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Research Article

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Use of Meropenem in Children Labeled with Penicillin and Cephalosporin Allergy: A Retrospective Study Based on Real-life Data

Merve Karaca Şahin [1], Güler Yıldırım [1], Nilay Çalışkan [1], Hamit Boloğur [1], Muhammed Fatih Erbay [1], Aslı Berivan Topçak [1], Hasan Tunç Şarman [1], Hilal Güngör [1], Çağla Öztürk [2], Şefika İlknur Kökcü Karadağ [1] & Deniz Özçeker [1]

[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
[2] Bezmialem Vakıf Üniversitesi, Pediatric Immunology and Allergy Department, İstanbul, Türkiye

Abstract

Objective: Beta-lactam antibiotics are among the most commonly used and frequently reported drug allergies. The beta-lactam ring has traditionally been considered to be responsible for cross-reactivity across all beta-lactam antibiotics. However, recent publications demonstrate that side chains, rather than the beta-lactam ring, are primarily responsible for cross-reactivity and that meropenem can be safely used in patients with beta-lactam allergies. The aim of our study was to evaluate the safety of meropenem in patients labeled with penicillin and cephalosporin allergies based on real-life data.

Materials and Methods: Children under the age of 18 years who were referred to the Pediatric Immunology and Allergy with a beta-lactam allergy label between January 1, 2017, and September 1, 2024, were retrospectively evaluated.

Results: A total of 95 children labeled with a beta-lactam allergy were referred to our Pediatric Allergy and Immunology Clinic for appropriate antibiotic selection. Among them, 64% were female and 36% were male. Fifty-eight patients were labeled as allergic to penicillins only, 31 to cephalosporins only, and 6 to both drug classes. Meropenem was administered to 23 patients. Of these, only three developed a rash following meropenem treatment and were re-referred for further evaluation. A total of 15 patients presented to our outpatient clinic for the diagnostic assessment of beta-lactam allergy. None of them had an allergy to meropenem. However, beta-lactam allergy was confirmed in three patients.

Conclusion: Meropenem appears to be a safe and effective alternative treatment option for patients labeled with beta-lactam allergy until a comprehensive beta-lactam allergy workup can be conducted.

Keywords Beta-lactam · Drug hypersensitivity · Meropenem · Cross-reactivity

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Corresponding author: Merve Karaca Şahin karacasahinmerve@gmail.com

INTRODUCTION

Beta-lactam antibiotics are the most commonly used group of antibiotics for infection (1). However, they are also the most frequently reported drug class responsible for allergic reactions in children (2). Beta-lactam antibiotics are subdivided into penicillins, cephalosporins, carbapenems, monobactam, and clavam (3). Meropenem, a member of the carbapenem group, is a broad-spectrum antibiotic effective against resistant gram-negative, gram-positive, and anaerobic bacteria. It is generally used for serious and hospital-acquired infections in hospitalized patients (4).

All beta-lactams share a common four-membered beta-lactam ring. In penicillins, this ring is attached to a five-membered thiazolidine ring, whereas in cephalosporins, it is linked to a six-membered sulfur-containing dihydrothiazine ring. Carbapenems differ structurally by having a five-membered ring in which the sulfur atom replaced by a carbon double bond. Penicillins and carbapenems contain a single side chain, whereas cephalosporins have two side chains. Among these, the R1 side chain is considered the main determinant of the cross-reactivity between beta-lactam antibiotics (5). The shared beta-lactam ring itself may also exhibit allergenic potential. Because this structure is common across all beta-lactams, it has traditionally been assumed to be a major contributor to cross-reactivity, leading to the recommendation that all beta-lactams be avoided in patients with a beta-lactam allergy. However, recent studies have shown that selective beta-lactam allergy is more common than previously thought, prompting a shift in treatment strategies (3).

Less than 10% of patients labeled as having a penicillin allergy are found to have a true beta-lactam allergy after diagnostic testing (6). Similarly, only about one in four patients with a reported history of allergic reaction to cephalosporins are confirmed to have a true cephalosporin allergy (7). Among children whose parents report beta-lactam allergy, approximately 7% are initially labeled as allergic; however, diagnostic testing reveals that the actual prevalence of true beta-lactam allergy is as low as 0.1% (8). In the pediatric population, rashes caused by viral infections can often be mistaken for allergic reactions, leading to the incorrect labeling of beta-lactam allergy. According to a recent meta-analysis, the cross-reactivity rate with carbapenems in individuals labeled as penicillin-allergic was found to be 0.87%, with rates of 0.3% for meropenem, 0% for ertapenem, and 0.79% for imipenem (9).

