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Prevalence of antibiotic allergy labels and their consequences in people presenting to a teaching hospital Emergency Department; a retrospective chart review

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Abstract

Background: Antibiotic allergy labels have a direct impact on individual patient care and on the consumption of broad-spectrum antibiotics.

Objective: Our aim was to establish the prevalence of antibiotic allergies and to determine whether patients with documented antibiotic allergy labels received guideline concordant antimicrobial therapy. Additionally we wanted to evaluate the quality of allergy documentation in the medical record.

Method: Prospective audit of all patients presenting to the Emergency Department of an adult teaching hospital in Sydney over a 4 month period. Documented allergy labels, diagnoses, antibiotic administration and outcomes were recorded. Appropriateness of antibiotic choice was based on the Australian National Antimicrobial Prescribing Survey.

Results: 9.9% of presentations had at least one antibiotic allergy recorded. Significantly more women than men had antibiotic allergies documented. One third of patients with documented antibiotic allergies were prescibed inappropriate antibiotic therapy and some had significant adverse events.

Conclusion: The documentation of antibiotic allergy labels and choice of antibiotic treatment can be significantly improved. Strategies to safely de-label people with documented allergies who are not truly allergic need to be implemented.

Key words: Antibiotic, allergy, appropriate prescribing, delabelling, anaphylaxis

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Introduction

It has been shown that a documented allergy or an allergy label does not always reflect true allergy. More than 90 percent of patients who believe they have a penicillin allergy can be administered penicillin safely after assessment including skin testing and oral challenge.[1,2,3] The impact of antibiotic allergy on clinical management is often underestimated. Several studies have shown that patients with documented antibiotic allergies are more likely to be treated with broad spectrum antibiotics.[1] This is a concern with the emergence of increasingly resistant microorganisms and the lack of new classes of effective antibiotics in development. One recent study found that 15% of vancomycin, 9.4% of fluoroquinolone and 3.8% of ceftriaxone use in one Australian hospital was due to reported antibiotic allergies.[4] In a study by Macy et al looking at over fifty thousand hospitalised patients, those with a documented allergy were significantly more likely to develop *Clostridium difficile*, vancomycin resistant enterococcus (VRE) and methicillin resistant *Staphylococcus aureus* (MRSA) infections and to have longer admissions.[5] Similar outcomes were found by Charneski et al, but in addition they found that patients with documented allergy had more frequent ICU admissions, higher readmission rates and higher mortality.[6]

This study aimed to establish the prevalence of antibiotic allergy labels, examine the detail of antibiotic allergy documentation and evaluate whether patients presenting to an Emergency Department with documented antibiotic allergy labels received guideline concordant treatment at an adult teaching hospital in Sydney. The study also examined whether patients were prescribed antibiotics to which they had documented allergies and whether any adverse effects occurred.

Methods

Study design

The audit was done at the Prince of Wales Hospital in Sydney, a 570 bed tertiary adult teaching hospital. All Emergency Department (ED) presentations on a convenience sample of 59 days between August and December 2015 were evaluated. The Human Research Ethics Committee determined this project to be a quality improvement or quality assurance activity not requiring ethical review. This clinical audit aimed to establish current standard of care given to patients with documented antibiotic allergy labels.

Data collection

All presentations to the ED on the 59 days were assessed. Each patient's electronic medical record (eMR) was reviewed. The allergy alert page was used to identify patients with documented allergy labels. Gender, age and drug allergy details (including type of reaction and severity) were collected. For presentations who received an antibiotic prescription, the medication chart and ED documentation were reviewed to record which antibiotics were administered. Subsequently, each prescription was assessed for appropriateness when compared to the Therapeutic Guidelines: Antibiotic, Version 15, 2014.[7] The Australian National Antimicrobial Prescribing Survey (NAPS) assessment of appropriateness scale was used to rate the antibiotic appropriateness.[8] This includes categories of optimal, adequate, suboptimal, inadequate and not assessable. For the purposes of this study, optimal and adequate prescribing were considered appropriate. Suboptimal and inadequate prescribing were considered inappropriate. If patients were prescribed an antibiotic to which they were documented to be allergic, the medical record was reviewed to determine if this led to a documented adverse outcome.

