How to Take a Good Clinical History in Cases of Allergic Reactions to Medications

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Abstract

The clinical history is the cornerstone of the doctor's work. When assessing patients consulting for a suspected hypersensitivity reaction to a drug, the details collected in the patient's clinical history are essential when deciding which tests to perform and for making recommendations about which drugs the patient should avoid and which can be taken. This area is especially important today, since many patients are labeled as allergic to drugs, especially penicillins, without this being the case. This article reviews the importance of the clinical history in a patient with a hypersensitivity reaction to a drug and considers which data should be collected. Likewise, a record-based model is proposed to help standardize the clinical history.

Key words: Clinical history. Allergy. Adverse drug reaction. Drug hypersensitivity. Diagnosis.

Resumen

La historia clínica es la piedra angular del trabajo del médico. En el estudio de los pacientes que consultan por una supuesta reacción de hipersensibilidad a un fármaco, los detalles recogidos en la historia clínica del paciente son fundamentales para decidir el estudio que hay que realizar y para, al final, dar recomendaciones al paciente sobre los fármacos que debe evitar o que puede tomar. Actualmente cobra especial importancia este tema, dado que hay un elevado porcentaje de la población que, sin serlo, está etiquetada de alergia a fármacos, sobre todo a las penicilinas. En este artículo se revisa la importancia que tiene la historia clínica ante un paciente con una reacción de hipersensibilidad a un fármaco y qué datos deben ser recogidos. Asimismo, se propone un modelo de ficha que puede ayudar a la estandarización de la historia clínica.

Palabras clave: Historia clínica. Alergia. Reacción adversa a medicamentos. Hipersensibilidad a medicamentos. Diagnóstico.

Introduction

Adverse drug reactions (ADRs) are a significant public health problem [1] because they generate health costs, increase bacterial resistance, and decrease patient quality of life. ADRs affect up to 10% of the population, with this figure increasing to 20% in hospitalized patients [2]. Problems currently arise both from underdiagnosis due to underreporting and from overdiagnosis because of misuse of the term "allergy" [3-5]. In this article, we make recommendations on how take a good clinical history in patients who have experienced an ADR and on how allergists can help family doctors and other specialists to avoid labeling patients with nonallergic symptoms as allergic and to refer patients with the most prominent reactions to allergists.

Definition of Adverse Reactions to Medications

Many patients, and even some health professionals, use the term "drug allergy" to refer to any adverse effect of a given drug [6]. ADRs are classified into type A (predictable), which comprise about 80% of all ADRs, and type B (unpredictable). Type A reactions include toxicity (overdose), adverse effects, and drug interactions and are generally known to the medical community and appear on the summary of product characteristics. Type B comprises unpredictable reactions and encompasses intolerance and idiosyncratic reactions, as well as hypersensitivity reactions (HSRs), which are all more patient-dependent than drug-dependent. HSRs are limited to susceptible individuals and can be caused by immunological mechanisms (allergic) or nonimmunological mechanisms [7]. Only when a definite immunological mechanism (IgE-mediated or T cell–mediated) is demonstrated should drug reactions be classified as an allergic drug HSR.

Classification of Hypersensitivity Reactions

Depending on the time of their appearance, HSRs can be classified clinically as immediate or nonimmediate [8].

- Immediate HSRs. These usually occur in the first hour after the first administration of a new course of treatment, although they can appear within the first 6 hours after the last dose administered [9]. When a combination of symptoms affects various organs, the reaction is considered anaphylactic. These immediate reactions include reactions mediated by IgE or by another mechanism. When the mechanism is not IgE-mediated, the reactions are referred to as anaphylactoid reactions [10], although the currently preferred term is nonallergic HSRs [11].
- Nonimmediate or delayed HSRs. These can occur at any time from the first hour after the initial administration of the drug, although they most commonly appear after the first or second day of treatment and are often associated with a delayed T cell–dependent allergic mechanism.