Considering that only a small proportion of patients labeled as having beta-lactam allergy actually have a true allergy and that cross-reactivity with meropenem is rare even among those with confirmed beta-lactam allergy, meropenem appears to be a safe therapeutic option in this patient group. However, data on the evaluation of meropenem allergy in children with a reported history of penicillin and cephalosporin allergy remain limited.

In our hospital, consultation requests for antibiotic selection in patients labeled with penicillin allergy are frequently referred to our allergy department. In our clinical practice, we recommend administering meropenem under anaphylaxis precautions without a prior intradermal test (IDT) in children labeled with beta-lactam allergy. In these cases, meropenem is given directly as a full dose. In this study, we aimed to retrospectively evaluate the frequency of meropenem allergy in hospitalized children labeled with penicillin or cephalosporin allergy based on real-life clinical data.

METHOD

Participants and the study design

Children under the age of 18 who were referred to the Pediatric Immunology and Allergy Department at Prof. Dr. Cemil Taşcıoğlu City Hospital with a beta-lactam allergy label between January 1, 2017, and September 1, 2024, were retrospectively evaluated.

Inclusion criteria:

1. Presence of a beta-lactam allergy label
2. Completion of diagnostic tests related to beta-lactam allergy

Exclusion criteria:

1. Patients whose beta-lactam allergy label was not assessed

Demographic characteristics, indications for antibiotic use, history of drug allergies, and beta-lactam antibiotics tolerated without adverse reactions were recorded. Following the consultation, allergy evaluations performed in the pediatric allergy outpatient clinic, including IDTs and DPTs, were reviewed. The final diagnoses of beta-lactam allergy (including labeled antibiotics and meropenem) and safe antibiotic alternatives were documented.

Allergic Evaluation in the Outpatient Clinic

Patients labeled with allergy were evaluated in the pediatric allergy and immunology outpatient clinic after hospital discharge. Initially, a skin prick test (SPT) was performed, and if the result was negative, an IDT was conducted. IDT was administered to the volar surface of the forearm by an experienced technician. Reactions were evaluated 20 min

after application, and a wheal diameter greater than 3 mm compared to the negative control was considered a positive result. The drug provocation test (DPT) was performed using an open challenge protocol in accordance with the European Network for Drug Allergy (ENDA) recommendations (10). All patients were clinically stable and their allergic conditions were under control. In line with the ENDA position paper on drug hypersensitivity, antihistamines and other interfering medications were discontinued before testing. The first dose administered was one-eighth of the therapeutic dose. The therapeutic dose, calculated according to the patient's age and weight, was administered in 3 to 4 incremental steps with 30-min intervals between each dose. The test was discontinued and considered positive if objective findings were observed. After the DPT, patients were observed for at least 2 h. In the absence of any reaction, patients were advised to continue taking the oral form of the drug at home for two additional days. All tests were conducted at least 4 weeks after the initial hypersensitivity reaction. Informed consent was obtained from all patients prior to IDT and DPT. A diagnosis of drug allergy was confirmed if either the IDT or DPT yielded a positive result.

Ethics Committee

The Ethics Committee of the xxx approved the study protocol (No: xxx). Our study was conducted in accordance with the principles of good clinical practice based on the Declaration of Helsinki. Ethics approval confirms that studies are conducted in compliance with ethical standards and human rights and that the rights of the participants were protected.

Statistical analyses

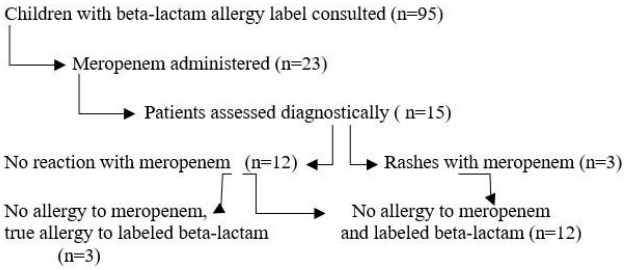
Statistical analyses were performed using SPSS 15.0 for Windows. Descriptive statistics are presented as frequencies and percentages for categorical variables and as mean ± standard deviation, median, and interquartile range [IQR] for continuous variables. Comparisons between groups were made using the chi-square test or Fisher's exact test, as appropriate, for categorical variables. For continuous variables, the Student's t-test was used when the assumption of normality was met; otherwise, the Mann–Whitney U test was applied. A p-value of <0.05 was considered statistically significant.

