ORIGINAL ARTICLE

Study of Hypersensitivity Reactions and Anaphylaxis During Anesthesia in Spain

T Lobera,[1] MT Audicana,[2] MD Pozo,[1] A Blasco,[1] E Fernández,[2] P Cañada,[3] G Gastaminza,[2] I Martinez-Albelda,[4] I González-Mahave,[1] D Muñoz[2]

[1]Department of Allergology, Hospital San Pedro/San Millán, Logroño, Spain
[2]Department of Allergology, Hospital Santiago Apóstol, Vitoria, Spain
[3]Department of Anesthesia, Hospital San Pedro/San Millán, Logroño, Spain
[4]Department of Anesthesia, Hospital Santiago Apóstol, Vitoria, Spain

Financial support by SERIS (Hospital San Pedro/San Millán, Logroño, Spain) and OSAKIDETZA (Hospital Santiago Apóstol, Vitoria, Spain)

Abstract

Background: Several studies have identified neuromuscular blocking agents as the most common cause of anaphylaxis during general anesthesia. The reported frequencies vary considerably between countries. There are few reports from Spain, probably due to the low prevalence of reactions.
Methods: For 5 years (1998-2002), all the patients who presented perioperative anaphylactic-type reactions, were studied in 2 Spanish allergy departments (Santiago Apostol, Vitoria-Gasteiz and San Pedro, Logroño). The diagnostic protocol consisted of a case history (age, gender, number of previous interventions, characteristics of the reaction, reaction phase, previously administered drugs), serum tryptase measurements, skin tests, and specific immunoassays (immunoglobulin [Ig] E determination against latex, penicillin, and *Echinococcus*).
Results: Forty-eight patients were studied, with ages ranging from 7 to 86 years. The ratio of women to men was 3:2. An IgE-mediated mechanism was confirmed in 27/48 patients (56%). The etiological agents were antibiotics in 12 cases (44%) (10 betalactams, 1 vancomycin, and 1 ciprofloxacin), muscle relaxants in 10 cases (37%), pyrazolones in 2 cases, latex in 2 cases, and *Echinococcus* in 1 case.
Conclusions: Fifty-six percent of the perianesthetic reactions studied were IgE-mediated. Antibiotics and neuromuscular blocking agents were the most frequent causal agents, as verified by skin tests, and specific IgE and/or challenge tests. It is important to keep appropriate documentation on any of the drugs used during surgery, since our results show that those drugs involved in the reaction as the etiological agent, such as antibiotics and nonsteroidal anti-inflammatory agents, can be used again outside the context of surgery.

Key words: Anesthesia. Hypersensitivity. Anaphylaxis. Muscle relaxants. Antibiotics. Perianesthetic reactions.

Resumen

Antecedentes: Los agentes miorelajantes son reconocidos por varios estudios como la causa más común de anafilaxia durante la anestesia general. Su frecuencia varía entre diferentes países. Hay pocas referencias españolas, probablemente debido a la baja prevalencia de reacciones.
Métodos: Durante 5 años (1998-2002), todos los pacientes que presentaron reacciones peroperatorias de tipo anafiláctico, se estudiaron en dos Servicios de Alergología de España (Hospital Santiago Apóstol de Vitoria y San Pedro de Logroño). El protocolo diagnóstico conjunto constaba de historia clínica (edad, sexo, número de intervenciones quirúrgicas previas, características de la reacción, fase de la reacción, fármacos administrados previamente), determinación de triptasa sérica, pruebas cutáneas y determinación de IgE específica (latex, penicilina y *Echinococcus)*.
Resultados: Se estudiaron 48 pacientes con edades comprendidas entre los 7 y 86 años. La proporción por sexo (F:M) fue 3:2. Se confirmó un mecanismo IgE mediado en 27/48 (56%). Los agentes etiológicos fueron antibióticos en 12 casos (44%)(10 betalactámicos, 1 vancomicina, 1 ciprofloxacino), relajantes musculares en 10 casos (37%), pirazolonas en 2 casos, y latex y Echinococcus en 2 casos y 1 caso, respectivamente.
Conclusiones: El 56% de las reacciones peranestésicas fueron mediadas por IgE. Los antibióticos y los relajantes musculares fueron las causas más frecuentes, confirmadas mediante pruebas cutáneas, determinación de IgE específica y/o pruebas de provocación. Creemos importante guardar documentación apropiada sobre todos los fármacos administrados en la intervención puesto que, de acuerdo a nuestros resultados, algunos de estos fármacos involucrados en la reacción como agentes etiológicos, como los antibióticos o antiinflamatorios, pueden ser usados de nuevo fuera del contexto quirúrgico.

