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Assessment of the residual neuromuscular blockade using the train of four stimulation and related factors in laparoscopic appendectomy

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Abstract
Background*: Neuromuscular blockade drugs (NMBD) during surgery and general anesthesia can lead to postoperative residuals. Besides the commonly used clinical method, one of the measures used is the Train of four stimulation (TOF) assessment.*
Objectives*: (1) Determine factors related to residual neuromuscular blockade (RNMB) in patients undergoing laparoscopic appendectomy. (2) Compare the difference in the assessment of RNMB by TOF ratio and by clinical signs.*
Materials and methods: *A cross-sectional study was carried out from December 2020 to May 2021 at the Anesthesia Department of Nguyen Tri Phuong Hospital on patients undergoing laparoscopic appendectomy.*
Results*: At admission, the highest RNMB rate accounted for 58.33% and gradually decreased to 0% after 120 minutes of extubation. The residual rate of RNMB was higher in the age group ≥ 60 and with repeated use of NMBD. There was a relationship between the overweight /obesity and the RNMB rate at the two-time points of resuscitation and extubation (p<0.05). Patients with ASA II ASA III showed a higher RNMB rate than patients with ASA I (p<0.05). There was no statistically significant relationship between the 5-second head lift factor and the RNMB rate at the time of extubation.*
Conclusions*: The residual rate of NMBD after laparoscopic appendectomy was highest at admission and decreased gradually over time. RNMB was found to be significantly higher in the age group that is more than or equal to 60 years old, overweight and obese, higher ASA grade, and repeated use of NMBD at different times. There was no relationship between the ability to lift the head for more than 5 seconds and the RNMB rate at the time of extubation.*
Keywords: *residual neuromuscular blockade, 5 seconds head lift, laparoscopic appendectomy, Train of four*

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I. Introduction

Neuromuscular blockage drugs are commonly used in surgery and anesthesia to facilitate intubation, airway control, and surgical patient manipulation. However, RNMB after surgery can bring many dangers to patients, such as pharyngeal weakness, gastric reflux, pulmonary aspiration, and an increased risk of respiratory complications after surgery. One of the evaluations being used is Train of four (TOF) watch monitoring, a muscle accelerator that has been shown to reduce RNMB and discomfort associated with muscle weakness in the postoperative care unit and improve recovery neuromuscular quality [1]. Muscle accelerometers measuring TOF index to monitor muscle relaxation and relaxation to limit residual muscle relaxation have been popular in many countries. However, this issue has not been routinely performed in Vietnam; extubation is mainly based on subjective clinical judgments. In addition, the monitoring and care of patients after muscle relaxation through the TOF index is still limited. Therefore, the epidemiological factors involved play an important role and should be investigated in order to provide suggestions for clinicians to make decisions at appropriate times. Therefore, we carried out the project "Evaluating residual muscle relaxation by TOF ratio and related factors in patients undergoing laparoscopic appendectomy" with the following objectives:

Objectives of research:
1. Determine factors related to a residual neuromuscular blockade in patients undergoing laparoscopic appendectomy.
2. Compare the difference in assessing residual neuromuscular blockage by TOF ratio and by clinical signs.

II. Methodology

Research design: Research described cross-section

Time and place: From 12/2020 to 05/2021 at Nguyen Tri Phuong Hospital, Ho Chi Minh City.

Sample selection object: The study was conducted on 96 patients aged 18 years or older, scheduled to undergo laparoscopic appendectomy, under general anesthesia with indications for the use of rocuronium muscle relaxants, ASA grades I, II, III; capable of understanding, directing, and voluntarily consenting to participate in the study. Excluding patients with neuromuscular disease, patients who were converted to open surgery during surgery had complications that required a stay in the intensive care unit after surgery.

Conduct method:

Systematic random sampling.

Sampling is done from the pre-operative room, and then the patient continues to be monitored in the operating room and recovery room. Measurement of muscle relaxation residuals (by TOF - Watch) will be performed at specific times: immediately after arrival in the recovery room, after extubation, 15 minutes, 30 minutes, 60 minutes, 90 minutes, 120 minutes after extubation.