RESULTS

Patients Labeled with Beta-Lactam Allergy

Among hospitalized children, 0.08% were referred to the allergy department because of a penicillin or cephalosporin allergy label. A total of 95 children labeled with beta-lactam allergy were referred to our Pediatric Allergy and Immunology Clinic for appropriate antibiotic selection. Among them, 64% were female and 36% were male. Fifty-eight patients were labeled as allergic to penicillins only, 31 to cephalosporins only, and 6 to both drug classes. Meropenem was administered to 23 patients. Meropenem was administered to 23 patients. Diagnostic tests were not performed on 4 patients who refused the provocation test, 2 patients who were lost to follow-up, and 2 patients who were receiving immunosuppressive treatment due to leukemia. However, these patients did not exhibit any reactions to meropenem during hospitalization. A total of 15 patients presented to our outpatient clinic for the diagnostic assessment of beta-lactam allergy (Figure 1). Of these, only three developed a rash following meropenem treatment and were re-referred for further evaluation.

Figure 1. Flowchart of Diagnostic Evaluation in Patients with Beta-lactam Allergy Label



Characteristics of the Study Population

Fifteen patients who were referred with a beta-lactam allergy label and subsequently evaluated in our clinic after discharge were included in the study. Of these patients, 27% were female and 73% were male. The mean age was 81 ± 107 months. Atopic comorbidities were absent in 73.3% of the patients; three had allergic rhinitis, and one had a diagnosis of asthma. Nine patients had a history of allergy to penicillins only, four to cephalosporins only, and two to both antibiotic classes. The mean age at which the allergy label was assigned was 89 ± 73 months (range: 2–204 months). The mean interval between drug administration and onset of the reaction was 1.6 ± 1.7 hours (range: 0.4–4 h). Eight patients received the allergy label during the same hospitalization. In 87% of cases, the label was based on physician assessment, and in 13%, it was based on the parental report. Reactions occurred following oral administration in 4 patients, intramuscular administration in 1, and intravenous administration in 10. Urticaria was reported in 8 patients, anaphylaxis in 2 patients, maculopapular rash in 2 patients, urticaria with angioedema in 1 patient, angioedema alone in 1 patient, and the reaction history was unclear in 1 patient.

Diagnostic Testing with Beta-lactams

No allergic reactions were observed in the 13 patients who received meropenem treatment during their hospitalization. In three of these patients, beta-lactam allergy was later confirmed by diagnostic tests: one patient had positive IDT for penicillin and ceftriaxone. In two patients, anaphylaxis developed during ceftriaxone provocation testing.

Three patients were reconsulted after developing urticaria following meropenem infusion during hospitalization. Non-beta-lactam antibiotic therapy was initiated for these patients. However, in these cases, IDTs and DPTs with meropenem were negative. Additionally, the allergy labels for the penicillin group in two patients and for ceftriaxone in the other were later removed. Detailed information is provided in Table 1.

Risk Factors for Beta-lactam Allergy

Patients with confirmed beta-lactam allergy were compared with those without. The age at which the first allergic reaction to beta-lactam occurred was significantly higher in those with beta-lactam allergy ($p < 0.007$). No significant differences were observed when comparing the presence of known allergic diseases, the antibiotic group, the person who assigned the allergy label (physician or family member), the route of drug administration, whether the reaction occurred on the first day of treatment, the duration between drug administration and the onset of reaction (one hour or more), whether the allergy label was assigned during the same hospitalization, total IgE levels, eosinophil percentage, eosinophil count, basophil percentage, and basophil count (Table 2).