Palabras clave: Anestesia. Hipersensibilidad. Anafilaxia. Relajantes musculares. Antibióticos. Reacciones peranestésicas.

Introduction

Anesthesiologists administer several drugs during surgery and many of these drugs have side effects that are similar to those induced by immunologic mechanisms. Anaphylactoid reactions, or nonallergic drug hypersensitivity, occur through direct nonimmunologic immunoglobulin (Ig) E-induced release of mediators from mast cells or from complement activation induced by the drugs, mainly neuromuscular blocking agents (NMBA) and opioids. Drug hypersensitivity reactions are considered allergic reactions to drugs when immunologic mechanisms have been demonstrated and IgE-mediated drug allergy when we wish to highlight the role of IgE antibody [1]. Anaphylaxis, considered an acute type I hypersensitivity reaction resulting primarily from rapid antigen induction—usually IgE-dependent release of potent mediators from mast cells and basophils—has been reported [2], although the term anaphylaxis should only be used for the most severe IgE-mediated, life-threatening, generalized, or systemic hypersensitivity reaction [1].

The perioperative adverse reactions described above are uncommon, and their frequency varies with the type of procedure. The estimated overall frequency has been reported to range from 2.8 per 10 000 procedures in French series to 0.5 per 10 000 in an Australian study [3-6]. An IgE-mediated mechanism has been confirmed in 40%-70% of cases [7].

Severe adverse reactions are infrequent during surgery, and IgE-mediated allergic reactions are the main contributors to morbidity and mortality in this kind of reaction during surgery [6]. Therefore, an allergologic study of patients who experience a suspected perianesthetic allergic reaction could prove useful for future interventions.

In Spain, there have been few reports of allergic reactions during anesthesia [8]. We present the experience of 2 hospitals that carried out a study following the same protocol coordinated by their allergy and anesthesiology teams from 1998 to 2002.

Materials and Methods

We carried out a 5-year prospective study (January 1998-December 2002) of all patients who presented a suspicious perianesthetic hypersensitivity reaction and were referred from the anesthesiology department to the allergy departments of Hospital Santiago

Table 1. Patient Characteristics

Drug	Prick Test	Intradermal Test
Benzodiazepines		
Midazolam	5 mg/mL	10^{-2}
Diazepam	5 mg/mL	0.1 mg/mL 10^{-2}
Opioid analgesics		
Morphine	Undiluted	10^{-5}
Fentanyl, alfentanil, remifentanil	Undiluted	10^{-2} 10^{-1}
Pentazocine	Undiluted	10^{-2}
Barbiturates		
Thiopental	Undiluted	10^{-2}
Pentothal	200 mg/mL	1 mg/mL
Muscle relaxants		
Succinyl-choline (Suxamethonium)		10^{-3} 10^{-2} 10^{-1}[a]
Pancuronium	Undiluted	10^{-3} 10^{-2} 10^{-1}
Cisatracurium	Undiluted	10^{-3} 10^{-2} 10^{-1}[a]
Atracurium	Undiluted	10^{-3} 10^{-2}[a]
Vecuronium	Undiluted	10^{-3} 10^{-2} 10^{-1}
Rocuronium	Undiluted	10^{-3} 10^{-2} 10^{-1}[a]
Mivacurium	10^{-1}	10^{-3} 10^{-2}[a]
Gallamine	Undiluted	10^{-3} 10^{-2} 10^{-1}[a]
Other induction drugs		
Propofol	Undiluted	10^{-2} 10^{-1}
Local anesthetics		
Procaine	Undiluted	0.05 mg/mL
Lidocaine	Undiluted	2 mg/mL
Mepivacaine	Undiluted	0.2 mg/mL
Analgesics		
Dipyrone (metamizole)	40 mg/mL	1 mg/mL-4 mg/mL
Betalactams		
Penicillin-G	10 000 U	10 000U
Ampicillin	10	10
Amoxicillin	10	10
PPL		
MDM		
Cefazolin	1	1
Ceftriaxone	1	1
Cefuroxime	1	1
Other antibiotics		
Vancomycin	0.005 mg/mL	0.005 mg/mL
Ciprofloxacin	0.02 mg/mL	0.02 mg/mL
Levofloxacin	5 mg/mL	0.05 mg/mL
Other drugs		
• Sterilizers: ethylene oxide modified prick by prick with a sterile glove		
• Latex commercial extracts		
Heparin	Undiluted	10^{-2} 10^{-1}
Gelatin	Undiluted	10^{-2} 10^{-1}
Monovalent haptens		
Etamsylate	Undiluted	10^{-1}
Cytidine-5-diphosphocholine	Undiluted	Undiluted

