

A multicenter survey on the use of neuromuscular blockade in Greece. Does the real-world clinical practice indicate the necessity of guidelines?

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Abstract

Background and Aims: The aim of this study was to investigate the current status of clinical practice regarding neuromuscular blocking drugs and their antagonists in Greece.

Material and Methods: This is a multicenter survey, including a questionnaire based on previous studies, which was translated and modified by a Task Force of the Hellenic Society of Anaesthesiology. It was completed on a web-based database after invitation via e-mail and was left online for a period of 2 months.

Results: A total of 1,100 questionnaires were sent, with a response rate of 7.9%. 13.7% stated that they do not use neuromuscular monitoring. Rocuronium was most commonly used for intubation ["often" stated by 19 (21.8%) and "very often" by 62 (71.2%)], followed by cis-atracurium, atracurium, and succinylcholine. Neostigmine and sugammadex were both used, with reversal not always administered by 23 (26.4%). Both agents were mostly used at fixed doses and not calculated based on TOF monitoring or body weight. Sugammadex was preferred in special patient groups and in operations of short duration. Reversal was most often administered based on clinical signs of neuromuscular recovery rather than objective monitoring. A significant percentage of respondents used an inadequate TOF ratio for extubation [37 (43.2%) used a TOF ratio <90%]. The reported incidence of observed residual neuromuscular blockade (RNMB) was 44.8%.

Conclusion: Great variability was observed in Greek clinical practice regarding the use of neuromuscular blockade, which indicates serious issues that must be addressed. The needs for educating anesthesia providers and developing official guidelines are obvious in order to improve patient outcomes.

Keywords: Antagonists, neuromuscular blocking drugs, neuromuscular blockade

Introduction

Neuromuscular blocking drugs and their antagonists are commonly used in Anesthesiology to achieve endotracheal


intubation and maintain neuromuscular blockade throughout surgery. However, their use, including the type and dose of administration, and their reversal at the end of surgery are not always evidence based.^[1-3] Several issues of significant clinical interest have been identified, such as the perioperative management of neuromuscular blockade,

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adequate monitoring, management of special patient groups, and residual neuromuscular blockade (RNMB) at the end of surgery.^[1-5]

Multiple surveys conducted worldwide indicate that neuromuscular blocking drugs and their antagonists are commonly administered without adequate rationalization and monitoring, leading to variable incidence of RNMB. Studies from the United States, Europe,^[6] Australia and New Zealand,^[7,8] Italy,^[9,10] Denmark,^[11] Morocco,^[12] and Brazil^[13] suggest that currently, only a small percentage of anesthesiologists monitor neuromuscular function in their clinical practice, even in special patient groups. In addition, the absence of internationally accepted clinical guidelines regarding neuromuscular blockade remains a major problem.^[14,15]

The need to clarify these critical issues and facilitate safe and appropriate clinical practice led the Hellenic Society of Anaesthesiology to create a task force of specialists to critically review current evidence on the subject and propose recommendations to improve the clinical practice in Greece. This project also aimed to apply the necessary alterations in education and clinical practice based on the formed recommendations. Therefore, the aim of this study was to investigate the current status of clinical practice regarding neuromuscular blocking drugs and their antagonists in Greece.

Material and Methods

This study was initiated by the Hellenic Society of Anaesthesiology on a national level. The requirement for written informed consent was waived by the IRB because we chose to conduct an anonymous internet-based survey. The task force included five anesthesiologists with significant clinical experience. The team developed a questionnaire based on the one published by Naguib *et al.*,^[6] after obtaining permission. The translated and modified questionnaire included various sets of questions. Some aspects of the questionnaire were adapted to the Greek National Health System organization, especially regarding the hierarchy of doctors' positions and the organization of Anaesthetic Departments.

An invitation to complete the questionnaire was sent to all members of the Hellenic Society of Anaesthesiology, with instructions for its online completion. Three reminder e-mails were sent to all anesthesiologists. The questionnaire was maintained online for 2 months. All respondents completed it anonymously, and measures were taken to ensure privacy and uniqueness.

Statistical analysis

Statistics for continuous variables were analyzed using the Shapiro–Wilk test. Results are presented as absolute or relative frequencies. Fisher's exact test was employed for comparisons between categorical variables. All statistical tests were two-tailed, with the level of statistical significance set at 5% ($P < 0.05$).

Because one of the major issues is the presence and prevention of RNMB, we decided to analyze the data first as a whole, and then to perform two different subgroup analyses: one based on the presence/absence of a Post-Anesthesia Care Unit (PACU) at the Department and the second based on whether the anesthesiologist reported incidences of RNMB at their hospital.

Power analysis was performed post-hoc based on responses regarding RNMB observation and the presence of a PACU. GPower 3.1.9.2 was used for power calculation. Statistical analysis of the results was performed using the Stata™ software (Version 13.1 MP, Stata Corporation Software, College Station, TX, USA).

Results

The questionnaire was translated into Greek by the Task Force of the Hellenic Society of Anaesthesiology. The Cronbach's alpha coefficient was calculated to be 0.78, indicating acceptable internal consistency. About 1100 questionnaires were sent via e-mail. Of those, 580 were read, and 87 were completed, yielding an overall response rate of 15%. If the total number of questionnaires sent is considered, the response rate was lower (7.9%). The demographic characteristics of participants are presented in Table 1. Two different subgroup analyses were performed: one based on the presence of a structured PACU and another on whether the anesthesiologist reported the incidence of RNMB in their hospital. A post-hoc power analysis based on these factors yielded a result of 56%.

