

Research article

Preferences of Mexican anesthesiologists for vecuronium, rocuronium, or other neuromuscular blocking agents: a survey

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Abstract

Background: Several neuromuscular blocking (NMB) agents are available for clinical use in anesthesia. The present study was performed in order to identify preferences and behaviors of anesthesiologists for using vecuronium, rocuronium or other NMB agents in their clinical practice.

Material and methods: The cross-sectional survey was applied at the Updated Course of the *Colegio Mexicano de Anestesiología* performed last year. Of 989, 282 (28.5%) surveys were returned.

Results: Most anesthesiologists were working at both public and private hospitals, performed anesthetic procedures for hospitalized and ambulatory patients, and anesthetized children as well as adults. Respondents did not consider mechanomyography as the gold standard method for neuromuscular monitoring. The T_{25} was not recognized as a pharmacodynamic parameter that represents the clinical duration of the neuromuscular block. Most answered that vecuronium induces less histamine release than rocuronium, had never used any neuromuscular monitor, did not know the cost of vecuronium and rocuronium, and preferred rocuronium in multiple-sampling vials and vecuronium in either a vial for single or multiple sampling. Rocuronium was preferred for emergency surgery in patients with full stomach only. Almost all of anesthesiologists that conserve the unused drug did it without refrigeration and more than 30% conserve the unused drug in one syringe for further use.

Conclusion: Vecuronium was preferred for most clinical situations, and the decision for this choice was not based on costs. Storage of unused drugs without refrigeration in a single syringe for purpose of future use in several patients represented a dangerous common practice.

Background

Neuromuscular blockade is an important component of most procedures that require general anesthesia to facili-

tate tracheal intubation and the surgical procedure. Non-depolarizing neuromuscular blocking (NMB) agents are usually preferred because of fewer adverse effects than de-

polarizing drugs [1–3]. According to their chemical structure, two classes of non-depolarizing NMB agents have been available for clinical use, the aminosteroidal (pancuronium, vecuronium and rocuronium) and benzyloisoquinoline drugs (atracurium, mivacurium and cisatracurium). Vecuronium has been used for many years in the clinical setting whereas rocuronium is available in Mexico only since 1999 [4]. Rocuronium has a faster onset of action than vecuronium [5,6], and its metabolites by lacking pharmacological effects avoid any residual neuromuscular block [7]. These characteristics favor rocuronium as a better alternative than vecuronium. In relation to the benzyloisoquinoline drugs, these type of NMB agents produce cardiovascular response and clinical evidence of histamine release even at recommended doses [8,9].

In our country, until 2000 rocuronium was only provided as an ampoule containing 50 mg/5 mL, and since last year the pharmaceutical presentation was modified to a vial containing a similar concentration but allowing multiple sampling. Whereas vecuronium is available in two pharmaceutical presentations, a single-sampling ampoule and a vial allowing multiple sampling. Each of the two presentations has only 4 mg of vecuronium.

It is estimated that 1.4 million of surgical procedures were performed last year at the IMSS [10], and three million of surgical procedures are being performed every year by the Mexican public health care systems [11]. According to cost obtained from different sources, rocuronium is significantly more expensive than vecuronium, therefore, a complete replacement of vecuronium by rocuronium could result into a significant increase in spending. The present survey was performed in order to identify the preferences of anesthesiologists, as primary users, in relation to the use of rocuronium, vecuronium or other NMB agents.

Material and Methods

The survey, printed in the two sides of one letter-size sheet of paper, was developed and validated by a group of four board-certified Mexican anesthesiologists and two epidemiologists. It was attached to the documents given to the 989 persons inscribed to the Annual Course of the *Colegio Mexicano de Anestesiología* (formerly the *Sociedad Mexicana de Anestesiología*) performed in July, last year. Conference participants were encouraged to fill out and return the survey at the end of each conference day during the three days of the course. Of 989, 282 (28.5%) surveys were returned. Data from returned surveys was captured in a pre-designed Microsoft 97[®]Excel form and reported as the number of respondents and proportions. In some cases, numbers could vary according to persons answering any specific question.

The survey included the following four sections:

Section 1: General information.

- 1) Your current maximal specialty training is: anesthesiologist, anesthesiologist with subspecialty training, or anesthesiology resident.
- 2) Have you been practicing anesthesia for < 5, 5 to 10, or >10 years?
- 3) Have you been working at a public, private or both types of health services?
- 4) Are your anesthetic procedures performed in pediatric, adults, or mixed patients? If mixed patients was selected, then the proportion representing the pediatric patients was asked (<25, 25 to 50, 50 to 75 or >75%).
- 5) Are your anesthetic procedures performed on ambulatory, hospitalized or mixed patients? If a mixed setting was selected, then the proportion representing the ambulatory patients was asked (<25, 25 to 50, 50 to 75 or >75%).

