

Penicillin sensitivity among hospital nurses without a history of penicillin allergy

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Abstract

Title. Penicillin sensitivity among hospital nurses without a history of penicillin allergy

Aim. This paper reports a study to document the prevalence of penicillin sensitivity among nurses who had no previous history of sensitivity and worked in an inner city hospital in Turkey.

Background. Frequent and prolonged exposure to any drug including penicillin may increase the risk of hypersensitivity to these drugs. Local administration of drugs increases the likelihood of sensitization. Nurses are the main group of healthcare workers who prepare and administer antibiotics to patients, so they may be at highest risk for sensitization. Skin testing with major and minor determinants of penicillin has proved useful for identifying penicillin-specific IgE antibodies in sensitized individuals.

Method. Skin prick tests were performed with benzyl penicilloyl polylysine (PPL) and a mixture of minor antigenic determinants (MDM) solution with 83 nurses who had been handling beta-lactam antibiotics. The study was conducted in 2004.

Findings. Ten nurses (12%) had positive skin reactions to penicillin antigens. Six were sensitive to PPL (7.2%) and four were sensitive to MDM (4.8%).

Conclusion. Occult sensitization to beta-lactam antibiotics, without symptoms, may develop in hospital nurses. It is possible that these healthcare workers might be at increased risk of hypersensitivity reactions should they be exposed to beta-lactams, administered for therapeutic purposes. Further research is needed to explore this important issue.

Keywords: drug allergy, drug hypersensitivity, empirical research report, healthcare workers, penicillin allergy, skin prick tests

Introduction

Penicillins and other beta-lactam antibiotics are among the most widely used antibiotics and some patients experience unpredictable reactions, which include allergic reactions (IgE mediated), drug intolerance, idiosyncratic reactions and pseudoallergic reactions. Some people, such as healthcare

workers, may develop sensitivity to beta-lactam drugs unintentionally. Unknown hypersensitivities are not routinely screened for in healthcare workers, but may potentially present unappreciated occupational hazards.

Frequent and prolonged exposure to any drug, including penicillin, may increase the risk of hypersensitivity to these drugs. Local administration of drugs increases the likelihood

of sensitization (Adkinson 1984). Nurses are the main group of healthcare workers who prepare and administer antibiotics to patients, so they may be at highest risk for sensitization. Skin testing with major and minor determinants of penicillin has proved useful for identifying the penicillin-specific IgE antibodies in sensitized individuals.

In this study, penicillin sensitivity was tested among nurses at a large city hospital without any history of adverse reactions to these drugs. We used both minor and major determinants of penicillin.

Study

Aim

The aim of the study was to document latent sensitization of hospital nurses who did not have drug allergy history with penicillins.

Design

This was an epidemiological screening study, and was performed in 2004.

Participants

The study site was a large tertiary care referral hospital, which generally accepts patients coming from lower socio-economic groups in Istanbul. Recruitment to the study was by advertisement within the hospital, seeking voluntary participant nurses who used beta-lactam antibiotics in their daily practice. Inclusion criteria were no history of drug sensitivity or any other systemic reactions – including non-IgE-mediated reactions – such as severe food allergies.

Data collection

All nurses were examined comprehensively by a family physician and a detailed medical and allergy history was taken. Only those without a history of a previous reaction to beta-lactam antibiotics were included in the study.

The participants avoided all antihistamines for 4 weeks before testing. Skin prick tests were performed by the allergy specialist in a location close to the emergency room where facilities – including ready epinephrine – and trained personnel were available to treat any systemic reactions.

The tests were performed with benzyl penicilloyl polylysine (PPL; Allergopen, Allergopharma, Germany) and mixture of minor antigenic determinants (MDM) solutions. PPL was used at the concentration of 7 nmol/mL. MDM consisted of

benzyl penicillin 1.7 nmol/mL and benzylpenicilloic acid 1.3 nmol/mL. Skin prick tests were performed by using a stallerpoint needle (Stallergenes, France) on the forearm. A wheal larger than 3 × 3 mm accompanied by erythema, along with a negative response to saline, within 20 minutes was considered positive. If the responses to prick tests were negative, intradermal tests were performed by using 0.02 mL of solutions. In this case, a wheal larger than 5 mm with erythema within 20 minutes was defined as positive. Skin test reactions were read at 15 minutes after application. Any participant with a positive response to any testing with PPL or MDM was considered sensitive to penicillin. Histamine phosphate (1 mg/mL) and normal saline were used as positive and negative controls, respectively.

Ethical considerations

The study was approved by the ethics committee of the hospital and conformed to the Declaration of Helsinki. The aim of the study and the risks of the penicillin skin testing were explained to all participants, and all gave written consent at the beginning of the study.

Data analysis

Data were recorded on a MICROSOFT EXCEL spreadsheet and descriptive statistics were obtained by using the SPSS for WINDOWS software (version 10.0, SPSS Inc, Chicago, IL, USA). As the sub-groups were very small, no statistical comparisons were made.

Results

Of the 320 nurses in the hospital, 83 participants aged 18–42 (mean 33.5) years were recruited. They had been working as nurses for between 6 months and 22 years (mean 8.4 years); 32 worked in surgical and 51 in medical areas. None of the nurses had a history of drug allergies, including penicillin, or any other systemic reactions such as severe food allergies. However, 13 had a history of some allergic disease (bronchial asthma in two, allergic rhinitis in seven, asthma plus rhinitis in two, venom allergy in one and atopic dermatitis in one).

Physical findings in all participants were within the normal limits and they had no systemic diseases during the study period. The overall frequency of positive skin reaction to penicillin antigens was 12% ($n = 10$).

