Guidance on Antibiotic Choice for Patients with Penicillin Hypersensitivity

Introduction

The phrase ‘allergic to penicillin’ is commonly seen in medical notes and on medicine charts. The diagnosis of ‘penicillin allergy’ is often simply accepted without obtaining a detailed history of the reaction. It has been reported that a significant percentage of patients labelled as ‘penicillin allergic’ are not truly allergic to the drug. As a result, penicillins are unnecessarily withheld from these patients, which may subsequently affect their clinical outcomes.

What is the True Incidence of ‘Penicillin Allergy’?

General hypersensitivity reactions (e.g. rashes) to penicillin occur in between 1 and 10% of exposed patients but true anaphylactic reactions (which can be fatal) occur in less than 0.05% of treated patients. Please note that patients who have a vague history of symptoms or gastro-intestinal intolerance are probably not truly allergic to penicillins.

Basic Immunology of Penicillin Allergy

Understanding the key classification systems and clinical presentations of penicillin allergy can help the practitioner make informed decisions about future therapy in order to treat the infection by the safest means.

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<th>Table 1. Definitions of terms relating to allergy</th>
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<td><strong>Adverse Drug Reaction</strong> is a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiologic function.</td>
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<td><strong>Drug allergy</strong> is an immunologically mediated reaction that exhibits specifically and recurrence on re-exposure to the offending drug. A Drug Allergy is a form of Adverse Drug Reaction.</td>
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<td><strong>Anaphylaxis</strong> is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance.</td>
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<td><strong>Immediate Onset Reactions (Type1)</strong> occur within 1 hour of administration of the drug. These are IgE mediated reactions and may progress to anaphylaxis.</td>
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<td><strong>Accelerated Onset Reactions</strong> occur between 1 and 72 hours of administration of drug. These are almost always IgE mediated reactions.</td>
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<td><strong>Early Onset Reactions</strong> is a collective term used to describe Immediate and Accelerated Onset Reactions.</td>
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<td><strong>Late Onset Reactions</strong> occur beyond 72 hours of administration of the drug.</td>
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Who is at risk?
Patients with a history of atopic allergy (e.g. asthma, eczema, hay fever) are not predisposed to anaphylaxis but may result in a more severe reaction. There is generally no hereditary link to anaphylaxis so a family history is irrelevant.

Who should not be prescribed or administered penicillins?
Individuals with a history of Early Onset or Type I allergy are clinically recognisable by features of urticaria, laryngeal oedema, bronchospasm, hypotension or local swelling within 72 hours of administration, or those who develop a pruritic rash (even after 72 hours) should NOT receive a penicillin.

Clinical Diagnosis
The clinician assessing a patient who presents with a history of penicillin allergy should attempt to define the type of reaction. The table below highlights some questions that may be useful.

Table 2. Taking a history of Penicillin allergy. What to Ask?

1. What antibiotics has the patient reacted to in the past?
2. What antibiotics has the patient taken and tolerated since the allergy diagnosis?
3. What was the nature of the reaction?
4. If rash then:
   a. Describe nature of rash (e.g. pustular, urticarial etc)
   b. Could rash be related to underlying condition (e.g. viral)
   c. How long after commencing antibiotic did rash appear?
5. Why was the patient taking the antibiotic?
6. Did this reaction result in hospitalisation?
7. Did the reaction resolve on stopping the antibiotic?

Are there situations where cephalosporins or other beta-lactam antibiotics can be prescribed for patients with penicillin hypersensitivity?
Clinical studies suggest that the incidence of cross-reactivity to cephalosporins in penicillin-allergic patients is around 10% but this is thought to be an overestimate. The true incidence of cross-sensitivity is uncertain. Second and third generation cephalosporins (e.g. cefuroxime, ceftriaxone, ceftazidime) are unlikely to be associated with cross reactivity as they have different side chains to penicillin.

- Patients with no evidence of Type I allergy to penicillin may be treated with any cephalosporin or beta lactam antibiotic for infections of any severity.
- Patients with symptoms suggestive of a Type I allergy should avoid cephalosporins and other beta-lactam antibiotics for mild or moderate infections when a suitable alternative exists. In life threatening infections, when use of a non-cephalosporin antibiotic would be sub-optimal, consider giving, under observation, a second or third generation cephalosporin (e.g. cefuroxime, ceftriaxone, ceftazidime). If necessary seek advice from ID or Microbiology.
Cross-reactivity of other classes of antimicrobials in patients with penicillin allergy?

Carbapenems (Meropenem, Imipenem, Ertapenem) have a cross reaction rate of about 1% in patients who have previously suffered IgE mediated reactions to penicillins. The risk of a life threatening reaction should be no more than the general population.

Monobactams (Aztreonam) Can be cautiously considered with close observation in patients with Type I hypersensitivity after discussion with micro/ID as the cross reactivity rate appears to be <10%.

Cephalosporin allergy is dependent on the generation of cephalosporin. First generation cephalosporins e.g. cefalexin, have a cross reactivity rate of around 10% in patients with a penicillin allergy.

Tetracyclines (e.g. doxycycline), macrolides (e.g. clarithromycin), aminoglycosides (e.g. gentamicin) and glycopeptides (e.g. vancomycin) are all unrelated to penicillins and are safe to use in the penicillin allergic patient.

Prescribing Issues

Always identify and document the nature of the reported allergy and drug name on the medicine chart and in the medical notes. The prescriber has the primary responsibility for ensuring that the allergy/sensitivity details are completed on all relevant medicine charts and medical notes.

What should be prescribed for truly penicillin allergic patients?

Alternative antibiotic options to use in penicillin allergic patients to treat specific infections are included in all sections of this antibiotic website.

Click here for information on which antibiotics should be avoided in penicillin allergy, those that should be used with caution, and those that are safe.

References

5. Pegler S, Healy B. In patients allergic to penicillin, consider second and third generation cephalosporins for life threatening infections. BMJ 2007;335:991