Section 2: Basic questions on neuromuscular relaxation.

Questions were elaborated with information obtained from different sources including textbooks [1,12], printed documents obtained by subscription [13], guidelines [14] and web-sites [15]. All sources were available in Spanish language, at any medical library or freely accessed on the Internet.

- 6) Neuromuscular relaxants are classified according to: chemical structure, duration of action, action at the neuromuscular junction or you do not know.
- 7) The pharmacodynamic parameter of T_{25} represents: the time to loss the muscular tone, the time to maximal block, the clinical duration of the neuromuscular block, or you do not know.
- 8) Which of the following methods is considered as the gold standard for neuromuscular monitoring system? Electromyography, mechanomyography, electrophysiology, acceleromyography, or you do not know.
- 9) Which is the recommended dose of rocuronium for any patient undergoing an elective surgery? 150, 300, 600, 900, 1200 $\mu\text{g} \cdot \text{kg}^{-1}$ or you do not know.
- 10) Which produces less histamine liberation: vecuronium, rocuronium, vecuronium and rocuronium in a similar potency, or you do not know?

Section 3: Clinical practice

11) In which percentage of daily surgical procedures do you utilize a neuromuscular blocking drug? In <25, 25 to 50, 50 to 75, or >75%.

12) Do you routinely use any neuromuscular monitoring system and if so, which method do you use?

13) Vecuronium is available for reconstitution in two forms, as an ampoule for single sampling or as a multiple sampling vial. Which one do you prefer?

14) Do you prefer rocuronium as: an ampoule for single sampling, a vial for multiple sampling, any of these two forms, or as a different form?

15) Do you know the unitary cost of vecuronium? Yes or no.

16) Do you know the unitary cost of rocuronium? Yes or no.

17) Have you ever used rocuronium? Yes or no.

SECTION 4: Preferences among rocuronium, vecuronium or other neuromuscular relaxant.

Question: Which neuromuscular blocking drug do you prefer: rocuronium, vecuronium or other NMB agent...?

18) For an ambulatory patient undergoing a surgical procedure of one to two hours of duration.

19) For a low surgical risk (ASA 1) male patient, aged 19 yr., undergoing a septorhinoplasty.

20) For a female patient, 32 years old, suffering appendicitis and undergoing general anesthesia with tracheal intubation for an emergency surgery with full stomach.

21) For a low surgical risk (ASA 1) pediatric patient, 6 yr. old, undergoing a planned surgical repair of a bilateral inguinal hernia of 1.5 h of duration.

SECTION 5: Behaviors in relation to the drug excess after obtaining one dose of either vecuronium or rocuronium.

22) What do you do with the excess of the neuromuscular blocking agent after one dose is obtained, to conserve it in the same syringe, to maintain it in the vial or ampoule, to conserve it in several syringes, or to discharge it?

23) If you conserve unused drug, do you refrigerate it? Yes or no.

Results

Of the 282 respondents, 244 (86.5%) were general anesthesiologists, 37 (13.1%) were anesthesiologists with another postgraduate study, and one resident (0.4%). Most of the anesthesiologists, 231 (81.9%), have been graduated more than 10 years ago, 41 (14.5%) between 5 to 10 years ago and only 10 (3.5%) have been graduated less than 5 years ago. Most worked at both public and private hospitals [n= 158 (56.0%)], but many worked at a public hospital only [n= 119 (42.2%)], and few [n= 5 (1.8%)] worked at a private hospital only.

Most of them, 220 (78.0%), answered that they performed anesthetic procedures in children and adult patients, 62 (22.0%) in adults only and none in children only. Of the 220 anesthesiologists performing anesthetic procedures in children and adults, 195 (88.6%) answered that <25%, 15 (6.8%) that between 25 to 50%, and 10 (4.5%) that >50% of the procedures were performed in children. Of the 282, 272 (96.5%) performed anaesthetic procedures for a combination of hospitalized and ambulatory patients, while 10 (3.5%) only for hospitalized and none provided anesthetic procedures exclusively for ambulatory patients.