The outcome variable: TOF is the ratio (%)displayed on the machine (T4/T1). The machine only displays the result % when stimulus 4 appears. If no stimulus 4 is present, the machine will display the result as 0, 1, 2 or 3 then count as 0%. The RNMB is TOF ratio < 0.9 (90%) [2].

III. Results and Discussion

The study was carried out on 96 subjects who met the sampling conditions.

Table 1. The rate of RNMB in laparoscopic appendectomy at different time points

Time points	RNMB (TOF < 90%)	
	Frequency	Ratio
Recovery room	56	58.33
Extubation	38	39.58
15 minutes after extubation	21	21.88
30 minutes after extubation	15	15.62
60 minutes after extubation	6	6.25
90 minutes after extubation	2	2.08
120 minutes after extubation	0	0.0

Residual neuromuscular blockade after surgery by the TOF index is < 0.9. At the time in the recovery room, the highest RNMB rate was 58.33%, followed by the time of extubation 39.58%, 15 minutes after extubation was 21.88%. Until 120 minutes after extubation, there was no residual neuromuscular blockade.

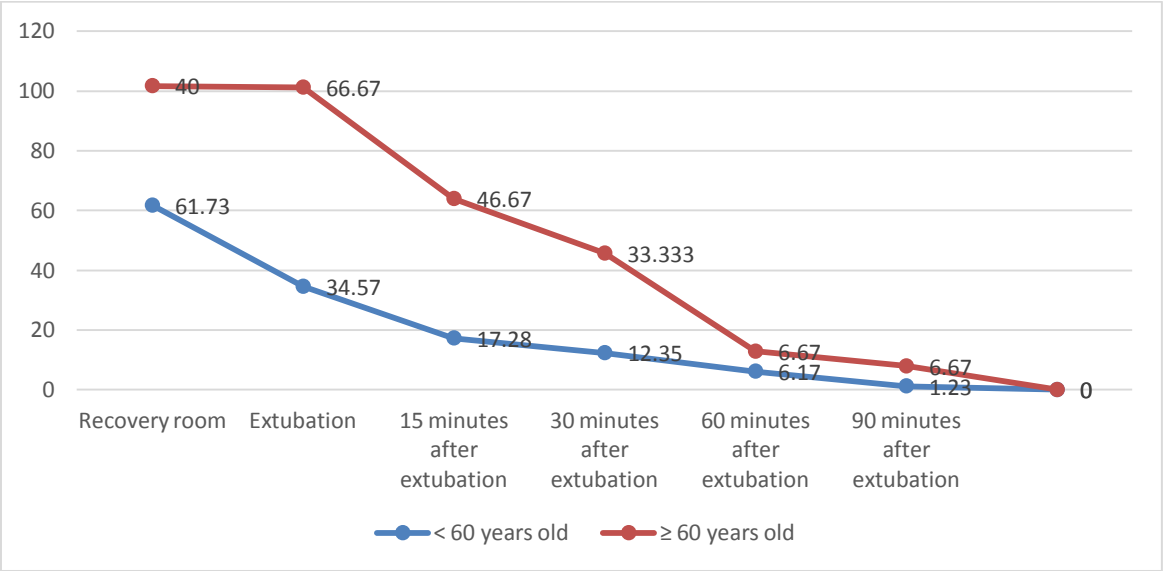

Chart 1. Relationship between age group and RNMNB

The study showed a statistically significant difference between the age group and the RNMB rate at clinical time points (p < 0.05). Accordingly, the RNMB rate of the age group that is more than or equal to 60 years old was higher than the RNMB rate of the age group that is less than 60 years old at all time points in the research.

Table 2. Relationship between BMI and RNMB

Timepoints	Overweight and obesity	Normal	p	PR (95%)
Recovery room	43 (67.19)	13 (40.62)	**0.013**	1.65 (1.05-2.60)
Extubation	30 (46.88)	8 (25.00)	**0.039**	1.87 (1.00-3.61)
15 minutes after extubation	16 (25.00)	5 (15.62)	0.295	1.60 (0.64-3.97)
30 minutes after extubation	10 (15.62)	5 (15.62)	1.00*	1.00 (0.37-2.68)
60 minutes after extubation	3 (4.69)	3 (9.38)	0.371*	0.50 (0.11-2.34)
90 minutes after extubation	1 (1.56)	1 (3.12)	0.613*	0.50 (0.03-7.74)

** Fisher's exact test*

There is a relationship between overweight and obesity with the residual neuromuscular rate at two-time points of the recovery room and extubation ($p < 0.05$).

