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SCIENTIFIC ARTICLE

Use of neuromuscular blockers in Brazil



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KEYWORDS

Neuromuscular blockers;
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Abstract The objective of this study was to evaluate how Brazilian anesthesiologists are using neuromuscular blockers, focusing on how they establish the diagnosis of postoperative residual curarization and the incidence of complications associated with the use of neuromuscular blockers. A questionnaire was sent to anesthesiologists inviting them to participate in the study. The online data collection remained open from March 2012 to June 2013. During the study period, 1296 responses were collected. Rocuronium, atracurium, and cisatracurium were the main neuromuscular blockers used in cases of elective surgery. Succinylcholine and rocuronium were the main neuromuscular blockers used in cases of emergency surgery. Less than 15% of anesthesiologists reported the frequent use of neuromuscular function monitors. Only 18% of those involved in the study reported that all workplaces have such a monitor. Most respondents reported using only the clinical criteria to assess whether the patient is recovered from the muscle relaxant. Most respondents also reported always using some form of neuromuscular blockade reversal. The major complications attributed to neuromuscular blockers were residual curarization and prolonged blockade. Eighteen anesthesiologists reported death attributed to neuromuscular blockers. Residual or prolonged blockade is possibly recorded as a result of the high rate of using clinical criteria to diagnose whether the patient has recovered or not from motor block and, as a corollary, the poor use of neuromuscular transmission monitors in daily practice.
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PALAVRAS-CHAVE

Bloqueadores neuromusculares;
Pesquisas sobre serviços de saúde;
Monitoração neuromuscular

Uso de bloqueadores neuromusculares no Brasil

Resumo O objetivo desta pesquisa foi avaliar como os anestesiológicos brasileiros estão usando os bloqueadores neuromusculares (BNM), com foco na forma de estabelecer o diagnóstico da curarização residual pós-operatória e a incidência de complicações atribuídas ao uso de BNM. Um questionário foi enviado a anestesiológicos convidando-os a participar da pesquisa (tabela 1). A coleta online de dados permaneceu aberta de março de 2012 a junho

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de 2013. Durante o período de estudo foram coletadas 1.296 respostas. Rocurônio, atracúrio e cisatracúrio foram os principais bloqueadores neuromusculares usados em casos de cirurgia eletiva. Succinilcolina e rocurônio foram os principais BNM usados em casos de cirurgia de emergência. Menos de 15% dos anesthesiologistas referiram que usam frequentemente monitores da função neuromuscular. Apenas 18% dos envolvidos no estudo referiram que todos os locais de trabalho têm tal monitor. A maioria dos entrevistados afirmou que usa somente o critério clínico para avaliar se o paciente está recuperado do relaxante. A maioria dos entrevistados também relatou que sempre usa algum tipo de reversão de bloqueio neuromuscular. As principais complicações atribuídas aos BNM foram curarização residual e bloqueio prolongado. Houve relato por 18 anesthesiologistas de óbito atribuído a BNM. O bloqueio residual ou prolongado se registra, possivelmente, como consequência do alto índice do uso de critérios clínicos para diagnosticar se o paciente está recuperado ou não do bloqueio motor e, como um corolário, o baixo uso de monitores da transmissão neuromuscular na prática diária.

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Introduction

Postoperative residual curarization (PORC) is a complication of considerable impact and proven side effects, sometimes potentially life-threatening.¹⁻⁶

The diagnosis of deep relaxation degrees at the end of anesthesia can be done with the use of bedside tests; however, curare residual blocks are only detected with the use of neuromuscular transmission (NMT) objective monitoring by train-of-four (TOF) and accelerometry.⁷⁻¹¹ Although there is a consensus in the literature on how to diagnose, as well as the consequences of this complication, the frequency of using NMT monitors remains very low, even in developed countries.¹²⁻¹⁴

The objective of this study was to evaluate how Brazilian anesthesiologists are using neuromuscular blockers (NMB), focusing on how to establish the diagnosis of PORC and the incidence of complications associated with the use of NMB, and compare the results with those obtained in a similar survey 10 years ago in Brazil¹⁵ (Table 1).

