

Allergy to anaesthetizing agents in Spain

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We have investigated the incidence of requests for allergy testing in 5005 patients attending an anaesthetic assessment clinic. Diagnosis of allergy to anaesthetic drugs was established using cutaneous tests. Allergy tests were requested in 151 (3.0%) patients, proving positive in 43 (0.86%). No allergic reactions were observed during subsequent anaesthesia.

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There is a relatively high incidence of allergic reactions during anaesthesia because of the large number of drugs administered in a short period of time. Data from various retrospective studies indicate that the frequency of reactions is 1 in 350 to 1 in 20 000.^{1–4}

Apart from the clinical consequences of allergic reactions to anaesthetic drugs, medico–legal implications are also relevant. Great controversy arose in Spain as a result of two court rulings. In both cases, the anaesthetist was found to be negligent for not having carried out allergy tests for anaesthetizing agents in patients who had no previous allergy record.⁵ As a consequence of social and professional anxiety arising from these rulings, the Spanish Society of Anaesthetics and Reanimation and the Spanish Society of Allergy and Clinical Immunology declared that ‘tests regarding allergy to anaesthetizing agents should only be carried out in patients with a history of adverse reactions to such agents, as is the case with other types of medication’.⁵

Consequently, in this study, we have assessed the incidence of requests for allergy testing to anaesthetizing agents, the reasons for such requests and the frequency of positive test results.

Methods and results

This was a retrospective study, investigating patients who attended the anaesthetic assessment clinic of Valladolid University Hospital (800 beds) from June 1, 1995 to May 31, 1996. The Hospital’s Research Committee approved the study.

All patients undergoing anaesthesia attended the clinic. Members of the Anaesthesiology and Reanimation Service of Valladolid University Hospital (21 anaesthetists) agreed

to carry out allergy tests if: (i) there was irrefutable, documented evidence of allergy to any drug; (ii) there was a history of atopy of clinical relevance that had required treatment in the past (allergic rhinitis, asthma, atopic dermatitis and urticaria); (iii) there had been previous adverse reactions to anaesthetics; or (iv) the patient requested tests.

In order to establish a diagnosis of allergy, intradermal reactions and prick tests were used. The skin prick test was performed using the anaesthetic agents and other drugs directly from the ampoules and vials, with no dilution, on the volar surface of the forearm. For atracurium, a 1 in 100 solution, and for latex, the Alk-Abello preparation were used. In the latter case, latex extract was prepared from an ammonia latex particle suspension by neutralization, semi-purification and further concentration. Final protein adjustment was performed using the method of Lowry. The prick test reading was regarded as positive when the weal was more than 3 mm. A saline control was used in all cases. The agents for which allergy tests were carried out and the individual concentrations used for the prick tests are shown in Table 1. Chi-square tests were used to compare data. $P < 0.05$ was regarded as significant.

We investigated 5005 patients, of whom 2339 (46.7%) were female. Age groups were as follows: 12.2% were aged 1–25 yr; 21.5% were aged 26–45 yr; 37.3 % were aged 46–65 yr; and 29.0% were aged more than 65 yr. Allergy tests were requested in 151 patients (3.0% of all patients), being more frequent (chi-square=6.533, $P=0.011$) in women ($n=86$, 3.8%) compared with men ($n=65$, 2.4%). Of these 151 patients, 43 (28.5%; 0.86% of all patients) tested positive, and again the values were

higher (chi-square=5.888, $P=0.015$) in women (1.2%) than in men (0.6%).

Results of allergy tests are shown in Table 1. The most frequent positive tests were for neuromuscular blocking agents ($n=44$, 69.8%), especially atracurium ($n=25$, 39.7%); latex was the second most frequent ($n=6$, 9.5%).

Of the 151 patients tested, 62 (41.1%) had a history of atopy, of whom 29 (46.8%) showed positive results. A total of 130 patients (86.1%) had a history of allergy to other drugs, and allergy tests proved positive in 34 of these patients (25.1%). Thirty-four patients (22.5%) had suffered a previous adverse effect related to anaesthetics and tests were positive in 15 (44.1%) of these patients. Seven patients (4.6%) requested allergy tests and a positive result was obtained in one patient (14.3%).

For those patients in whom cutaneous tests were carried out, the following steps were taken by the anaesthetist. For 39 patients (90.7%), the substance or substances to which the patient was positive in the prick test was avoided. In four other patients (9.3%), the substance which caused the positive prick test was administered (fentanyl in two patients, droperidol in one and Thalamonal in one). In these cases, administration of dexchlorpheniramine 5 mg i.v. every 8 h, ranitidine 1 mg kg⁻¹ i.v. every 8 h and methylprednisolone 1 mg kg⁻¹ i.v. every 6 h was commenced 24 h before operation and continued for another 24 h after surgery.

During anaesthesia, there were no signs or symptoms suggestive of an allergic reaction in the 43 patients who had positive tests. This was also the case for the 108 patients for whom allergy tests were requested and proved negative.

Comment

In this study, we found that allergy tests were requested for 3 in every 100 patients, and of those tested, 1 in 116 showed allergy to agents used in anaesthesia; neuromuscular blocking agents, particularly atracurium, were the most frequent agents involved. No allergic reaction was observed during anaesthesia itself. In common with other studies,^{1,3} we found allergic reactions to be more frequent in women.

The target population for predictive allergy tests is debatable. Laxenaire¹ defended the systematic use of prick tests in the anaesthetic assessment clinic for every individual who is to receive neuromuscular blocking agents, given the fact that more than 25% of severe allergic reactions caused by neuromuscular blocking agents occur on the first exposure to anaesthesia. However, Fisher and colleagues,^{3,4} the Spanish Society of Anaesthetics and Reanimation, and the Spanish Society of Allergy and Clinical Immunology⁵ consider that allergy tests should be requested only when

Table 1 Frequency (%) of positive allergy tests to anaesthetizing agents. *For the prick test, a 1 in 100 solution was used

Drug	n	%	Concn of drug (mg ml ⁻¹)
Atropine	3	4.8	1
Droperidol	2	3.2	2.5
Fentanyl	2	3.2	0.05
Flumazenil	1	1.6	0.1
I.v. anaesthetics	3	4.8	
etomidate	0	0.0	2
diazepam	2	3.2	5
midazolam	0	0.0	1
propofol	0	0.0	20
thiopental	1	1.6	2.5
Metoclopramide	0	0.0	5
Naloxone	1	1.6	0.4
Neuromuscular blocking agents	44	69.8	
Atracurium	25	39.7	1*
Pancuronium	5	7.9	2
Succinylcholine	8	12.7	50
Vecuronium	6	9.5	1
Thalamonal	1	1.6	droperidol 2.5+fentanyl 0.05
Latex	6	9.5	0.5
Total	63	100	

an allergy reaction to an anaesthetic agents has taken place, and do not believe it is useful to carry out a test in those patients deemed to be at risk (e.g. atopy, previous anaesthesia, etc). Our study would suggest that the incidence of allergic reactions during anaesthesia is less than 1 in 5000, a value in the middle of the wide reported range of 1 in 350 to 1 in 20 000.¹⁻⁴

Our study had several limitations. It was retrospective, and despite the fact that all members of the service agreed to adopt definite criteria, we cannot be sure that this was actually the case. It is possible that we underestimated the 'at risk' population. Perhaps a prospective study and tests on all patients would be more accurate.

The clinical relevance of our results lies in the fact that it is relatively common for patients to be allergic to anaesthetic agents, and that it is possible to avoid allergic reactions during anaesthesia by requesting prior investigation of possible allergy.

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