General findings

The majority of respondents (66.6%) lived in the capital and worked in large hospitals. Junior consultants, who have less experience, responded at a higher percentage than did consultants and directors [Table 1].

Presence/absence of a structured PACU

Only 43 (49.4%) respondents reported the presence of a structured PACU in their Department. This percentage did not differ between respondents based in the capital and those located in other areas ($P = 0.17$). Similarly, no significant difference was observed regarding the presence of a PACU depending on the type of hospital ($P = 0.33$). Hospitals

Table 1: Demographic characteristics of the total number of respondents, n (%)

Geographical region		Academic title	
Attica	58 (66.67%)	Academic	16 (18.39%)
Other areas	29 (33.33%)	Nonacademic	71 (81.61%)
Hospital		Years since completion of training	
NHS	58 (66.67%)	1-4 years	28 (32.18%)
Private	15 (17.24%)	5-9 years	24 (27.59%)
Military	8 (9.2%)	10-15 years	9 (10.34%)
University	6 (6.9%)	15-20 years	7 (8.05%)
Size of hospital-number of beds		>20 years	19 (21.84%)
<50	8 (9.2%)	Number of trainees in Anesthesiology Department	
50-100	7 (8.05%)	<10	48 (55.17%)
100-200	14 (16.09%)	>10	39 (44.83%)
>200	58 (66.67%)	Number of trained anesthesiologists in Anesthesiology Department	
Number of operating rooms		None	33 (37.93%)
1-5	31 (35.63%)	<10	44 (50.57%)
5-10	42 (48.28%)	>10	10 (11.49%)
>10	14 (16.09%)	Number of nurse anesthetists Anesthesiology Department	
Doctor's position at the Department		None	5 (5.75%)
Specialized anesthetist in temporary cooperation with the department	20 (22.99%)	<10	42 (48.28%)
Junior Consultant (<3 years)	20 (22.99%)	>10	40 (45.98%)
Senior Consultant (3-6 years)	14 (16.09%)	Is there a PACU in your hospital?	
Consultant (>6 years)	18 (20.69%)	No	44 (50.57%)

with more anesthesiologists (>10) and with more academic personnel had a structured PACU more often ($P = 0.01$ and $P = 0.02$, respectively). In addition, hospitals with a structured PACU reported the recognition of RNMB more often ($P = 0.008$) [Table 2].

Observation or not of RNMB

The total perceived percentage of identifying symptoms of RNMB was 44.8%. The reported frequency of clinically important RNMB was <1 observed episode per month for 68 (78.1%) respondents. Anesthesiologists with more experience and those who worked at departments with a structured PACU reported RNMB at a greater rate ($P = 0.02$ and 0.008 ; Table 2).

Monitoring devices

Objective monitoring of neuromuscular function

In most Anesthesiology Departments, only one train-of-four (TOF) device existed for all operating rooms [33 (37.9%)]. However, 27 (31%) of the respondents stated that their department has one device for each operating room, and 24 (27.5%) that there is no device for objective monitoring of neuromuscular blockade. The TOF-watch was the most commonly available device (51.7%), followed by TOF-Guard (37.5%) and Datex-NMT (26.7%). Sixty (68.9%) respondents thought that objective monitoring devices should be available in all operating rooms, and 53 (60.9%) that they should be part of the minimum monitoring [Table 3].

Conventional nerve stimulators

Conventional nerve stimulators were more widely available compared to TOF-monitoring devices [56 (64.3%)], especially in departments with an organized PACU ($P = 0.03$). Respondents stated that they prefer to use TOF-monitoring devices [54 (62.1%)] compared with the conventional ones, whereas 12 (13.7%) stated that they do not utilize neuromuscular monitoring at all [Table 3].

Clinical use of neuromuscular blocking drugs

Details on the type of neuromuscular blocking drugs used are presented on Table 4, with the most common being succinylcholine, rocuronium, and cis-atracurium. Sixty-eight (78.1%) respondents stated that they administer neuromuscular blocking agents for endotracheal intubation also in patients with anticipated difficult airway. In this case, the most commonly administered agent was rocuronium (54%), followed by succinylcholine (41.3%) [Table 4].

Reversal of neuromuscular blockade

Neostigmine was available in all departments, and sugammadex in 97.7%. Twenty-three (26.4%) respondents stated that they do not always administer reversal. Of those, 81 (93.1%) reported that they do not reverse in 1%–25% of cases. The main reasons for not reversing were a long time since the last dose of the neuromuscular blocking drug (79.6%), the absence of clinical signs of muscle weakness (67.8%), the TOF-ratio (52.5%), the use of a specific neuromuscular blocker (40.6%), and the absence of fade (38.9%) [Table 5].

Table 2: Residual neuromuscular blockade (RNMB) observation by anesthesiologists in Greece

RNMB	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
Have you ever observed at your hospital a patient at the PACU having symptoms of residual neuromuscular paralysis?				
No	43 (49.43%)	27 (61.36%)	16 (37.21%)	0.008*
Yes	39 (44.83%)	13 (29.55%)	26 (60.47%)	
I don't know/no answer	5 (5.75%)	4 (9.09%)	1 (2.33%)	
What is the estimated incidence of clinically significant residual neuromuscular paralysis at your hospital?				
Never	15 (17.24%)	9 (20.45%)	6 (13.95%)	0.835
Rarely (<1 episode/month)	68 (78.16%)	33 (75%)	35 (81.4%)	
Often (>1 episode/week)	-	-	-	
Very often (>1 episode/day)	-	-	-	
I don't know/no answer	4 (4.6%)	2 (4.55%)	2 (4.65%)	
Do you believe that residual neuromuscular blockade represents a serious public health problem?				
Totally agree	73 (83.91%)	35 (79.55%)	38 (88.37%)	0.383
Agree	14 (16.09%)	9 (20.45%)	5 (11.63%)	
Disagree	-	-	-	
Totally disagree	-	-	-	
I don't know/no answer	-	-	-	
Do you think that routine use of a conventional nerve stimulator or a quantitative TOF monitor would decrease the incidence of residual neuromuscular blockade?				
Totally agree	71 (81.61%)	36 (81.82%)	35 (81.4%)	0.999
Agree	15 (17.24%)	8 (18.18%)	7 (16.28%)	
Disagree	1 (1.15%)	0	1 (2.33%)	
Totally disagree	-	-	-	
I don't know/no answer	-	-	-	

