanomyography with a force displacement transducer attached to the thumb. Subsequent to a few TOF nerve stimulations, atracurium was administered. Tracheal intubation was done when no response to nerve stimulation was observed at the display of the TOF-Guard. The patients' lungs were then mechanically

ventilated with a tidal volume of 10 ml/kg and a respiratory rate of 12/min to maintain end-tidal carbon dioxide partial pressure (PETCO<sub>2</sub>) at around 38 mmHg. Anesthesia was maintained with isoflurane 1-1.2% with a fresh gas flow of 4 L/min (50% N<sub>2</sub>O in O<sub>2</sub>).

Core temperature was measured with a tympanic membrane probe and it was directed at maintaining the temperature more than 35°C.<sup>5</sup> At the end of surgery, if TOF-ratio was  $\leq 0.9$ , neostigmine 40  $\mu\text{g}/\text{kg}$  i.v. was given. If TOF-ratio was  $\geq 0.9$ , no neostigmine was given, but the anesthetist stayed at the bedside until the patient became conscious before extubation of the trachea was performed.

In addition to demographic data, the following variables were recorded: duration of surgery, time of tracheal extubation, peripheral and central temperature each thirty minutes during surgery and just after arrival to the post anesthesia care unit (PACU), hypoxia (SPO<sub>2</sub> < 90%), and the length of PACU stay based on the modified Aldrete Score system.<sup>12</sup>

Also, in awake patients with TOF > 0.9, residual neuromuscular paralysis was evaluated by using clinical tests (i.e., the head lift test, the tongue depressor test, and the hand grip).

Student's t-test was utilized for comparison of continuous variables. If distribution of continuous variables was not normal, nonparametric test such as Mann-Whitney U was used for analysis of data. Data are presented as mean  $\pm$  SD or range. Ordinal variables are presented as numbers (%). A value of  $p < 0.05$  was considered the minimum level of statistical significance. Analysis of data was performed by Statistical Package for the Social Sciences (SPSS) 16.0 for Windows.

## Results

Two-hundred sixteen patients met the inclusion criteria and were then studied. Demographic data of patients and duration of operation are shown in Table 1. Mean (SD) peripheral temperature of patients each thirty minutes during surgery and just after arrival to the

PACU was  $36.0 \pm 0.8^\circ\text{C}$  (range: 35-37.7).

Duration of thirty three surgeries was between 93-120 minutes. One-hundred eighty three surgeries lasted more than 120 minutes. Ninety minutes after administration of NDMR, TOF was less than 0.9 in 48 (22.2%) patients while after 120 minutes, no patients had TOF less than 0.9. Of 33 patients whose operation lasted less than 120 minutes, 4 patients had TOF less than 0.9 at the end of surgery. The mean (SD) extubation time was significantly more in these 4 patients compared with the other 29 patients ( $7.2 \pm 2.2$  vs.  $5.4 \pm 1.5$ , respectively,  $p = 0.034$ ). Due to wide difference in the numbers of patients in the two groups, analysis of data by using Mann-Whitney U test was performed which showed the difference was also statistically significant ( $p < 0.05$ ). Of 183 patients whose operation lasted more than 120 minutes, there was no cases with TOF less than 0.9 at the end of operation.

The mean (SD) extubation time in these patients was not significantly different from patients whose operation lasted less than 120 minutes and had TOF more than 0.9 ( $6.32 \pm 1.7$  vs.  $5.6 \pm 1.7$ , respectively,  $p = 0.33$ ).

There was no case of hypoventilation or hypoxia (SPO<sub>2</sub> < 90%) at PACU. The frequency distribution of different clinical tests (i.e., the head lift test, the tongue depressor test, and the hand grip) for evaluation of residual neuromuscular paralysis in awake patients with TOF > 0.9 at PACU is shown in Table 2.

As Table 2 shows, the incidence of negative value in clinical tests was high so it can be concluded that clinical tests can not differentiate existence of residual paralysis. The duration of PACU stay in patients whose operation lasted less than 120 minutes was not significantly different in patients who had TOF less than 0.9 with those had TOF more than 0.9 ( $35 \pm 18$  vs.  $32 \pm 7$ , respectively,  $p = 0.54$ ).