Table 1 shows the main symptoms of immediate and nonimmediate allergic reactions.

Value of the Clinical History

Guidelines for diagnosing drug allergy [1,12] establish that the first steps in the diagnostic algorithm are the record of a detailed clinical history, followed by skin tests and in vitro tests, with controlled challenge tests comprising the final step [13]. Clinical histories are a fundamental tool in the practice of medicine, and in the case of ADRs, they help to classify and stratify patients, thus enabling personalized and precision treatments [14]. Each history contains important data, whose collection requires an adequate methodology and a basic knowledge of the patient. Some publications consider the clinical history an unreliable diagnostic method in the treatment of drug allergy, as in other diseases [15,16]. Indeed, the value of the clinical history is affected to a greater or lesser extent by a series of factors, as follows:

- Limits when taking a clinical history in children [17].
- Drug type. Nonimmunological HSRs with nonsteroidal anti-inflammatory drugs (NSAIDs) have a high positive predictive value [18].
- Reduced reliability when the interval between the drug reaction and the allergology study is long.
- Simultaneous administration of several drugs can confound the usefulness of the clinical history.
- Very heterogeneous clinical presentation of ADRs.

The algorithms that use clinical history data in pharmacovigilance systems also lack diagnostic sensitivity [19].

Nevertheless, there are several reasons why interviewing the patient and preparing an accurate clinical history are essential when diagnosing drug allergies, as follows:

- To avoid a definitive diagnosis of an ADR if the patient has symptoms not compatible with an allergic reaction (eg, diarrhea, mycosis, extrapyramidal symptoms).
- To avoid diagnosing a patient as allergic without carrying out an allergology study.
- To distinguish which patients require an allergology study.
- To choose the best time to perform the allergology study.
- To determine which tests should be performed, with which drugs, and in what sequence.
- To provide the patient with recommendations once the study is complete.

False Allergy Labels

It is common for some patients to be labeled as allergic to a medication without being so. This can happen for different reasons:

- The symptoms coincided with administration of the drug and were attributed to the drug.
- Subjective symptoms could be confused with allergy (eg, isolated itching, malaise, dizziness, or digestive symptoms).
- A reaction provoked by another cause as a cofactor.

– Known adverse effects of the drug (eg, intertrigo after antibiotic treatment).
– Patients may assign themselves the allergy label and report this to their doctor [6].
– Patients may also be labeled as allergic because a direct family member was allergic.

These and other situations help to explain the fact that a high number of people who are labeled as allergic to a drug are

Table 1. Data From the Clinical History With Specific Diagnostic Value

Data from the clinical history that indicate a high probability of a drug allergy
Immediate reactions
Reaction <1 h after administration of the first dose in a new course of treatment
Skin symptoms: generalized wheals and/or facial or oropharyngeal angioedema or palmoplantar pruritus
Consider anaphylaxis if there are multisystem symptoms with or without skin involvement - Respiratory symptoms: dyspnea, wheezing, cough, respiratory arrest, and hoarseness - Cardiovascular symptoms: hypotension, tachycardia, weak pulse, and palpitations - Neurological symptoms: dizziness, loss of consciousness, and confusion. - Gastrointestinal symptoms: diarrhea and vomiting.
Treatment with adrenaline
Multiple reactions with the same drug (and in the case of NSAIDs, with drugs from 2 different groups)
Hospital admission due to an immediate reaction
High-risk comorbidities (bronchial asthma or nasal polyposis)
Increased serum tryptase
Delayed reactions
Maculopapular rash
Vesiculobullous rash
Ulceration of the oral, ocular, or genital mucosa
“Target” lesions
Skin denudation (Nikolsky sign)
Multiple pustules
Purpuric lesions
Arthralgia or lesions consistent with serum sickness
Systemic involvement (liver, kidney, fever, lymphadenopathy, eosinophilia)
Elements of clinical histories that indicate a low probability of a drug allergy
Remote history of symptoms not suggestive of a severe reaction (>5 y previously)
Delayed-onset urticaria (>6 h after the dose)
Acute urticaria and recurrence of urticaria for several days (except for NSAIDs)
A mild self-limiting rash, especially in childhood/adolescence
The interval between taking the drug and the onset of symptoms is not suggestive of an immediate or nonimmediate allergic reaction
Known drug tolerance after the index reaction
Reaction occurring in childhood with few known details
Symptoms probably related to the underlying disease
Not remembering the drug causing the reaction
Itching without a rash
Isolated symptoms: gastrointestinal/headache/malaise/palpitations/dizziness
Only a family history of allergy
Drug avoidance solely out of fear
The patient does not remember having any type of reaction