Table 3. Relationship between ASA grand and RNMB

Time points	ASA I	ASA II	ASA III	P^1 PR (95%)	P^2 PR (95%)
Recovery room	40 (70.18)	15 (42.86)	1 (25.00)	**0.022** 0.61 (0.40-0.93)	0.238 0.36 (0.06-1.98)
Extubation	20 (35.09)	15 (42.86)	3 (75.00)	0.454 1.22 (0.72-2.06)	**0.026** 2.14 (1.09-4.18)
15 minutes after extubation	10 (17.54)	9 (25.71)	2 (50.00)	0.349 1.46 (0.66-3.26)	0.071 2.85 (0.91-8.76)
30 minutes after extubation	5 (8.77)	8 (22.86)	2 (50.0)	0.071 2.60 (0.92-7.37)	**0.008** 5.70 (1.56-20.82)
60 minutes after extubation	2 (3.51)	4 (11.43)	0 (0.00)	0.162 3.26 (0.62-17.00)	**<0.001*** **None**
90 minutes after extubation	1 (1.75)	1 (2.86)	0 (0.00)	0.728 1.63 (0.10-25.59)	**<0.001*** **None**

** Fisher's exact test;*

P^1 test the difference between ASA II and ASA I

P^2 test the difference between ASA III and ASA I

At the time in the recovery room, the RNMB rate of ASA II was 0.61 times as high as the RNMB rate of ASA I (p=0.022). The RNMB rate of ASA III was 2.14 times as high as RNMB rate of ASA I (p=0.026) at extubation time. In addition, the RNMB rate of ASA III was 5.7 times as high as RNMB rate of ASA I at 30 minutes after extubation (p=0.008).

Table 4. Relationship between repeated NMBD and RNMB

Timepoints	Repeat NMBD		p	PR (95%)
	Yes	No		
Recovery room	19 (79.17)	37 (51.39)	**0.017**	1.54 (1.14-2.09)
Extubation	15 (62.50)	23 (31.94)	**0.008**	1.96 (1.24-3.09)
15 minutes after extubation	6 (25.00)	15 (20.83)	0.669	1.20 (0.52-2.74)
30 minutes after extubation	4 (16.67)	11 (15.28)	1.00*	1.09 (0.38-3.11)
60 minutes after extubation	2 (8.33)	4 (5.56)	0.638*	1.50 (2.29-7.68)
90 minutes after extubation	1 (4.17)	1 (1.39)	0.439*	3.00 (0.19-46.1)

** Fisher's exact test*

There was a statistically significant difference between the residual neuromuscular blockage rate in patients with repeat neuromuscular blockage drugs at the two-time points: recovery room and extubation ($p<0.05$). The residual neuromuscular blockage rate in patients with repeat neuromuscular blockage drugs at the recovery room time was 1.54 times as high as the patients without repeat (p=0.017). At the extubation time, the proportion of patients with RNMB in patients with repeated NMBD was 1.96 times as high as in patients without repeated intraoperative NMBD (p=0.008).

Comparing the relationship between the clinical recovery of neuromuscular criteria and residual neuromuscular blockade at the time of extubation, the number of patients able to lift the head more than 5 seconds is 59 patients, accounting for 61.45%. Evaluation of neuromuscular recovery based on the criteria of lifting the head more than 5 seconds has a sensitivity of 57.89%, a specificity of 36.21%, a positive predictive value of 37.29%, a predictive value of 37.29%, negative is 56.76%. The study showed no statistically significant

relationship between the ability to lift the head more than 5 seconds factor and the residual neuromuscular blockage rate at the time of extubation (p=0.561).

