Anaphylaxis Incidence with Rocuronium, Succinylcholine, and Atracurium: How Risk Communication Can Influence Behavior

To the Editor:

Reddy et al. studying neuromuscular-blocking drug (NMBD)-induced perioperative anaphylaxis concluded that “the rate of anaphylaxis to succinylcholine and rocuronium is approximately 10-fold higher than to atracurium.” However, we believe that major methodological issues should be highlighted in this article as the authors’ resulting statement might mislead clinical care.

First, a small series including 21 cases of NMBD-induced allergic anaphylaxis among 89 patients who were referred to the Anesthetic Allergy Clinic during a 7-yr study period was presented, but NMBD-induced anaphylaxis was not proven in 9 of these 21 reported cases (42.8%) as skin tests remained negative to the culprit NMBD. Except in one case (patient 9 with mastocytosis), the negative skin tests to the culprit NMBD in the eight remaining cases including succinylcholine (n = 2), rocuronium (n = 4), and atracurium (n = 2) may be explained by false-negative results as follows. Only intradermal tests (IDTs) to NMBDs were performed, whereas optimal investigation of drugs should be performed by prick-tests followed by IDTs without exceeding the maximal concentrations. Accordingly, IDTs are more sensitive but less specific than prick-tests. In addition, lower concentrations of NMBDs, that is, up to 100-fold lower, were used than those currently recommended in Europe and in France, explaining that one patient (patient 21) experienced further anaphylaxis on reexposure to atracurium despite negative skin tests to atracurium. Anaphylaxis to NMBD after negative skin testing has been previously reported by Fisher et al. and Fraser and Smart using the same drug dilutions and skin-testing protocol. We thus respectfully disagree with the authors who claim that “no one test unequivocally allows diagnosis of anaphylaxis to NMBDs” because skin testing is the definitive standard for the detection of anaphylaxis mediated by type E immunoglobulin (IgE) and the assessment of cross-reactive drugs and safe alternative regimens.

Second, despite negative skin tests to the culprit NMBD, these patients were nonetheless considered to “warrant inclusion on consideration of the clinical picture and relevant tests including serum tryptase and specific immunoglobulin E testing available.” Although the measurement of tryptase concentration is a very valuable tool to support the diagnosis of IgE-mediated anaphylaxis, identification of serum IgE to succinylcholine in two patients (patients 1 and 14) with negative skin tests to succinylcholine provides possible evidence of IgE sensitization but does not confirm that the drug induced the immediate reaction per se.

Precisely, only the suxamethonium-specific assay is commercially available among the different NMBDs.

Third, one of these patients (patient 9) with negative skin tests had systemic mastocytosis and received atracurium. In this case, moderate features including hypotension and rash associated with an increased tryptase level and negative skin tests to atracurium rather suggest nonallergic immediate hypersensitivity. Unfortunately, increase in tryptase level was not compared with the patient’s baseline level that may be markedly increased in systemic mastocytosis, whereas skin tests should also have been performed until the maximal recommended concentration. Indeed, mastocytosis is not a risk factor for perioperative drug-induced IgE-mediated anaphylaxis, and mast cell degranulation usually occurs secondary to a variety of nonimmune triggers specific for each patient. The best way to avoid mast cell degranulation in mastocytosis is therefore to avoid potential triggers including histamine-releasing benzylisoquinolines, such as atracurium and mivacurium.

Thus, in this series, only 12 cases of NMBDs-induced anaphylaxis can be considered to be definitively supported by positive skin tests including suxamethonium (n = 10) and rocuronium (n = 2). The claim that “the rate of anaphylaxis to succinylcholine and rocuronium is approximately 10-fold higher than to atracurium” should therefore be softened because this has not been proved while one should keep in mind that all NMBDs may elicit anaphylaxis.

Besides, effective risk communication must take into account how various publics perceive risk influenced by societal and cultural factors rather than just focusing on science. The last French survey of anesthesia-related mortality demonstrated that 3% of anesthesia-related deaths involved either NMBDs-induced or antibiotics-induced anaphylaxis, whereas 20% were due to pulmonary aspiration in 1999. The analysis of aspiration-related deaths in surgical patients with known full stomach (26 cases) showed significant deviations from standard practices. Particularly, succinylcholine was not used by French anesthetists in two third of these patients. The expert panel suggested that the most common interpretation of this limited use of succinylcholine may be explained by the fear of the risk of succinylcholine-induced anaphylaxis largely publicized in France since the 1980s. Thus, the risk communication on NMBD-induced anaphylaxis brought to the foreground a more severe adverse event such as pulmonary aspiration. This emphasizes the complicated process of disseminating risk messages.

In conclusion, the statement that “anaphylaxis is more common with rocuronium and succinylcholine than with atracurium” has not yet been proven and we believe that such a message is hazardous because it may have deleterious influences on anesthetists’ behavior.

Competing Interests

Dr. Dewachter received symposium and lecture travel fees from MSD France, Courbevoie, France. Dr. Mouton-Paivre declares no competing interests.
References


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