Method

After approval by the Human Research Ethics Committee under the protocol # 2205/2011, an e-mail was sent to anesthesiologists registered in the database of the Brazilian Society of Anesthesiology and Anestech, inviting members to participate in the survey "Use of neuromuscular blockers in Brazil". In the email message body, participants were informed that participation was not mandatory, the collection of responses would be anonymous and data would be confidential and untraceable. The questionnaire consisted of 10 questions, 2 about demographics and 8 about the choice of using NMB, neuromuscular function monitoring, blockade reversal, and complications associated with the use of these drugs.

The participants accessed a link to a website for online data collection (Survey Monkey, USA). Data collection remained open from March 2012 to June 2013. To increase the response rate, three invitations were sent to the participants. Data are presented as frequency (percentage).

Results

The invitation to participate in the survey was sent to 9910 anesthesiologists. During the study period, 1296 responses were collected.

Regarding the years in practice of anesthesiology, there was a predominance of anesthesiologists with over 11 years of practice (53.8%); 30.7% and 15.5% of responders with up to 5 years of specialty and between 6 and 10 years, respectively.

Most participants were from the Southeast region (52.4%), followed by participants from the South (20.6%), Northeast (15.6%), Midwest (8.4%), and North (3%) regions.

Most anesthesiologists who responded to the questionnaire reported that rocuronium, atracurium, and cisatracurium were the main NMB used in cases of elective surgery. These data are shown in Fig. 1.

Most anesthesiologists indicated that succinylcholine and rocuronium were the main NMB used in cases of emergency surgery. Data are shown in Fig. 2.

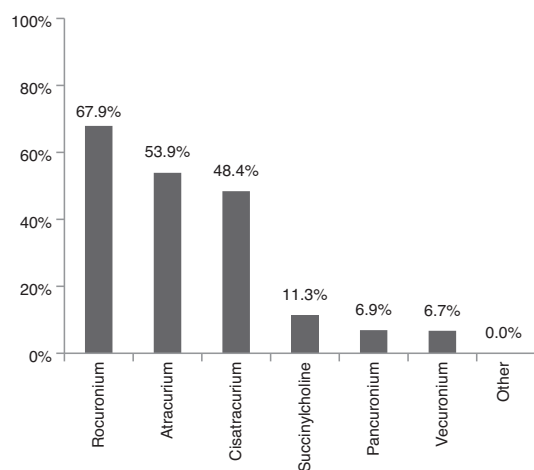


Figure 1 Most commonly used NMB for tracheal intubation in cases of elective surgery. Total of 1296 responses.

Table 1 Questionnaire sent to survey participants.

1. How many years have you been in practice of anesthesiology?
 - Up to 5 years
 - Between 6 and 10 years
 - Over 11 years
2. What is the region where you exercise your occupation?
 - North
 - Northeast
 - Midwest
 - Southeast
 - South
3. Check the two (2) neuromuscular blockers you use most for tracheal intubation in cases of elective surgery.
 - Atracurium
 - Cisatracurium
 - Rocuronium
 - Vecuronium
 - Pancuronium
 - Succinylcholine
 - Other
4. Check the two (2) neuromuscular blockers you use most for tracheal intubation in cases of emergency surgery.
 - Cisatracurium
 - Rocuronium
 - Vecuronium
 - Pancuronium
 - Succinylcholine
 - Others
5. Regarding the use of neuromuscular transmission monitor:
 - Never
 - Rarely
 - Sometimes
 - Often
6. Hospital(s) in which you work:
 - All have the TOF neuromuscular transmission monitor
 - Some have the TOF neuromuscular transmission monitor
 - None has the TOF neuromuscular transmission monitor
7. As a criterion "the patient has recovered from the muscle relaxant", you use:
 - Only the clinical criteria only
 - Only the TOF neuromuscular transmission monitor
 - The clinical criteria and the TOF neuromuscular transmission monitor
8. Do you use any type of neuromuscular blockade reversal (neostigmine or sugammadex)?
 - Always
 - It depends on the outcome of the TOF monitor
 - I do not use
9. Have you ever had any complication that you assigned to the muscle relaxant?
 - Prolonged blockade
 - Residual curarization
 - Severe bronchospasm
 - Allergic reaction