With regard to questions related to basic concepts on neuromuscular relaxation, of 282 only 7.8% considered the mechanomyography as the gold standard to measure the neuromuscular response (Table 1). Most of respondents considered that rocuronium 600µg/kg was the recommended dose for an elective surgery. Approximately 40% answered that T₂₅ was a pharmacodynamic parameter representing the clinical duration of the neuromuscular block. Of 280, only 11.4 answered that vecuronium and rocuronium were similar in relation to histamine release, and 85.7% and 2.9% answered that either vecuronium or rocuronium, respectively, induce less histamine release. Furthermore, 75.5% answered they administered a neuromuscular blocking agent in <25% of patients, 28.1% in 25 to 50%, 3.9% in 50 to 75% and 1.8% in >75% of patients.

Of the 282 respondents, 277 (98.2%) have never used any neuromuscular monitor and 45 (16%) have not used rocuronium. In relation to the pharmaceutical presentations of vecuronium and rocuronium, most of the anesthesiologists preferred rocuronium in a vial for multiple sampling and considered that vecuronium could be presented either in a vial for single or multiple sampling (Table 2). Of 281, 249 (88.3%) and 256 (90.8%) did not know the cost of vecuronium and rocuronium, respectively.

In relation to the clinical cases, rocuronium was preferred for tracheal intubation of patients undergoing an emergency surgery with full stomach, while vecuronium was

Table 1: Concepts on neuromuscular monitoring

	Correct	Wrong	Do not know
Which method of neuromuscular monitoring is considered the gold standard?	22 (7.8)	250 (88.7)	10 (3.5)
What does T ₂₅ represent?	112 (39.7)	167 (59.2)	3 (1.1)
Which is the recommended dose of Rocuronium undergoing an elective surgery?	217 (77.0)	65 (23.0)	-
Which produce more histamine liberation, Rocuronium or Vecuronium?	32 (11.4)	240 (85.7)	8 (2.9)

n (%)

Table 2: Preferences of pharmaceutical presentations for rocuronium and vecuronium

	For single use	For multiple sampling	Either for single or multiple sampling	Other form
Vecuronium 4 mg	27 (9.6)	103 (36.5)	96 (52.5)	4 (1.4)
Rocuronium 50 mg	79 (29.1)	156 (55.3)	36 (12.8)	8 (2.8)

n (%)

Table 3: Anesthesiologists preferences to use a NMR in different clinical situations.

	Vecuronium	Rocuronium	Either Vecuronium or Rocuronium	Other
Ambulatory surgery of 1–2 h of duration	266 (94.6)	10 (3.6)	0	5 (1.8)
Patient 19 years old, undergoing an elective rinoseptumplastia under general anesthesia	150 (53.2)	79 (28.0)	40 (14.7)	12 (4.1)
Patient with full stomach undergoing an emergency surgery under general anesthesia	30 (10.7)	160 (56.9)	64 (22.8)	27 (9.6)
Patient 6 years old, ASA I, undergoing general anesthesia for an elective surgery of 1.5 h of duration	161 (57.3)	29 (10.3)	57 (20.3)	34 (12.1)

N= 281 (100%)

preferred for all the other situations also including the pediatric patient (Table 3). Finally, only one third of respondents discharge the drug excess after one dose is obtained, while approximately 25% conserve the excess in a single syringe for purpose of future use in several patients (Table 4).

Discussion

A non-conventional form of questionnaire was used for the present survey. Questions to be answered in a multiple option format, by a simple yes or no, to complete the answer, or to select more than one response were included in different sections. However, our results can be widely supported, e.g. demographic data have also been observed

in two previous surveys performed at the same setting [16,17]. It is estimated that the public health care covers approximately 80% of all the Mexican inhabitants [18], and almost 60% are attended at the *Instituto Mexicano del Seguro Social* (IMSS). Therefore, it was expected that most of the anesthesiologists were working in a combination of the public and private services. Furthermore, to our knowledge only two Mexican pediatric hospitals confer the official certificate of Pediatric Anesthesiologist recognized by the major public health university [19], which in turn provides the official title. At the *Hospital Infantil de México* (HIM) only 1 to 4 residents are graduated each year. It was therefore expected that general anesthesiologists attending both pediatric and adult patients were

dominant. Unfortunately, we could not compare respondents with the general population attending the course due to the fact that data from the latter were not available. Finally, the fact that most of the anesthesiologists had >10 years of clinical practice is positive in relation that they are attending updated courses. However, young anesthesiologists are not. This interesting educational aspect merits further attention in order to stimulate the recently graduated students to attend the continuing education courses.

