

Antibiotic allergy labels—the impact of taking a clinical history

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Summary

Background: Many patients admitted to hospital have an antibiotic allergy (AAL) documented in their medical record. In many of these, the reaction is not a hypersensitivity reaction or may no longer be relevant. Despite this, the label adversely affects patient care directly in terms of antibiotic selection, and indirectly in terms of patient costs and the development of antimicrobial resistance.

Aims: To estimate the prevalence of AALs in a cohort of hospitalised patients, to investigate the feasibility of de-labelling through re-challenge based solely upon clinical grounds.

Design: This is a cross-sectional study conducted over a 6-month period on adult inpatients. An allergy history was taken from each patient and compared with medical record data regarding allergy. Antibiotic selection data were collected (if relevant). It was then determined whether immediate de-labelling was appropriate, if direct provocation test (DPT) could be relatively safely performed, and if antibiotic selection was appropriate.

Results: Three thousand eight hundred and fifty five patients were screened, 553 (14.35%) had an AAL, and 352 were interviewed. There were 426 AALs; 276 (64.8%) towards a penicillin. After taking a detailed clinical history of the type of reaction, approximately 20% could be immediately de-labelled and educated (non-allergic, non-severe reactions) and another 38% with either a definite or vague history of mild cutaneous reaction would be suitable for an attempt at clinical de-labelling DPT.

Conclusions: These simple measures to 'de-label' patients appropriately, would increase the quality of care of this group known to have higher costs, infection with more resistant bacteria and worse health outcomes than 'non-labelled' patients.

1 | INTRODUCTION

Antibiotic allergies affect a significant proportion of hospitalised patients. Eighteen per cent of hospitalised patients have at least 1 antibiotic allergy label (AAL), penicillin being the most common with a prevalence of 13%.¹ Studies have found that up to 90% of patients who claim to be allergic to penicillin are actually able to tolerate penicillins.² The large proportion of inappropriate AALs is a significant issue as it contributes to poor antimicrobial stewardship (AMS), increased antibiotic resistance, worse patient outcomes, longer hospital stay and increased healthcare costs.^{1,3,4} An association with increased *C difficile*, MRSA and VRE prevalence has also been shown.⁵ There

have now been a number of studies which have directly linked AALs to increased prescription of second line, multiple and restricted antibiotics and increased overall antibiotic costs.^{6–8} So, as well as optimising individual patient outcomes, appropriate allergy labelling and de-labelling has also become an antimicrobial stewardship issue.^{6,9} Antibiotic allergy testing is very helpful in both de-labelling penicillin-allergic patients and identifying real beta-lactam allergies¹⁰ but is not always readily accessible, especially for hospital inpatients.¹¹ This study aims to estimate the prevalence of AALs recorded in medical records in an Australian tertiary hospital over an 18-week period that could be removed immediately (as inappropriate) as well as identifying those in whom it would be relatively safe to perform a direct

re-challenge with a drug provocation test (DPT) based upon clinical grounds. Secondary outcomes of this study included quality of allergy documentation, and the appropriateness of antibiotic prescriptions in patients with an AAL.

2 | METHODS

This study was a cross-sectional study performed at Prince of Wales hospital, a large, tertiary referral hospital. Eighteen weeks of data collection was performed between April 2016 and September 2016 on patients, admitted during that period. Patients were identified through electronic medical records with the initial inclusion criteria being that they were a new hospital inpatient with a documented suspicion of antibiotic allergy, aged 18 or over. Exclusion criteria included admission to wards in which it was not possible to get adequate clinical history (emergency department, intensive care unit, high dependency unit, mental health unit, surgical recovery unit and prison ward), cognitive impairment, patients unable or unwilling to communicate or previous admission during study period. Allergy information was collected through direct patient history within 72 hours of admission. Information gathered included: antibiotic name and reason for use date of first reaction, nature of reaction, reaction resolution, antibiotic re-use and reaction recurrence, chronology, prior antibiotic allergy testing and antibiotic identification banding. Data were also collected from patient records regarding allergy documentation and antibiotic prescription. Reactions were then classified as inappropriate (non-allergic adverse reaction - NAAR), vague or convincing (Table 1). Vague and convincing histories of allergy were then further classified by reaction into mild cutaneous reactions, severe cutaneous reactions, anaphylaxis/high risk of anaphylaxis, single organ involvement hypersensitivities, other allergic reactions or unclassifiable. Inappropriate histories were also further classified into mild non-allergic reaction, severe non-allergic reaction, inconsistent history, symptoms likely disease related, and those in which the patient claimed to not be allergic and/or claimed to be able to tolerate the antibiotic. Based upon the history and allergy classification, it was then determined whether the patient could be immediately de-labelled or if it would be appropriate to perform a direct clinical re-challenge. For those patients who received antibiotics during this admission, the antibiotics were classified relative to current national guidelines as either optimal, adequate or inappropriate based upon criteria adapted from the National Antimicrobial Prescribing Survey (NAPS)¹² which details best prescribing practices. Analysis was descriptive with categorical data summarised using frequency and percentage. Continuous variables were analysed using median and interquartile range.