Table 1 (Continuación)

- Prolonged apnea after succinylcholine
 - Malignant hyperthermia
 - Serious cardiac dysrhythmias
 - Recurarization
10. If you checked any condition in question 9, in the case considered most serious, the patient:
- Without sequelae
 - With sequelae that I considered mild/moderate
 - With sequelae
 - With death

Less than 15% of anesthesiologists who participated in the study said they often use neuromuscular function monitor (Fig. 3). Only 18% of respondents reported that all work-places have such a monitor (Fig. 4).

Regarding the reversal of neuromuscular blockade at the end of anesthesia, the majority of respondents said that they use only the clinical criteria to assess whether the patient has recovered from the muscle relaxant. Most respondents also reported always using some sort of neuromuscular blockade reversal agent (neostigmine or sugammadex) at the end of anesthesia. Data are shown in Figs. 5 and 6.

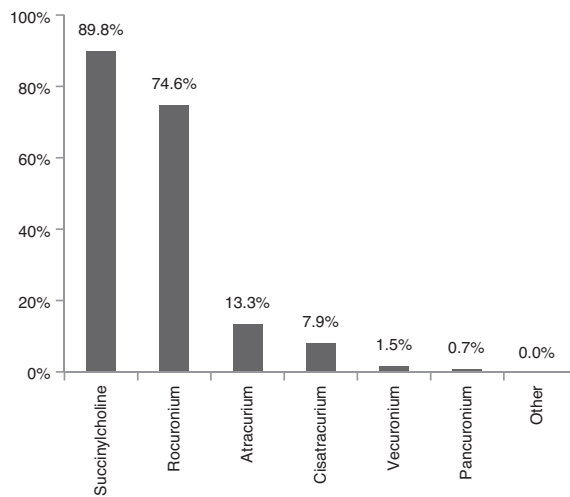


Figure 2 Most commonly used NMB for tracheal intubation in cases of emergency surgery. Total of 1294 responses.

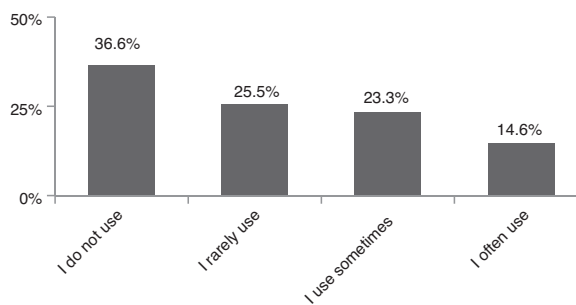


Figure 3 Standard use of neuromuscular function monitor. Total of 1296 responses.

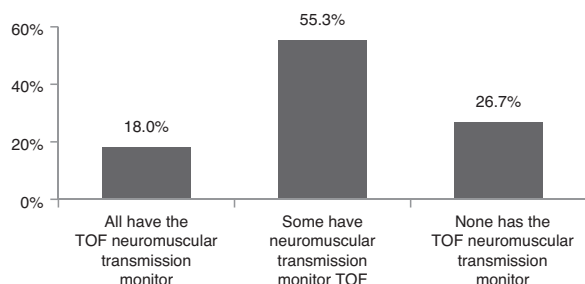


Figure 4 Availability of TOF neuromuscular transmission monitor at the workplaces of 1292 anesthesiologists.