[a]The test can be irritative at the last concentration.

Apostol in Vitoria, Spain and Hospital San Millán-San Pedro in Logroño, Spain.

Patients

An anaphylactic or anaphylactoid reaction [9] was the criterion for inclusion. All patients presented reactions in the operating room and/or recovery room.

Each patient was referred from the anesthesiology department to the allergy department for examination approximately 2 months after the reaction. The diagnostic workup included the clinical history, skin tests, controlled challenge tests, and serum-specific immunoassays.

The medical history included data on age, sex, number of previous interventions, characteristics of the reaction, reaction phase (induction/premedication, maintenance, recovery) and previously administered drugs. Data on the characteristics of the reaction, reaction phase, and drugs administered were submitted by the anesthetist.

Tryptase Determination

Two blood samples were taken by the anesthetist, the first within 15 minutes and the second 2 hours after the reaction. Levels of serum tryptase were measured by fluoroimmunoassay (CAP System, Pharmacia Diagnostics AB, Uppsala, Sweden). Values higher than 13.5 µg/L were considered positive.

Skin Tests

All patients underwent skin prick tests and intradermal tests with a battery of muscle relaxants (mivacurium, atracurium, suxamethonium, gallamine, vecuronium, pancuronium, and rocuronium) and a skin prick test with latex (Leti SL, Barcelona, Spain). All drugs and/or substances suspected of being involved in the reaction were also tested. Histamine 10 mg/mL and physiologic saline solution were used as positive and negative controls, respectively, for skin prick tests. The concentrations used are shown in Table 1. Skin tests involved 2 different steps: a prick test and, if this was negative, intradermal tests using increasing concentrations of the drugs. Readings were taken after 15 minutes and assessed according to the criteria of the EAACI [10]. When skin tests were positive with any of the NMBA tested, a study with monovalent haptens, etamsylate (Hemo 141, Esteve SA, Barcelona, Spain), or cytidine 5-diphosphocholine choline (SOMAZINA, Almirall Prodesfarma SA, Barcelona, Spain) was carried out. The shift to a negative result in the intradermal test by mixing the muscle relaxant (which had been positive alone) at the same concentration with the monovalent hapten 50:50 was considered to be confirmation of an IgE-mediated mechanism [11].

Other Determinations

When other substances were involved, we also carried out an IgE determination (penicillin, latex), if possible, and controlled challenge tests to rule out sensitization to those drugs.

The patient signed a written informed consent form before the controlled challenge test was performed. This was a single-blind subcutaneous or oral challenge with the suspect drug: oral challenge was performed with nonsteroidal anti-inflammatory drugs (NSAIDs) or benzodiazepines, and subcutaneous challenge and parenteral challenge were performed with cephalosporins. We administered progressively higher doses until the therapeutic dose was reached for each drug. Doses were administered 30 minutes apart.

A descriptive statistical analysis (mean, median, percentage, and confidence interval) was performed using G-Stat 2.0.