Descriptive statistical analysis in the total number of respondents and according to the presence/absence of a Post-anesthesia Care Unit (PACU) at the Department. Description of statistics: Absolute and relative frequencies (%). Statistical tests applied: Fisher's exact test. *Significance ($P < 0.05$)

Reversal was mostly administered using clinical signs of neuromuscular recovery [20 (22.9%): totally agree; 40 (45.9%): agree] rather than objective monitoring. Regarding the ability to reverse neuromuscular blockade based on tetanic stimulation, most respondents agreed that it is feasible [39 (44.8%)], but some disagreed [31 (35.5%)]. Notably, 17 respondents (19.5%) did not know or did not answer this question [Table 5].

Sugammadex was the preferred agent to reverse rocuronium for 71.2% of respondents. Regarding neostigmine, 46 (52.8%) respondents stated that they extubate patients 3–5 min after its administration, 22 (25.3%) after 6–10 min, and 14 (16.1%) after <2 min. Only 5 (5.75%) stated that they extubate patients 10 min after neostigmine administration [Table 5].

Thirty-three respondents (37.9%) stated that the TOF-ratio is the most important factor for administering neostigmine, with 36.7% administering reversal at a TOF count of 3–4 and 25.29% at 1–2. The most commonly administered dose of neostigmine (75.8%) was 2.5 mg. Only 11.4%

of respondents stated that the dose they administer is 0.05 mg/kg, 6.9% >0.05 mg/kg, and 5.7% <0.05 mg/kg. About 88.5% of the anesthesiologists stated that they do worry about adverse effects of reversal drugs, with the most common being cardiovascular (82.1%), respiratory (52%), inadequate reversal (52%), and nausea/vomiting (35.6%) [Table 5].

Most respondents [47 (54%)] stated that they administer sugammadex at any TOF count; 31 (35.6%) at a TOF count of 0–2, and 9 (10.3%) at a TOF count of 3–4. However, a significant number of respondents stated that they use an inadequate TOF-ratio for extubation: (24.1% use a TOF-ratio up to 80%, and 42.5% up to 90%. In addition, 48.2% reported that the TOF-ratio used to determine extubation should be 91–100%, 18.3% 81–90%, 24.1% 60–80%, and 9.2% stated that they do not think it is important to know.

The majority of anesthesiologists (41.38%) also stated that they administer sugammadex at a dose of 2 mg/kg, and only 19.54% administer the drug based on TOF count. Overall,

Table 3: Monitoring practices regarding neuromuscular blockade management

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
Monitoring devices for neuromuscular function				
No	24 (27.59%)	12 (27.27%)	12 (27.91%)	0.264
Yes	60 (68.97%)	32 (72.73%)	28 (65.12%)	
I don't know/no answer	3 (3.45%)	0	3 (6.98%)	
If yes, which of the following devices are available?				
TOF Guard	21 (37.5%)	10 (34.48%)	11 (40.74%)	0.783
TOF Watch	29 (51.79%)	16 (55.17%)	3 (48.15%)	0.789
Datex NMT	15 (26.79%)	9 (31.03%)	6 (22.22%)	0.552
Other	1) Model MS-IVA της Life-Tech, Inc, 2) TOFSCAN			
If quantitative TOF monitors are available, how are they distributed?				
1 per 1 operating room	27 (31.03%)	14 (31.82%)	13 (30.23%)	0.948
1 per 2 operating rooms	10 (11.49%)	4 (9.09%)	6 (13.95%)	
1 per 3 operating rooms	17 (19.54%)	9 (20.45%)	8 (18.6%)	
1 for all operating rooms (when >3)	33 (37.93%)	17 (38.64%)	16 (37.21%)	
Are there conventional nerve stimulators available in your department?				
No	28 (32.18%)	19 (43.18%)	9 (20.93%)	0.037*
Yes	56 (64.37%)	23 (52.27%)	33 (76.74%)	
I don't know/no answer	3 (3.45%)	2 (4.55%)	1 (2.33%)	
If conventional nerve stimulators are available, how are they distributed?				
1 per 1 operating room	43 (49.43%)	27 (61.36%)	16 (37.21%)	0.061
1 per 2 operating rooms	6 (6.9%)	4 (9.09%)	2 (4.65%)	
1 per 3 operating rooms	10 (11.49%)	4 (9.09%)	6 (13.95%)	
1 for all operating rooms (when >3)	28 (32.18%)	9 (20.45%)	19 (44.19%)	
Do conventional nerve stimulators display the delivered current?				
No	10 (11.49%)	4 (9.09%)	6 (13.95%)	0.083
Yes	66 (75.86%)	31 (70.45%)	35 (81.4%)	
I don't know/no answer	11 (12.64%)	9 (20.45%)	2 (4.65%)	
If you have both quantitative TOF monitors and conventional nerve stimulators, which device do you use more frequently?				
TOF monitor	54 (62.07%)	29 (65.91%)	25 (58.14%)	0.858
Conventional nerve stimulator	18 (20.69%)	8 (18.18%)	10 (23.26%)	
None	12 (13.79%)	6 (13.64%)	6 (13.95%)	
Both	3 (3.45%)	1 (2.27%)	2 (4.65%)	
If you had at least one monitor of neuromuscular function, TOF or conventional, when would you prefer to use it intraoperatively?				
During induction of anesthesia	12 (13.79%)	6 (13.64%)	6 (13.95%)	0.999
During emergence from anesthesia	26 (29.89%)	13 (29.55%)	13 (30.23%)	
During both, induction and emergence	12 (13.79%)	6 (13.64%)	6 (13.95%)	
During the whole anesthetic procedure	37 (42.53%)	19 (43.18%)	18 (41.86%)	
Do you think that a sustained response to a 50 Hz tetanic stimulation reflects the adequacy of the recovery of the neuromuscular function?				
Totally agree	19 (21.84%)	14 (31.82%)	5 (11.63%)	0.051
Agree	20 (22.99%)	10 (22.73%)	10 (23.26%)	
Disagree	19 (21.84%)	5 (11.36%)	14 (32.56%)	
Totally disagree	12 (13.79%)	5 (11.36%)	7 (16.28%)	
I don't know/no answer	17 (19.54%)	10 (22.73%)	7 (16.28%)	
Conventional nerve stimulators compared to TOF monitoring devices				
In your opinion, conventional nerve stimulators (choose all that apply)				
Should be part of the minimal essential monitoring (in patients under neuromuscular blockade)	49 (56.32%)	26 (59.09%)	23 (53.49%)	0.668
Should be available in all operating rooms	51 (58.62%)	25 (56.82%)	26 (60.47%)	0.829
Should be used in special cases	9 (10.34%)	1 (2.27%)	8 (18.6%)	0.015*
Are not necessary	6 (6.9%)	5 (11.36%)	1 (2.33%)	0.202