In relation to the aspects considered as basic concepts for purpose of the study, it is clear that efforts to extend the knowledge on neuromuscular relaxation should be performed. Despite topics in NMB agents are usually included in the course, a more efficient method of dissemination of these concepts is needed. It is alarming that practically none of the anesthesiologists answered that they used any neuromuscular monitoring method. How are Mexican anesthesiologists assessing the advantages of the new neuromuscular blocking drugs without the use of any neuromuscular relaxation monitor? According to the results shown in Table 3, the respondents favored vecuronium in most clinical cases. However, there was an important remaining group that considered rocuronium or either vecuronium or rocuronium as the preferred NMB agent. Probably preferences are being based on clinical experience and observations of success and failure. For example, despite potentially dangerous, Mexican pediatric anesthesiologists have been administering an elevated dose of bupivacaine by caudal block according to a technique described several years ago because it has been safe and effective in their own clinical experience [20]. Despite the intensive publicity, we therefore assume that vecuronium has been replaced by rocuronium in a small percentage of cases because using the former has proven to be safe and effective for a long time. However, we believe that drug promotion to support rational and safe drug utilization instead of drug choices based on custom, conservation, or publicity, should be encouraged and studied in order to prevent an unjustified preference for using the expensive NMB agents with similar efficacy than the older and cheaper drugs. Rational use guidelines can be established for each institution with a direct impact into improving clinical practice and cost of services at short and long terms [21]. Furthermore, the availability of generic drugs may result into a benefit of a high rate of population with low economic resources [22]. In our country, vecuronium is available as a generic drug which in turn is being produced as the potentially best pharmaceutical form.

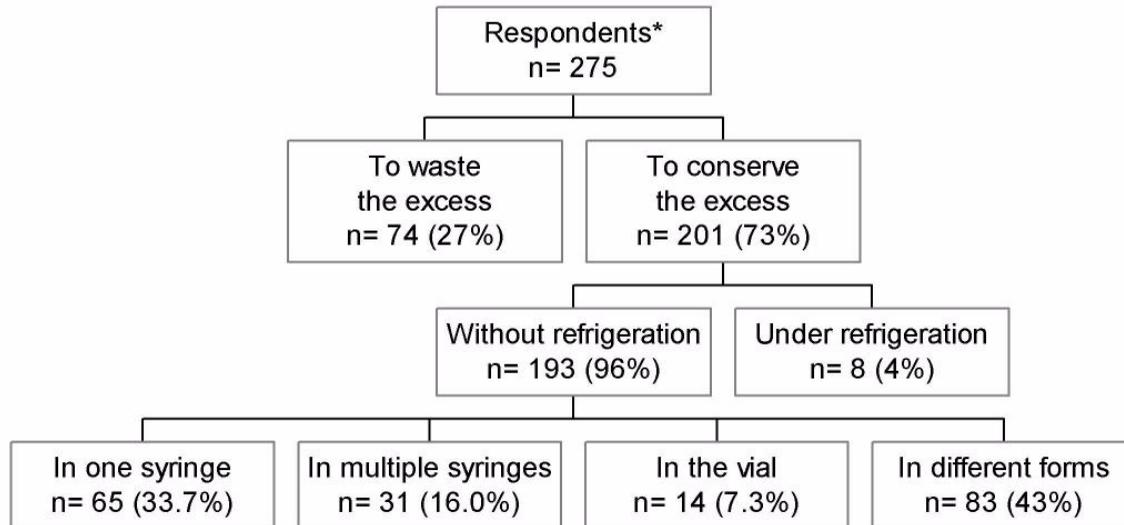
The idea that rocuronium could be used for rapid intubation was present, even if the anesthesiologists did not have any method to corroborate it. Vecuronium was con-

sidered to produce higher histamine liberation than rocuronium. Some NMB agents can induce histamine liberation even at recommended doses, e.g. mivacurium and atracurium [8,9]. However, vecuronium and rocuronium are drugs that practically do not produce histamine liberation even at high doses [9,23], while rocuronium is intermediate in its propensity to cause allergy in known neuromuscular blocking agents reactors compared with vecuronium [24].

In Mexico, we only speak Spanish and do not have a second language. Despite this fact, knowledge of the English language is being evaluated as a prerequisite for postgraduate studies. However, further improvement is obtained by entering private courses usually not required in the workplaces. Therefore, we could hypothesize that information is mainly being searched by our colleagues in national journals or promotional documents provided by pharmaceutical companies. This topic deserves urgent attention in order to promote the availability of updated and unbiased information in Mexican journals.