Statistical analysis

All statistical analysis were conducted using online calculators available from Statistical Computation Vassar College.[9] The chi-square test was used to determine whether there was a statistically significant difference between the documentation of allergies in presentations requiring antibiotics during the current admission and those who did not. The same test was used to determine if there was statistically significant difference in the number of men and women presenting to ED and the number of men and women reporting antibiotic allergies. Differences between the ages of men and women were examined with a Mann-Whitney test.[9] Significance was set at $p < 0.05$ for all comparisons.

Results

The number of ED presentations who were seen by a doctor or a nurse over the 59 selected days was 8518. There were a total of 8902 presentations to ED on the days of the study, including patients who did not wait to be seen. 4436 of these were women and 4466 were men.[10] 844 (9.9%) of those seen by a doctor or nurse had an antibiotic allergy label documented in the EMR. There was a significant gender difference in the presentations with documented allergies with 275 men (32.6%) and 569 women (67.4%) having a documented allergy label ($\chi^2 = 115.34$, $p < 0.001$). The median age of the cohort with allergy labels was 56 years (range 16-98 years). There was no difference between the ages of men and women ($p = 0.28$).

A description of the adverse drug reaction was documented in 526/844 (62.3%) patients, including true allergies and other adverse effects. The type of reaction was documented more commonly for patients who were prescribed antibiotics 142/201 (70.6%) compared to those that were not 384/643 (59.7%) ($\chi^2 = 7.786$, $p = 0.0053$). **Table 1** outlines the type and severity of adverse drug reaction in the allergy label record.

Table 1. Description of adverse reactions documented in the medical records. Some patients had more than one reaction documented.

Adverse drug reaction	Presentations n (%)
No description given	318 (37.7%)
Rash	217 (25.7%)
Only severity of adverse reaction documented	149 (17.7%)
Mild	49 (5.8%)
Moderate	54 (6.4%)
Severe	46 (5.5%)
Possible anaphylaxis	97 (11.5%)
Anaphylaxis	40 (4.7%)
"Swelling"	25 (3.0%)
Tongue/lips/throat/face swelling	16 (1.9%)
Angioedema	12 (1.4%)
"Nearly died"	2 (0.2%)
Chest tightness/respiratory distress	2 (0.2%)
Side effects/intolerances	62 (7.3%)
Vomiting	26 (3.1%)
Nausea	17 (2.0%)
Diarrhoea	8 (0.9%)
GI upset/abdominal pain	7 (0.8%)
Deranged LFTs	1 (0.1%)
Jaundice	1 (0.1%)
Red man syndrome	1 (0.1%)
Peripheral neuropathy	1 (0.1%)

Table 1. (Continued)

Adverse drug reaction	Presentations n (%)
Urticaria/hives/itch	19 (2.3%)
Peeling of skin/mucus membranes	3 (0.4%)
DRESS	1 (0.1%)
Others*:	13 (1.5%)

* Other adverse reactions only reported from 1 presentation each: Headache, visual disturbance, lethargy, renal tubular acidosis, myositis, coldsores, mouth ulcers, seizures, swelling of scrotum, gastric bleed, fever, hallucinations, Meniere's disease.

Table 2. The number and proportion of patients with documented allergy labels to different antimicrobials.

Antibiotic allergy	Number of presentations reporting allergy to each drug	Percentage of the 844 presentations reporting the allergy
Penicillin	591	70.0%
Amoxycillin	50	5.9%
Cephalexin	41	4.9%
Erythromycin	40	4.7%
Amoxycillin/clavulanic acid	28	3.3%
Trimethoprim	25	3.0%
Trimethoprim/sulfamethoxazole	22	2.6%
Roxithromycin	20	2.4%
Doxycycline	20	2.4%
Cefaclor	17	2.0%
Tetracycline	17	2.0%
Cephalosporins	12	1.4%
Clarithromycin	9	1.1%
Cephazolin	8	0.9%
Flucloxacillin	8	0.9%
Metronidazole	8	0.9%
Ampicillin	6	0.7%
Clindamycin	6	0.7%
Streptomycin	6	0.7%
Vancomycin	6	0.7%
Ciprofloxacin	5	0.6%
Norfloxacin	4	0.5%
Azithromycin	3	0.4%
Ceftazidime	3	0.4%
Ceftriaxone	3	0.4%
Voriconazole	3	0.4%