Contd...

Table 3: Contd...

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
Conventional nerve stimulators compared to TOF monitoring devices				
I don't know/no answer	9 (10.34%)	5 (11.36%)	4 (9.3%)	0.999
In your opinion, quantitative TOF monitors (choose all that apply)				
Should be part of the minimal essential monitoring (in patients under neuromuscular blockade)	53 (60.92%)	32 (72.73%)	21 (48.84%)	0.029*
Should be available in all operating rooms	60 (68.97%)	34 (77.27%)	26 (60.47%)	0.108
Should be used in special cases	19 (21.84%)	7 (15.91%)	12 (27.91%)	0.203
Are not necessary	0	-	-	
I don't know/no answer	0	-	-	

Descriptive statistical analysis in the total number of respondents and according to the presence/absence of a Post-Anesthesia Care Unit (PACU) at the Department. Description of statistics: Absolute and relative frequencies (%). Statistical tests applied: Fisher's exact test. *Significance (P<0.05)

Table 4: Use of neuromuscular blocking agents

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
Neuromuscular blocking agents and administration strategies				
Which of the following drugs are available in your department? Choose all those that apply (no vs yes)				
Succinylcholine	0 vs 87 (100%)	-	-	
Rocuronium	1 (1.15%) vs 86 (98.85%)	1 (2.27%) vs 43 (97.73%)	0 vs 43 (100%)	0.999
Vecuronium	76 (87.36%) vs 11 (12.64%)	41 (93.18%) vs 3 (6.82%)	35 (81.4%) vs 8 (18.6%)	0.118
Cis-atracurium	3 (3.45%) vs 84 (96.55%)	1 (2.27%) vs 43 (97.73%)	2 (4.65%) vs 41 (95.35%)	0.616
Atracurium	43 (49.43%) vs 44 (50.57%)	17 (38.64%) vs 27 (61.36%)	26 (60.47%) vs 17 (39.53%)	0.054
Pancuronium	87 (100%) vs 0	-	-	
Which of the following neuromuscular blocking agents do you use to facilitate tracheal intubation? Estimate the incidence of each. Choose all those that apply				
Succinylcholine				
Never	12 (13.79%)	6 (13.64%)	6 (13.95%)	0.399
Rarely	58 (66.67%)	29 (65.91%)	29 (67.44%)	
Often	12 (13.79%)	8 (18.18%)	4 (9.3%)	
Very often	5 (5.75%)	1 (2.27%)	4 (9.3%)	
Rocuronium				
Never	2 (2.3%)	0	2 (4.65%)	0.516
Rarely	4 (4.6%)	3 (6.82%)	1 (2.33%)	
Often	19 (21.84%)	10 (22.73%)	9 (20.93%)	
Very often	62 (71.26%)	31 (70.45%)	31 (72.09%)	
Vecuronium				
Never	80 (91.95%)	43 (97.73%)	37 (86.05%)	0.058
Rarely	7 (8.05%)	1 (2.27%)	6 (13.95%)	
Often	-	-	-	
Very often	-	-	-	
Cis-atracurium				
Never	11 (12.64%)	7 (15.91%)	4 (9.3%)	0.4
Rarely	36 (41.38%)	15 (34.09%)	21 (48.84%)	
Often	28 (32.18%)	14 (31.82%)	14 (32.56%)	
Very often	12 (13.79%)	8 (18.18%)	4 (9.3%)	
Atracurium				
Never	58 (66.67%)	25 (56.82%)	33 (76.74%)	0.149
Rarely	18 (20.69%)	11 (25%)	7 (16.28%)	

Contd...

Table 4: Contd...