This table was produced using data from references 12, 13, 18, 21, 25, 27, 29, and 33.

not actually allergic. In the United States, 8%-15% of patients carry a penicillin allergy label [20], and only 4% of them or fewer actually have penicillin allergy [21]. This has created a serious problem, in that overprescription of less effective antibiotics can lead to more serious infections, with increased length of stay, spread of multiresistant bacterial strains, and higher costs [21,22].

To solve this problem, some authors propose directly administering a dose of penicillin to specific patients to confirm their tolerance [23,24]. Others have proposed different ways of stratifying risk [13,21,25-28], namely, identifying data suggestive of a true allergy requiring more careful evaluation in the clinical history before considering a direct provocation test [13]. However, attempts to replace conventional allergy testing with risk stratification to avoid time- and resource-consuming allergy testing also have the potential to cause reactions and do not take into account the possibility of resensitization [8]. In addition, some patients are reluctant to receive a direct dose of penicillin without first carrying out an allergology study, indicating that removing the allergy label based solely on the clinical history is not exempt from difficulties [23]. Attempts have been made to design prospectively applied predictive models to predict whether a patient is allergic [29,30], although their actual predictive ability has not been optimal.

Therefore, false labeling can be associated both with the patient and with the health professional. Many false labels should either not be applied or be removed as they become known. This requires adequate training for doctors to allow them to safely filter out cases that should not be labeled as allergic, thereby curbing the problem. Family doctors and specialists should be able to decide not to label certain symptoms or reactions as allergic. Similarly, they should not delay the referral of patients who experience reactions suspected of being allergic or who present with doubtful symptoms to an allergist.

Although the study of drug allergies has a nonnegligible cost to the health system and direct and indirect costs to the patient, the cost of falsely labeling allergies could be higher, because more expensive and less effective antibiotics are prescribed, leading to an increase in the average length of stay [31]. Moreover, having experienced an allergic reaction to a drug affects patient quality of life, which improves once an allergology study is completed [32].

Allergology Studies

A specific allergology study is performed preferably 4-6 weeks after complete resolution of all the clinical signs and symptoms of the allergy [1] and up to 6-12 months after the reaction.

These studies should include a complete and accurate clinical history to establish a study protocol. Depending on the clinical presentation, the appropriate tests will usually comprise skin prick and intradermal tests with immediate and delayed readings, patch tests, in vitro tests (measurement of specific IgE, a basophil activation test, lymphocyte transformation test, complete blood count, liver and kidney function), and controlled challenge tests.

What Should Be Asked When Taking the Clinical History?

The clinical history can provide very important data when planning allergy studies. Some findings may lead us to be more cautious in performing skin tests, while others can indicate that the drug in question is very unlikely to be the cause of the reaction, or that the suspected drug is different from that initially presumed to be the culprit. Several studies [12,13,18,21,25,27,29,33] highlight data for and against a suspected reaction being considered an allergic reaction (Table 1).

The doctor who saw the patient during the reaction should record in detail the sequence of the onset of symptoms, the times of introduction and withdrawal of each drug, the type of skin lesions and their distribution, clinical course, and treatment.

In immediate reactions, it is important to quickly assess the serum tryptase value as the only marker of mast cell activation, usually by an IgE-mediated mechanism [34]. In nonimmediate reactions, other parameters, such as blood count, liver and kidney function, and serology, should be determined [35].