Six participants were sensitive to PPL (7.2%) and four were sensitive to MDM (4.8%). No systemic reaction was observed in any of the participants during the test period.

What is already known about this topic

- Hypersensitivity to beta-lactam antibiotics is a common and frightening health problem.
- When people are known to be sensitive to beta-lactams, it may be possible to protect them, while those with unknown sensitivity may be at risk of severe systemic reactions.
- Sensitivity to drugs including beta-lactams increases with exposure to them, and therefore nurses and some other healthcare workers who prepare and administer beta-lactam antibiotics to patients may be more likely to become sensitized.

What this paper adds

- Nurses in large hospitals are extensively exposed to penicillins and other beta-lactam antibiotics and hence it is important to identify nurses handling penicillin with clinically unrecognized hypersensitivity.
- The overall frequency of positive skin reaction to penicillin antigens was more than 12% in our study group. These and other latent sensitized nurses may be at risk of subsequent severe systemic reactions.
- Nurses handling beta-lactam antibiotics should be alert to latent sensitization and should be tested periodically.

Two of the penicillin-sensitive participants also had allergic rhinitis, The remaining eight penicillin-sensitive nurses had had not any other allergic disease.

Discussion

Between 80% and 90% of patients who report a history of penicillin sensitivity have a positive skin test for penicillin allergy (Salkind *et al.* 2001). Positive skin reactions are not necessarily followed by allergic responses to administration of penicillin (Sogn *et al.* 1992). Despite some uncertainties over definitions, the incidence of anaphylaxis in the United States of America is estimated to be 10–20/100,000 population (Sampson *et al.* 2005). Variable frequencies of hypersensitivity responses are difficult to explain, but may be due to differences in drug sensitization among populations, length of time elapsed as sensitization occurred and heterogeneity in techniques and interpretation of skin tests. There are no data indicating that anaphylaxis and other severe hypersensitivity responses are more common in healthcare workers other than latex allergies. However, we know that sensitization to penicillin may result from environmental or occupational

exposures. Even occupational contact with airborne drugs may cause sensitization. Nurses are in close contact with drugs and are more likely to be exposed to beta-lactam antibiotics than other healthcare workers, including physicians. Despite a negative history of allergic reactions to penicillins, clinically silent drug sensitization was documented in 12% of the nurses in our study group by skin tests. This subgroup may represent those who have become sensitized through occupational contact with penicillins. Wearing gloves is required in every kind of contact with patients for protection of both patients and healthcare workers and may reduce allergies and infection.

Potential anaphylactic reactions to penicillin skin tests limit their routine use in daily practice. When applied with the correct technique and antigens, the frequency of systemic reactions is <1% during test procedures (Valyasevi & Van Dellen 2000). When 1710 participants with a history of penicillin allergy who underwent penicillin skin test were evaluated retrospectively, mild systemic reactions were observed in only two cases (0.12%; Valyasevi & Van Dellen 2000). In our study group, no systemic reactions were observed in 83 nurses. If penicillin skin tests are positive, a patient can be considered to be at risk for a subsequent clinical reaction if challenged with a beta-lactam antibiotic (Anderson 1992). On the other hand, some people may develop non-IgE mediated reactions, such as contact dermatitis, after taking beta-lactam antibiotics, although this was not seen in our participants.

Our study would have been strengthened by the use of radioallergosorbent test, total serum IgE determination and lymphocyte transformation tests (Hamilton & Adkinson 2003). Despite the minimal risks of *in vitro* tests compared with reactions to skin testing, *in vitro* detection of drug-specific IgE antibodies is generally less sensitive than skin testing with the suspected agent. Skin prick testing alone is often sufficient to identify or exclude IgE-mediated penicillin hypersensitivity (VanArsdel & Larson 1989). Negative skin tests, however, do not completely rule out IgE-mediated reactivity and the risk of anaphylaxis in response to penicillin administration in patients with negative skin tests is about one percent (Chosidow *et al.* 2005). Administering penicillin to those people with a positive skin test leads to clinical allergy in about two-third of the participants (Chosidow *et al.* 2005).

Conversely, it is well known that negative skin test reaction to penicillin antigens reduces the risk of anaphylaxis (Salkind *et al.* 2001). Patients with a history of penicillin allergy and a positive skin test have at least a 50% chance of an immediate reaction if they are exposed (Salkind *et al.* 2001). These data suggest that in the diagnosis of penicillin

allergy, the history of allergy – with the exception of documented anaphylaxis – is less reliable than skin test results. It follows that those who are often exposed to penicillins should be tested occasionally, despite a negative history of penicillin allergy. We do not have reliable figures for the prevalence of penicillin sensitivity in general population in Istanbul, but we have recently reported that frequent use of penicillin and other beta-lactam antibiotics leads to sensitization in 10.2% of children without any known penicillin allergy in our population (Cetinkaya & Cag 2004). It is not possible to judge the significance of our findings because we did not compare our results to the prevalence of penicillin/beta lactam sensitivity in a general population. Therefore, further studies are needed with other occupational groups in regular contact with penicillins to compare the results of the present study.

Conclusion

Nurses should protect themselves from exposure to beta-lactam antibiotics as much as possible, and those who are inadvertently and frequently exposed to these drugs should be periodically tested for occult sensitization. We advise nurses to wear gloves while preparing and administering beta-lactam antibiotics.

Author contributions

FC, AOO and GK were responsible for the study conception and design and FC, GK and EE were responsible for the drafting of the manuscript. AOO, GK and EE performed the data collection and FC, GK and EE performed the data analysis. FC, AOO, EE and GK provided administrative support. FC, EE and GK made critical revisions to the paper. FC supervised the study.

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