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
Often	9 (10.34%)	7 (15.91%)	2 (4.65%)	
Very often	2 (2.3%)	1 (2.27%)	1 (2.33%)	
Pancuronium				
Never	87 (100%)			
Rarely	-			
Often	-			
Very often	-			
None of the above				
Never	76 (87.36%)	42 (95.45%)	34 (79.07%)	0.031*
Rarely	10 (11.49%)	2 (4.55%)	8 (18.6%)	
Often	0	0	0	
Very often	1 (1.15%)	0	1 (2.33%)	
Which of the following neuromuscular blocking agents do you use to provide surgical relaxation intraoperatively? Estimate the incidence of each. Choose all those that apply				
Succinylcholine				
Never	85 (97.7%)	42 (95.45%)	43 (100%)	0.494
Rarely	2 (2.3%)	2 (4.55%)	0	
Often	-	-	-	
Very often	-	-	-	
Rocuronium				
Never	5 (5.75%)	0	5 (11.63%)	0.088
Rarely	7 (8.05%)	5 (11.36%)	2 (4.65%)	
Often	23 (26.44%)	12 (27.27%)	11 (25.58%)	
Very often	52 (59.77%)	27 (61.36%)	25 (58.14%)	
Vecuronium				
Never	82 (94.25%)	43 (97.73%)	39 (90.7%)	0.234
Rarely	4 (4.6%)	1 (2.27%)	3 (6.98%)	
Often	0	0	0	
Very often	1 (1.15%)	0	1 (2.33%)	
Cis-atracurium				
Never	17 (19.54%)	9 (20.45%)	8 (18.6%)	0.38
Rarely	30 (34.48%)	14 (31.82%)	16 (37.21%)	
Often	24 (27.59%)	10 (22.73%)	14 (32.56%)	
Very often	16 (18.39%)	11 (25%)	5 (11.63%)	
Atracurium				
Never	56 (64.37%)	25 (56.82%)	31 (72.09%)	0.479
Rarely	17 (19.54%)	10 (22.73%)	7 (16.28%)	
Often	10 (11.49%)	6 (13.64%)	4 (9.3%)	
Very often	4 (4.6%)	3 (6.82%)	1 (2.33%)	
Pancuronium				
Never	87 (100%)			
Rarely	-			
Often	-			
Very often	-			
None of the above				
Never	74 (85.06%)	43 (97.73%)	31 (72.09%)	0.003*
Rarely	8 (9.2%)	1 (2.27%)	7 (16.28%)	
Often	4 (4.6%)	0	4 (9.3%)	
Very often	1 (1.15%)	0	1 (2.33%)	
Would you use neuromuscular blocking agents to intubate a patient with anticipated difficult intubation?				

Contd...

Table 4: Contd...

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
No	19 (21.84%)	10 (22.73%)	9 (20.93%)	0.999
Yes	68 (78.16%)	34 (77.27%)	34 (79.07%)	
I don't know/no answer	-	-	-	
If yes, which of the following neuromuscular blocking agents do you use to intubate a patient with anticipated difficult intubation? Estimate the incidence of each. Choose all that apply				
Succinylcholine				
Never	35 (40.23%)	17 (38.64%)	18 (41.86%)	0.768
Rarely	16 (18.39%)	10 (22.73%)	6 (13.95%)	
Often	17 (19.54%)	8 (18.18%)	9 (20.93%)	
Very often	19 (21.84%)	9 (20.45%)	10 (23.26%)	
Rocuronium				
Never	26 (29.89%)	13 (29.55%)	13 (30.23%)	0.981
Rarely	14 (16.09%)	7 (15.91%)	7 (16.28%)	
Often	22 (25.29%)	12 (27.27%)	10 (23.26%)	
Very often	25 (28.74%)	12 (27.27%)	13 (30.23%)	
Vecuronium				
Never	87 (100%)			
Rarely	-			
Often	-			
Very often	-			
Cis-atracurium				
Never	85 (97.7%)	44 (100%)	41 (95.35%)	0.241
Rarely	1 (1.15%)	0	1 (2.33%)	
Often	1 (1.15%)	0	1 (2.33%)	
Very often	-	-	-	
Atracurium				
Never	85 (97.7%)	44 (100%)	41 (95.35%)	0.241
Rarely	1 (1.15%)	0	1 (2.33%)	
Often	1 (1.15%)	0	1 (2.33%)	
Very often	-			
Pancuronium				
Never	87 (100%)			
Rarely	-			
Often	-			
Very often	-			

*Significance (P<0.05)

17.2% of respondents stated that the dose of sugammadex is dependent on the last dose of the neuromuscular blocking drug, whereas others administer 1 or 4 mg/kg (11.4 and 10.3%, respectively). The dose of 16 mg/kg was not reported to be used [Table 5].

Sugammadex was preferred in special patient groups (73.5%), in operations of small duration (51.7%), and in most cases when rocuronium was administered (37.9%). Fewer respondents seemed to worry about sugammadex's adverse effects compared with neostigmine (37.9% vs. 88.5%). The most worrisome adverse effects were anaphylaxis (60.9%), cardiovascular (31.7%), inadequate reversal (31.7%), respiratory (14.6%), and nausea/vomiting (7.3%).

Discussion

Various studies have demonstrated the importance of the appropriate use, antagonism, and monitoring of neuromuscular blockade to prevent adverse effects, including the occurrence of postoperative RNMB.^[1-5,15-26] This study details the real-life clinical practice of neuromuscular blockade in Greece, where almost all current available neuromuscular blocking agents and antagonists are available.

The response rate of this survey was low, reaching 7.9% of the total number of questionnaires sent and 15% of those that were read. The results of similar studies are conflicting, with large variation exhibited between surveys around the world.