Approximately 75% of our respondents administered a neuromuscular blocking drug for <25% of surgical procedures. Most of them preferred rocuronium in multiple sampling presentation while allowing vecuronium to be presented either in a single or a multiple sampling vial while ignoring the commercial cost of the two drugs. It is estimated that 1.4 million of surgical procedures were performed last year at the IMSS [10], and three million of surgical procedures are being performed every year by the Mexican public health care systems [11]. According to cost obtained from different sources, rocuronium is between four to seven times more expensive than vecuronium, and a complete replacement of vecuronium by rocuronium could result in significant increases in spending. For example, it would represent US\$30,000 each year at HIM, an amount equivalent to the annual salary of approximately 1.8 pediatric anesthesiologists. Therefore, any increment of budgets for exchanging new for old drugs (e.g. neuromuscular blocking drugs) should be supported by evidence also based on cost-effectiveness studies and not only on efficacy studies.

Rocuronium until 2000 was available in a single sampling vial only. Since last year it is available in a vial for multiple sampling also containing 50 mg. However, the fact that only one pharmaceutical presentation is available for pediatric and adult patients could generate a waste of resources. Furthermore, we considered that rocuronium only available as 50 mg and vecuronium as 4 mg are favoring to conserve the unused drug in some instances under unsatisfactory conditions, i.e. in a single syringe without refrigeration. Although rocuronium conserved at certain ambient conditions is stable for a brief period of



* Respondents to this question

Figure 1

Practice of anesthesiologists in relation to the drug excess after one dose of the NMB agents is obtained.

time, refrigeration is mandatory [6]. However, after the ampoule is broken it is recommended to waste the unused drug. Vecuronium, however, can be stored without refrigeration until reconstitution is performed although conservation is recommended for a period not longer than 24 hours. This can be easily performed when using the vial for multiple sampling.

Furthermore, anesthesiologists preferences in relation to presentation of rocuronium or vecuronium in a vial for single or multiple samplings was certainly not supported by cost-saving attitudes because almost none of the respondents knew the cost of either drug. This year one of the sectors of the IMSS acquired vecuronium for single sampling (personal communication, *Departamento de Adquisiciones, Delegación 3, IMSS*). Despite the fact that this alternative is more expensive than the multiple sampling option, by being designed for single sampling it can

be argued that it might result in fewer dangerous conservation practices. Since our results suggests that dangerous conservation practices are being used, we believe that urgent efforts to educate and to inform anesthesiologists in the correct use of vecuronium and rocuronium are required.

Economical impact cannot be examined if corrections in the clinical practice are not performed, e.g. through the development of guidelines which in turn require participation of practitioners. Rational use guidelines have been shown to result in safe, cost-effective improvement in the provision of analgesia, sedation and neuromuscular blockade to critical ill patients requiring ventilator management [21]. Impact of formulary substitution of e.g. glyburide for glipizide, two hypoglycemic drugs, has resulted in significant (approximately 50%) reduction in overall hospital expenditures [25], and a joint anesthesia-phar-

macy program has produced a cost-saving exceeding US\$950,000 during a 3-year period at an American hospital [26]. In fact, NMB agents are appropriate targets of cost-minimization strategies in anesthesia by different approaches [21,27–31]. Clinical Pharmacology does not formally exist as a postgraduate option in our country, and only one unit formally devoted to pharmacological research is available at the IMSS. At the HIM, the Department of Clinical Pharmacology and the service of Hospital Pharmacy are available although none of their personnel is involved in the activities of the Department of Anesthesiology. Therefore, the lack of such programs in our country might favor a lack of planned and permanent programs designed to identify and solve controversies on drug utilization. For example, drug dispensing by a pharmacy service directly involved within the anesthesiology departments might provide the drug doses in one sterile syringe while the excess is properly conserved.

Finally, according to different surveys some deficiencies have been identified among Mexican anesthesiologist including indication of preoperative fasting periods unnecessary prolonged for adult patients [17], transfusional practices different from international recommendations [32], and conservation of the NMB agents excess in one syringe for using it in multiple patients (current study). We therefore considered that we have a valuable opportunity to implement alternative programs in order to improve anesthetic clinical practices and diminish cost of medical services.

Competing Interests

None declared

Authors' Contributions

AAANO participated in the study design, statistical analysis, data interpretation and manuscript preparation. JCRM participated in the study design and data interpretation and carried out the survey. DMG, JGE and JS participated in the study design, data interpretation and manuscript preparation.

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