

The Value of Skin Testing for Penicillin Allergy in an Inpatient Population: Analysis of the Subsequent Patient Management

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ABSTRACT

It was decided to assess the value of skin testing in a group of inpatients with a remote history of penicillin allergy, in terms of whether or not beta-lactams were subsequently given, if any adverse reactions occurred as a result of this therapy, and if labeling of the patient record was changed subsequent to skin testing and/or challenge. All patients seen in consultation with a history of penicillin allergy were assessed. When done, skin tests were performed with the major and minor determinants of penicillin and semisynthetic penicillins. Charts were reviewed after discharge in terms of the antibiotics given during admission, adverse events, and the medical record and hospital database labeling for drug allergy at discharge. Skin testing was carried out in 79% of 67 patients assessed and in all, the tests were negative. Beta-lactam therapy was recommended in 51/53 patients but was given in only 57% of these cases. At discharge, 49% of patients' records still carried the penicillin allergy label, despite negative skin testing and/or successful completion of a course of beta-lactam therapy. So, in approximately half of the patients reviewed, beta-lactams were not given despite negative skin tests and a recommendation to do so, if indicated, and 49% of patients were still inappropri-

ately labeled as being penicillin-allergic on discharge. (Allergy and Asthma Proc 21:297-299, 2000)

It is common in tertiary care hospitals for allergy specialists to be asked to assess patients with a remote history of penicillin allergy, with a view to using beta-lactam antibiotics during the admission. Because skin testing for immediate hypersensitivity to penicillins is a safe, reliable, and sensitive method of excluding IgE-mediated penicillin allergy, it is presumed that (a) this assessment is of value to the patient if it allows beta-lactams to be used, and that (b) if cheaper but equally effective and safe antibiotics can be given, this also will benefit the institution.

We decided to examine these assumptions directly, by determining what happened to a group of inpatients with a remote history of penicillin allergy, recently admitted to a large tertiary care hospital. The Allergy and Clinical Immunology Service assessed the patients at the request of the referring physician. Skin testing to exclude immediate hypersensitivity to penicillins was carried out, and recommendations regarding the use of beta-lactam antibiotics during the current admission were made. Subsequently, after discharge, a review was carried out to determine (a) whether or not beta-lactam antibiotics were administered to the patients; (b) if the use of beta-lactams resulted in adverse effects; (c) if beta-lactams were not given, what alternative antibiotics were used and did their use result in adverse effects; and (d) what Medic Alert label was given to the patients on discharge from the hospital and whether it accurately reflected the true state of the patient regarding the previous history of penicillin allergy, as determined by subsequent skin testing and/or the successful administration of beta-lactams during admission.

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METHODS

Between 1995 and 1997 we reviewed all adult inpatients seen by the Allergy and Clinical Immunology Service for assessment of possible penicillin allergy identified by history on admission. In each case, the referring physician had requested that current penicillin allergy be excluded, with a view to using beta-lactams during the admission. The following were assessed: (a) whether skin testing for penicillin allergy was carried out by the service; (b) the results of skin testing for penicillin allergy, when it was performed; (c) what recommendations were given in consultation regarding the use of beta-lactam antibiotics; (d) whether these recommendations were followed; (e) if they were not followed, whether alternative antibiotics were used; (f) what was the outcome of therapy in terms of adverse reactions; and (g) whether the patient was still labeled as being penicillin-allergic on discharge from the hospital and subsequently.

It should be noted that a recommendation to give beta-lactam antibiotics was not made if the previous history of penicillin allergy was indicative of an unpredictable and serious adverse event such as Stevens-Johnson syndrome or toxic epidermal necrolysis. A follow-up review was performed at three months to determine whether the course of beta-lactam therapy was completed successfully and whether the discharge labeling of penicillin allergy had been changed.

Skin Testing for Penicillin Allergy

Tests were carried out as described previously using benzylpenicilloyl poly-L-lysine, 6×10^{-5} mol/L (Pre-Pen, Kremers-Urban, Milwaukee, WI), benzylpenicillin minor determinant mixture containing penicillin, penilloate, and penicilloate, 1×10^{-2} mol/L, and semisynthetic MDM for ampicillin, amoxicillin, and cloxacillin, all prepared by the method of Levine and Redmond¹ as lyophilized preparations that were dissolved in isotonic saline just before use, as described previously.² Phosphate buffered saline and histamine 1 mg/mL were used as negative and positive controls. Skin tests were carried out by epicutaneous prick, then if negative, by intradermal testing. The tests were read at 12 minutes and a positive reaction had a wheal 3 mm or more than the saline control, as well as an obvious flare.

Testing was only carried out on patients who had a previous history compatible with penicillin allergy and who were not on medications that suppressed immediate skin test reactivity, i.e., H1 antagonists.

RESULTS

A total of 67 patients were assessed for penicillin allergy, of which 24 were male. The mean age of the group was 56.2 ± 18.3 years. Skin testing for immediate hypersensitivity to penicillins was carried out on 79.1% (53) of these patients. In 14 patients, skin testing could not be

carried out because of the administration of histamine H1 antagonists or because of a negative histamine response for unidentified reasons. In seven of these patients beta-lactam antibiotics were subsequently still given, with no adverse reactions.

