

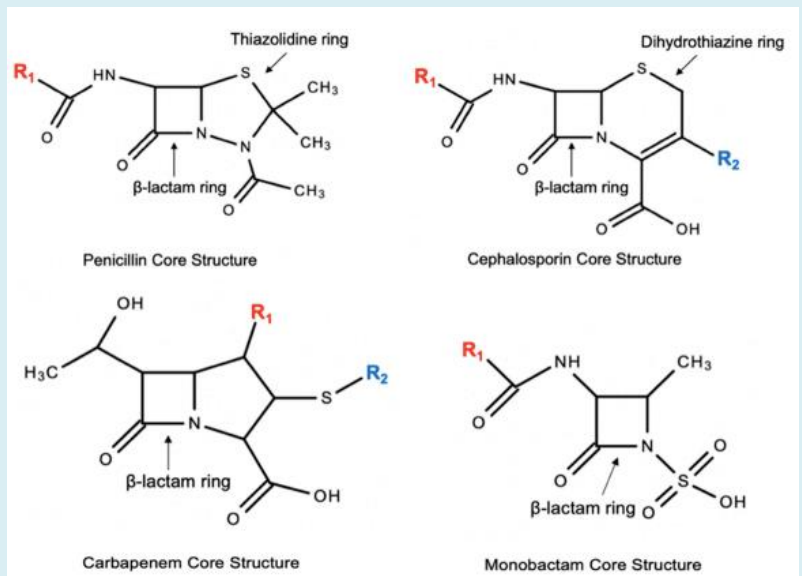
Penicillin Allergy & Cross-Reactivity

Introduction

1. Only 0.5% to 2% of patients with a documented penicillin allergy that are administered a penicillin will exhibit a hypersensitivity reaction, usually presenting as a rash or hives.
2. True IgE-mediated penicillin allergies that cause anaphylaxis are rare.
3. An IgE-mediated penicillin allergy can diminish over time, as 80% of patients become tolerant after a decade.
4. Patients with a documented penicillin allergy may be inappropriately exposed to alternative antibiotics, resulting in increased treatment failures, adverse effects, and antimicrobial resistance.
5. Penicillins, cephalosporins, and carbapenems all share a beta-lactam core structure, thus raising the potential for cross-reactivity among these agents.

Pharmacology

- The following drugs in each group **may have cross-reactivity to each other due to similar side chains**
- Cross-reactivity between penicillins and cephalosporins is about **2%**
- Cefazolin is **NOT likely to cross react** with penicillin (side chains NOT similar)
- Cross-reactivity with monobactams (i.e. aztreonam) is **negligible**
- Cross-reactivity between penicillins and carbapenems is **<1%**



Group 1	Group 2	Group 3	Group 4
Penicillin Cefoxitin Cefuroxime	Amoxicillin Ampicillin Cefaclor Cephalexin Cefadroxil	Ceftriaxone Cefotaxime Cefuroxime Cefepime Cefpodoxime Ceftaroline	Aztreonam Ceftolazane Ceftazidime

Overview of Evidence

Author	Design	Intervention & Comparison	Outcome
Why Cross-Reactivity?			
Nagakura, 1990 Mayorga, 1995	Animal study	-Studied antibodies formed when animals were immunized with protein-beta-lactam conjugates	-92% of the antibodies recognized an epitope in which the side chain was the main constituent -The side chain is the most important determinant in penicillin immunogenicity
Cephalosporins			
Goodman, 2001	Retrospective review (n=2933)	-Orthopedic patients with penicillin allergy receiving cefazolin prior to a procedure	-Only 1 patient may have had an allergic reaction to cefazolin -Cross-reactivity rate with cefazolin was 0.33%
Daulat, 2004	Retrospective review (n=606)	-Patients with penicillin allergy receiving cephalosporins -42% 1 st gen., 21% 2 nd gen., and 37% 3 rd or 4 th gen. cephalosporins	-Only 1 patient had an allergic reaction that was documented as worsening of underlying eczema after being placed on cefazolin -Cross-reactivity was 0.17%
Apter, 2006	Retrospective review (n=3920)	-Patients with a prescription for penicillin followed by a prescription for a cephalosporin -Identified allergic-like events within 30 days after each prescription	-Only 43 patients who experienced an allergic-like reaction after both penicillin and cephalosporin -Cross-reactivity rate was 1.1% -70% of these patients just had urticaria -The risk of anaphylaxis to cephalosporins was only 0.001%
Carbapenems			
Romano, 2006	Prospective study (n=112)	-Skin tested to penicillins and then skin tested to imipenem -If skin test to imipenem was negative, then challenged with IM dose	-Only 1 patient of the penicillin skin-test positive patients had a positive skin test to imipenem -Cross-reactivity rate was 0.9% -None of the 110 patients with a negative imipenem skin test that underwent IM challenge had a reaction
Romano, 2007	Prospective study (n=104)	-Skin tested to penicillins and then skin tested to meropenem -If skin test to imipenem was negative, then challenged with IV dose	-Only 1 patient of the penicillin skin-test positive patients had a positive skin test to meropenem -Cross-reactivity rate was 1% -All 103 patients with a negative meropenem skin test tolerated the IV challenge
Atanaskovic-Markovic, 2008	Prospective study (n=108)	-Children with penicillin allergy were skin tested to penicillin and meropenem -If skin test to meropenem was negative, then challenged with IV dose	-Only 1 patient with a positive penicillin test reacted to the meropenem skin test -Cross-reactivity rate was 0.9% -All 107 patients with a negative meropenem skin test tolerated the IV challenge

Conclusions

1. True penicillin allergies are less common than reported, and anaphylaxis is uncommon.
2. Cross-reactivity among penicillins and cephalosporins is attributed to similarity in side chains.
3. Cephalosporin cross-reactivity with penicillins is much lower than reported in early studies partly due to contamination of study drugs with penicillin.
4. Cross-reactivity between cephalosporins is about 2% and with carbapenems is <1%.

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