Diagnosis is more difficult when patients are not seen during the symptomatic phase or if many years have passed since the reaction, making it impossible to confirm the chronology of the reaction, type of lesions, and names and number of suspect drugs. Photographs of the lesions can help considerably in these cases. The primary objective of the clinical history is to identify whether the reaction is compatible with an HSR in order to decide whether an allergology study is indicated. Supplementary Table 1 indicates factors that can help in this decision.

Ideally, these data should be recorded in a uniform format. EAACI-DAIG/ENDA members have developed a questionnaire to harmonize diagnostic procedures in HSRs [36]. We have adapted and reduced the questionnaire (Figure). Collecting reaction data in this way helps physicians to remember important data and homogenizes the information for use in further studies with different researchers. Below, we list the various items that should be collected in the clinical histories (Supplementary Table 2).

Date of the reaction

The first question asked should be "When did the reaction occur?" Important details about the reaction are lost when the clinical history is taken after a long interval. It is preferable to wait 4-6 weeks before carrying out the allergology study [1]. In IgE-mediated reactions, the specific IgE levels decline rapidly over months [37], and skin tests can become negative, especially a year after the reaction [38]. The frequency of resensitization varies in the literature from 2% to more than 20% of cases [39-41]. Although there is no consensus on this point, retesting is recommended, particularly in patients who have experienced serious reactions with ß-lactams more than a year previously [1,8].

Reason for the prescription

The presence of an infectious agent can cause skin rashes. For example, a reaction occurring in the context of infectious

RESEARCHER: _____ PATIENT: _____

SEX

☐ M ☐ F NAT / Age: _____ DATE OF REACTION: ____ / ___ / ____

☐ Unknown

CURRENT DISEASE: _____ _____

DRUG REACTION: *fill in the table with the drug(s)*

Similar symptoms without taking these drugs:

ATOPY

☐ NO

☐ YES ☐ Rhinitis / Asthma ☐ Atopic dermatitis ☐ Food allergy

Skin symptoms:

☐ Macules
☐ Itching
☐ Papules
☐ Hives
☐ Angioedema
☐ Eczema
☐ Vesicles
☐ Blisters
☐ Purpura
☐ Target lesions
☐ Fixed rash
☐ Pustules
☐ Purpura
☐ Nickolsky sign

Duration of lesions:

_____

Evolution:

☐ No residual lesion
☐ Desquamation
☐ Hyperpigmentation

Cardiovascular symptoms:

☐ Hypertension
☐ Hypotension
☐ Tachycardia
☐ Arrhythmia

Gastrointestinal symptoms:

☐ Nausea/vomiting
☐ Diarrhea
☐ Abdominal pain

Respiratory symptoms:

☐ Cough
☐ Dysphonia
☐ Dyspnea
☐ Wheezing
☐ O_2 desaturation
☐ Sneezing/rhinorrhea/ nasal congestion
☐ Conjunctivitis

Onset of symptoms:

☐ IMMEDIATE reaction: <1 hour after first dose
☐ IMMEDIATE reaction: 1 to 6 hours after first dose
☐ LATE reaction: > 6 hours after first dose on day 1
☐ LATE reaction: _____ days from first dose
☐ LATE reaction: _____ days from last dose

Contributing factors:

☐ Viral infection
☐ Fever
☐ Photosensitivity
☐ Physical exercise
☐ Stress
☐ Autoimmune diseases
☐ Cancer
☐ Other: _____

Treatment of the reaction:

Drug discontinued:

☐ NO ☐ YES

Antihistamines:

☐ Oral ☐ Systemic

Corticosteroids:

☐ Oral ☐ Systemic ☐ Topical

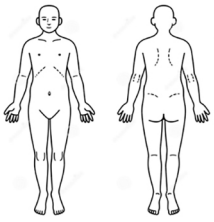
Epinephrine

Other: _____

Other symptoms:

☐ Fear
☐ Syncope
☐ Paresthesia
☐ Hyperventilation
☐ Fever
☐ General discomfort
☐ Hematological involvement
☐ Renal involvement
☐ Liver involvement
☐ Neurological involvement

Location of skin lesions



Suspected drugs	Dose	Day / h first dose	Day last dose

10 9 8 7 6 5 4 3 2 1 0 1 2 3 4 5 6 7 8 9 10

Figure. Medical History Questionnaire on Drug Allergy. Proposed questionnaire to collect important data from the clinical history of a patient with suspected drug allergy (adapted from P Demoly [36]). 0 marks the first day of the reaction. Each mark to the left and right of day 0 indicates a day before or after, respectively, the onset of the reaction. Below the line, the first and last day of each medication can be noted.

Table 2. Points to Consider in the Clinical History: Specific Drug Groups

Medication	Points to consider
ß-Lactams	Check tolerance to the suspected drug or other ß-lactams. Assess the possibility of concomitant infection (eg, mononucleosis, cytomegalovirus) in diagnosis.
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Check subsequent tolerance to other NSAIDs. Evaluate the possibility that NSAIDs are acting as a cofactor in a reaction to a food. Investigate respiratory symptoms (eg, asthma, nasal polyps) due to suspicion of NSAID-exacerbated respiratory disease. Ask about the possibility of underlying urticaria.
Radiological contrast media	Pre- and postadministration. Assess the possibility of previously unreported delayed reactions.
Quinolones	Assess photosensitivity. Possibility of a non–IgE-mediated mechanism (through MRGPRX2).
Corticosteroids	Consider excipients and preservatives (eg, sorbitan, polyethylene glycol). Consider delayed eczema or dermatitis with a poor course and treated with corticosteroids. Assess tolerance in different ways. Facial rash syndrome as an adverse effect.
Low-molecular-weight heparins	These agents almost always cause delayed local reactions at the injection site. High probability of cross-reactivity.
Sulfonamides	These can cause all kinds of allergic reactions including immediate reactions, fixed drug reactions, or severe cutaneous adverse reactions. No evidence of cross-reactivity between antibiotic sulfonamides and nonantibiotic sulfonamides.
Drugs used in anesthesia	Record all the drugs administered before the reaction, including nonpharmacological products (eg, dyes, chlorhexidine). Possibility of an allergy to latex (assess related allergens such as fruits). Later tolerance to some of the drugs. Evaluate nonimmunological reactions (eg, problems with intubation, cardio-circulatory adverse effects of drugs). Evaluate other diagnoses (eg, cold urticaria, irritative reactions caused by antiseptics, plasma expanders due to α-gal).
Anticonvulsants	Can cause severe skin reactions. Presence of systemic symptoms: fever ≥38.5°C, lymphadenopathy, eosinophilia, atypical lymphocytes, skin rash, involvement of other organs (eg, liver, kidney, lung, muscle, heart, pancreas); resolution ≥15 days. Rule out other causes (eg, antinuclear antibodies, blood cultures, hepatitis serology, *Chlamydia*, *Mycoplasma*, C-reactive protein). Frequent cross-reactivity between aromatic anticonvulsants (phenytoin, carbamazepine, and phenobarbital).
Biological drugs	Possibility of cytokine storm.
Local anesthetics	Anesthetics of the ester group can cause delayed allergic reactions that do not present cross-reactivity with those of the amide group (which very rarely cause allergic reactions).
Chemotherapy	Platins usually induce an IgE-mediated reaction when the patient has received several cycles. Taxanes usually induce a reaction after the first or second dose, rarely IgE-mediated.
Drugs that cause delayed allergic reactions related to human leukocyte antigen (HLA) polymorphisms	Dapsone and HLA-B 13:01. Phenytoin and HLA-B*15:13 and 15:02. Carbamazepine and HLA-B 15:02 and HLA-A 31:01. Vancomycin and HLA-A 32:01. Abacavir and HLA-B 5701. Allopurinol and HLA-B 58:01. Benznidazole and HLA-A 68, HLA-A 11:01, and HLA-A 29:02.
Cremophor EL	Included in cyclosporine, tacrolimus, taxol, and Stesolid (diazepam), among others.
Protamine (fish allergy, postvasectomy, or previous contact with protamine)	To be considered in reactions involving insulin or heparin.
Gelatin capsules of bovine or porcine origin.	Patients allergic to α-gal.
Proton pump inhibitors	Three patterns: *1*) Allergy exclusively to omeprazole; *2*) Allergy to pantoprazole and omeprazole; *3*) Allergy to rabeprazole and lansoprazole.
Vancomycin	Infusion rate–dependent red man syndrome.

