

# Anaphylaxis Is More Common with Rocuronium and Succinylcholine than with Atracurium

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## ABSTRACT

**Background:** Intraoperative anaphylaxis is a rare but serious occurrence, often triggered by neuromuscular-blocking drugs (NMBDs). Previous reports suggest that the rates of anaphylaxis may be greater for rocuronium than for other NMBDs, but imprecise surrogate metrics for new patient exposures to NMBDs complicate interpretation.

**Methods:** This was a retrospective, observational cohort study of intraoperative anaphylaxis to NMBDs at two hospitals between 2006 and 2012. Expert anesthetic and immunologist collaborators investigated all referred cases of intraoperative anaphylaxis where NMBDs were administered and identified those where a NMBD was considered responsible. New patient exposures for each NMBD were extracted from electronic anesthetic records compiled during the same period. Anaphylaxis rates were calculated for each NMBD using diagnosed anaphylaxis cases as the numerator and the number of new patient exposures as the denominator.

**Results:** Twenty-one patients were diagnosed with anaphylaxis to an NMBD. The incidence of anaphylaxis was 1 in 22,451 new patient exposures for atracurium, 1 in 2,080 for succinylcholine, and 1 in 2,499 for rocuronium ( $P < 0.001$ ).

**Conclusions:** In Auckland, the rate of anaphylaxis to succinylcholine and rocuronium is approximately 10-fold higher than to atracurium. Previous estimates of NMBD anaphylaxis rates are potentially confounded by inaccurate proxies of new patient exposures. This is the first study to report anaphylaxis rates using a hard denominator of new patient exposures obtained directly from anesthetic records. (*ANESTHESIOLOGY* 2015; 122:39-45)

**I**NTRAOPERATIVE anaphylaxis is a rare but serious event that may cause significant morbidity and mortality.<sup>1-3</sup> Neuromuscular-blocking drugs (NMBDs) are common causative agents during anesthesia.<sup>2,4-8</sup> There is controversy whether the incidence of anaphylaxis is higher with rocuronium than with other NMBDs. Evidence that this might be so has been reported from France,<sup>1,6</sup> Norway,<sup>5,9</sup> and some parts of Australia,<sup>4,7</sup> whereas no difference has been found from the limited data available for the United States.<sup>10</sup>

Such comparisons are complicated by difficulties in obtaining accurate numerator and denominator data with which to calculate an incidence for the various drugs. Deriving accurate numerators relies on capture of all relevant anaphylaxis cases and thorough and consistent case investigation. Denominators based on cases actually exposed to each agent are even harder to obtain because of the difficulties associated with retrieval of administration records from many thousands of anesthetics. For the latter reason, relevant denominators have usually been estimated from sales data or similar metrics that fail to account for confounders such as vials opened but not used, discarded date-expired vials, and repeat administrations or infusions. These problems, combined with the previously mentioned potential

### What We Already Know about This Topic

- Neuromuscular-blocking drugs are common causative agents of intraoperative anaphylaxis
- Comparisons of neuromuscular-blocking drug anaphylaxis rates are complicated by difficulties in obtaining accurate numerator and denominator data

### What This Article Tells Us That Is New

- Search of a database containing more than 400,000 anesthetic records identified 92,858 new patient exposures to neuromuscular-blocking drugs between 2006 and 2012
- Twenty-one of 89 patients referred to the Anaesthetic Allergy Clinic had anaphylaxis attributed to muscle relaxants
- Use of credible numerator and denominator data found similar rates of anaphylaxis after succinylcholine and rocuronium administration, rates that were nearly an order of magnitude higher than those for atracurium and other neuromuscular-blocking drugs

for geographical variation, result in divergent estimates of anaphylaxis incidence for the same drug. For example, the reported incidence of anaphylaxis to rocuronium varies from approximately 1:3,500 to 1:445,000.<sup>5,11</sup>

We undertook a 7-yr retrospective review of the incidence of intraoperative anaphylaxis to NMBDs in Auckland, New

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Zealand. All cases of intraoperative anaphylaxis in the city were referred to a single clinic for investigation, facilitating capture of cases. Moreover, hospital catchment areas are strictly defined and maintained, and two of the three large hospitals in the city used an electronic system to record all anesthetics during this 7-yr period. The associated database contains more than 400,000 anesthetic records which can be searched for administration of particular drugs. These local practices provide accurate numerators and denominators for the calculation of anaphylaxis rates for anesthetic drugs. We compared anaphylaxis rates for various NMBDs, with the null hypothesis being that there is no difference in anaphylaxis rates between agents.