Table 1. Patient characteristics and diagnostic test results

Patient Number	Age at labeling	Sex	Concomitant allergic disease	Culprit drug	The first reaction with the labeled drug	Reaction to meropenem during hospitalization	Intradermal Test Result	Drug provocation test with the culprit drug
1	13 years	Male		Ceftriaxone	Anaphylaxis	No	Negative	Anaphylaxis
2	12 years	Male		Ceftriaxone	Anaphylaxis	No	Negative	Anaphylaxis
3	17 years	Male	Allergic rhinitis	Penicillin	Urticaria+angioedema	No	Positive skin prick test with penicillin G	Not done
4	8 years	Female	Asthma	Ampicillin-Sulbactam	Maculopapular rash	No	Negative	Negative
5	2 months	Male		Ampicillin-Sulbactam	Urticaria	No	Negative	Negative
6	Unknown	Male		Amoxicillin+Clavulanate	Unknown	No	Negative	Negative
7	2 years	Male		Amoxicillin+Clavulanate	Urticaria	No	Negative	Negative
8	13 years	Male		Piperacillin+Tazobactam	Urticaria	No	Negative	Negative
9	5 months	Male		Piperacillin+Tazobactam	Urticaria	No	Negative	Negative
10	Unknown	Female		Cefpodoxime	Angioedema	No	Negative	Negative
11	3 months	Male	Allergic rhinitis	Amoxicillin + Clavulanate and Cefuroxime	Urticaria	No	Negative	Negative
12	7 years	Female	Allergic rhinitis	Ampicillin-Sulbactam and Ceftriaxone	Urticaria	No	Negative	Negative
13	8 months	Female		Penicillin	Maculopapular rash	Urticaria	Negative with labeled drug and meropenem	Negative with labeled drug and meropenem
14	7 years	Male		Piperacillin + tazobactam and ampicillin-sulbactam	Urticaria	Urticaria	Negative with labeled drug and meropenem	Negative with labeled drug and meropenem
15	16 years	Male		Ceftriaxone	Urticaria	Urticaria	Negative with labeled drug and meropenem	Negative with labeled drug and meropenem

Table 2. Characteristics of patients with and without confirmed beta-lactam allergy

			Beta-lactam allergy		
Variable		**Total (n=15)**	**No (n=12)**	**Yes (n=3)**	**p**
Label age	Mean ± SD/Median [IQR]	89.38 ± 76.00/87.00 [8.00-156.00]	65.70 ± 69.12 / 52.50 [5.75-96.00]	168.33 ± 31.56/157.00 [150.50-180.50]	0,007†
Reaction duration	Mean ± SD/Median [IQR]	1.59 ± 1.66/1.00 [0.57-1.50]	1.89 ± 1.83/1.00 [0.60-3.00]	0.70 ± 0.26/0.60 [0.55-0.80]	0,395*
Allergic disease	None	11 (73.3%)	9 (75.0%)	2 (66.7%)	0,739§
	Allergic rhinitis	3 (20.0%)	2 (16.7%)	1 (33.3%)	
	Asthma	1 (6.7%)	1 (8.3%)	0 (0.0%)	
Labeled drug class	Penicillin	9 (60.0%)	8 (66.7%)	1 (33.3%)	0,202§
	Cephalosporin	4 (26.7%)	2 (16.7%)	2 (66.7%)	
	Both	2 (13.3%)	2 (16.7%)	0 (0.0%)	
Label during current hospitalization	No	7 (46.7%)	6 (50.0%)	1 (33.3%)	1,000‡
	Yes	8 (53.3%)	6 (50.0%)	2 (66.7%)	
Label given by	Family	2 (13.3%)	2 (16.7%)	0 (0.0%)	1,000‡
	Doctor	13 (86.7%)	10 (83.3%)	3 (100%)	
Route of administration	Oral	4 (26.7%)	4 (33.3%)	0 (0.0%)	0,392§
	IV	10 (66.7%)	7 (58.3%)	3 (100%)	
	IM	1 (6.7%)	1 (8.3%)	0 (0.0%)	
Total IgE	Mean ± SD/Median [IQR]	188.12 ± 165.64/142.00 [84.25-231.50]	205.43 ± 170.92/155.00 [109.50-278.00]	67.00	0,500*
Eosinophil %	Mean ± SD/Median [IQR]	2.27 ± 1.87/2.00 [0.65-3.65]	2.38 ± 1.74/2.25 [1.03-3.62]	1.80 ± 2.69/0.40 [0.25-2.65]	0,749†
Eosinophil count	Mean ± SD/Median [IQR]	0.37 ± 0.28/0.36 [0.14-0.52]	0.33 ± 0.22/0.32 [0.15-0.43]	0.54 ± 0.49/0.60 [0.31-0.80]	0,540†
Basophil %	Mean ± SD/Median [IQR]	0.31 ± 0.18/0.30 [0.20-0.45]	0.31 ± 0.19/0.25 [0.18-0.50]	0.33 ± 0.12/0.40 [0.30-0.40]	0,769*
Basophil count	Mean ± SD/Median [IQR]	0.04 ± 0.02/0.03 [0.02-0.05]	0.04 ± 0.02/0.03 [0.02-0.05]	0.05 ± 0.03/0.04 [0.03-0.06]	0,603*