Results

During the study period, 71 063 surgical interventions were carried out under general anesthesia. Forty-eight patients suffered a perianesthetic hypersensitivity reaction (6.7/10 000 interventions or 1/1480 interventions). Eighteen were male (37%) and 30 female (63%), with ages ranging from 7 to 86 years (mean 45.3).

With regard to the reaction phase, 31 reactions occurred during the induction/preparation phase (Table 2), 6 during the maintenance phase (Table 3), and 11 during the recovery phase (Table 4). All the patients were treated effectively with epinephrine, antihistamines, ß-mimetics, and/or fluid therapy. No patients died.

Most patients (32/48), had already undergone 1 or 2 surgical interventions under general anesthesia (mean 1.2 per patient). Eleven patients had not had previous surgery and it is surprising that an allergic mechanism was involved in 4 out of these 11 patients: NMBAs were responsible in 2 cases and antibiotics were responsible in 2 cases. In contrast, only 5 cases had had 3 previous surgical operations and 4 of these were included in the study. Two of these patients were positive to NMBAs and 1 to ciprofloxacin.

As for clinical symptoms, skin eruption was recorded in 40 cases (83%), cardiovascular involvement (hypotension, tachycardia) in 13 cases (27%), and respiratory symptoms (bronchospasm, increased airway resistance, breathlessness) in 11 cases (23%). Thirty-seven out of 48 patients presented only 1 type of symptom: 31 were skin-related, 3 cardiovascular, and 3 respiratory. Although cutaneous manifestations were predominant in all phases of anesthesia, as usually occurs in drug allergy, respiratory and cardiovascular manifestations show equal ratios in the maintenance phase. During the induction and/or premedication phase, the most frequent type of reaction was cutaneous (generalized erythema, rash, or urticaria/angioedema in 26 out of 31 patients). During the recovery phase, cutaneous symptoms were once again predominant.

Tryptase was determined in 22 patients and high values were detected in 4. In 3, a sensitizing agent was confirmed (amoxicillin, latex, and dipyrone).

An allergic IgE-mediated mechanism was confirmed in 27 cases (56%): 1 *Echinococcus*, 2 pyrazolones (dipyrone), 2 latex, 12 antibiotics (6 cephalosporins, 4 penicillins, 1 vancomycin, 1 ciprofloxacin), 10 NMBA (5 rocuronium, 3 pancuronium, 3 mivacurium, 3 vecuronium, 2 suxamethonium, and 1 gallamine). The 17 positive skin tests found in 10 patients were due to cross-reactivity between the NMBA (Tables 2, 3, and 4). Only 2 patients refused to finish the skin test (patients number 10 and 13).

All allergic reactions were analyzed in relation to the phase when the reaction was induced, and differences can be

Table 2. Thirty-one Cases of Adverse Reaction Induced During the First Phase: Premedication and Induction

Case	Sex	Age	Previous Surgery	Reaction Phase	Type Of Reaction[a]	Tryptase	Confirmed Allergic Reaction
2	F	45	1	Induction	2,3	NT	Yes (*Echinococcus*)
5	F	49	2	Induction	1	(-)	Yes (penicillin)
6	F	37	1	Premedication	1	NT	No
7	F	31	1	Induction	1,2,3	(-)	Yes (cefuroxime)
8	M	49	2	Induction	1,2	NT	No
9	F	39	0	Induction	1	(-)	No
10	F	60	2	Induction	1	(-)	NT
12	M	57	2	Premedication	1	(-)	Yes (cefazolin)
15	F	51	2	Induction	1	(-)	Yes (muscle relaxants)
16	M	51	0	Premedication	3	(-)	Yes (cefazolin)
17	F	49	0	Induction	1	(-)	No
18	M	28	2	Premedication	3	(-)	Yes (cefazolin)
19	F	46	2	Induction	1	NT	Yes (muscle relaxants)
24	F	81	1	Induction	2	NT	No
29	F	60	3	Induction	1	(-)	No
30	F	67	1	Induction	1	(-)	No
32	M	34	2	Induction	1	NT	Yes (ceftriaxone)
33	F	64	3	Induction	1	NT	Yes (muscle relaxants)
34	F	54	2	Induction	1	(-)	Yes (muscle relaxants)
35	F	74	1	Induction	1	NT	Yes (latex)
36	F	64	0	Induction	1	(-)	No
37	F	19	2	Induction	1	(-)	Yes (muscle relaxants)
38	F	40	1	Induction	1	NT	Yes (amoxicillin)
39	M	18	0	Induction	1,2	NT	No
41	M	32	1	Induction	1	NT	Yes (vancomycin)
42	M	70	1	Induction	1	NT	No
43	F	41	3	Induction	1	NT	Yes (ciprofloxacin)
44	F	69	3	Induction	2,3	NT	Yes (muscle relaxants)
45	M	33	1	Induction	1	NT	Yes (amoxicillin)
46	F	13	1	Induction	1	(-)	No
48	M	57	0	Induction	1,2,3	(+)	Yes (amoxicillin)