## Materials and Methods

This retrospective, observational cohort study was approved by the Health and Disability Ethics Committee (Reference: 12/NTA/65) and institutional approval was granted by Auckland District Health Board (Auckland, New Zealand) and Waitemata District Health Board (Auckland, New Zealand). Approval was also granted to release the full, anonymized dataset.

### Denominator Data

Auckland City Hospital and North Shore Hospital are the two principal public hospitals within Auckland District Health Board and Waitemata District Health Board, respectively. Both hospitals use the SAFERSleep™ electronic anesthetic record keeping and safety system (SAFERSleep: Safer Sleep LLC, Nashville, TN).<sup>12</sup> This system was fully implemented in all theaters before the study period from January 1, 2006 to December 31, 2012. All drug administrations during an anesthetic are entered by the anesthesiologist using either bar code scanning of specific drug labels on syringes or manual entry (*via* a keyboard) and are permanently recorded by the system.

SAFERSleep maintains anesthetic records in a secure database. Using relevant search criteria in Structured Query Language, we identified all anesthetics in which NMBDs were used. For each record, we extracted the patient's unique National Health Index number, sex, age, name of NMBD used, total number of administrations of NMBD, and use of infusions. After excluding duplication of patients undergoing multiple procedures, we calculated the number of new patient exposures to each NMBD. A new patient exposure was defined as the administration of an NMBD to a patient, for the first time (during the study period). That is, if the same patient received the same NMBD during one or more anesthetics, a single new exposure was considered to have occurred during the period of analysis.

### Numerator Data

The Auckland Anesthetic Allergy Clinic is a multidisciplinary clinic staffed by anesthesiologists, immunologists, and immunology technologists. Case referrals listed all medications and

substances administered before the episode of anaphylaxis, the clinical features, and details of treatment. The anesthetic record was also attached. Patients were seen at the clinic approximately 6 weeks after receipt of referral for consultation and skin testing. The consultation elucidated any other relevant history and established the patient's fitness and consent for skin testing. Skin testing was carried out according to the clinic's protocol which is based on the methodology first described by Fisher and Bowey.<sup>13</sup> The clinical features, serial tryptase results, specific immunoglobulin E testing, and skin testing were then used to confirm the diagnosis and identify the likely causative agent. All medications administered before the anaphylaxis were tested. All patients had skin testing for chlorhexidine (skin prick test 2% aqueous) and latex.

Intradermal skin testing was generally performed on the patient's back. A volume of 0.02 ml of each drug was injected intradermally, and the size of the wheal was measured with calipers after 15 min for comparison with the size of the wheal produced by the injection of 0.02 ml of 0.9% saline (negative control). The test was regarded as positive if the wheal diameter obtained with the drug was larger than the negative control wheal by 3 mm or more. The test was regarded as equivocal if the wheal diameter increased by 1 to 2 mm, with a surrounding flare. A skin prick test with histamine 10 mg/ml was used as a positive control. The drug dilutions used for intradermal testing of muscle relaxants are provided in table 1. If any muscle relaxant had been administered, skin tests were carried out with the full range of muscle relaxants available to detect cross-sensitization.

We included all patients from the two hospitals who were referred after intraoperative anaphylaxis and who had received NMBDs during the study period. Relevant correspondence, referral forms, anesthetic records, and the skin testing results were examined. All the cases were reviewed independently by an anesthetist and an immunologist and then discussed. In the cases confirmed as NMBD-induced allergic anaphylaxis, severity grading was made according to the guidelines published by Mertes *et al.* (table 2).<sup>14</sup> Peak serum tryptases were also recorded.

Diagnostic classification of the patients was based on clinical consensus on all of the following points:

1. Whether or not the patient had one or more manifestations of anaphylaxis as described by Mertes *et al.*<sup>14</sup>;
2. The temporal relation between the administration of an NMBD and the onset of anaphylaxis;
3. The supporting laboratory evidence of allergic anaphylaxis to the relevant NMBD based on intradermal testing with NMBDs, the serum tryptase result, and specific immunoglobulin E testing when available;
4. Ensuring that skin testing had been carried out for other substances or medications that may have caused the anaphylaxis.