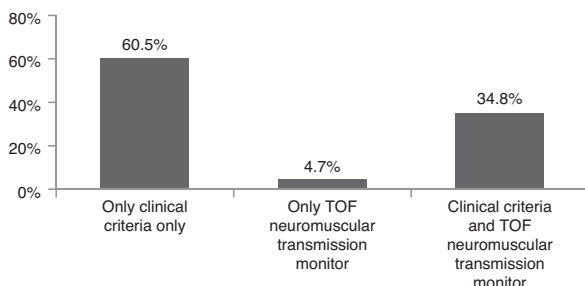


Figure 5 Criterion used to evaluate patient recovery after neuromuscular blockade by 1291 anesthesiologists.

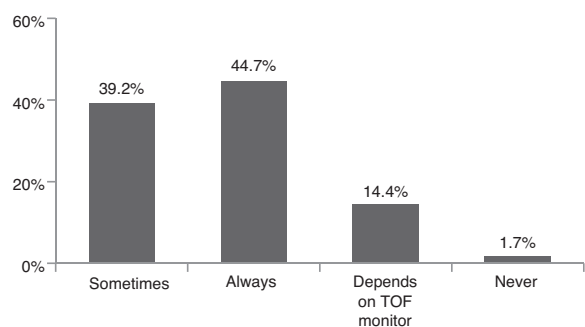


Figure 6 Use of neuromuscular blockade reversal (sugamdemax or neostigmine) at the end of anesthesia. Total of 1296 responses.

The complications associated with the use of NMB are described in Fig. 7. Residual curarization and prolonged blockade were the main complications. Most respondents indicated that patients evolved without sequelae after complications, but 18 anesthesiologists reported death associated with NMB (Fig. 8).

Discussion

In this study, 13% of questionnaires were completed (1296 of 9910 questionnaires sent). We found a percentage of responses similar to Naguib et al.,¹⁶ whose percentage was 10% (1792 of 17,870) in the United States and 15% (844 of 4807) in Europe. Phillips et al.,¹⁷ in Australia and New Zealand, reported a slightly higher number in percentage terms (21%). However, the total number of respondents was limited to 678.

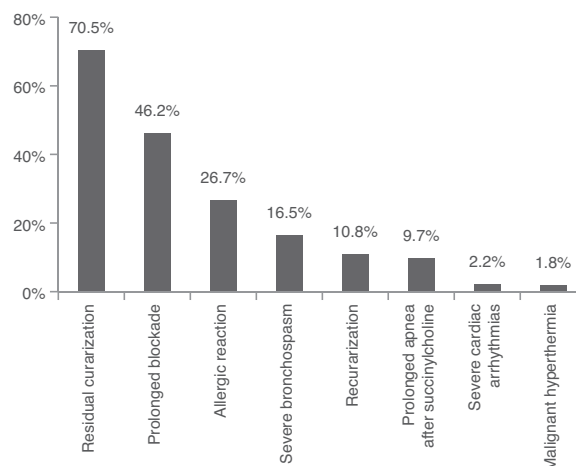


Figure 7 Complications attributed to the use of NMB by 1160 anesthesiologists.

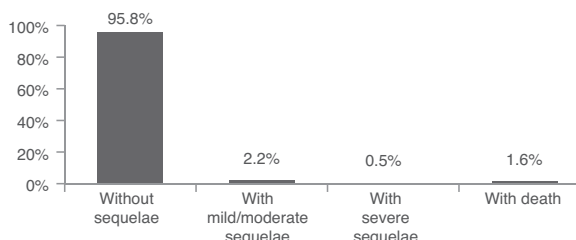


Figure 8 Evolution of patients with complications attributed to the use of NMB. Total of 1156 responses.