Statistical tests used: * Mann–Whitney U test; † Student's t-test; ‡ Fisher's exact test; Chi-square test.
IQR = Interquartile Range, SD = Standard Deviation

DISCUSSION

Penicillin allergy is the most frequently reported drug allergy (11). 75% of children receive a drug allergy label before the age of 3 (12). In 66% of children with a beta-lactam allergy label and negative DPT results, at least one test for a viral infection was found to be positive (13). In patients using beta-lactam during a viral infection, the differential diagnosis should consider viral exanthems or benign rashes induced by the viral infection (13). In our study, diagnostic tests confirmed a beta-lactam allergy diagnosis in one-fifth of the patients tested. Furthermore, no meropenem hypersensitivity was observed in the 23 patients with a beta-lactam allergy label. The results of our study are supported by the fact that only a small proportion of betalactam-labeled patients had true betalactam allergy and there was a low risk of cross-reaction between betalactams and meropenem. Our real-world data indicate that administering meropenem at full dose until the beta-lactam allergy label is removed in hospitalized patients is a safe approach.

In our study, similar to the literature, the culprit drug in patients with a beta-lactam allergy label was commonly amoxicillin + clavulanate. It has been shown that 27% of patients with a history of allergy to amoxicillin + clavulanate developed a selective allergy to amoxicillin and 36% to clavulanate while tolerating penicillin (14). Similarly, it has been shown that one-third of reported allergies to piperacillin + tazobactam were selective, with patients tolerating other penicillins (15). The cross-reactivity between penicillins and cephalosporins is thought to be related to the R1 side chains, indicating that selecting an antibiotic with a different side

chain would be safer. Note that the only common chemical structure with meropenem is the beta-lactam ring, which is not the major allergenic determinant (16).

Penicillin allergy labels are more frequently observed in hospitalized patients (11). In hospitalized pediatric patients, a beta-lactam allergy label has been reported in 4.2% of cases (17). Having a penicillin label significantly influences physicians' antibiotic selection. Children with a penicillin allergy label are more likely to be treated with macrolides, quinolones, lincosamide, and metronidazole (17). Similarly, in adults, there is a higher preference for reserve antibiotics such as tetracyclines, quinolones, macrolides, and clindamycin. These reserve antibiotics are not only more expensive but also carry a higher risk of side effects and may contribute to the development of antibiotic resistance. They have been more frequently associated with MRSA, vancomycin-resistant enterococci, and Clostridium difficile infections. The use of these drugs often leads to ineffective treatment and subsequent hospital readmissions (18). A beta-lactam allergy label leads to the treatment of patients with multiple antibiotics and is associated with higher mortality (19). This results in poorer outcomes and more costly treatments, posing a significant risk to public health (6).

Due to the comorbidities associated with a beta-lactam allergy label, various label removal strategies have been developed (20,21). Removing an antibiotic allergy label from patients usually requires at least two outpatient visits. First, allergic history and IDT are conducted, followed by DPTs (20). Allergy specialists and immunologists perform these evaluations; however, they do not meet the current demand. A study conducted in Australia found that the median waiting time for evaluation at drug allergy referral centers was 178 days (22). Due to healthcare resource limitations and long waiting times, various guidelines have been developed to enable other physicians to remove labels (23). Additionally, computer-assisted algorithms have been developed to identify low-risk patients and recommend alternative beta-lactams that can be safely used (24). these algorithms increase beta-lactam use during hospitalizations in patients with a penicillin allergy label.