Where skin testing (described earlier in this section) was equivocal, all the above features were used to determine

**Table 1.** Drug Dilutions Used for Intradermal Testing

Drug	Concentration
Succinylcholine	0.05 mg/ml 1:1,000 dilution of 100 mg in 2 ml
Mivacurium	0.0002 mg/ml 1:10,000 dilution of 10 mg in 5 ml
Atracurium	0.001 mg/ml 1:10,000 dilution of 50 mg in 5 ml
Pancuronium	0.002 mg/ml 1:1,000 dilution of 4 mg in 2 ml
Vecuronium	0.004 mg/ml 1:1,000 dilution of 4 mg in 1 ml
Rocuronium	0.01 mg/ml 1:1,000 dilution of 50 mg in 5 ml
Saline (negative control)	0.9%

**Table 2.** Clinical Grading of Anaphylaxis

Grade	Symptoms
1	Cutaneous signs: generalized erythema, urticaria, angioedema
2	Measurable but not life-threatening symptoms: cutaneous signs, hypotension, tachycardia
3	Respiratory disturbances: cough, difficulty inflating
4	Life-threatening symptoms: collapse, tachycardia or bradycardia, arrhythmias, bronchospasm
5	Cardiac and/or respiratory arrest

Adapted from Mertes *et al.* J Invest Allergol Clin Immunol 2011; 21:442–53.<sup>14</sup> Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

the cause, as is appropriate in clinical decision making. It is important to emphasize that no one test unequivocally allows diagnosis of anaphylaxis to NMBDs. It is difficult to use a rigid case definition with the sensitivity and specificity of all the available tests being incompletely understood.

### Statistical Analysis

The rate of anaphylaxis to NMBDs was calculated using confirmed cases of anaphylaxis to each drug as the numerator and the number of new patient exposures to the drug as the denominator. Fisher exact test was used to compare the incidence of anaphylaxis to the various NMBDs during the entire interval. CI (95%) were calculated based on the Poisson distribution. A *P* value of less than 0.05 was considered to indicate statistical significance. All analyses were conducted in R, version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria). Because of the large numbers in the denominator, *P* values for Fisher exact test were computed using Monte Carlo simulation with 10<sup>7</sup> replicates. Additional details of our statistical analysis are given in Supplemental Digital Content 1, <http://links.lww.com/ALN/B110>.

### Results

During the 7-yr period from January 1, 2006 to December 31, 2012, there were 92,858 new patient exposures to NMBDs. Database queries and analyses are available in Supplemental

Digital Content 2, <http://links.lww.com/ALN/B111>. The full (deidentified) dataset is available online.\* Eighty-nine of these patients were referred to the Anesthetic Allergy Clinic for follow-up investigation of an intraoperative event that was thought to be anaphylaxis (table 3).

Two referred cases did not attend the clinic and were lost to follow-up. In five cases, we excluded anaphylaxis with a high level of certainty on historical grounds, and in 36 cases with negative skin testing, a diagnosis of nonallergic (nonimmunoglobulin E mediated) anaphylaxis was made. In 25 cases, the causative agent was identified as a substance other than a muscle relaxant (chlorhexidine 8, cefazolin 7, *Gelofusine*® 5, latex 1, tramadol 1, diclofenac 1, paracetamol 1, and protamine 1). Twenty-one cases of allergic anaphylaxis were attributed to muscle relaxants. Table 3 summarizes these cases and lists all use of muscle relaxants in all cases, including those cases lost to follow-up and those considered either due to nonallergic anaphylaxis or not to represent anaphylaxis at all.

Demographics and clinical features of these 21 cases are shown in table 4. The average age of patients was 59 yr and females accounted for 17 of 21 (81%) cases. Four cases were categorized as clinical grade 2, 12 as grade 3, and 5 as grade 4. The median peak tryptase level was 59 µg/l (range, 7.8 to >200 µg/l), with only one patient (20) having a tryptase of

**Table 3.** Classification of Patients Referred to the Anesthetic Allergy Clinic and Muscle Relaxants Received

	Count
Nonallergic anaphylaxis	
Atracurium	11
Succinylcholine	12
Succinylcholine and atracurium	2
Pancuronium	1
Vecuronium	2
Rocuronium	8
Total	36
Did not attend clinic	
Atracurium	1
Succinylcholine	1
Total	2
Allergic anaphylaxis to a muscle relaxant	
Atracurium	3
Rocuronium	6
Succinylcholine	12
Total	21
Allergic anaphylaxis to drugs that are not muscle relaxants:	25
Not allergy	
Atracurium	1
Succinylcholine	2
Succinylcholine and atracurium	1
Rocuronium	1
Total	5
Grand total	89

\* Available at: [http://www.anaesthetist.com/R/allergy2014/nmba\\_anaphylaxis\\_supplement\\_3.zip](http://www.anaesthetist.com/R/allergy2014/nmba_anaphylaxis_supplement_3.zip). Accessed June 19, 2014.