Main NMB used

The main NMB used in Brazil for elective surgical procedures are rocuronium, atracurium, and cisatracurium. Results reported in a previous study showed that the NMB commonly used 10 years ago were atracurium, pancuronium, and succinylcholine.¹⁵ In other parts of the world its use is slightly different. Naguib et al.¹⁶ reported that, in Europe, the three most commonly used neuromuscular blocking agents are rocuronium (75%), atracurium (49%), and succinylcholine (47%) and, in the United States, rocuronium (89%), vecuronium (63%), and atracurium (47%). Specifically in France, the most used NMB are atracurium and cisatracurium.¹⁸ We could say that, in the USA, there is a greater tendency toward using steroidal NMB, whereas in France are the benzylisoquinoline neuromuscular blocking agents. In Brazil there is a more even distribution of both steroidal NMB and benzylisoquinoline agents. We could explain this difference between countries by market supply reasons and the incidence of adverse effects, particularly anaphylactic reactions, which seem to be different in different parts of the world.^{19–22}

Emergency tracheal intubation

Succinylcholine remains the drug of choice by respondents for emergency tracheal intubation, a result similar to that found in a previous study,¹⁵ with rocuronium as a second option currently. The same result was found by

Eldawlatly et al.²³ in the Middle East and by Naguib et al.¹⁶ in Europe and the USA. This can be explained by the rapid onset of action and the clinical ultrashort duration of succinylcholine. Rocuronium has emerged as an option due to its similar profile of onset of action and especially the possibility of rapid reversal with sugammadex. Sugammadex at a dose of 16 mg kg⁻¹ is able to completely reverse the deep neuromuscular blockade induced by rocuronium in less time than the spontaneous recovery of 1 mg kg⁻¹ dose of succinylcholine.²⁴ With such flexibility of use, it can be supposed that the introduction of sugammadex in the European market is the cause of increased rocuronium consumption in France.¹⁸

Clinical criteria to diagnose the end of the blockade

Most Brazilian anesthesiologists remain using clinical criteria to diagnose the end of muscle relaxation,¹⁵ such as the registered in Australia and New Zealand.¹⁷ This is a questionable conduct, as several authors have shown that the clinical tests alone or in combination have low sensitivity and specificity in the diagnosis of residual neuromuscular blockade.

Residual neuromuscular blockade may be present despite the use of subjective monitors of neuromuscular function, clinical trials, and reversing agents.^{25,26} Only the objective monitoring of neuromuscular function is able to diagnose the degree of residual neuromuscular blockade, and currently it is considered that the T4/T1 ratio by TOF must be equal to or preferably higher than 0.9 to be considered absence of residual neuromuscular blockade. Di Marco et al., in a study of the residual curarization knowledge in Italy, reported that only 24% of anesthesiologists responded that the safe T4/T1 ratio for tracheal extubation was 0.9.²⁷ This result is similar to others reported in Australia and New Zealand, where anesthesiologists considered the T4/T1 ratio ≥ 0.9 as an acceptable criterion for safe tracheal extubation.¹⁷ The present survey results show that in Brazil only 4.6% use only monitor for the diagnosis of muscle relaxation recovery. Probably it is not only due to the outdated scientific knowledge by the anesthesiologist, but also the lack of neuromuscular function monitors.

Monitor use and availability of monitors

This survey showed that only 14% of Brazilian anesthesiologists routinely use objective monitoring of neuromuscular function, a result quite close to that found in Australia and New Zealand (17%)¹⁷ and much lower than the percentage in France, which is 52% when using single dose of NMB and 74% when using maintenance doses.²⁸

In this survey, only 18% of the Brazilian respondents' workplaces have neuromuscular function monitor. These results are similar to those found in the USA (22%) and differ widely from those found in Europe (70%),¹⁶ although in the Brazilian study there is no separation of qualitative and quantitative monitors. In Australia and New Zealand, quantitative neuromuscular function monitors are available in

58% of hospitals where respondents practice anesthesia, a number greater than that found in Brazil.¹⁷

Reversing NMB

Regarding the reversal of neuromuscular blockade, we found that almost half the anesthesiologists always uses reversal agents, either sugammadex or neostigmine. This fact may be a result of the unavailability of NMT monitors in most Brazilian hospitals. However, this approach may be questioned as the use of neostigmine after neuromuscular blockade complete recovery may result in muscle weakness. We found that only 14% stated that the use of reversal agent is conditioned to the results of TOF. This percentage is lower than that found among anesthesiologists in the Middle East²³ and could be explained by the lack of NMT monitors in Brazil.

