

Letter to the Editor

IgE antibody detection in the diagnosis of hypersensitivity to neuromuscular blocking agents

doi: 10.1111/j.1399-6576.2011.02540.x

Sir,

The diagnostic procedure of immediate hypersensitivity reactions to neuromuscular blocking agents (NMBAs) is mainly based upon an evocative clinical history and positive skin tests, and should be supplemented by laboratory assays, such as specific IgE antibody detection.¹ Baldo et al. have demonstrated that substituted ammonium (SA) groups are the major allergenic epitopes of NMBAs.² Nevertheless, cross sensitization studies have raised the importance of the accessibility of the SA ions and their adjacent or adjoining structures for IgE binding.² IgE detection assays have thus used different providers of SA groups: either single individual NMBAs³ or generic compounds containing a SA epitope.⁴ Furthermore, different strategies exist to detect SA-specific IgE: radioimmunoassays (RIAs) were first developed, while today, fluorescent enzyme immunoassays (FEIAs) become more popular.

We compared the different available strategies for SA-specific IgE detection in the diagnosis of NMBA allergy. The tested assays are either commercial FEIAs (Phadia, Uppsala, Sweden), directed against single NMBAs (suxamethonium-CAP and rocuronium-CAP) or the SA (tertiary ammonium) structure of morphine (morphine-CAP), or a RIA using quaternary ammonium structures of p-aminophenylphosphoryl-choline

(PAPPC-RIA, previously described⁴). Eighteen patients were consecutively investigated (from February 2007 to April 2008) in our outpatient unit on the basis of a suggestive clinical history and a severe allergic reaction (grade III or IV according to the Ring and Messmer classification) and positive skin tests to NMBAs. Culprit molecules were suxamethonium (11 patients), atracurium (2), pancuronium (1), mivacurium (1), cisatracurium (2), or alcuronium (1). Twenty individuals exposed to NMBAs who have experienced anaphylaxis to agents other than NMBAs (antibiotics, latex, and dyes) were used as controls for the study of IgE specificity.

Sensitivity, specificity, positive, and negative predictive values of the different assays are summarized in Fig. 1.

Our first findings confirm the low sensitivity of suxamethonium test (44%, Fig. 1A), as previously described.⁵ It is of note that this sensitivity is not improved in patients who experienced anaphylaxis to suxamethonium (45%, Fig. 1B). On the contrary, the sensitivity of the rocuronium assay appears to be excellent, either for the whole population (83%) or for the suxamethonium allergic patients (100%). Unfortunately, this assay is hampered by its low specificity. The other strategy tends to detect IgE against SA residues, either using RIA or FEIA. PAPPC-RIA is known to display excellent characteristics,⁴ which is confirmed in our population (Fig. 1). Unfortunately, the use of radioisotopes in this test has limited its wide spreading. Thus, we compared this assay with the recently introduced FEIA morphine-CAP. The new test displays similar performances to the PAPPC-RIA, regardless of the offending NMBA (Fig. 1).

In conclusion, we show, in a limited number of patients, that to detect sensitization against any NMBA, it is more clinically useful to detect specific IgE directed against SA structures than