Of the 53 patients who were skin tested for penicillin allergy, all were found to be skin test negative. Treatment with beta-lactams was recommended in 51 of these patients. This advice was followed in 27 cases, without adverse effects. Therefore, in only 57% of individuals shown to be skin test negative for penicillin allergy were the recommendations to use beta-lactams followed by the referring physicians. In other patients, alternative antibiotics vancomycin, ciprofloxacin, clindamycin, TMP-SMX, gentamicin, and metronidazole were used. However, the use of these medications was also not associated with adverse reactions.

At discharge, despite the negative skin tests and recommendations regarding beta-lactam allergy, 49% (26) of the 53 patients who were not skin test positive to beta-lactams were still labeled as penicillin-allergic on their charts. Thirteen of these individuals (50%) had successfully completed a course of beta-lactam therapy during the admission. An additional seven patients were not skin tested but received beta-lactams without adverse reactions, and four of these individuals were still labeled as penicillin-allergic at discharge. Therefore, overall there was a 50% mislabeling of patients as penicillin-allergic despite negative skin tests and/or negative challenge. A total of 17 of 34 patients who completed the course of beta-lactam therapy without an adverse reaction were still labeled as being penicillin-allergic at discharge.

DISCUSSION

It is important, in this time of health care restraint, to assess the significance of what we do as allergists and to determine whether our recommendations have a beneficial impact upon patient care and institutional costs.

In this study we found that our assessment of patients with a remote history of penicillin allergy had an impact on management in approximately half of the cases in which negative skin testing for penicillin allergy and our clinical evaluation resulted in a recommendation to use beta-lactam antibiotics during the current admission. This advice was followed in only 57% of cases. Of course, such decisions are up to the primary or consulting physician, and there may have been valid reasons to leave patients on their original antibiotic regimens, such as the results of subsequent bacterial cultures or the clinical status of the patient. All patients with a remote history of penicillin allergy who were skin test negative and received beta-lactam antibiotics, did so without developing any adverse drug reactions. But certainly the demonstration of negative skin tests for penicillin allergy and the recommendation that beta-lactams can be used, cannot be assumed to mean that this will result in the use of such antibiotics in an individual patient.

Of more significance, perhaps, is the finding that 49% of patients were still labeled as penicillin-allergic at discharge, even after negative skin tests had been recorded on the hospital chart. The mislabeling also applied to 4 of 7 patients who had not been skin tested but were given beta-lactams without adverse effects during the admission. The risks of this mislabeling are that (a) the cycle of presumed penicillin allergy and skin testing will be repeated on subsequent admission, and (b) the patient will continue to not be given beta-lactam antibiotics in the future when these would be tolerated.

On the positive side, all of the patients with a remote history of penicillin allergy who were skin test negative and were given beta-lactams tolerated this treatment without adverse effects. In addition, no patients with a remote history of penicillin allergy had positive immediate skin tests for penicillin allergy. This may in part reflect the older age group of our patient population. In children, Mínguez et al.³ found 20 of 219 (9.1%) cases of adverse reactions to penicillins and related antibiotics had positive IgE antibodies and provocation tests, while Gadde et al.⁴ reported from an STD clinic that 7.1% of patients with a positive history had positive skin tests. In contrast, Kerr⁵ considered only 1.11% of hospital patients to be allergic to penicillins by history in a prospective survey without skin testing and Surtees et al.⁶ could confirm penicillin allergy in only 4 of 132 patients (3%) claiming penicillin allergy.

Now it may be argued that negative skin testing for penicillin allergy in the absence of treatment with beta-lactams does not constitute irrefutable evidence for the absence of penicillin allergy. For example, patients could develop a delayed onset morbilliform eruption in the presence of negative skin tests for immediate hypersensitivity. All that can be said is that the patients who received beta-lactams in the present study did not have any adverse reactions. In most circumstances, the potential for such a reaction would not preclude the use of beta-lactams if clearly indicated.

This study does point out a deficiency in terms of the labeling of patient charts. Charts can be given a label of penicillin allergy based often solely on the uncorroborated history of the patient, but there may be no defined process in place to remove that labeling. Preston et al.⁷ found that a description of the allergic reaction was present in the chart in only 34% of patients who reported being penicillin-

allergic. It is clearly not sufficient to remove the label from the chart, because this will not change the hospital patient database. It is also not sufficient to have successfully completed a course of therapy with beta-lactams to have the label removed. In the institution itself, there appeared to be no accepted mechanism in place that would permit both the removal of the chart label and a change in the hospital medic alert label for the individual patient, based upon recognized criteria such as negative skin testing and completion of a course of beta-lactam therapy. However, the chart of the patient could be labeled as "penicillin-allergic" based on the uncorroborated history of the patient on admission, or would receive this label if a reaction occurred during admission when a beta-lactam was administered. Adverse reaction forms completed at such a time are forwarded to the pharmacy and the hospital medic alert data base of the patient is labeled "penicillin allergy."

It is clearly important to institute measures whereby the results of diagnostic skin testing for penicillin allergy and the results of challenge with beta-lactam antibiotics are communicated to medical record departments, so that appropriate labeling of these patients can be carried out. Otherwise, the cycle of being considered penicillin-allergic and allergy testing will continue. It is also likely that agents will then continue to be used as substitutes for penicillin, and these will often be more toxic and more costly.⁷

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