Complications of using NMB and reversal

The complications most often cited in this survey are the residual neuromuscular blockade followed by prolonged neuromuscular blockade. Esteves et al.²⁹ found an incidence of residual neuromuscular blockade of 26% (TOF < 0.9). This demonstrates that, despite the scientific knowledge of the problem and the use of sugammadex, a high incidence of this complication still remains.³⁰

In Brazil, the use of clinical criteria to monitor the end of neuromuscular blockade and the lack of objective monitoring of NMT may be one of the causes of this problem. In Australia and New Zealand, 71% of respondents in a survey underestimate the incidence of residual curarization.¹⁷

Residual neuromuscular blockade may result in severe clinical complications.^{31,32}

The data of this survey show that 26% reported allergic reactions as a complication of using NMB. Among the agents used in anesthesia, NMB are the ones that cause most anaphylaxis, with a percentage of 58%.^{19,33} The incidence of allergic reactions during anesthesia retrieved from the French national database is greater than the previous estimate.³³ Chong et al. found that NMB were the causative agents of anaphylaxis during general anesthesia in a series of 23 patients with anaphylactic shock.³⁴

Prolonged apnea reported by 9% and serious cardiac arrhythmias by 2% of respondents to this survey are listed in the results of the study by Karanović et al.³⁵ who reported the most common adverse events reported for succinylcholine: myalgia (47%), prolonged blockade (36%), allergic reaction (13%), and asystole (12%). A systematic review by Abrishami et al.³⁶ demonstrated that there is no evidence of differences in the prevalence of adverse events between sugammadex, placebo, or neostigmine.

In this survey, malignant hyperthermia has also been reported as a complication of using NMB by 1.8% of respondents. This demonstrates the concern about this extremely serious complication, with the outcome almost always unfavorable. This information needs further clarification, given that the role of non-depolarizing NMB does not seem to be involved in the pathogenesis of malignant hyperthermia and the role of succinylcholine as a trigger of malignant hyperthermia remains controversial.³⁷

Evolution of patients with complications after the use of NMB

In this survey, the consequences arising from complications of using NMB were considered severe in 0.5% of cases and with death 1.6%. This result demonstrates that the use of NMB may be related to unfavorable outcomes, as demonstrated by Naguib et al.,¹⁶ Eikermann et al.,⁵ and Murphy et al.^{7,38,39} The justification could be found in the very results of this survey: the use of clinical criteria for residual neuromuscular blockade diagnosis, low use and low availability of quantitative NMT monitors, inappropriate use of reversal agents, and possibly the proper inadequate diagnosis and treatment of complications could explain the serious adverse outcomes.

Study limitations

The electronic means used did not reach all recipients, due to spam type mechanism or some outdated e-mails in the database used, which may have hampered the participation of a larger number of anesthesiologists.

We conclude by this survey on the use of NMB in Brazil that the following aspects stood out: succinylcholine is still the most frequently used NMB for emergency situations, the rates of PORC and prolonged muscular block are high, as well as the record of sequelae considered serious or even death as complications of using these drugs. The residual or prolonged blockade is possibly seen as a result of the high rate of using clinical criteria to diagnose whether the patient has recovered or not from motor block and, as a corollary, the low use of NMT monitors in daily practice.

Conflicts of interest

The authors declare no conflicts of interest.

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