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Successful removal of penicillin allergy label in a tertiary hospital in Paraguay

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Abstract: Objective: To develop a treatment algorithm for patients with penicillin allergy.

Methods: Retrospective study, carried out in adult patients with penicillin allergy, who remained in group 3 or 4 of the established classification, and attended outpatient consultation in the Department of Pulmonology and Allergy of the Central Hospital of the Social Security Institute, between January 2021 and December 2022. Each patient underwent a provocation test with amoxicillin, after informed consent.

Results: 60 patients were registered, who were able to remove the penicillin allergy label and whose medical history was corrected, resulting in financial benefits for both the patient and the Paraguayan health service.

Conclusion: Penicillin allergy labels can lead to irrational antibiotic prescribing, prolonged hospital stays, and increased need for outpatient visits. Risk stratification based solely on historical characteristics can reliably identify ideal patients for direct challenge testing. This study demonstrates the feasibility of the first penicillin delabeling program applicable in an outpatient setting, which can be implemented even outside of hospital allergy departments.

Key words: allergy; penicillin allergy; amoxicillin; Paraguay; risk stratification; feasibility; antibiotic prescription

1 Background

Penicillins are a group of antibiotics frequently associated with a high risk of drug allergy and anaphylaxis [1,2]. The prevalence of penicillin allergy ranges from 5% to 15% worldwide [3-7]. However, only 2% to 10% of cases test positive for penicillin allergy [8,9]. Although various types of allergy are mislabeled and the proportion of genuine allergies is low, it remains a significant concern when prescribing penicillin and considering it as a treatment option [10]. Due to insufficient knowledge of drug allergies, some clinicians accept existing penicillin allergy labels or self-reported penicillin allergies without further verification. Therefore, it is common for patients diagnosed or labeled with penicillin allergy to receive alternative antibiotics to avoid the risk of severe reactions. Furthermore, physicians tend to avoid prescribing other beta-lactam antibiotics, especially first- and second-generation cephalosporins, for fear of cross-reactivity. This often results in the unnecessary prescription of broad-spectrum, second-line antibiotics in patients with unconfirmed penicillin allergy. Children and pregnant women are no exception [11,12]. Over time, this leads to increased surgical site infections [13], drug-resistant bacterial infections [14,15], and treatment failures [16]. Some studies suggest that documented penicillin allergy is a risk factor for higher medical costs [4] and prolonged hospital stays [14]. In addition, for patients infected with COVID-19 diagnosed with penicillin allergy, it also affects COVID-19-related outcomes, such as

hospitalization, acute respiratory failure, intensive care unit (ICU) requirements, and mechanical ventilation [17]. Therefore, eliminating false penicillin allergy labels is considered an important aspect of antibiotic stewardship [18,19].

While the delabeling of penicillin allergy has gained increasing attention worldwide [19], there are still no reports on its prevalence and impact in Paraguay, where penicillin allergy labels are suspected to be inaccurate due to the lack of a reference diagnostic algorithm for penicillin allergy. Therefore, the objective of this study was to develop a simple, easy, and safe treatment algorithm for patients with penicillin allergy.

2 Methods

Retrospective study, carried out in adult patients who consulted for allergic pathologies, who were questioned if they knew or had a history of penicillin allergy, and who attended the Pulmonology and Allergy service at the Central Hospital of the Social Security Institute, Paraguay, between January 2021 and December 2022. A detailed clinical history was prepared for each patient and they were classified into one of the groups shown in Table 1.