Table 5: Reversal strategies

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
When a nondepolarizing neuromuscular blocking drug has been used, do you always administer a reversal agent at the end of surgery?				
No	23 (26.44%)	10 (22.73%)	13 (30.23%)	0.473
Yes	64 (73.56%)	34 (77.27%)	30 (69.77%)	
I don't know/no answer-		-	-	
If the answer to the above question was "No," what is the percentage of cases not given a reversal agent?				
1%-25%	81 (93.1%)	43 (97.73%)	38 (88.37%)	0.142
26%-50%	3 (3.45%)	0	3 (6.98%)	
51%-75%	3 (3.45%)	1 (2.27%)	2 (4.65%)	
76%-100%	-	-	-	
If you choose not to administer a reversal agent, which of the following factors contributes to that decision? Choose all that apply				
Time since the last dose of non-depolarizing neuromuscular blocking agent	47 (79.66%)	23 (82.14%)	24 (77.42%)	0.752
Absence of fade when using a conventional nerve stimulator	23 (38.98%)	12 (42.86%)	11 (35.48%)	0.602
Measurement of TOF ratio	31 (52.54%)	13 (46.43%)	18 (58.06%)	0.439
Absence of clinical signs of weakness	40 (67.8%)	20 (71.43%)	20 (64.52%)	0.591
Use of a specific nondepolarizing neuromuscular blocking drug	24 (40.68%)	10 (35.71%)	14 (45.16%)	0.597
Other		(I always administer reversal)		
Do you think that the clinical signs, such as the ability to sustain a 5-s head lift, are reliable indicators of the adequacy of neuromuscular recovery?				
Totally agree	20 (22.99%)	14 (31.82%)	6 (13.95%)	0.012*
Agree	40 (45.98%)	23 (52.27%)	17 (39.53%)	
Disagree	19 (21.84%)	4 (9.09%)	15 (34.88%)	
Totally disagree	7 (8.05%)	3 (6.82%)	4 (9.3%)	
I don't know/no answer	1 (1.15%)	0	1 (2.33%)	
Do you think that a sustained response to a 50 Hz tetanic stimulation reflects the adequacy of the recovery of the neuromuscular function?				
Totally agree	19 (21.84%)	14 (31.82%)	5 (11.63%)	0.051
Agree	20 (22.99%)	10 (22.73%)	10 (23.26%)	
Disagree	19 (21.84%)	5 (11.36%)	14 (32.56%)	
Totally disagree	12 (13.79%)	5 (11.36%)	7 (16.28%)	
I don't know/no answer	17 (19.54%)	10 (22.73%)	7 (16.28%)	
In your department which of the following neuromuscular reversal agents are available?				
Neostigmine	87 (100%)	-	-	
Sugammadex	85 (97.75%)	42 (95.45%)	43 (100%)	0.494
When using rocuronium, how often do you administer the following?				
Neostigmine				
Never	17 (19.54%)	11 (25%)	6 (13.95%)	0.531
Rarely	29 (33.33%)	15 (34.09%)	14 (32.56%)	
Often	31 (35.63%)	13 (29.55%)	18 (41.86%)	
Very often	10 (11.49%)	5 (11.36%)	5 (11.63%)	
Sugammadex				
Never	4 (4.6%)	2 (4.55%)	2 (4.65%)	0.532
Rarely	21 (24.14%)	9 (20.45%)	12 (27.91%)	
Often	23 (26.44%)	10 (22.73%)	13 (30.23%)	
Very often	39 (44.83%)	23 (52.27%)	16 (37.21%)	
When using neostigmine, how much time do you allow from time of administration of neostigmine to extubation?				
<2 min	14 (16.09%)	9 (20.45%)	5 (11.63%)	0.716
3-5 min	46 (52.87%)	23 (52.27%)	23 (53.4%)	
6-10 min	22 (25.29%)	10 (22.73%)	12 (27.91%)	
>10 min	5 (5.75%)	2 (4.55%)	3 (6.98%)	

Table 5: Contd...