Table 3. Hypersensitivity Reaction Data That Can Increase or Decrease the Value of the Clinical History

	Less accurate clinical history ←		→ More accurate clinical history
Reaction date	> 3 y	1 to 3 y	< 1 y
Reason for the prescription	Pharyngitis + fever		
Drug(s)	> 3	2	1
Route of administration	Topical	Local (eg, ocular, intrathecal)	Systemic
Treatment administered	Spontaneous resolution	Home treatment	Emergency/adrenaline
Symptoms without taking the drug	Same symptoms repeated		Asymptomatic
Related factors	Fever (except DRESS)	Atopy	
Chronic urticaria			
Asthma/polyposis	None		
Immediate reactions			
No. of doses	> 4	2 or 3	1
Time	> 6 h	1 to 6 h	< 1 h
Duration of symptoms	Seconds to minutes	> 24 h	< 24 h
Nonimmediate reactions			
No. of doses	1	2 or 3	> 4
Time	> 1 h	1 to 6 h	> 6 h
Duration of symptoms	< 1 d	< 3 d	> 3 d

Abbreviation: DRESS, drug reaction with eosinophilia and systemic symptoms.

mononucleosis treated with amoxicillin-clavulanate [42] cannot be considered in the same way as a rash occurring in the context of the prophylactic administration of this drug prior to an invasive technique. In addition, knowing the reason for the prescription of the drug can help us to rule out other potentially involved drugs.

Drugs used

It is also important to obtain a complete list of all the medications administered to the patient at the time of the reaction. This is particularly true in specific situations, such as surgery, hospital environment, and radiological/endoscopic examinations. When the symptoms are typical of immediate reactions, it would be enough to note the drugs received in the previous 6 hours. In the case of hives associated with an NSAID, the treatment time could be longer, even up to 12-24 hours [18].

In the case of a nonimmediate reaction, the information should cover the 2 or 3 days prior to the onset of the rash and, depending on the type of reaction, even the previous 4-8 weeks [1]. We must remember that since the symptoms appearing during the first hours or days may have been very mild, the start of a delayed reaction may not be very precise. Table 2 shows various points to consider with specific drugs.

Administration route

A medication can produce a reaction, irrespective of the administration route. However, it is important to bear in mind the following: (*i*) the intravenous route can produce extravasation of the drug; (*ii*) it is common for the reaction to appear locally at the site of administration after topical or subcutaneous application; (*iii*) the oral route is the route most often involved in allergic reactions because it is the most commonly used [43].

Number of doses administered until the onset of symptoms

The number of doses is also important. In fact, if the reaction occurred immediately after the first dose administered, it should alert us to a possible IgE-mediated reaction. Delayed reactions usually occur after more than 1 dose.

Time between drug administration and onset of symptoms

This is of particular importance when the patient is exposed to several drugs. Immediate reactions are those that occur within the first 6 hours of the first dose (especially within the first hour). Some reactions with symptoms of an IgE-mediated reaction (eg, in reactions to NSAIDs) can appear after the first hour.