Abbreviation: NT, not tested

[a] Type of reaction: 1, cutaneous (erythema, rash, urticaria/angioedema); 2, cardiovascular (hypotension, tachycardia); 3, respiratory (bronchospasm, increased airway resistance, breathlessness).

Table 3. Six Cases of Adverse Reaction Induced During the Maintenance Phase

Case	Sex	Age	Previous Surgery	Reaction Phase	Type Of Reaction[a]	Tryptase	Confirmed Allergic Reaction
1	F	57	2	Maintenance	1,2,3	(-)	No
3	F	65	1	Maintenance	1	NT	No
13	M	51	3	Maintenance	2	(-)	Not tested
20	M	9	0	Maintenance	1	NT	Yes (muscle relaxants)
21	F	50	0	Maintenance	2	NT	No
26	F	43	1	Maintenance	1,2,3	(+)	Yes (latex)

Abbreviation: NT, not tested
[a] Type of reaction: 1, cutaneous (erythema, rash, urticaria/angioedema); 2, cardiovascular (hypotension, tachycardia); 3, respiratory (bronchospasm, increased airway resistance, breathlessness).

Table 4. Eleven Cases of Adverse Reaction Induced During the Recovery Phase

Case	Sex	Age	Previous Surgery	Reaction Phase	Type Of Reaction[a]	Tryptase	Confirmed Allergic Reaction
4	M	20	1	Recovery	1	NT	No
11	M	86	2	Recovery	3	(+)	No
14	M	82	0	Recovery	1	(-)	No
22	F	20	1	Recovery	1	NT	No
23	M	22	0	Recovery	1	NT	No
25	F	7	0	Recovery	1	NT	Yes (muscle relaxants)
27	M	36	1	Recovery	1,2	NT	Yes (cefazolin)
28	M	42	1	Recovery	1,2,3	(+)	Yes (dipyrone)
31	F	29	1	Recovery	1	NT	Yes (muscle relaxants)
40	F	35	1	Recovery	1,3	NT	Yes (muscle relaxants)
47	F	45	1	Recovery	1	NT	Yes (dipyrone)

Abbreviation: NT, not tested
[a] Type of reaction: 1, cutaneous (erythema, rash, urticaria/angioedema); 2, cardiovascular (hypotension, tachycardia); 3, respiratory (bronchospasm, increased airway resistance, breathlessness).

observed regarding the type of allergy and its etiology. During the induction phase, the allergic mechanism was confirmed in 19 out of 30 cases, which is slightly higher than the global mean (63% vs. 56%), although not statistically significant. Skin testing confirmed that allergic reactions to antibiotics were predominant (11/19), followed by NMBA (6/19), and 2 isolated cases of latex and *Echinococcus*. During the maintenance phase, the allergic mechanism was only confirmed in 2 patients (latex and NMBA) out of 5 studied cases (40%). During the recovery phase, the number rose to 6 out of 11 (54%) and the drugs were NMBA (3), dipyrone (2), and cefazolin (1). Interestingly, 2 of these reactions were caused by an NSAID, namely, magnesium dipyrone.

Allergy to antibiotics was confirmed in 12 out of 48 cases: 10 with betalactams, 6 with cephalosporins, and 4 with penicillins.