Table 1. Penicillin exposure groups

Group 1 H. type 1	Group 2 H. Type IV	Group 3 Unlikely H. type 1	Group 4 Vague history
One or more of the following symptoms at the time of the first dose	One or more of the following symptoms > 6 hours after drug exposure	No temporal association between symptoms and exposure	The temporal association between drug administration and the onset of symptoms is vague/unknown
Hives: redness, itching	Maculopapular rash, urticaria/angioedema, itching, redness	Exposure to the same medication without reaction	Vague history with no details. E.g., a child's penicillin allergy label
Angioedema, rhinitis or rhinconjunctivitis, bronchospasm, chest tightness, rhonchi, cough, desaturation, cyanosis	FDE, DRESS, SJS,TEN, AGEP	The symptoms do not suggest an immune reaction, such as headache, blurred vision, or isolated gastrointestinal symptoms.	It is not clear or certain whether the symptoms occurred after the first dose or after subsequent doses.
Hemodynamic instability (syncope, arrhythmias, seizures, cardiac arrest)	**Other types of H. type II or III are rare and can cause hemolysis, acute interstitial nephritis, vasculitis, etc.**	**Limited urticaria**	**Adverse reaction following administration of more than one drug. Parents' history of penicillin allergy.**

Each patient with penicillin allergy, who was in group 3 or 4, underwent a provocation test with amoxicillin. Only patients who signed the informed consent were included (Figure 1).

3 Results

Sixty patients with penicillin allergy were selected:

29 in group 3 and 31 in group 4. After the provocation tests, no patient reported a hypersensitivity reaction. Forty-one women and 19 men were registered, and the provocation test was performed on them (Figure 2).

Figure 3 shows the number of allergy patients by age group. According to the results, 33 patients were registered in group 3 and 27 in group 4 for provocation.

Regarding the type of allergy by type of antibiotic, 40 cases of penicillin allergy and 20 cases of amoxicillin allergy were reported.

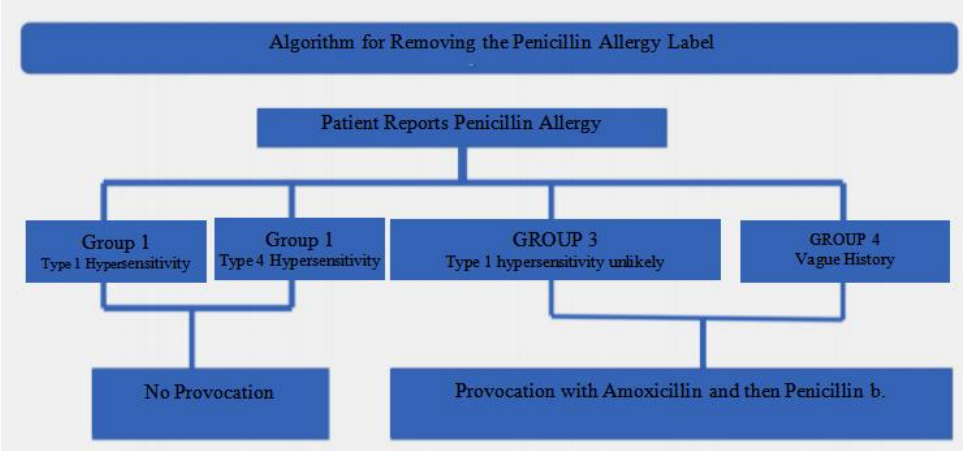

Figure 1. Algorithm to determine which patients can receive the amoxicillin provocation test