	Total (n=87)	PACU		P
		No (n=44)	Yes (n=43)	
At what TOF count do you think that neostigmine would lead to a rapid and reliable reversal?				
1-2	22 (25.29%)	13 (29.55%)	9 (20.93%)	0.447
3-4	32 (36.78%)	17 (38.64%)	15 (34.88%)	
Any response to neuromuscular stimulation	0	0	0	
What matters is the TOF ratio (%)	33 (37.93%)	14 (31.82%)	19 (44.19%)	
What is the dose of neostigmine that you usually administer?				
2.5 mg	66 (75.86%)	35 (79.55%)	31 (72.09%)	0.857
<0.05 mg/kg	5 (5.75%)	2 (4.55%)	3 (6.98%)	
0.05 mg/kg	10 (11.49%)	4 (9.09%)	6 (13.95%)	
>0.05 mg/kg	6 (6.9%)	3 (6.82%)	3 (6.98%)	
When using antimuscarinic/anticholinergic drugs, do you have any concern regarding their potential adverse effects?				
No	10 (11.49%)	7 (15.91%)	3 (6.98%)	0.314
Yes	77 (88.51%)	37 (84.09%)	40 (93.02%)	
I don't know/no answer	-	-	-	
If yes, what are they? Choose all that apply (no vs yes)				
Cardiovascular effects	60 (82.19%)	28 (82.35%)	32 (82.05%)	0.999
Respiratory effects	38 (52.05%)	18 (52.94%)	20 (51.28%)	0.999
Increased nausea and vomiting	26 (35.62%)	11 (32.35%)	15 (38.46%)	0.631
Inadequate reversal of neuromuscular blockade	38 (52.05%)	17 (50%)	21 (53.85%)	0.816
Other		Increase of respiratory secretions, anticholinergic syndrome in the elderly		
In your opinion, at what TOF count would sugammadex lead to a rapid and reliable reversal?				
0-2	31 (35.63%)	19 (43.18%)	12 (27.91%)	0.342
3-4	9 (10.34%)	4 (9.09%)	5 (11.63%)	
Any response to neuromuscular stimulation	47 (54.02%)	21 (47.73%)	26 (60.47%)	
What is the dose of sugammadex do you most commonly administer?				
1 mg/kg	10 (11.49%)	7 (15.91%)	3 (6.98%)	0.538
2 mg/kg	36 (41.38%)	16 (36.36%)	20 (46.51%)	
4 mg/kg	9 (10.34%)	5 (11.36%)	4 (9.3%)	
16 mg/kg	0	0	0	
Depends on the time of the last dose of neuromuscular blocking agent	15 (17.24%)	9 (20.45%)	6 (13.95%)	
Dose depends on TOF ratio	17 (19.54%)	7 (15.91%)	10 (23.26%)	
In which of the following cases would you choose to use sugammadex? Select all that apply				
In surgical cases of short duration	45 (51.72%)	24 (54.55%)	21 (48.84%)	0.67
Patients with specific comorbidities (obesity, elderly, chronic respiratory disease)	64 (73.56%)	30 (68.18%)	34 (79.07%)	0.332
Always when rocuronium is administered	33 (37.93%)	21 (47.73%)	12 (27.91%)	0.077
Other		Emergency operations, operations during night shifts, ENT operations, pediatric surgeries (adenoidectomies), reversal of neuromuscular blockade by rocuronium at a dose >1.2 mg/kg for rapid sequence intubation, cases of difficult airway/intubation		
Do you have any concerns about the adverse effects associated with the administration of sugammadex?				
No	52 (59.77%)	26 (59.09%)	26 (60.47%)	0.458
Yes	33 (37.93%)	18 (40.91%)	15 (34.88%)	
I don't know/no answer	2 (2.3%)	0	2 (4.65%)	
What adverse effects associated with the administration of sugammadex are of concern? Choose all that apply (no vs yes)				
Cardiovascular effects	13 (31.71%)	5 (27.78%)	8 (34.78%)	0.742

Contd...

Table 5: Contd...

		Total (n=87)	PACU		P
			No (n=44)	Yes (n=43)	
Respiratory effects		36 (14.63%)	3 (16.67%)	3 (13.04%)	0.999
Nausea and vomiting		3 (7.32%)	2 (11.11%)	1 (4.35%)	0.573
Anaphylaxis		25 (60.98%)	12 (66.67%)	13 (56.52%)	0.54
Inadequate reversal of neuromuscular blockade		13 (31.71%)	4 (22.22%)	9 (39.13%)	0.321
Other		-			
The appropriate TOF ratio prior to extubation should be					
61%-70%	12 (13.79%)	37 (43.2)	9 (20.45%)	3 (6.98%)	0.058
71%-80%	9 (10.34%)		4 (9.09%)	5 (11.63%)	
81%-90%	16 (18.39%)		4 (9.09%)	12 (27.91%)	
91%-100%	42 (48.28%)		21 (47.73%)	21 (48.84%)	
Knowing TOF ratio before extubation is not important	8 (9.2%)		6 (13.64%)	2 (4.65%)	

Descriptive statistical analysis in the total number of respondents and according to the presence/absence of a Post-Anesthesia Care Unit (PACU) at the Department. Description of statistics: Absolute and relative frequencies (%). Statistical tests applied: Fisher's exact test. *Significance (P<0.05)

In a study by Naguib *et al.*, the questionnaire was available online for 60 days, and the response rate was 40.1% for the United States and 15.6% for Europe. Similarly, the Australia and New Zealand's survey^[7] revealed a response rate of 21%. In contrast, the Italian survey^[9,10] revealed a response rate of 88.7%, but this might be because the questionnaire was distributed during a national congress. These differences may be attributed to the methodological issues, the distribution method, or social and cultural differences interfering with the interest in participating. In Greece, it seems that anesthesiologists with less experience, who are likely younger, were most inclined to respond, whereas those with higher positions at the departments and more experience were in the minority. This might be due to a heavier workload, the absence of interest in surveys, or the general disappointment of doctors in the Greek region due to the economic crisis and the recession of the last decade, reflecting general negativity. However, since the response rate is in accordance with previous studies,^[6,7] it can be considered acceptable, albeit low. The members of the Hellenic Society of Anaesthesiology represent the majority of anesthesiologists in Greece, and therefore can be considered a representative sample of current clinical practice, including public as well as private healthcare facilities.

Regarding the type of neuromuscular blocking drugs used in Greece, nearly all are available, except for mivacurium and pancuronium. For the clinical management of anticipated difficult airways, it is of interest that most respondents reported using rocuronium, with succinylcholine being the second choice. Naguib *et al.*^[6] also revealed that succinylcholine continues to be used in both Europe and United States for endotracheal intubation, with percentages being very high (reaching 85.8% and 92.8%, respectively) and not restricted to cases of difficult airway.^[6]

Reversal of neuromuscular blockade was most commonly performed using neostigmine. Although it was available in all departments, its dose seems to be standardized to 2.5 mg and not calculated per kg of body weight nor guided by neuromuscular monitoring. This is in accordance with the survey conducted by Naguib *et al.*,^[6] wherein the dose of neostigmine was also revealed to be 2.5 mg across most of Europe, but mainly calculated based on body weight in the United States. It is also interesting to note that neostigmine was not administered on time for its maximum effect.^[20-22] So, the fixed dose of neostigmine, combined with the fact that most anesthesiologists seem to extubate patients < 10 min after administration and do not rely on TOF count as a measure of the adequacy of neuromuscular function, indicates an increased risk for postoperative RNMB.