Of the 10 patients with confirmed allergy to NMBA (21%), 7 had had at least 2 previous operations, 1 had had 1 operation, and 2 (numbers 20 and 25 in Tables 3 and 4) had never undergone surgery. Interestingly, these last 2 cases were children, a girl aged 7 and a boy aged 9.

Discussion

Few studies have analyzed adverse reactions to general anesthetics in Spain [8] and the incidence is currently unknown.

Previous studies have demonstrated the usefulness of skin tests to confirm allergy to NMBA, antibiotics, and other drugs [12,13]. In our study, the diagnosis of an allergic or nonallergic reaction was made by skin tests, IgE determination, or both.

The age range of the present series is wide (7-86 years), with a higher percentage of females (63%), which is consistent

with previous reports [3,4]. An IgE-mediated allergic reaction was confirmed in 56% of patients, also consistent with previous reports [7,8,14].

Generally, reactions were predominant in the induction and recovery phases, and manifested mainly as cutaneous symptoms. Reactions to drugs coincide with the phases when they were administered. Reactions to antibiotics were more frequent in the induction phase, NMBA in the initiation and maintenance phases, and the NSAID (dipyrone) in the recovery phase.

We found differences regarding the etiological agents: in most studies, NMBA are the most frequent followed by latex [7,15-17]; however, in our study, betalactam antibiotics caused 44% of allergic reactions and NMBA caused 37% of allergic reactions. In previous case studies, reactions to antibiotics could have been underdiagnosed, since prophylaxis was administered in the patient's room immediately before the patient was taken to the operating room, where the reaction developed.

The most frequently involved antibiotics were cephalosporins. We believe that the predominance of cephalosporin allergy is due to their widespread use in the context of general anesthesia. In the general population in Spain, however, allergy to aminopenicillins is predominant [18]. Penicillin and other betalactams are also considered to be emerging antigens [19], and antibiotic therapy occupies the third cause of anaphylaxis and could increase [7,20].

Latex caused allergic reactions in only 2 cases. In 2003, Dybendal et al [21] reported 1 out of 18 cases induced by latex. This and other reports show that the incidence of latex allergy is decreasing [3,7].

As for curare derivative drugs (NMBA), some intradermal tests could be irritative due to nonspecific histamine release or a result of the direct vasodilating effects [22], so that the interpretation of the cutaneous response could be difficult. Although some studies note that a high percentage of the control subjects had a positive prick test to undiluted NMBA [23], our previous controls did not react to undiluted NMBA, except for mivacurium and atracurium, which were tested at a dilution of 1:10. The highest concentration used for our intradermal tests is similar to that suggested elsewhere [22]. None of our patients diagnosed as allergic to NMBA reacted to the prick test, although they all reacted at different concentrations to the intradermal test. Associating curare with cytidine 5-diphosphocholine or etamsylate (monovalent haptens) during performance of the test facilitates diagnosis. When the intradermal test was negative after mixing the muscle relaxant with monovalent haptens (50:50), this was considered to confirm that an IgE mechanism was involved [11].

It is highly recommendable to perform skin tests with all the commercially available NMBAs. On the one hand, since skin tests with muscle relaxants remain positive for several years, sensitization may be identified as a result of previous surgery. On the other hand, because of the high frequency of cross reactivity between NMBA, testing all the drugs available increases the chances of finding a drug with a negative skin test that could be used as an alternative. Cross reactivity to NMBA was found in most of our sensitized patients. In these cases, the use of a drug with a negative skin test was recommended as an alternative, according to the results of previous publications [24-26].

If we look at those cases with 3 or more previous operations separately, a higher proportion of allergy is detected than in the rest of the cases (3 out of 4 studied were positive). These results coincide with previous reports [7] regarding the number of operations as a risk factor for allergy. In children, drug allergy is not common [27], although we found 2 cases of skin allergic reaction to NMBAs. These results agree with the results of a 12-year survey at a French pediatric center [28]. However, these 2 cases had no previous history of surgical intervention.