The recent EAACI position paper on beta-lactam hypersensitivity recommends that, in patients with a beta-lactam allergy label, all beta-lactams should be avoided until the allergy label is removed, or different approaches should be adopted based on the time of reaction onset and risk assessment (25). Among these approaches, in patients with penicillin and cephalosporin allergy labels, penicillins, cephalosporins with different side chains, and meropenem may be administered at full dose or gradually, without the need for IDT (24).

Some centers administer meropenem by performing bedside IDT in patients with a beta-lactam allergy label. A study conducted in adults reported that bedside IDT with meropenem for allergic evaluation was safe and effective. In patients over 13 years old with a penicillin allergy, the positive rate of IDT with meropenem was found to be 0.9%, and those with negative IDT results tolerated meropenem safely (26). Similarly, in a study by Atanaskovic-Markovic et al., the positive rate of IDT with meropenem in children aged 3-14 years with a penicillin allergy label was found to be 0.9%. All children with negative IDT result tolerated meropenem (27). However, performing bedside IDT is not always possible due to factors such as working conditions, staff availability, and technical issues. Generally, patients are evaluated for beta-lactam allergy in elective settings after discharge (20). In our clinic, bedside IDT is not performed. Patients are evaluated after discharge, but when consulted regarding antibiotic selection, in patients with penicillin and cephalosporin allergy labels, we generally recommend administering a single dose of a penicillin, cephalosporin with a different side chain or meropenem, with anaphylaxis precautions.

Studies based on real-world data have shown no significant difference in the frequency of allergic reactions to meropenem between hospitalized patients with and without a beta-lactam allergy label (28,29). Additionally, it has been reported that meropenem is well tolerated in patients with a history of anaphylactic reactions to penicillin (30). In our study, two patients who experienced anaphylaxis to ceftriaxone also tolerated meropenem treatment.

Due to the retrospective design of our study, data were obtained from patient files, and some data could not be accessed in full. Diagnostic tests could only be performed on 15 patients with a beta-lactam allergy label who received meropenem treatment. In other cases, testing was not possible due to reasons such as the patient not seeking consultation to remove the beta-lactam allergy label, inability to obtain parental consent, or clinical contraindications. Another limitation of the study is that some physicians opted for antibiotic changes instead of allergy consultations, which may have led to the exclusion of some patients. Additionally, the single-center nature of the study and the small sample size reduce the generalizability of the findings. Our study provides clinical observations consistent with the literature, indicating that meropenem is a safe option in patients with penicillin and cephalosporin allergies (31). These findings need to be confirmed in larger, prospective studies.

CONCLUSION

Viral rashes in the pediatric age group are often misdiagnosed as drug allergies. After diagnostic testing, a significant proportion of the beta-lactam allergy labels were excluded. However, during this process, particularly in hospitalized patients, beta-lactam allergy labels are associated with poor outcomes due to the use of non-beta-lactam drugs. Meropenem appears to be a safe and effective alternative treatment option for patients labeled with beta-lactam allergy until a comprehensive beta-lactam allergy workup can be conducted.

Ethics Committee Approval	This study was approved by the ethics committee of the University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital (07.10.2024 - 225).
Informed Consent	Written consent was obtained from the participants.
Peer Review	Externally peer-reviewed.
Author Contributions	Conception/Design of Study- M.K.Ş.; Data Acquisition- H.B., M.F.E., A.B.T., H.T.Ş., N.G., G.Y.; Data Analysis/Interpretation-Ş.İ.K.K., H.G.; Drafting Manuscript- M.K.Ş., N.G.; Critical Revision of Manuscript- G.Y.; Final Approval and Accountability- M.K.Ş., G.Y., N.G., H.B., M.F.E., A.B.T., HT.Ş., Ş.İ.K.K., D.Ö.
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Author Details

Merve Karaca Şahin
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0001-8783-0514 karacasahinmerve@gmail.com

Güler Yıldırım
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0001-7852-9252

Nilay Çalışkan
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0002-5546-0034

Hamit Boloğur
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0003-1092-8833

Muhammed Fatih Erbay
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0002-4128-3081

Aslı Berivan Topçak
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0009-0007-8300-6430

