

BRIEF COMMUNICATION

Negative predictive value of skin tests to neuromuscular blocking agents

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To cite this article: Ramirez LF, Pereira A, Chiriac AM, Bonnet-Boyer M-C, Demoly P. Negative predictive value of skin tests to neuromuscular blocking agents. *Allergy* 2011; DOI: 10.1111/j.1398-9995.2011.02753.x.

Keywords

anaesthesia; anaphylaxis; negative predictive value; neuromuscular blocking agents; skin tests.

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Abstract

Allergy to neuromuscular blocking agents (NMBAs) is the most important cause of perioperative anaphylaxis in France. The diagnosis relies on a careful clinical history, the search of serum IgE antibodies, and the realization of skin tests. Although the skin tests are the most important tool and their sensitivity is widely recognized, the lack of information about their negative predictive value represents an important issue in the management of patients who require a new procedure with NMBA injection. We present a series of 49 patients with confirmed allergy to NMBAs, six of whom required a subsequent surgery with neuromuscular blockade. Negative skin tests allowed the selection of an alternative NMBA, which was well tolerated in all 6 cases. We found an excellent negative predictive value of skin tests in our series but larger studies are required to properly address this question.

Edited by: Werner Aberer

Accepted for publication 25 October 2011

DOI:10.1111/j.1398-9995.2011.02753.x

Perioperative anaphylactic reactions are dramatic and unexpected and could be fatal. Their incidence in France is estimated in 100.6 cases per million general anaesthetics, of which 58% are because of neuromuscular blocking agents (NMBAs) (1). A detailed medical history, the performance of skin tests (STs) and the search for specific IgE antibodies allow an aetiological diagnosis to be determined, and the risk of further surgeries reduced. The determination of specific IgE may not match with the NMBA involved in the patient's reaction. In fact, the presence of IgE against various NMBA is often found, and an NMBA with the highest power of inhibition may not be the cause of the reaction (2). Skin tests are the cornerstone of the diagnosis of NMBA allergy (1, 3, 4), and a positive ST (following the current guidelines and the published dilutions) (3) confirms allergy to the product, with a high sensitivity.

However, there is no clarity with regard to the negative predictive value (NPV) of STs. Given the severity of the reactions, it is recommended to avoid any further use of these drugs in patients who have already suffered a severe reaction to NMBAs (5). Cross-reactivity, as assessed by STs or IgE antibody tests, is frequent amongst NMBAs (1–3), because of

the presence of substituted ammonium ions (2). IgE antibody tests appear to be less clinically relevant than STs for cross-reactivity analysis (2). However, certain types of surgery require the use of an NMBA. In these cases, it is very important to have a test reliable enough to predict a low risk of a new severe reaction.

There are no recent publications of case series available on this topic. A 1998 retrospective study analysed 13 patients who had experienced a perioperative anaphylactic shock because of NMBAs. These patients were all re-injected with an NMBA for which the STs were negative. There was no recurrence of an allergic reaction (6). However, the current guidelines for the study of perioperative allergic reactions (3) were published some years later, and new NMBAs have since been commercialized.

In recent literature, we have found only a few case reports regarding patients who were injected with an NMBA for which the ST was negative, with no adverse reactions (7). Nevertheless, anaphylaxis after injection of a negatively skin-tested NMBA has also been reported (8).

To determine the NPV of the STs for NMBAs, we analysed all patients who were addressed to our allergy department

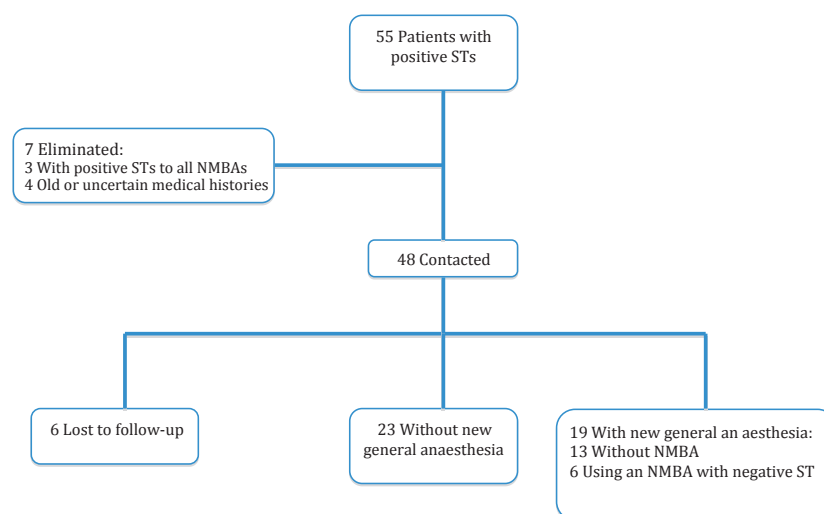


Figure 1 Patients with confirmed allergy to a NMBA.

Table 1 Patients with allergy to a NMBA who subsequently received another NMBA injection

	Sex	Year of birth	Severity of accident	Injected NMBA	Delay between reaction and ST, months	Positive ST	Delay between reaction and further NMBA injection	Used NMBA	Absolute indication for an NMBA injection
1	F	1962	III	Sux	2	Sux	2 years	Cis	Yes
2	M	1968	III	Gal-Pan	2	Alc, Gal, Pan	14 years	Cis	Yes
3	M	1961	III	Cis-Sux	4	Sux	4 months	Cis	Yes
4	F	1944	I	Atr	3	Atr	12 years	Cis	Yes
5	M	1942	IV	Atr	4	Atr	13 years	Cis	Yes
6	F	1935	IV	Gal	8	Gal, Pan	30 years	Cis	Yes

Alc, alcuronium; Sux, suxamethonium; Atr, atracurium; Cis, cisatracurium; Gal, gallamine; NMBA, neuromuscular blocking agent; Pan, pancuronium; Roc, rocuronium; ST, skin test.

between January 2006 and May 2011 with a diagnosis of perioperative anaphylaxis. Amongst 502 consecutive medical consultations, 55 patients were diagnosed with an allergy to NMBA, confirmed by clinical history, presence of specific IgE and/or positive STs according to the 2005 guidelines (3). All of the patients and referring physicians were contacted and asked whether further surgery had been performed, following the allergic work-up. Charts of subsequent surgical procedures were obtained and reviewed, in search of NMBA injection and/or perioperative incidents. Monitoring results are shown in Fig. 1. Amongst the 55 patients, 48 were contacted, 19 of which have had a new general anaesthesia, 13 without NMBA and six using an NMBA for which STs were negative. None had had a new reaction to the injected NMBA. Data concerning patients who subsequently received an NMBA injection are shown in Table 1. In our series, the negativity of STs enabled the choice of a safe NMBA for the patients, who could then undergo subsequent procedures without complication. Two of our patients had positive STs to

more than one NMBA, the first one to gallamine and two aminosteroids and the second one to an aminosteroid and a benzylisoquinoline (Table 1). As cross-reactivity of the NMBA does not depend on the pharmacological class, but rather on the distance between the two substituted ammonium ions, with or without the neighbouring structures (2, 9), STs are so far the only mean to predict clinical cross-reactivity.

The excellent predictive value of STs in our series is obviously biased by the small number of patients. Given the low frequency of perioperative reactions, the odds of having a significant number of patients in a single hospital are very low. We therefore consider it mandatory to establish a database that would assemble the findings of several hospitals and, if possible, a multinational database, in the hope of clarifying the true NPV of the STs for NMBA.

Conflict of interest

None of the authors had any conflict of interest.

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