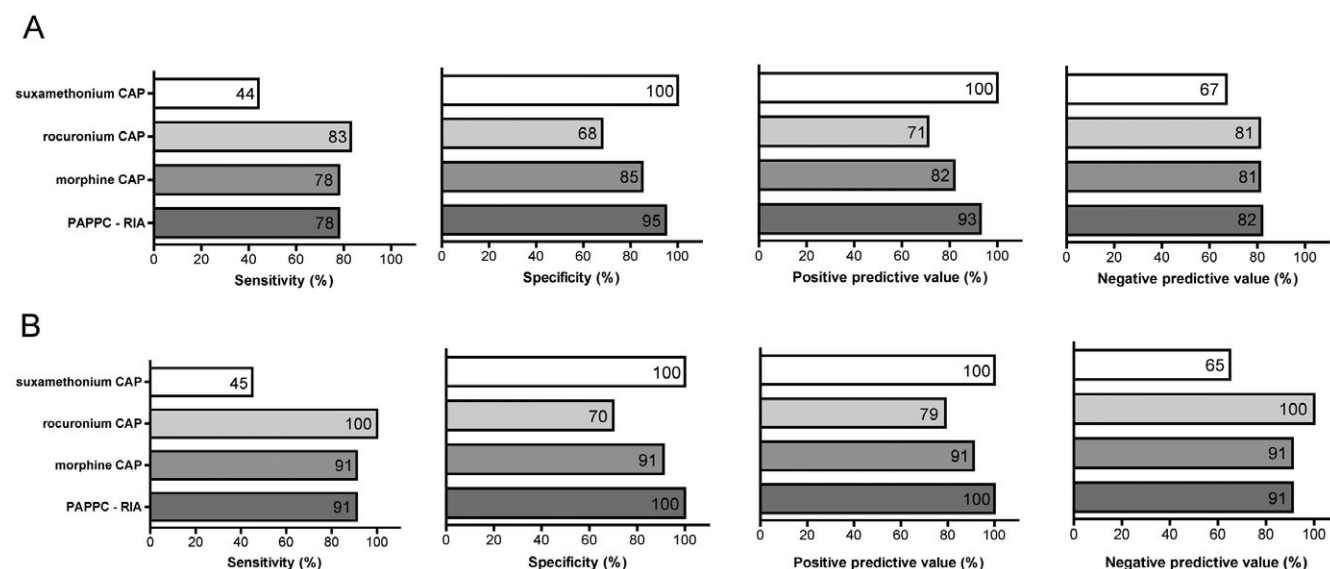


Fig. 1. Characteristics of the different NMBA IgE assays. Sensitivity, specificity, negative, and positive predictive values of the tests are presented for the whole population (A) and for the suxamethonium allergic patients (B). NMBA, neuromuscular blocking agent; PAPPC-RIA, p-aminophenylphosphoryl-choline radioimmunoassay.

Letter to the Editor

against individual molecules. This is true even if a specific test against the offending drug is used (i.e., suxamethonium). Our results demonstrate the excellent characteristics of the morphine-CAP, in agreement with a recent publication.⁶ In our hands, the test performed as well as the validated SA provider PAPPC. The good practicability and easy availability of the morphine-CAP will certainly facilitate its widespread use as a routine laboratory test for an efficient diagnosis of NMBA allergy in combination with skin tests.

*P. Rouzaire
G. Proton
F. Bienvenu
L. Guilloux
Y. Benoit
V. Piriou
J. Bienvenu
P. Mertes*

References

1. Mertes PM, Laxenaire MC, Lienhart A, Aberer W, Ring J, Pichler WJ, Demoly P, Working Group for the SFAR; ENDA; EAACI Interest Group on Drug Hypersensitivity. Reducing the risk of anaphylaxis during anaesthesia: guidelines for clinical practice. *J Invest Allergol Clin Immunol* 2005; 15: 91–101.
2. Baldo BA, Fisher MM, Pham NH. On the origin and specificity of antibodies to neuromuscular blocking (muscle relaxant) drugs: an immunochemical perspective. *Clin Exp Allergy* 2009; 39: 325–44.
3. Baldo BA, Fisher MM. Detection of serum IgE antibodies that react with alcuronium and tubocurarine after life-threatening reactions to muscle-relaxant drugs. *Anaesth Intensive Care* 1983; 11: 194–7.
4. Guilloux L, Ricard-Blum S, Ville G, Motin J. A new radioimmunoassay using a commercially available solid support for the detection of IgE antibodies against muscle relaxants. *J Allergy Clin Immunol* 1992; 90: 153–9.
5. Harboe T, Guttormsen AB, Irgens A, Dybendal T, Florvaag E. Anaphylaxis during anesthesia in Norway: a 6-year single-center follow-up study. *Anesthesiology* 2005; 102: 897–903.
6. Laroche D, Chollet-Martin S, Leturgie P, Malzac L, Vergnaud MC, Neukirch C, Venemalm L, Guéant JL, Roland PN. Evaluation of a new routine diagnostic test for immunoglobulin E sensitization to neuromuscular blocking agents. *Anesthesiology* 2011; 114: 91–7.

Address:
Paul Rouzaire
Laboratoire d'Immunologie
Centre de Biologie Sud
CHU Lyon-Sud
69495 Pierre-Bénite
France
e-mail: paul.rouzaire@chu-lyon.fr