3 | RESULTS

During the study period, 3855 patients were admitted, met inclusion criteria and were screened for AALs. Of these patients, 553 (14.35%)

What's known

- Antibiotic allergy labels, particularly to beta-lactam antibiotics are commonly recorded in the records of patients (approximately 13% of hospitalised patients, for beta-lactams).
- These patients often receive second line antibiotics, have poorer outcomes and have a higher incidence of more resistant organisms.
- Skin testing (ST) for beta-lactam allergies can be helpful but is often not available, particularly in the acute hospital inpatient setting.

What's new

- A detailed history of reaction allows immediate de-labelling of about 20% of patients with allergy labels (although in patients with severe non-allergic reactions, the antibiotic is still contraindicated).
- In almost another 40% of patients, the reaction reported is either mild or distant enough, that after consent, a clinical re-challenge would be appropriate.

TABLE 1 Details of 'allergy' history and reaction

Classifications of the history and reaction	N=426
Convincing history (% total)	225 (52.8%)
Mild cutaneous reactions (% subgroup; % total)	109 (48.4%; 25.6%)
Severe cutaneous reactions (% subgroup; % total)	12 (5.3%; 2.8%)
Anaphylaxis/High risk of anaphylaxis (% subgroup; % total)	94 (41.8%; 22.1%)
Single organ involvement hypersensitivities (% subgroup; % total)	8 (3.6%; 1.9%)
Other allergic reactions (% subgroup; % total)	2 (0.9%; 0.5%)
Vague history (% total)	92 (21.6%)
Mild cutaneous reactions (% subgroup; % total)	53 (57.6%; 12.4%)
Unclassifiable (% subgroup; % total)	39 (42.4%; 9.2%)
Inappropriate history (% total)	109 (25.6%)
Mild non-allergic reactions (% subgroup; % total)	50 (45.9%; 11.7%)
Severe non-allergic reactions (% subgroup; % total)	10 (9.2%; 2.3%)
Inconsistent histories (% subgroup; % total)	9 (8.3%; 2.1%)
Likely as a result of the disease at the time (% subgroup; % total)	9 (8.3%; 2.1%)
Patient denies allergy/claims to tolerate (% subgroup; % total)	31 (28.4%; 7.3%)

were identified as having an AAL on their electronic record, 352 were included in this study after exclusion criteria. Baseline demographics are unremarkable.

3.1 | Antibiotic allergy labels

In 352 patients, there were a total of 426 AALs. Two hundred seventy-six (64.8%) were towards penicillins, 41 (9.6%) towards cephalosporins, 36 (8.5%) towards macrolides and 32 (7.5%) to sulphonamides/trimethoprim.

In this cohort, 109 patients (25.6%) gave a clinical history that was a NAAR, 225 (52.8%) patients provided a convincing allergic history, and 92 (21.6%) cases, a vague allergic history. Of the 109 NAAR, 50 (45.9%) historically were mild non-allergic reactions, based on clinical history. Details of the other reactions are shown in Table 1. Three hundred and seventeen patients had histories consistent with an allergic reaction (either convincing or vague), the majority of reactions, (162/317, 51.1%) were mild cutaneous reactions whilst 94 (29.7%) were consistent with anaphylaxis or high risk of progressing to anaphylaxis, 12 (3.8%) were classified as severe cutaneous reactions, 8 (2.5%) as single organ involvement hypersensitivities, 2 (0.6%) as other allergic reactions and 39 (12.3%) were unclassifiable.

3.2 | Quality of allergy documentation

Of the 426 AALs, 417 (97.9%) were recorded in the 'allergy' section of the patient's file. The remaining 9 (2.1%) were found in other sections of the medical documentation. Of the 417 AALs recorded in the allergies section of the patient's electronic record, only 179 (42.9%) had a description or detail of the reaction recorded, 237 (56.8%) had no description, and 1 (0.2%) was inaccessible.

3.3 | Antibiotic appropriateness

In this patient cohort, 162 of patients with 'antibiotic allergy' labels recorded in their file, had clinical indications for which antibiotics were prescribed during this admission. Of these, only 60 (37.0%) of these antibiotic courses prescribed were deemed optimal (according to Australian antibiotic guidelines of alternative recommendation for allergic patients), 60 (37.0%) were deemed adequate and 42 (25.9%) were deemed inappropriate.