**Table 4.** Clinical Features of Cases with Anaphylaxis to Neuromuscular-blocking Drugs

Case	Index Drug	Age (yr)	Sex	Grade	Tryptase (peak: $\mu\text{g/l}$ )	Wheal/Flare Size (mm)		Positive by Skin Test Criteria	Cross-sensitivity	Prominent Clinical Features	Notes
						Saline	Relaxant				
1	sux	64	F	2	49	7	7/0	No		HYT, BSM, HYPOX, R	+IgE succinylcholine, negative ID test
2	roc	69	F	3	37.2	7	10/25	Yes	vec	HYT, BSM, R, arrhythmia	
3	sux	70	F	4	>200	7	12/29	Yes		HYT, BSM, R, BRADY	
4	roc	78	F	4	147	9	10/32	No		HYT, BSM, HYPOX, R	ID equivocal, strongly positive clinical features
5	roc	70	M	2	16.3	7	7/10	No	sux	HYT, R	On retest rocuronium 8/30 saline 6mm, equivocal
6	sux	41	F	3	127	6	10/35	Yes	roc	HYT, BSM, TACHY	+IgE succinylcholine
7	roc	46	M	3	154	7	9/31	No	vec, sux	HYT, BSM, TACHY, HYPOX, R	ID equivocal, multiple other positives
8	sux	56	F	3	63	6	9/59	Yes		HYT, HYPOX, TACHY	
9	atrac	67	M	2	76	6	8/12	No		HYT, R	Systemic mastocytosis
10	sux	65	F	3	174	7	11/196	Yes	miv, atrac	HYT, BSM, R	
11	sux	49	M	2	22.8	7	12/81	Yes		HYT, BSM, R	
12	roc	96	F	4	30.4	6	8/23	No	vec, panc	HYT, TACHY, R	ID equivocal, multiple other positives
13	sux	36	F	3	38	5	13/53	Yes		HYT, BSM, HYPOX, R	+IgE succinylcholine
14	sux	69	F	3	16.5	7	7/56	No	roc	HYT, BSM, HYPOX, R, urticaria	+IgE succinylcholine, ID for rocuronium positive
15	sux	31	F	3	58.5	8	12/35	Yes		HYT, BSM, FS	
16	sux	65	F	3	79.3	8	14/40	Yes	vec	HYT, TACHY, R	
17	atrac	32	F	3	39.6	7	9/35	No		HYT, TACHY, R	ID equivocal, strongly positive clinical features
18	sux	66	F	4	>200	7	16/32	Yes		HYT, R	
19	sux	50	F	3	67.8	8	13/32	Yes		HYT, R	
20	roc	50	F	3	7.8	6	12/125	Yes	sux, vec	HYT, BSM, TACHY, R	
21	atrac	65	F	4	59	7	6/0	No		HYT, TACHY, flushing, ventricular fibrillation	Severe anaphylaxis $\times$ 2 related to atracurium, retested 6/0

atrac = atracurium; BRADY = bradycardia; BSM = bronchospasm; FS = facial swelling; HYPOX = hypoxemia; HYT = hypotension; ID = intradermal; IgE = immunoglobulin E; miv = mivacurium; panc = pancuronium; R = rash; roc = rocuronium; sux = suxamethonium; TACHY = tachycardia; vec = vecuronium.

less than 12  $\mu\text{g/l}$ . This compared with a median peak tryptase of 7.5  $\mu\text{g/l}$  (range, 1 to 33.2  $\mu\text{g/l}$ ) in the group with nonallergic anaphylaxis, which also exhibited lower severity scores (4 were grade 1, 20 were grade 2, and 12 were grade 3).