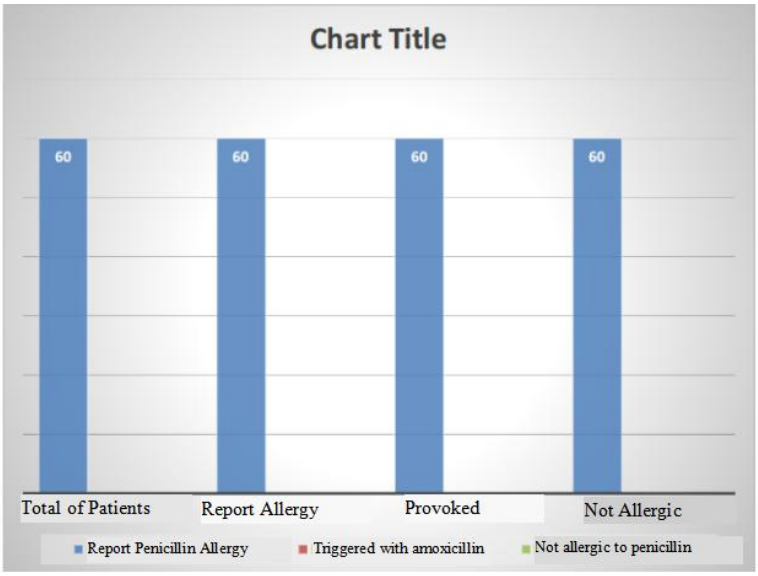

Figure 2. Results of the provocation test

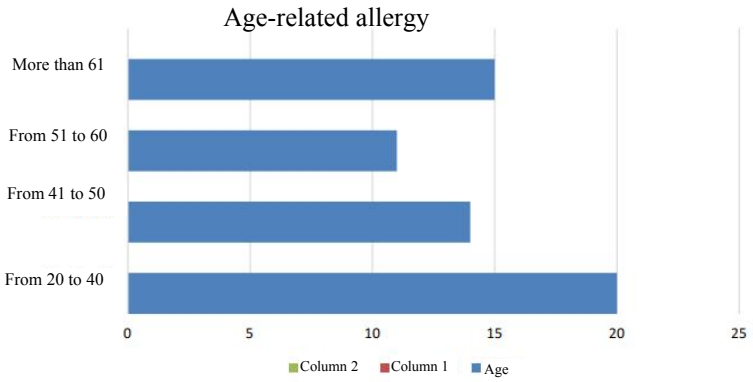

Figure 3. Patients with allergies by age group

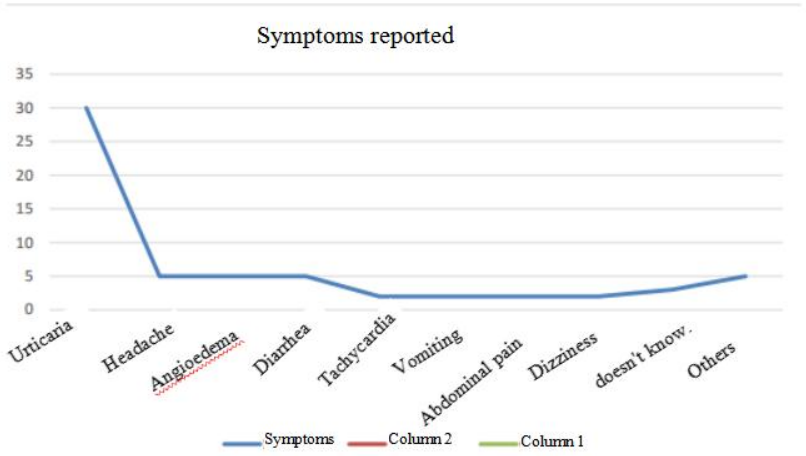

Figure 4. Clinical manifestations reported by patients

The most frequent symptom of penicillin allergy was urticaria, followed by headache, angioedema, diarrhea, tachycardia, vomiting, abdominal pain, and dizziness. A small group did not recall their symptoms, as they were pediatric patients. The allergy was reported by the mother (Figure 4).

The time of evolution of the allergic reaction after receiving penicillin was variable; however, most reported symptoms after 12 hours of exposure and others were unaware of this fact, because the allergy reference was provided by the mother (Figure 5).

The treatment protocol to reduce or control the symptoms of the alleged penicillin allergy consisted of antihistamines (48%) and discontinuation of the drug (48%); the remaining 4% did not remember the type of medication or protocol they received.

4 Discussion

Penicillin skin provocation testing, with major and minor determinants, may not be necessary to remove the label from low-risk patients. This study described the utility and safety of a penicillin allergy algorithm, which incorporates challenges in the outpatient management of penicillin allergy.