NSAIDs, and more specifically pyrazolone derivatives, are uncommonly reported as causal agents of anaphylaxis during surgery. We found 2 cases, both during the recovery phase; this is consistent with the high consumption of pyrazolones in Spanish hospitals. These 2 patients tolerated oral challenge tests with other nonpyrazolone-derivative NSAIDs (indomethacin and aspirin). The use of dipyrone is controversial.

Another unusual finding is IgE-mediated anaphylaxis within the context of a hydatid cyst operation due to sensitization to *Echinococcus*. It is known that this condition is highly dependent on the geographic origin of the patient and it is endemic in some areas of Spain [29,30].

Finally, we were unable to confirm a high yield for serum tryptase determination, which was only positive in 4 out of 22 patients who underwent testing. An allergic cause of the reaction was confirmed in 3. The low sensitivity of the test in this series may be due to the fact that in 19 out of 22 cases, only a single first determination was performed, at the time of the reaction. Therefore, levels were still low. Unfortunately, in most cases, the second extraction was not performed, due to lack of coordination between the different departments of the hospital.

To conclude, we would like to stress the importance of carrying out an allergy study to detect an allergic cause in more than 50% of the perioperative reactions studied. This is of paramount importance, since allergic reactions are the main causes of morbidity and mortality during anesthesia and the postoperative period [6]. Our study also highlights the importance of drugs such as antibiotics and NSAIDs, which play a vital role in perianesthetic allergic reactions and can be used again outside the operation room.

References

1. Johansson SGO, Biber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, Motala C, Ortega Martell JA, Platts-Mills TAE, Ring J, Thien F, van Cauwenberge F, Williams HC. Revised nomenclature for allergy for global use. Report of the Nomenclature Review Committee of the World Allergy Organization. J Allergy Clin Immunol. 2004;113:832-36.
2. Mertes PM, Laxenaire M. Allergy and anaphylaxis in anaesthesia. Minerva Anestesiol.. 2004;70:285-91.
3. Fisher MM, Baldo BA. The incidence and clinical features of anaphylactic reactions during anaesthesia in Australia. Ann Fr Anesth Réanim. 1993;12:97-104.
4. Watkins J. Adverse reactions to neuromuscular blockers: frequency, investigation and epidemiology. Acta Anesthesiol Scand. 1994;38:6-10.
5. Vervloet D, Magnam A, Birnbaum J, Pradal M. Allergic emergencies seen in surgical suites. Clin Rev Allergy Immunol. 1999;17:459-67.