Nine of the 21 cases of allergic anaphylaxis did not meet the standard skin test criteria but were nevertheless considered to warrant inclusion on careful consideration of the clinical picture and relevant tests. The notes on the right hand side of table 4 give an indication as to why this diagnosis was made,

despite the absence of a wheal increase of 3 mm or more in these nine cases. Two succinylcholine cases (1, 14) showed the presence of immunoglobulin E antibodies specific for succinylcholine with one (14) also showing cross-sensitization to rocuronium (which had not been administered). Three rocuronium patients (5, 7, and 12) with equivocal skin tests were cross-sensitized to various other NMBDs (not administered). One patient (21) with negative skin tests to atracurium experienced further anaphylaxis on reexposure



**Table 5.** Intraoperative Incidence of Neuromuscular-blocking Drug-related Anaphylaxis

	Succinylcholine	Rocuronium	Atracurium	Other
Anaphylaxis	12	6	3	0
95% CI (Poisson)	6–21	2–13	0–9	0–4
Exposure	24,960	14,995	67,354	15,042
Rate	1:2,079	1:2,498	1:22,450	—
Range (from CI)	1:1,190–4,030	1:1,150–6,810	1:7,680–109,000	1:4,080–∞

to atracurium. One rocuronium (4) and two atracurium (9, 17) patients showed a 1 to 2-mm wheal increase, with flare, no other cause, positive tryptase and timing consistent with the NMBD being causative. Cross-sensitization was demonstrated overall in 9 of the 21 cases (43%).

The number of new patient exposures, number of confirmed cases of anaphylaxis, and rates of confirmed anaphylaxis to succinylcholine, rocuronium, atracurium, and a composite of other NMBDs (vecuronium, pancuronium, and mivacurium) are shown in table 5. These data suggest that there is a large (10-fold) difference between the rate for atracurium and the rates for succinylcholine and rocuronium ( $P < 0.001$ ). Unsurprisingly, individual  $2 \times 2$  comparisons reveal that the differences reside in the rates of anaphylaxis to succinylcholine and rocuronium compared with the other agents. For example, the  $P$  value for rocuronium *versus* atracurium is approximately 0.002.

To test the robustness of our results, we performed two main sensitivity analyses. In the first analysis, we assumed a worst-case scenario: anaphylaxis to NMBDs in all patients who either did not attend or are labeled as “nonallergic anaphylaxis” in table 3. Rates of anaphylaxis to succinylcholine, rocuronium, atracurium, and other agents are then 1:920, 1:1,070, 1:5,000, and 1:4,000, respectively. We did not observe any cases of anaphylaxis to vecuronium in our dataset (0 of 9,585 new exposures). Application of Fisher test as before still results in rejection of the null hypothesis at a  $P$  value of  $6 \times 10^{-7}$ .

The second “restrictive” sensitivity analysis took the opposite approach, rejecting all cases in table 4 that do not strictly conform to “standard criteria” and abandoning the clinical judgment of the anesthesiologist and immunologist who assessed the cases. Even here, a  $P$  value of  $2 \times 10^{-6}$  mandates rejection of the null hypothesis although the difference is then mainly due to succinylcholine.

## Discussion

The principal finding of this study was that in the Auckland region, the use of succinylcholine and rocuronium was associated with a substantially higher rate of intraoperative anaphylaxis compared with atracurium and other NMBDs. There was similarity between the incidence of anaphylaxis to rocuronium and succinylcholine (approximately 1:2,500 and 1:2,000, respectively); in contrast, the rate of anaphylaxis to atracurium was substantially lower (1:22,000). This difference is unlikely to be an artifact due to the large numbers

in the denominators, and this observation is supported by several large European studies.<sup>1,6,8</sup> No cases of anaphylaxis were observed for vecuronium (0 of 9,585 new exposures). The proportion of anaphylaxis events during anesthesia resulting from sensitization to NMBDs (46%) is similar to that reported in France, Norway, Spain, and Australia.<sup>2,4–8,15</sup> The characterization of our patient series, with 56% of anaphylaxis cases being found to be allergic and associated with higher tryptase and greater severity than nonallergic cases, is similar to that in other published studies.<sup>1,2,4,8</sup>

The study provides direct calculation of comparative rates of anaphylaxis based on actual measurement of denominator data. Previous studies have used surrogate denominators based on metrics such as drug sales data, which are prone to inaccuracies. The use of drug sales as an index of patient exposures is confounded by the discarding of expired drugs, multiple administrations, and infusions in long cases. Wastage of NMBDs can be substantial, suggesting that denominators based on drug sales or supply may substantially overestimate exposure, resulting in a potential underestimation of anaphylaxis rates. Notwithstanding such concerns, other studies have reported a higher rate for anaphylaxis to rocuronium than to other nondepolarizing NMBDs,<sup>1,4–7</sup> in agreement with the results from our region.

