

# Hypersensitivity to Penicillin V With Good Tolerance to Other $\beta$ -Lactams

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## ■ Abstract

A 24 year-old man developed an anaphylactic reaction within thirty minutes of an oral administration of penicillin V. He suffered from recurrent streptococcal pharyngitis that was usually treated with penicillin V with good tolerance.

Skin prick and intradermal tests with penicilloyl-polylysine, minor determinant mixture, amoxicillin, ampicillin and cefuroxime were negative. However, a skin prick test with penicillin V was positive in the patient and negative in 10 controls. Determination of specific (Immunoglobulin (Ig) E to penicillin V was 0.64 kU/L. Specific IgE to penicillin G, amoxicillin and ampicillin were all negative. Single blind controlled oral challenge with amoxicillin and cefuroxime were both negative.

This is an exceptional case of an anaphylactic reaction induced by phenoxymethylpenicillin with positive allergologic study *in vivo* and *in vitro* tests and with negative allergological study to other  $\beta$ -lactams.

**Key words:**  $\beta$ -lactams. Hypersensitivity. Penicillin V. Penilevel

## ■ Resumen

Paciente de 24 años que 30 minutos después de tomar una dosis de penicilina V oral, presentó una reacción anafiláctica. El paciente había tolerado previamente la penicilina V en varias ocasiones por presentar faringitis estreptocócicas recurrentes.

Las pruebas cutáneas (prick e intradermo) realizadas con peniciloil polilisina, mezcla determinantes menor, amoxicilina, ampicilina y cefuroxima fueron negativas, sin embargo, el prick test con penicilina V fue positivo en el paciente y negativo en 10 controles. La determinación de IgE específica con penicilina V fue 0.64 kU/L. La IgE específica con penicilina G, amoxicilina y ampicilina fueron negativas. Las pruebas de provocación oral controlada con amoxicilina y cefuroxima fueron ambas negativas.

Este es un caso excepcional de anafilaxia inducida por phenoxymethylpenicilina con estudio alergológico positivo *in vivo* e *in vitro* y estudio alergológico negativo con otros betalactámicos.

**Palabras clave:** Betalactámicos. Sensibilización. Penicilina V. Penilevel

## Introduction

We present a case of immediate systemic reaction to penicillin V in a patient frequently exposed to the drug, and in which cross-reactivity to other  $\beta$ -lactam antibiotics was ruled out.

## Case Description

A 24-year-old man was referred to our clinic because of an anaphylactic reaction with Penilevel (penicillin V) for treatment of acute amygdalitis. One week after the beginning of this treatment, he developed a systemic reaction within thirty minutes of the last dose. His symptoms were pruritus

on the head, erythema and edema in the lips, tongue and both hands, dyspnea and foreign body at the pharynx, sickness and nausea. He was treated in an emergency room with systemic corticosteroids and oxygen. Subsequently, the patient was treated with azitromicin and deflazacort because of persistent amygdalitis. He had previously tolerated penicillin V on several occasions for recurrent streptococcal pharyngitis. The personal and family history for atopic diseases was negative. He had no previous history of drug allergy.

Written informed consent was obtained and diagnostic studies were performed following the European Network for Drug Allergy recommendations for the diagnosis of immediate allergic reactions to  $\beta$ -lactams [1]. Skin tests were carried out with penicilloyl-polylysine (PPL), minor determinant mixture (MDM), benzylpenicillin (penicillin

Cutaneous Tests Performed in Patient: Drugs and Highest Concentrations Used\*

Reagent	Concentration
PPL (Allergopen, Allergopharma)	$6 \times 10^{-5}$ M
MDM (Allergopen, Allergopharma)	0.5 mg/mL
Penicillin G	10 000 IU/mL
Penicillin V	25 mg/ml (40 000 IU/mL) (in prick) 2.5 mg/ml (4 000 IU/mL) (in ID)
Amoxicillin	25 mg/mL
Ampicillin	25 mg/mL
Cefuroxime	25 mg/mL

\* MDM indicates minor determinant mixture; PPL, penicilloyl-polyslysine; ID, intradermal

G), phenoxymethylpenicillin (penicillin V), amoxicillin, ampicillin and cefuroxime (table). The patient exhibited an immediate positive response (6x6 mm wheal with erythema) to penicillin V in the skin prick test. The penicillin V concentrations used were shown to be specific and nonirritant by testing in ten control subjects. The prick and intradermal tests with the rest of the reagents were all negative. Total (Ig) E immunoglobulin was 504 kU/L. Determination of serologic specific IgE (CAP-System; Pharmacia, Sweden) to penicillin V was 0.64 kU/L, in a serum sample obtained within one month of the reaction. Specific IgE to penicillin G, amoxicillin and ampicillin (CAP-System; Pharmacia, Sweden) were all negative. Single-blind controlled oral challenges with increasing doses of cefuroxime to a dose of 500 mg (cumulative dose of 925 mg) and with amoxicillin to a dose of 500 mg (cumulative dose of 987 mg) were both negative. Two years later, the allergological study was repeated. Prick and intradermal tests at a concentration of 25 mg/mL and 2.5 mg/mL, respectively, became negative. However, specific serologic IgE was 0.55 kU/L. In the same process specific IgE in freeze serum from the initial sample was also determined and was found to be 0.84 kU/L.

## Discussion

Allergic reactions to  $\beta$ -lactams are the most common cause of immunological drug reactions. Currently, amoxicillin is reported to be the most commonly consumed  $\beta$ -lactam in our country. In contrast, Penicillin V is seldom used.

Over the last 15 years an increasing amount of data have accumulated supporting the role of side chain structure as a unique allergenic determinant [1]. Penicillin G and V have the same  $\beta$ -lactam ring, and penicillin V results from the substitution of the phenyl acetic acid of benzylpenicillin by the phenoxy methyl side-chain.

This is an exceptional case of an anaphylactic reaction induced by phenoxymethylpenicillin with positive allergologic study results using in vivo and in vitro tests and with negative allergological study results to other  $\beta$ -lactams. The patient tolerated oral amoxicillin and cefuroxime which have the same  $\beta$ -lactam ring as penicillin. The lack of cross-reactivity with other  $\beta$ -lactam antibiotics, including amoxicillin and

cefuroxime, lead us to believe that the side-chain of penicillin V was probably the antigenic determinant in our patient.

Blanca et al [2] reported the other published case of selective immediate allergy to penicillin V. In this case, specific serologic IgE determination was also positive but skin tests to phenoxymethylpenicillin were negative. They also reported the decrease in the immunological response over time.

To the best of our knowledge, this is the first reported case of selective allergy to penicillin V with positive allergologic study results from both in vivo and in vitro tests.

## References

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