



A REVIEW ON PENICILLIN ALLERGIES

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ABSTRACT

Penicillin allergies are the most common miss diagnosed and wrongly diagnosed allergies in children. Many children are labeled penicillin allergic without getting them tested prior. Misdiagnosis of penicillin allergy may result in the unnecessary use of more expensive and less effective antibiotics as well as the emergence of multidrug-resistant cases. Skin testing remains standard practice for the evaluation of patients with immediate hypersensitivity reactions to penicillin. A DPT test can also be performed for diagnosing a child with penicillin allergies. Correct diagnosis of penicillin allergy is needed to avoid the morbidity, mortality and economic cost associated with it.

Key words: Penicillin, Allergies, SPT, DPT etc.

INTRODUCTION

In the children it is not uncommon to see a skin rash during a course of treatment with a penicillin antibiotic [1]. This is often assumed to be due to penicillin allergy and most children are simply labeled as 'penicillin allergic' which is not correct. Penicillin and penicillin-based antibiotics are the most widely used antibiotics for common infections. They are the antibiotics which most often causes allergic reactions with the frequency of life-threatening anaphylaxis [2]. The incidence of self-reported penicillin allergy varies between 1% and 10%⁴ but more than 80-90% of these have no evidence of IgE antibodies to penicillin on skin-testing [3]. Penicillin-based antibiotics are usually less expensive and have fewer side-effects than alternative broad-spectrum antibiotics and are also more effective. This is especially important for patients on long-term penicillin treatment [4].

Classification

The drug allergies can be classified in number of ways [5]. From a clinical perspective a practical method is to divide adverse drug reactions according to the time interval between exposure and onset of reaction – immediate, accelerated and delayed reactions [6]. Immediate hypersensitivity reactions (IgE-mediated) occur up to 1 hour after exposure to the offending agent. Non-immediate reactions include accelerated reactions (1-72 hours) and delayed reactions (>72 hours).

Immediate reactions may present with anaphylaxis, urticaria, angio-oedema and bronchospasm; accelerated/ delayed reactions may manifest as serum sickness, interstitial nephritis, haemolytic anaemia, morbilliform eruptions and Stevens-Johnson syndrome [7].

Diagnosis

• History

Diagnosis of any disease or an allergy begins with history taking. A personal or family history of drug allergies may be relevant as this may predispose to penicillin allergy. The signs, symptoms and severity of the reaction and any previous reactions should also be noted. The dose and route of administration are also important as prolonged parenteral administration is more likely to cause a hypersensitivity reaction than the oral or topical route. Any history of viral illness should also be noted as this may cause a rash that is mistaken for penicillin allergy [8].

• Physical Examination

The the skin, mucous membranes and the chest should be examined carefully. On the skin one should distinguish between an urticarial and a morbilliform or involvement may indicate Stevens-Johnsons syndrome or toxic epidermal necrolysis. The presence of wheezing or stridor should be noted on examination of the respiratory system [9].

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Investigations

Penicillin is metabolized into major (penicilloyl) and minor (penicilloate and penilloate) antigenic determinants. It is essential to test sensitivity to both minor and major determinants, as testing only for major determinants would miss at least 10% of penicillin-sensitive subjects [9]. Different tests for testing penicillin allergies include

• Blood Tests

During a case of acute hypersensitivity reaction, a serum tryptase level should be performed which is a highly sensitive and specific test of mast-cell activation. In it, blood is taken at 0, 1 and 6 hours after the reaction and placed in a lithium-heparin tube. A peak at 1 hour with a fall to normal levels within 12-24 hours is diagnostic of mast-cell de-granulation and an IgE-mediated reaction. The blood should be taken from 6 weeks after the acute reaction has taken place in order to get the most accurate results [10].

• Skin Tests

The skin test panel includes a positive (histamine 10 mg/ml) and a negative (0.9% saline) control as well as a major determinant mixture and minor determinant mixture. A wheal 3 mm or more greater than the negative control is considered a positive test result. Skin-prick testing (SPT) is a reliable and relatively safe procedure for detecting IgE-mediated penicillin allergy. Anaphylaxis has never been reported in a skin-test-negative individual challenged with the medication. SPT is cannot be used if a non-IgE-mediated hypersensitivity reaction such as Stevens-Johnson syndrome or serum sickness is suspected in an individual [11].

• Drug Provocation Test (DPT)

A DPT test is performed in case when penicillin skin test is negative and the IgE antibody levels are normal. A suggestive history of allergy together with a positive CAP-RAST and/or a positive skin test is sufficient for the diagnosis of penicillin allergy without the need to perform a DPT. A DPT cannot be done if there is a history of anaphylaxis [12].

Management

The management of penicillin allergy consists of discontinuing the drug use and treating the clinical

reactions occurring like anaphylaxis, urticaria or wheeze. Later once the condition comes in control, confirming the diagnosis, strict avoidance of the offending drug and patient education can be done [13]. A Medic Alert bracelet should also be obtained for the safeguard of the patient. De-sensitization to the drug should also be considered in children with IgE-mediated reactions. De-sensitization must be conducted in an intensive care unit by experienced personnel or doctor. The aim of De-sensitization is to convert a patient who is highly allergic to penicillin to a state in which they can tolerate the drug. The basic principle is to start with a minute dose and then double it every 15 minutes until a full dose is reached. Penicillin therapy must be commenced immediately after completing desensitization as the tolerance is only temporary or for short time only [14]. De-sensitization must be repeated if a course of penicillin is required again. Minor adverse reactions may occur but no fatal or life-threatening reactions may occur.

Cross-Reactivity with Other Antibiotics

Patients who consume cephalosporins may complain of penicillin allergy sometimes. The rate of cross reactivity with the 3rd and 4th generation cephalosporins is much lower than that of 1st and 2nd generations. Cross-reactivity between these drugs is believed to be due to the drugs having similar R-group side chains and not due to the -lactam ring itself.

In a patient with a known allergy to a cephalosporin, substitution with a cephalosporin with a different side chain is usually recommended. Cross-reactivity between penicillin and carbapenems is also reported in some cases [15].

CONCLUSIONS

Penicillin allergic reactions are less common in children. The majority of children with the label of penicillin allergy can safely take this drug without fear of an allergic reaction whatsoever. Improper diagnosis of penicillin allergy may result in the unnecessary use of more expensive and less effective antibiotics as well as the emergence of multi drug resistant organisms. SPT remains the standard practice for the evaluation of patients with immediate hypersensitivity reactions (IgE-mediated) to penicillin. Patients with known penicillin allergy can undergo de-sensitization if they require penicillin therapy as no alternative is available.

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