Hasan Tunç Şarman
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0009-0000-7234-5516

Hilal Güngör
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0002-8923-1897

Çağla Öztürk
[2] Bezmialem Vakıf Üniversitesi, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0002-8645-0373

Şefika İlknur Kökcü Karadağ
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0001-9234-633X

Deniz Özçeker
[1] The University of Health Sciences, Prof. Dr. Cemil Taşcıoğlu City Hospital, Pediatric Immunology and Allergy Department, İstanbul, Türkiye
0000-0002-0032-6727

REFERENCES

1 Brauer R, Ruigómez A, Downey G, Bate A, Garcia Rodriguez LA, Huerta C et al. Prevalence of antibiotic use: a comparison across various European health care data sources Pharmacoepidemiol Drug Saf. 2016 Mar 7;25(S1):11–20.

2 Gomes ER, Brockow K, Kuyucu S, Saretta F, Mori F, Blanca-Lopez N et al. Drug hypersensitivity in children: report from the pediatric task force of the <scp>EAACI</scp> Drug Allergy Interest Group. Allergy. 2016 Feb 17;71(2):149–61.

3 Montañez MI, Ariza A, Mayorga C, Fernandez TD, Torres MJ. Cross-reactivity in betalactam allergy: alternative treatments. Curr Treat Options Allergy. 2015 Jun 28;2(2):141–54.

4 Steffens NA, Zimmermann ES, Nichelle SM, Brucker N. Meropenem use and therapeutic drug monitoring in clinical practice: a literature review J Clin Pharm Ther. 2021 Jun 3;46(3):610–21.

5 Romano A, Gaeta F, Poves MFA, Valluzzi RL. Cross-reactivity among beta-lactams. Curr Allergy Asthma Rep. 2016 Mar 22;16(3):24.

6 Sáenz de Santa María R, Bogas G, Labella M, Ariza A, Salas M, Doña I et al. Approach for relabeling beta-lactam allergy in children Frontiers in Allergy. 2023 Nov 15;4.

7 Yilmaz Topal O, Kulhas Celik I, Turgay Yagmur I, Toyran M, Civelek E, Karaatmaca B et al. Evaluation of the Clinical Properties and Diagnostic Test Results of Cephalosporin Allergy in Children Int Arch Allergy Immunol. 2021;182(8):709–15.

8 Erkoçoğlu M, Kaya A, Civelek E, Özcan C, Çakır B, Akan A et al. Prevalence of confirmed immediate-type drug hypersensitivity reactions among school children Pediatric Allergy and Immunology. 2013;24(2):160–7.

9 Picard M, Robitaille G, Karam F, Daigle JM, Bédard F, Biron É, et al. Cross-reactivity to cephalosporins and carbapenems in penicillin-allergic patients: two systematic reviews and meta-analyses. J Allergy Clin Immunol Pract. 2019;7(8):2722-2738.e5.

10 Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J et al. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations Allergy. 2003;58(9):854–63.

11 Gomes ER, Demoly P. Epidemiology of hypersensitivity drug reactions Curr Opin Allergy Clin Immunol. 2005;5(4):309–16.

12 Vyles D, Chiu A, Simpson P, Nimmer M, Adams J, Brousseau DC. Parent-reported penicillin allergy symptoms in the pediatric emergency department. Acad Pediatr. 2017 Apr;17(3):251–5.

13 Caubet JC, Kaiser L, Lemaître B, Fellay B, Gervaix A, Eigenmann PA. The role of penicillin in benign skin rashes in childhood: A prospective study based on drug rechallenge Journal of Allergy and Clinical Immunology. 2011;127(1):218–22.

14 Torres-Rojas I, Pérez-Alzate D, Somoza ML, Pfeifer APM, Diaz EH, Jimenez-Rodriguez TW, et al. Clavulanic Acid is a leading culprit beta-lactam in immediate allergic reactions to penicillins. Allergy Asthma Immunol Res. 2023;15(2):201.

15 Casimir-Brown RS, Kennard L, Kayode OS, Siew LQC, Makris M, Tsilochristou O et al. Piperacillin-Tazobactam Hypersensitivity: A Large, Multicenter Analysis. J Allergy Clin Immunol Pract. 2021 May;9(5):2001–9.