The time elapsed between taking the drug and the onset of the symptoms of a delayed reaction can be as short as 30 minutes, such as in fixed drug eruption [44], or take several weeks, as in DRESS syndrome [35].

Symptoms and signs presenting during the allergic reaction

It is essential to record each of the symptoms that appear, changes over time, and their course. It is also important to make a detailed description of any skin lesions, including

their distribution and progress. For example, skin peeling may indicate a true nonimmediate reaction. Table 1 shows symptoms in both immediate and delayed allergic reactions. In the case of immediate reactions, some symptoms (for example, digestive or respiratory symptoms, or even loss of consciousness) must be considered typical of an allergic reaction if they appear in the context of anaphylaxis, but not if they appear in isolation.

Nonetheless, not all information from the clinical history has the same weight for allergology studies. Table 3 highlights the relevance of certain types of data in this respect.

Treatments given during allergic reactions

The main data to be collected are treatments administered to reverse the reaction, their doses and routes of administration, and whether the patient required treatment by a doctor or in the emergency department or had to be admitted to hospital. We should also record whether the allergic reaction simply receded spontaneously and how long this took (minutes, hours, or days). Having received urgent medical attention or adrenaline or having been admitted to a hospital/intensive care unit indicates more severe reactions and a greater probability of an allergic reaction.

The presence of the same symptoms without administration of the drug

It is also important to know whether the patient has experienced the same symptoms when not taking the suspected drug. For example, a reaction attributed to a drug could in fact be caused by a food [45], and chronic urticaria can be exacerbated by NSAIDs [46]. In turn, some symptoms can occur as an adverse effect and can lead a patient to be falsely labeled as allergic (Supplementary table 3). These symptoms are indicated in the summary of product characteristics.

If a patient reports similar symptoms with drugs from different pharmaceutical groups, then the probability of a true allergy decreases. However, multiple HSRs to drugs have been reported, as have delayed reactions mediated by lymphocytes through stimulation of T cells via the p-i mechanism [47,48].

Previous drug exposures

Intermittent and prolonged exposure to a drug increases the probability of sensitization [49], while gradually beginning administration of a drug can reduce the likelihood of delayed onset [50,51]. Information regarding previous reactions with the same drugs will also help raise or lower our suspicions with respect to the drugs involved. In IgE-mediated reactions, it is not uncommon for the patient to have recently tolerated the same drug several weeks before the reaction, with this pattern usually indicating a true allergic reaction.

Subsequently tolerated drugs

We should record any treatments the patient has tolerated after the reaction (eg, a patient reporting an allergy to penicillin who has tolerated amoxicillin). When these data come from the patient without confirmation, it is important to seek confirmation. If the patient has subsequently tolerated potentially cross-reactive drugs, for example, in the case of a reaction involving an NSAID, it is essential to know what analgesics or anti-inflammatory drugs were used after the reaction.

Other data

We should record other diseases that could explain symptoms and influence the need for specific medications in the future (eg, patient requiring periodic scans or antibiotics). Similarly, it is important to know whether the patient is atopic or has chronic urticaria or osteoarticular conditions that will often need treatment with NSAIDs.

It also helps to assess comorbidities that may contraindicate the drug allergy study [14,35,52]. The clinical history can help to detect other diseases that can simulate an allergic reaction to a drug. These include allergic reactions to specific foods and food allergens (eg, plant lipid transfer proteins, ω-5 gliadin, and shellfish), which often require a cofactor such as an NSAID for the allergic reaction to occur [53].

Conclusion

The clinical history is a basic tool in medicine and plays a key role in guiding the study of a supposed allergic reaction to a drug. Attempts to replace them with a series of data collected using a questionnaire have thus far been unsuccessful. Therefore, we must prioritize adequate training of doctors from various specialties to ensure that the most important data in the clinical history are collected and that the safety and efficiency of subsequent allergology studies can be improved. Further research is needed to show that taking the clinical history appropriately can help in making correct diagnoses and reliable recommendations that will not lead to the avoidance of important drugs.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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