

## Original Article

# Asthma, Family History of Drug Allergy, and Age Predict Amoxicillin Allergy in Children

Yoram Faitelson, MD<sup>a,b</sup>, Mona Boaz, PhD<sup>c,d</sup>, and Ilan Dalal, MD<sup>b,e</sup> *Holon, Tel Aviv, and Ariel, Israel*

**What is already known about this topic?** To date, physicians are unable to predict who will fail or pass oral graded challenge with amoxicillin, which is commonly used to rule out alleged amoxicillin allergy in children.

**What does this article add to our knowledge?** The presence of asthma, family history of drug allergy, and older age at reaction are associated with a higher risk of failing the oral challenge. Skin prick test was not helpful in diagnosing amoxicillin allergy.

**How does this study impact current management guidelines?** Recognizing risk factors for amoxicillin allergy in the pediatric population can assist the allergist in deciding what will be the optimal setting of an oral challenge for individual patients.

**BACKGROUND:** Suspected adverse reactions to amoxicillin are common, but there are no known factors that can predict amoxicillin allergy in children. In addition, methods used for the diagnosis of amoxicillin allergy are not standardized and their role in diagnosis is not clear.

**OBJECTIVE:** To identify predictive factors and to assess the role of skin test in the diagnosis of amoxicillin allergy in children.

**METHODS:** Children with a history of immediate (excluding anaphylaxis) or nonimmediate reactions to amoxicillin were tested by skin prick test, followed by oral graded challenge with amoxicillin. Clinical characteristics of the reaction before and after the challenge were recorded, and data of personal and relatives' drug allergies and atopy were collected for statistical analysis.

**RESULTS:** Skin prick tests followed by an oral graded challenge with amoxicillin were performed on 133 children. The skin test result was not of clinical value because it was negative in all children. Three children (2%) had an immediate reaction and 7 children (5%) had a nonimmediate reaction. Asthma (odds ratio [OR], 0.12; 95% CI, 0.017-0.869;  $P = .03$ ), family history of drug allergy (OR, 0.12; 95% CI, 0.026-0.613;  $P = .01$ ), older age at reaction (OR, 0.837; 95% CI, 0.699-1;  $P = .05$ ), and

angioedema (OR, 0.22; 95% CI, 0.043-1.12; marginally significant at  $P = .069$ ) were associated with reduced chance to pass the oral challenge.

**CONCLUSIONS:** Skin prick test did not contribute to the diagnosis of amoxicillin allergy. The presence of asthma, family history of drug allergy, and older age at reaction can be used as predictive factors for true amoxicillin allergy in children. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

**Key words:** Amoxicillin; Children; Drug allergy; Oral challenge; Predictive factors

Antibiotics, mainly the  $\beta$ -lactams, are one of the most frequent drug groups prescribed for children worldwide. Approximately 5% of children and 10% of adults report a history of penicillin or beta-lactam allergy, although only a few of these patients are truly allergic.<sup>1-4</sup> In children, viral infection plays an important factor in the presentation of these so-called allergic reactions.<sup>5</sup> Children and adults who were labeled "penicillin-allergic" without appropriate testing may not get the optimal antimicrobial coverage and are often treated with alternative broad-spectrum antibiotics (vancomycin, macrolides, cephalosporins), which have been associated with additional costs<sup>6</sup> and significant morbidities, such as those caused by vancomycin-resistant *Enterococcus* and *Clostridium difficile*-associated diarrhea.<sup>7-9</sup>

Currently, the diagnosis of penicillin allergy is mostly assessed by using skin tests (to exclude penicillin-specific IgE sensitization), followed by an oral graded challenge (OGC)<sup>10</sup> in those who have a negative skin test result. However, the role of skin tests in the diagnosis of amoxicillin allergy is not clear and there is no consensus about which reagents should be used for the skin tests or whether skin tests are at all needed. In some centers, skin tests include a skin prick test (SPT) followed by an intradermal test (IDT) injection with the major antigenic determinant, and various minor determinants, the most commonly used being penicillin G.<sup>11,12</sup> Other centers recommend adding

<sup>a</sup>Allergy and Immunology Unit, Edit Wolfson Medical Center, Holon, Israel

<sup>b</sup>Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

<sup>c</sup>Department of Nutrition Sciences, Ariel University, Ariel, Israel

<sup>d</sup>Department of Epidemiology & Research Unit, Edit Wolfson Medical Center, Holon, Israel

<sup>e</sup>Department of Pediatrics, Edit Wolfson Medical Center, Holon, Israel

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication June 12, 2017; revised November 1, 2017; accepted for publication November 15, 2017.

Available online ■■

Corresponding author: Yoram Faitelson, MD, Unit of Allergy and Immunology, Wolfson Medical Center, Ha-Lokhamim St 62, Holon, Israel. E-mail: [yfaitelson@gmail.com](mailto:yfaitelson@gmail.com).