Table 5. Relationship between clinical recovery of neuromuscular criteria and RNMB at the time of extubation

Ability to lift the head more than 5 seconds	RNMB at the time of extubation		p	PR (95%)
	TOF <90 Frequency (%)	TOF ≥ 90 Frequency (%)		
Yes	22 (37.29)	37 (62.71)		1
No	16 (43.24)	21 (56.76)	0.561	1.10 (0.79-1.54)

The most critical time after surgery is the time of recovery room and extubation. At these two points in time, our results are similar to those of author Nguyen Ngoc Han, but there are also differences compared with Dam Trung Tin and Hoang Quoc Khai [3-5].

Table 6. Compare the percentage of patients with RNMB after surgery

Authors	Percentage of patients with RNMB (%)	
	Time at the recovery room	*Time at extubation*
Nguyen Ngoc Han [3]	60%	40%
Dam Trung Tin [5]	68%	47%
Hoang Quoc Khai [4]	79%	34%
Murphy [6]	30%	-
Our research	58.33%	39.58%

The differences between the studies were explained by the different procedures, along with the location of extubation in the operating room or the recovery room. However, it can be seen that the degree of difference between studies is not high. For example, in the study of author Dam Trung Tin, the median time from using reverse neuromuscular blockage drugs to the recovery room after was 10 minutes. Besides, in Hoang Quoc Khai's study, the patient used reverse neuromuscular blockade drugs after being admitted to the recovery room. This result is much higher than Murphy's study because the sample was conducted on gynecological surgery, so the muscle relaxation degree was not as deep as a laparoscopic appendectomy.

Regarding the related factors, the study showed a relationship between the age group and the RNMB rate (TOF < 0.9) at clinical time points ($p < 0.05$). The results are similar to Yamamoto's study showing that RNMB rate increase with age (OR=0.94, 95%: 0.91-0.98) (OR=3.5, 95%: 1.79-6.86) [7]. Research by Nguyen Thi Minh Thu shows that the likelihood of residual neuromuscular blockage rate in the group over 50 years old is 5.73 times as high as the other groups. ($p<0.01$) [1]. Studies show that age is an epidemiological factor closely related to r residual neuromuscular blockade after surgery. In addition, the patient's physical condition also needs to be taken into account when showing higher prevalence indicators at some points in time. There were ASA grades I-III in our study; no patients were grade IV-V. The results are similar to the result of some authors. Khamtuikrua's study reported that the likelihood of residual neuromuscular blockade in the group of patients with ASA II class compared with the ASA I group was 2.31 times [8]. However, some studies by Lain Kunthou and Dam Trung Tin confirmed that ASA grade did not affect residual muscle relaxation [5], [9]. In all cases, the neuromuscular blockade drug that was used was Rocuronium. Most cases did not repeat intraoperative neuromuscular blockade drugs (75%). Only 25% of patients had repeated intraoperative neuromuscular blockade drugs (Rocuronium). On average, each patient received a total dose of 40.72mg rocuronium, with 50% of patients using the total dose in the range of 35 - 40.2mg, the highest being 100mg. The study found a statistically significant association between the repetition of neuromuscular blockage drugs and residual neuromuscular blockade ($p<0.05$). At the time of recovery room and extubation, the proportion of residual neuromuscular blockade with repeat residual neuromuscular blockage drugs was higher than the group of patients without neuromuscular blockade drugs.

In addition, the data showed no association between the criteria of lifting the head for more than 5 seconds and the residual neuromuscular blockage rate at the time of extubation ($p > 0.05$). The test of lifting the head for more than 5 seconds is influenced by many factors such as the patient's consciousness, cooperation, and even the evaluator's subjective feelings when performing extubation in cases where it is necessary to monitor neuromuscular blockade with quantitative devices [2].

IV. Conclusion

The residual neuromuscular blockage rate after laparoscopic appendectomy was high during recovery room and extubation, 58.33%, and 39.58%, and RMNB has tended to decrease gradually over time. The residual neuromuscular blockade was significantly higher in the age group that is more than or equal to 60 years old. Overweight and obesity, ASA grade, and repeated use of neuromuscular blockade drugs are associated with RNMB at some point in time. There was no statistically significant relationship between the test of lifting the head more than 5 seconds and the RNMB rate at the time of extubation.

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