4 | DISCUSSION

Our study found a 14.35% prevalence of AALs over a 6-month period of hospital admissions. This is well within the margins of other studies which have found between 10%-24%.^{1-3,13-15} Allergy testing for penicillin has been found to be safe and efficacious when used appropriately, but despite this, it is not widely available within Australia.¹⁰ Accurate classification of adverse drug reactions (ADRs) to antibiotics has emerged as a very important component of de-labelling,¹⁵ as the differentiation between allergic and non-allergic ADRs is often poorly documented and leads to inappropriate allergy labelling in medical records. ADRs can typically be categorised as Type A (non-immune mediated) and Type B (pharmacologically unpredictable, often immune mediated) reactions. Even many Type B reactions are now thought

to be non-IgE-mediated and not necessarily long lasting in terms of recurrence.¹⁵⁻¹⁷ It is important to note however, that severe, non-hypersensitivity reactions are still a contraindication to using the offending drug again.

This study found that it would be safe to immediately de-label just over 20% of the total cohort solely on the basis of a detailed allergy history. These were patients who had either a mild, non-allergic reaction (such as nausea or vomiting), had inconsistent histories or were inappropriately labelled in their medical record. In this significant group of patients, medical education alone should be sufficient to remove the 'label' of antibiotic allergy. Other studies have found that, whilst taking a detailed clinical history may exclude penicillin allergy, it is not a good predictor of antibiotic hypersensitivity in patients with a history consistent with an IgE-mediated reaction to penicillin,¹⁸ and has a poor correlation with penicillin skin tests results.¹⁹

The gold standard for de-labelling patients with suspected allergy to beta-lactam antibiotics is still felt to be skin testing (pricks and ID tests, if prick-tests are negative), followed by provocation tests (PT) if skin tests are negative.^{6,16,20} Because of the significant consequences of inappropriate AALs, many hospitals are developing dedicated multidisciplinary teams including pharmacists, nurses, infection control practitioners and physicians and using computer-derived algorithms to stratify patients.^{21,22} The data from our study suggest that ST/IDT would be beneficial in 72.8% (201/276) of patients with a penicillin allergy label, but unfortunately it is not always available, particularly in a timely manner for hospitalised patients. In this context, in patients with either a convincing or vague history of a mild cutaneous reaction (ie, non-immediate) it would be relatively safe to perform a direct clinical re-challenge (OC) and this has been shown in other studies after appropriate stratification of patient risk,²³ especially if there history was of a reaction in the distant past or in childhood (when allergy is frequency over-diagnosed).^{2,9,24} This group made up 38% of the total cohort. In children with non-immediate benign skin rashes, the OC tests are now said to be the gold standard and guidelines recommend an oral drug challenge to diagnose beta-lactam allergy.²⁵ Fewer than 7% develop allergic rashes on re-exposure.^{24,26}

Two other issues which have a significant impact on patient management are highlighted in this study – allergy documentation and alternative antibiotic prescribing. Only 42.9% (179/417) of AALs had an actual description of the reaction documented in the medical record. This is similar to reports by Knezevic¹ (57%) and Lutomski²⁷ (36.3%). This is concerning as it points towards a low level of awareness among healthcare professionals regarding the importance of allergy details, both true and false. In patients with previous severe, non-allergic adverse reaction, a detailing of the 'adverse reaction' would provide more clarity.

The findings of this study were consistent with others, which have highlighted inappropriate AALs as an AMS issue. Of the 162 antibiotic courses prescribed in the 352 patients with AALs, our study found that 25.9% (42/162) were inappropriate (according to national guidelines²⁸). Other studies have also found that patients with an AAL are more likely to receive alternative, less effective antibiotics

with broader spectrums of action, more toxic profiles and resultant complications such as *C. difficile* infection.^{1,6} The importance of this is further highlighted by the fact that almost 50% of the study cohort required antibiotics during their hospital admission, so there is a likelihood that the AAL had a significant impact on the quality of antibiotic prescribing.⁶ This is not a benign inaccuracy. As a result of this, many hospitals are incorporating AMS pharmacists and even microbiologists as part of their teams for addressing reported beta-lactam allergies.²⁰ De-labelling is a low cost and simple approach to resolving some of these problems.

In conclusion, this study found that an appropriate history alone would allow removal of an 'allergy' label from at least 20% of hospitalised patients with AALs. It would also allow clinically appropriate DPT, dependent on patient acceptance in about another 38%, which is useful in the context of minimal ST/IDT availability. These simple measures, even without SPT/IDT would have a significant impact on both the quality of care of these patients, hospital costs and antimicrobial stewardship within hospitals. Ethics approval was received from the Local Health District – Human Research Ethics Committee.

DISCLOSURES

No conflict of interest for either author.

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