2213-2198

© 2017 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2017.11.015>

**Abbreviations used**

*IDT*- Intra-dermal test  
*NPV*- Negative predictive value  
*OGC*- Oral graded challenge  
*OR*- Odds ratio  
*PPV*- Positive predictive value  
*SPT*- Skin prick test

aminopenicillins to the skin tests in patients who reacted to these drugs or may need them in the future.<sup>13</sup> There is cumulative evidence supporting the safety and accuracy of performing the OGC to confirm an allergic reaction to penicillin or amoxicillin in children with only a minimal skin test including selected reagents preceding it or no skin test at all.<sup>4,14,15</sup> The latter approach is supported by the fact that although the negative predictive value (NPV) of penicillin skin testing (when performed with the major determinant plus penicillin G or a full minor determinants panel) is very high, the positive predictive value (PPV) is low<sup>5</sup> or not known, because data are limited due to ethical concerns of challenging skin test—positive patients with penicillin.<sup>16-19</sup>

Because of the weak PPV of the skin test, there is a strong need for identification of reliable risk factors that could help select the population that has a higher risk for true amoxicillin allergy. Given such risk factors, one can choose to proceed with OGC without the burden of skin testing or, in contrast, patients who have significant risk factors might need further testing before an OGC is done. In this study, we focused on finding clinical predictive factors, such as the history of the reaction and the personal or family history of atopy, that can predict true allergic reaction to amoxicillin. In addition, because SPT is time consuming and painful, especially for young children, we assessed the role of SPT in the diagnosis of amoxicillin allergy in the pediatric population and calculated its sensitivity and specificity.

**METHODS****Study cohort**

The study was performed at the Wolfson Medical Center, Holon, Israel. Included in the study were children who had been referred to the Allergy unit in our center from January 1, 2013, to December 31, 2015, with a suspected allergic reaction to amoxicillin or amoxicillin-clavulanate antibiotic. Patients with a history of a severe cutaneous adverse reaction (eg, Stevens-Johnson syndrome/toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis) were excluded from this study. The study was approved by the Wolfson Medical Center Ethical Board (#0065-017-WOMC).

**Study questionnaire**

Before skin testing and oral challenge, a standardized questionnaire based on the European Network of Drug Allergy questionnaire was completed by the physician with the child guardian. The questionnaire included questions about the clinical characteristics of the reaction, comorbidities (including a history of atopy, use of medications before, after, and during the suspected reaction), family history regarding atopy and drug allergy, and management of the reaction.

**TABLE I.** Patient characteristics (n = 133)

Characteristic	Value
Sex, n (%)	
Male	70 (52)
Female	63 (48)
Age (y), median (min-max)	
At initial reaction	2 (0.1-17.5)
At time of challenge	4.1 (0.7-18)
Type of antibiotics, n (%)	
Amoxicillin	126 (95)
Amoxicillin-clavulanate	7 (5)
Atopy*, n (%)	
Personal	29 (22)
Asthma	9 (7)
Food allergy	8 (6)
Allergic rhinitis	8 (6)
Atopic dermatitis	6 (4.5)
Family	42 (32)
Family History of drug allergy, n (%)	35 (26)
Time to initial reaction, n (%)	
Immediate (<1 h)	6 (5)
Delayed (>1 h)	101 (75)
Unknown	26 (20)
Type of reaction, n (%)	
Skin	129 (97)
Angioedema	22 (16.5)
Gastrointestinal	2 (1.5)
Respiratory	1 (0.7)

\*Atopy—Presence of asthma, food allergy, allergic rhinitis, or atopic dermatitis.

**Skin testing procedure**

Skin testing was performed by 1 of 2 experienced nurses. Penicillin G (at a concentration of 10,000 U/mL) and amoxicillin (at a concentration of 50 mg/mL) were used for skin prick testing as previously described. Normal (0.9%) saline and 2 mg/mL of histamine were used as negative and positive controls, respectively. Reading of test result was done by 1 of 2 experienced nurses 15 minutes after the test and was documented in the patient medical chart. The test result was considered positive if it elicited a wheal greater than 3 mm compared with the negative control. Intradermal injections of penicillin or penicillin derivative were not given in this study.

**Graded drug challenge procedure**

If the SPT result was negative, as it was in all of our patients, a 3-dose graded drug challenge was performed to the drug incriminated in the allergic reaction (or amoxicillin if the culprit drug could not be identified). All children received 10% of the therapeutic dose (50 mg/kg/dose, up to a maximum of 500 mg/dose of amoxicillin), then 20 minutes later 30% of the therapeutic dose, and after another 20 minutes the rest of the therapeutic dose, that is, 60% of the therapeutic dose. Children were observed for at least 1 hour after receiving their last dose. Parents were asked to continue with the drug challenge by giving 100% of the therapeutic dose as a single dose in the following 2 days after their clinic visit. Parents and patients were warned about the possibility of a delayed reaction and asked to contact the allergy clinic by email or phone if any delayed reaction was noticed. If no immediate or delayed reaction occurred, the child was considered not allergic to amoxicillin, and parents and

Download English Version:

<https://daneshyari.com/en/article/8714128>

Download Persian Version:

<https://daneshyari.com/article/8714128>

[Daneshyari.com](https://daneshyari.com)