6. Fasting S, Gisvold SE. Serious intraoperative problems: a five-year review of 83,844 anesthetics. Can J Anesth. 2002;49:545-53.
7. Mertes PM, Laxenaire MC; GERAP. Anaphylactic and anaphylactoid reactions occurring during anaesthesia in France. Seventh epidemiologic survey (January 2001-December 2002). Ann Fr Anesth Reanim. 2004;23:1127-8
8. Tamayo E, Pérez M, Gómez JI, Alvarez FJ. Allergy to anaesthetizing agents in Spain. Br J Anaesth. 1999;83:336-337.
9. Kroigaard M, Garvey LH, Johansson SGO, Mosbech H, Florvaag E, Harbel T, Eriksson LI, Dhlgren G, Seeman-Lodding H, Takala R, Wattwill M, Hirlekar F, Dahlen B, Guttmormsen AB. Scandinavian clinical practice guidelines on the diagnosis, management and follow-up of anaphylaxis during anaesthesia. Acta Anaesthesiol Scand. 2007;51:655-70.
10. Mallíng HJ. Allergen standardization and skin tests. Methods of skin testing. Position Paper. Allergy. 1993;48(Suppl 14):55-6.
11. Moneret-Vautrin DA, Motin J, Mata E, Guéant JL, Kanny G, Widmer S, Laxenaire MD. Preventing muscle relaxant anaphylaxis with monovalent haptens. A preliminary study. Ann Fr Anesth Réanim. 1993;12:190-202.
12. Baldo BA, Pham NH, Zhao Z. Chemistry of drug allergenicity. Curr Opin Allergy Clin Immunol. 2001;4:327-35.
13. Brockow K, Romano A, Blanca M, Ring J, Pichler W, Demoly P. General considerations for skin tests procedures in the diagnosis of drug hypersensitivity. Allergy. 2002;57:45-51.
14. Moscicki RA, Sockin SM, Corsello BF, Ostro MG, Bloch KJ. Anaphylaxis during induction of general anesthesia; Subsequent evaluation and management. J Allergy Clin Immunol. 1990;86:325-32.
15. Harboe T, Guttormsen AB, Igens A, Dybendal T, Florvaag E. Anaphylaxis during anesthesia in Norway. Anesthesiology. 2005;102:897-903.
16. Lieberman P. Anaphylactic reactions during surgical and medical procedures. J Allergy Clin Immunol. 2002;110:64-9.
17. Hepner DL, Castells MC. Anaphylaxis during the perioperative period. Anesth Analg. 2003;97:1381-95.
18. Audicana M, Bernaola G, Urrutia I, Echechipía S, Gastaminza G, Muñoz D, Fernández E, Fernández de Corres L. Allergic reactions to betalactams: studies in a group of patients allergic to penicillin and evaluation of cross-reactivity with cephalosporin. Allergy. 1994;49:108-13.
19. Lee CW, Castells MC. Perioperative anaphylaxis to cefazolin. Allergy Asthma Proc. 2004;25:23-6.
20. Occelli AJ, Pradier C and Grimaud D. Impact of the development of anesthesia protocols on the incidence of perianesthetic anaphylactoid reactions. Allerg Immunol (Paris). 2002; 4:277-80.
21. Dybendal T, Guttormsen AB, Elsayed S, Askeland B, Harboe T, Florvaag E. Screening for mast cell tryptase and serum IGE antibodies in 18 patients with anaphylactic shock during general anaesthesia. Acta Anaesthesiol Scand. 2003;47:1211-8.
22. Levy JH, Gottge M, Szlam F, Zaffer R, McCall C. Weal and flare responses to intradermal rocuronium and cisatracurium in humans. Br J Anaesth. 2000;5:844-9.
23. Dhonneur G, Combes X, Chassard D, Merle JC. Skin sensitivity to rocuronium and vecuronium: A randomized controlled prick-testing study in healthy volunteers. Anest Analg. 2004;8:986-9.
24. Fisher MM, Merefield D, Baldo B. Failure to prevent an anaphylactic reaction to a second neuromuscular blocking drug during anaesthesia. Br J Anaesth. 1999;2:70-3.
25. Villas Martínez F, Joral A, Garmendia FJ and Navarro JA. Anaphylactic reaction to suxamethonium (succinylcholine). J Invest Allergol Clin Immunol. 1999;9:126-8.
26. Dewatcher P, Mouton-Faivre C, Pertek JP, Boudaa C, Mertes PM. Value of skin tests for the choice of a neuromuscular blocking agent after an anaphylactic reaction. Ann Fr Anesth Reanim. 2005;24:543-6.
27. Le J, Nguyen T, Law AV, Hodding JH. Adverse drug reactions among children over 10-year period. Pediatrics. 2006;118:555–62.
28. Karila C, Brunet-Langot D, Labbez F, Jacqmarcq O, Ponvert C, Paupe J, Scheinmann P, de Blie J. Anaphylaxis during anesthesia: results of a 12-year survey at a French pediatric center. Allergy. 2005;60:828-34.
29. Saenz de San Pedro B, Cazana J.L, Cobo, J, Serrano C.L, Quiralte J, Contreras J, Martinez F. Anaphylactic shock by rupture of hydatid hepatic cyst. Follow-up by specific IgE serum antibodies. Allergy. 1992;47:568-70.
30. Blanco I, Cardenas E, Aguilera L. Camino E, Arixaga A, Telletxea S. Serum tryptase measurement in diagnosis of intraoperative anaphylaxis caused by hydatid cyst. Anaesth Intens Case. 1996;24:489-91.

Manuscript received November 26, 2007; accepted for publication January 28, 2008.

Dr Teófilo I. Lobera

C/ Gran Vía, 40 - 8º Dcha
26005 Logroño
Spain
E-mail: tlobera@riojasalud.es