This finding will likely give anesthetists pause to consider the place of rocuronium in their clinical armamentarium. It is a popular drug for a variety of reasons, not least of which is that it exhibits the fastest onset of all the nondepolarizing NMBDs and it can be used as an acceptable substitute for succinylcholine in a rapid sequence induction. A further reason to use rocuronium in the latter application, despite slower onset when compared with succinylcholine,<sup>16</sup> may be that its effect can be rapidly reversed by sugammadex. Other than to discourage the selection of rocuronium over succinylcholine on the basis of a lower risk of anaphylaxis, our finding is unlikely to change the use of rocuronium in rapid sequence inductions because there are still many reasons why succinylcholine may be contraindicated or why anesthetists may prefer to avoid it. The present authors would have no hesitation in using rocuronium under such circumstances. In contrast, our findings suggest that when all other factors are equal, it may be prudent to reconsider the use of rocuronium in routine cases where it is not being used for any of its particular properties, at least in those regions where there is some evidence that sensitivity is prevalent. Atracurium seems a safer alternative, and although we cannot comment on the basis

of our data which contained too few vecuronium exposures, others have also shown vecuronium to be safer.<sup>1,6,7</sup>

There are several potential limitations to our study. First, the data are limited to the Auckland region of New Zealand and the results can only be extrapolated to other regions and nations with caution. Geographical differences in sensitivity to NMBDs are likely to be real and may be based on regional differences in exposure to other sensitizers such as pholcodine.<sup>17,18</sup>

Second, studies of this nature are vulnerable to any systematic error that leads to an unequal likelihood of identifying cases due to one drug relative to others. In our study, such errors would be possible either in the selection of cases for referral to the regional anesthetic allergy clinic or in the clinical evaluation of the cause of anaphylaxis.

Regarding potential referral errors, despite the single anesthetic allergy clinic in the Auckland region, it is possible that some patients with anaphylactic reactions were not referred from study hospitals for evaluation at the clinic. However, this would represent a serious departure from mandated practice at these institutions (or indeed from accepted anesthetic practice anywhere). Moreover, there is no convincing reason to suspect that any such departures would favor one drug. One possible concern is that the well-understood propensity for atracurium to cause histamine release may have inclined anesthesiologists to overlook anaphylaxis of a minor degree related to this agent, but the severity grading of the identified reactions (table 3) appears balanced across agents and therefore does not support this hypothesis. We do acknowledge that there may have been underreferral of minor reactions to all agents, as there were few grade 1 reactions diagnosed in the study.

In respect of potential evaluation errors, the evaluation of referred cases at the clinic followed a standard protocol (outlined earlier) including application of a consistent case definition, and the determination of causation for each case reported in this study was independently reviewed by an anesthetic allergy specialist and an immunologist. Although it is acknowledged that there is variation in the way in which the clinical histories, skin testing results, and other tests are evaluated, there is widespread acceptance that all features should be considered in diagnosis.<sup>19</sup> All the relevant clinical features and available test results have been transparently provided. It was not always possible to identify the agent on skin testing even though there was a convincing history of anaphylaxis. In 46 cases, the drug or substance was identified on skin testing, but in 36 cases (44%), it was not. This reaction rate is consistent with other large surveys.<sup>1,3</sup>

Third, there is a small potential for inaccuracies in the denominator data and the other associated data gathered from the electronic database of anesthetic records. For example, the records rely on anesthesiologists entering details such as the drug type and dose. These details are checked intra- and postoperatively and a printout requiring a signature by the anesthesiologist certifies this as a legal record of the

procedure. Previous research in our institution, which took place during the period of the current study, demonstrated a rate of omission of drug administration from the electronic record of 2.31 per 100 drug administrations.<sup>20</sup> Finally, we did not formally account for the increased risk of family-wise error rate by correcting our *P* values for multiple testing; this topic is further explored in Supplemental Digital Content 1, <http://links.lww.com/ALN/B110>.

In conclusion, we have used credible numerator and denominator data to demonstrate similar rates of anaphylaxis after administration of succinylcholine and rocuronium—these rates were approximately an order of magnitude higher than those for atracurium and other nondepolarizing NMBDs. Rocuronium remains a useful alternative to succinylcholine in rapid sequence inductions where succinylcholine is contraindicated, but its routine use as a muscle relaxant in preference to other NMBDs deserves careful consideration, particularly, in regions where presensitization is thought to be common.

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## Competing Interests

The authors declare no competing interests.

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