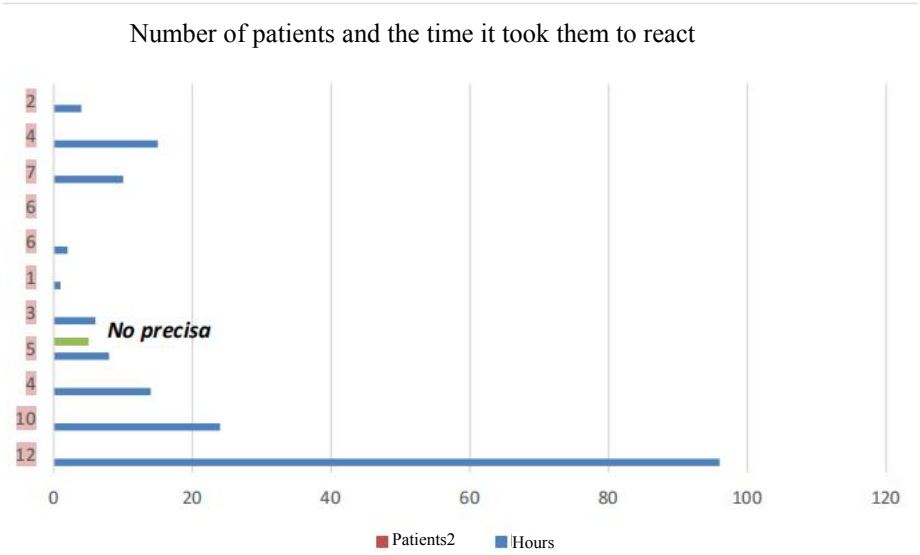

Figure 5. Time of evolution of the allergic reaction

Table 2. PEN-FAST score for the diagnosis of penicillin allergy

Quick score	Points	Points
Five years or less since the reaction	No 0 points	Yes +2 points
Anaphylaxis, angioedema or severe cutaneous adverse reaction	No 0 points	Yes +2 points
Treatment required for the reaction	No 0 points	Yes +1 points

Beta-lactams are the most prescribed antimicrobials due to their safety and efficacy. The immunoallergist is the best-qualified specialist to identify patients with penicillin allergy, as well as to develop challenge and desensitization protocols in a controlled environment [20]. In Paraguay, it is difficult to obtain major and minor determinants for the penicillin provocation test due to the high cost and limited access to the test; therefore, a tangible, practical, and efficient mechanism that allows for penicillin administration based on the patient's medical history is important.

The algorithm we are presenting, although insufficient in the number of patients to confirm its validity, is low-cost, easy to use, and safe for family physicians, general practitioners, and pediatricians (who represent the first line of care) to implement, considering that we only have 45 allergists, concentrated in the capital, for a population of 7 million. The World Health Organization recommends 1 allergist for every 50,000 inhabitants, which indicates that Paraguay requires at least 140 allergists. Based on the above, it is urgent to take this type of measure to address allergies through primary care physicians [21,22].

In addition to the algorithm suggested by the authors of this study, the PEN-FAST scoring system, designed to facilitate treatment with β-lactams for patients, can be used. A maximum of 5 points should be achieved with the PEN-FAST system. If the score remains below 3, a diagnosis or label of penicillin allergy is unlikely. This scoring system facilitates rapid assessment, particularly in relation to severe reactions (analyxemia or angioedema within the last 5 years), and aids in therapeutic decision-making; however, there is no experience with this method [23]. Table 2

5 Conclusion

Multiple strategies exist for delabeling penicillin allergy, based primarily on patient's history of the reaction and comorbidities. It is important to perform penicillin skin testing (major and minor determinants) in patients with a history of anilaxia or a recent reaction, with a high suspicion of IgE-mediated involvement. Risk stratification based solely on historical characteristics can reliably identify ideal candidates for direct challenge testing. Patients with a history of penicillin allergy who fall within groups 3 and 4, and who undergo direct amoxicillin challenge testing without prior skin tests, should be subjected to the diagnostic algorithm, according to our context.

The penicillin allergy label should be removed from all available health records, and the patient should be clearly and empathetically informed that they can safely and confidently receive penicillin-based antibiotics.

Conflicts of interest

The author declares no conflicts of interest regarding the publication of this paper.

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