Also, there was no significant difference in duration of PACU stay between patients whose operation lasted more than 120 minutes with those lasted less than 120 minutes.

**Table 1.** Patient demographic data and duration of surgery

Variable		Range
Age (years)	31.9 ± 10.8	18-65
ASA (I/II)	200/16	
Sex (M/F)	100/116	
Weight (kg)	67.5 ± 11.5	42-120
Duration of surgery (minutes)	130 ± 13.2	93-185
Data are presented as mean ± SD and range.		

**Table 2.** The frequency distribution of different clinical tests in patients with TOF > 0.9

Clinical test	Number	Positive	Negative
Head lift	152	18 (11.7)	134 (88.3)
Tongue depressor	144	15 (10.3)	129 (89.7)
Hand grip	149	20 (13.2)	129 (86.8)

Data are presented as number (%).

TOF: Train of Four ratios

## Discussion

Analysis of our data demonstrated that subsequent to a single intubating dose of intermediate-acting nondepolarizing muscle relaxant (atracurium), residual paralysis did not happen in the PACU more than 2 hours after administration.

The rates of residual paralysis were 41% and 52% when a TOF ratio less than 0.7 or 0.8 was applied, respectively, signifying that the occurrence of residual paralysis increases as the TOF threshold for its recognition enhances.<sup>13-15</sup> Our investigation showed that a long interval (more than 120 minutes) between the last administration of muscle relaxant and the evaluation of the measured TOF ratio in the PACU ensure full recovery.

We administered one single dose of atracurium in all patients. If operation time was less than 120 minutes and TOF-ratio was  $\geq 0.9$ , reversal of neuromuscular blockade was performed. Ninety minutes after administration of atracurium, TOF was less than 0.9 in 48 (22.2%) patients while after 120 minutes, no patients had TOF less than 0.9. So, if operation time lasted more than 120 minutes, no reversal of neuromuscular blockade was done but anesthesiologist monitored patients till extubation of trachea was performed. In this group, due to

TOF  $\geq 0.9$ , the patients were extubated early. In group of patients whose operation was lasted less than 120 minutes, if TOF-ratio was less than 0.9, reversal of neuromuscular blockade was done. So, it was expected that extubation time and PACU stay time were not different between these two groups.

Prior studies<sup>14,16,17</sup> have obviously confirmed a high incidence of residual paralysis when an anticholinesterase was not administered. In this background, our study showed that the overall incidence of residual paralysis (characterized by a TOF ratio less than 0.9) ninety minutes after administration of NDMR reached 22%. However, there was no case of residual paralysis (defined by a TOF ratio less than 0.9) 120 minutes after administration of NDMR.

Administration of reversal agents at the end of anesthesia seems signified to avoid the recognized harmful consequences of partial paralysis.<sup>18,19</sup> On the other hand, the administration of reversal agents does not ensure the lack of partial paralysis in all patients when they enter in the PACU.

Hayes et al<sup>6</sup> reported that there was no significant difference in the frequency of postoperative residual block among patients who did or did not have their block reversed. When there is obvious evidence of satisfactory neu-

romuscular function evaluated by quantitative monitoring, the administration of reversal agents seems needless. On the contrary, when neuromuscular monitoring identified residual block routine administration of an anticholinesterase would be needed.

Whatsoever the thresholds used to identify residual paralysis, our results showed that the accuracy of the clinical (head lift, tongue depressor, and hand grip) tests to distinguish neuromuscular blockade was too low to advise these tests in the clinical setting.

In the PACU, residual paralysis can be evaluated by clinical tests (head lift test and tongue depressor test) and qualitative instrumental tests (visual or tactile fade detection subsequent to TOF or DBS stimulation). Whereas instrumental tests can be simply carried out in all patients, the quality of the evaluations of neuromuscular function provided by the clinical tests necessitates that patients are awake and cooperative and devoid of the residual effects of other anesthetic drugs on arrival in the PACU. These circumstances are not always possible to accomplish, except in awake volunteers.<sup>20,21</sup>

In the present study, as a minimum, 32% of our patients were incapable to do these clinical tests appropriately. Undoubtedly, these results indicates that when patients were incapable to sustain the head lift or to maintain a tongue depressor clenched between their incisor teeth, neuromuscular recovery was not complete. Nevertheless, when these tests were successfully carried out, the existence of a certain degree of residual paralysis could not be excluded.