16 Zagursky RJ, Pichichero ME. Cross-reactivity in β-Lactam Allergy. J Allergy Clin Immunol Pract. 2018;6(1):72-81.e1.

17 Lucas M, Arnold A, Sommerfield A, Trevenen M, Braconnier L, Schilling A et al. Antibiotic Allergy Labels in Children Are Associated with Adverse Clinical Outcomes J Allergy Clin Immunol Pract. 2019;7(3):975–82.

18 van Dijk SM, Gardarsdottir H, Wassenberg MWM, Oosterheert JJ, de Groot MCH, Rockmann H. The High Impact of Penicillin Allergy Registration in Hospitalized Patients J Allergy Clin Immunol Pract. 2016 Sep;4(5):926–31.

19 Charneski L, Deshpande G, Smith SW. Impact of an Antimicrobial Allergy Label in the Medical Record on Clinical Outcomes in Hospitalized Patients. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy. 2011 Aug 6;31(8):742–7.

20 Armitage KF, Porter CE, Ahmed S, Cook J, Boards J, Bongard E et al. Penicillin allergy status and its effect on antibiotic prescribing, patient outcomes and antimicrobial resistance (ALABAMA): protocol for a multicentre, parallel-arm, open-label, randomized pragmatic trial. BMJ Open. 2023 Sep 4;13(9):e072253.

21 Mir A, Lanoue D, Zanichelli V, van Walraven C, Olynych T, Nott C et al. Introduction of a penicillin allergy de-labeling program with direct oral challenge and its effects on use of beta-lactam antimicrobials: a multicenter retrospective parallel cohort study Allergy, Asthma & Clinical Immunology. 2024 Mar 5;20(1):20.

22 Ali S, Hughes T, Smith A. Long waitlists for outpatient drug allergy referrals: An Australian tertiary center experience. World Allergy Organization Journal. 2024 Feb;17(2):100863.

23 Savic L, Ardern-Jones M, Avery A, Cook T, Denman S, Farooque S, et al. BSACI guideline for the set-up of penicillin allergy de-labelling services by non-allergists working in a hospital setting. Clinical and Experimental Allergy. 2022 Oct 21;52(10):1135–41.

24 Blumenthal KG, Wickner PG, Hurwitz S, Pricco N, Nee AE, Laskowski K et al. Tackling inpatient penicillin allergies: Assessing tools for antimicrobial stewardship. Journal of Allergy and Clinical Immunology. 2017;140(1):154-161.e6.

25 Romano A, Atanaskovic-Markovic M, Barbaud A, Bircher AJ, Brockow K, Caubet J et al. Toward a more precise diagnosis of hypersensitivity to beta-lactams — an EAACI position paper. Allergy. 2020 Jun 29;75(6):1300–15.

26 Romano A, Viola M, Guéant-Rodriguez RM, Gaeta F, Valluzzi R, Guéant JL. Brief Communication: Tolerability of meropenem in patients with IgE-mediated hypersensitivity to penicillins Ann Intern Med. 2007 Feb 20;146(4):266–9.

27 Atanasković-Marković M, Gaeta F, Medjo B, Viola M, Nestorović B, Romano A. Tolerability of meropenem in children with IgE-mediated hypersensitivity to penicillins Allergy. 2008 Feb 4;63(2):237–40.

28 Wall GC, Nayima VA, Neumeister KM. Assessment of hypersensitivity reactions in patients receiving carbapenem antibiotics who report a history of penicillin allergy Journal of Chemotherapy. 2014 Jun 6;26(3):150–3.

29 Sodhi M, Axtell SS, Callahan J, Shekar R. Is it safe to use carbapenems in patients with a history of allergy to penicillin? J Antimicrob Chemother. 2004;54(6):1155–7.

30 Cunha BA, Hamid NS, Krol V, Eisenstein L. Safety of Meropenem in Patients Reporting Penicillin Allergy: Lack of Allergic Cross Reactions Journal of Chemotherapy. 2008 Apr 18;20(2):233–7.

31 Torres MJ, Adkinson NF, Caubet JC, Khan DA, Kidon MI, Mendelson L et al. Controversies in Drug Allergy: Beta-Lactam Hypersensitivity Testing J Allergy Clin Immunol Pract. 2019;7(1):40–5.