Only 19.54% of the respondents stated that the use of sugammadex was supported by TOF monitoring, even when used in special patient groups or in operations of short duration.^[20-22] A fixed dose of sugammadex was also used by most participants, without titration. In contrast, some respondents stated that the dose of sugammadex was only guided by the last dose of neuromuscular blocker, whereas others used a dose of 1 mg/kg. It is of certain that the use of sugammadex alone does not preclude RNMB^[23] if it is not appropriately administered. These findings are in accordance with a previous study,^[24] indicating an oversimplification of the dose of sugammadex, with a wide variation in clinical practices. Most anesthesiologists used the standard dose of 200-mg sugammadex without adjustment based on TOF-count or on body weight, posing a problem for patients who are overweight or who present with co-morbidities. This leads to underdosing or overdosing, respectively. The same result was reported by Lebowski *et al.*, who found that sugammadex was often mildly overdosed, with 200 mg being the most common "standard" dose.^[25] This oversimplification of the doses of

both, sugammadex and neostigmine, is equally dangerous, since it is not adjusted to body weight and does not prevent residual neuromuscular blockade.

Another significant point of interest revealed was that the majority of anesthesiologists (93.1%) stated that they omit reversal in only 1%–25% of cases, whereas in the United States and Europe, the relevant percentage was 57.5% and 38.3%.^[6] This is likely because in Greece, the application of neuromuscular monitoring is very low; thus, the level of neuromuscular function is not routinely assessed before extubation to omit reversal in selected cases. The criteria for extubation were conflicting and require a closer look. Almost half of the participants answered that they use a TOF ratio of >0.9 for extubation. This indicates that the other half of the respondents use different criteria, indicating inadequate knowledge about monitoring devices and management of reversal. In fact, most respondents stated that they use only clinical signs for extubation (68.9%), or they extubate at a TOF of <0.8 (24.1%) and <0.9 (42.5%). In contrast, in the study by Naguib *et al.*,^[6] the majority of respondents answered that a TOF >0.9 is required in both the United States and Europe. In a similar survey in Australia and New Zealand,^[7] the findings were more similar to ours, with only 25% of the respondents stating that the TOF should be >0.9 for safe extubation and 52% using only clinical criteria. Surprisingly, in the Italian survey 73% stated that they also use only clinical signs for the assessment of neuromuscular function.^[10]

Naguib *et al.*^[6] also reported that most anesthesiologists (78%) knew that a sustained response to a tetanic stimulus could not exclude the presence of neuromuscular weakness, whereas in Greece, only 35.63% knew that, and 19.54% did not know what to answer. Knowledge of different types of monitoring, depending on the type of devices each department owns, is mandatory in order to prevent RNMB. Although it was revealed that most departments owned at least one monitoring device, they were not appropriately used. The recent AAGBI guidelines clearly state that peripheral nerve stimulators are mandatory for all patients who receive neuromuscular blocking drugs from induction of anesthesia until recovery and return of consciousness.

Another major issue revealed was that the presence of a structured PACU, as supported by the ASA and ESA guidelines,^[19,20] was not reported in all Departments. This issue was correlated with significantly less recognition of RNMB. The observed RNMB was revealed to be 44.8%, whereas in the survey in Europe and United States,^[6] a high percentage of respondents stated that they had never observed RNMB (88.1% in the United States vs 78.6% in Europe). The presence of a structured PACUs played a major role.

After careful consideration of these findings, our major concern continues to be residual neuromuscular blockade, since extubation is still often performed using clinical criteria or an inadequate TOF-ratio. The significance of recognizing and preventing the occurrence of RNMB has been clearly recognized during the last decade^[1-5] due to its various complications, such as increased perioperative morbidity and mortality, dysfunction of the upper airway muscles, increased risk of aspiration, and increased postoperative pulmonary complications.^[1-5]

This study is not without limitations. First of all, the low response rate, which probably indicates the low interest of anesthesiologists in such surveys. Furthermore, since the response was anonymous, completion bias cannot be excluded. Although we included questions addressing limitations reported in other studies^[6-10] in order to develop a more complete questionnaire, a validation of the instrument was not performed prior to administration.

The results of this survey have been used to develop national guidelines regarding the management of neuromuscular blockade in Greece. Our primary findings, such as the low response rate, the use of clinical criteria to determine reversal and extubation, the absence of monitoring, and the incorrect usage of reversal agents, reveal the main points that must be addressed. The Hellenic Society of Anaesthesiology guidelines on the management of neuromuscular blockade have been completed and are available online.

Our results reveal great variability in clinical practice regarding neuromuscular blockade and antagonism. The worrisome observations that only a small percentage of anesthesiologists use neuromuscular monitoring for reversal and that doses of reversal agents are not appropriately calculated require further focus and thought. It is of great importance to point out the necessity of adequate use of neuromuscular blocking drugs in everyday clinical practice, the correct dosing and use of antagonists, regardless of the type used, calculated per kg of body weight and not administered at fixed doses, and also the requirement of neuromuscular monitoring, especially in patients with severe comorbidities or whenever subsequent doses of neuromuscular blockers are being used. The needs for educating anesthesia providers and developing official guidelines are, therefore, obvious to reduce the overall incidence of residual postoperative neuromuscular blockade and to improve patient outcomes.

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Conflicts of interest

There are no conflicts of interest.

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