It is, nonetheless, obvious that 18 patients were incapable to sustain a head lift, 15 could not hold a tongue depressor, and 20 had not satisfactory hand grips while quantitative measurements of TOF showed a ratio higher than 0.9 assessed by acceleromyography.

Three reasons can be proposed to elucidate these unexpected results. First, most favorable conditions for clinical evaluation of neuromuscular function require that patients are awake and co-operative and without the residual effects of other anesthetics drugs on arrival in

the recovery area, conditions which are not constantly probable to accomplish. On the other hand, even in apparently awake patients, it may be difficult accurately to evaluate clinical function in the immediate postoperative period owing to factors such as pain.<sup>22,23</sup>

Second, the relation among TOF ratio values and clinical tests is not invariable in all persons.<sup>24</sup> For instance, Kopman et al.<sup>20</sup> showed that the range of TOF values upon which the tongue depressor test was accepted in height persons ranged between 0.68 and 0.95. Hence, it is possible that some of our patients could not maintain a tongue depressor between their teeth at TOF values of 0.9 or greater.

Lastly, acceleromyography overestimates the TOF ratio when compared with mechanomyography. A TOF ratio of 0.9 measured by acceleromyography corresponds to a TOF ratio of 0.85 achieved by mechanomyography.<sup>25</sup> It has been formerly shown that DBS is more sensitive than TOF in the manual detection of residual neuromuscular blockade.<sup>26</sup> Nonetheless, the limit of manual fade detection using DBS corresponds to a TOF ratio of 0.6.<sup>27</sup>

Previous investigation demonstrated that a TOF ratio greater than 0.9, not 0.7,<sup>8</sup> is needed to avoid partial paralysis; it is not unexpected that lack of fade subsequent to DBS nerve stimulation does not indicate complete recovery. Therefore, neither the clinical tests nor the qualitative instrumental tests are accurate enough to identify residual paralysis.

On the contrary, when fade is detected by tactile means, a certain degree of residual paralysis can be expected with a high degree of confidence. Residual blockade (TOF < 0.9) is present in 92–96% of individuals who show fade in response to TOF or DBS stimulation (positive predictive value). Conversely, complete recovery is seen in only half of the patients with no fade (negative predictive value, 53–62%). In other words, complete recovery cannot be confirmed by employing either qualitative instrumental tests or clinical tests but needs the use of measured TOF ratio.

As our study showed, duration of PACU



stay was no significantly different between patients whose operation lasted more than 120 minutes with those lasted less than 120 minutes. This may be owing to the use of only a single dose of the neuromuscular blocking drug in the vast majority of patients and the moderately long time between administration of the last dose of the neuromuscular blocking drug and entrance to the recovery ward.

### Conclusion

Our study showed that a long duration (more than 2 hours) between the administration of a single dose of an intermediate-acting nondepolarizing muscle relaxant (atracurium) and the entrance to the PACU can probably guarantee the lack of a residual paralysis. This conclusion needs further evaluation before final assumption can be elucidated. It must be emphasized that the technique of anesthesia including use of narcotics, inhalation anesthetics, or any drugs that can be related to the neuromuscular blockade were similar in all patients.

Also, as it is currently accepted that the TOF ratio threshold permitting complete recovery is

closer to 0.9 than 0.7, clinical tests (i.e., head lift, leg lift, or tongue depressor tests) and qualitative instrumental tests (i.e., manual detection of fade following TOF stimulation) are not adequately sensitive to evaluate full recovery.

Lastly, even after administration of a single intubating dose of intermediate-acting muscle relaxant, quantitative evaluation of TOF ratio is obligatory at the end of surgical procedure to evaluate the presence or absence of residual paralysis.

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### Conflict of Interests

Authors have no conflict of interests.

### Authors' Contributions

MRV has planned the study and finalized it; SMR and SR have planned the study and finalized it too; MRS and AH did the statistical analysis and prepared the first version of manuscript and revised final version for publish. All authors read and approved the final manuscript.

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