Table 2. (Continued)

Antibiotic allergy	Number of presentations reporting allergy to each drug	Percentage of the 844 presentations reporting the allergy
Chloramphenicol	2	0.2%
Minocycline	2	0.2%
Nitrofurantoin	2	0.2%
Piperacillin/tazobactam	2	0.2%
Cefuroxime	1	0.1%
Cephalothin	1	0.1%
Mebendazole	1	0.1%
Dicloxacillin	1	0.1%
Gentamicin	1	0.1%
Meropenem	1	0.1%
Quinine	1	0.1%
Rifampicin	1	0.1%
Ticarcillin/clavulanate	1	0.1%
Total	978	

Table 2 summarises the frequency of reported allergy label by drug. The most common allergy was to penicillin with 591 (70%) of presentations being labelled as penicillin allergic. Amoxycillin was the next most frequent with 50 (5.9%) presentations reporting allergy followed by cephalexin and erythromycin, reported by 41 (5.3%) and 40 (4.7%) subjects, respectively. More than one antibiotic allergy was documented in 99/844 (11.7%) of presentations. Seventy one (71) patients reported two allergies, 22 reported three allergies and five reported four allergies and one reported five allergies. In total, 978 allergies were reported in the 844 presentations with documented allergies.

201 of the 844 (23.8%) presentations with documented allergies were prescribed antibiotics. In 129 of these, the documented allergy may have affected the choice of antibiotic as the patient was allergic to the recommended first line choice of antibiotic according to the therapeutic guidelines. Of patients with documented allergy 90/129 (70%) received appropriate alternate antibiotics. Of these, 83 were treated with optimal and 7 with adequate treatment. 38/129 (30%) received inappropriate antibiotics, including 36 suboptimal and 2 inadequate prescriptions according to the NAPS assessment.

Of the 38 in the inappropriate group, 14 had an allergy mismatch causing the inappropriateness. Ten of these were given or prescribed the drug they were 'allergic' to, including two who had documented anaphylaxis. Five were prescribed amoxycillin/clavulanate despite having a documented allergy to penicillin. One of these five was detected by an outside pharmacy, two were lost to follow up and two had no evidence of allergic reaction whilst inpatients. Two of the ten were prescribed ampicillin for urinary tract infection (UTI) despite documented penicillin allergy. One of these two was

detected and ampicillin was subsequently changed to ceftriaxone, which was appropriate as the allergic phenotype was mild. The other one had no adverse reaction. One was administered piperacillin/tazobactam for sepsis when penicillin allergic with no adverse effect detected. One was given flucloxacillin despite documented penicillin allergy. However, the documented reaction was a delayed maculopapular rash in childhood and the prescribing was done in consultation with the infectious disease team. This patient developed a rash after 2 days of flucloxacillin. One was given ceftriaxone with a documented allergy to cephalexin. Four were treated with a cephalosporin (three got first generation, one got third generation cephalosporin) despite a documented anaphylaxis to penicillin with no apparent adverse reactions. The other reasons for placing patients in the inappropriate group were overlapping spectra of antibiotics given (e.g. clindamycin and metronidazole prescribed simultaneously) and overly broad spectrum therapy administered when a narrower spectrum would have been sufficient (e.g. moxifloxacin given for pneumonia when no immediate hypersensitivity to penicillin documented).

Discussion

We found that 9.9% of ED presentations had an antibiotic allergy documented in the period of the study. This is at the low end of the range published in the literature, where 10-20% have been reported to have allergy labels.[1,2,11] The results show that even though the majority of people with antibiotic allergies received guideline concordant treatment, almost one third did not. Ten people (approximately 1%) were treated with the antibiotic they had a documented allergy to. Two of these had anaphylaxis documented, with potentially serious consequence. The practice of providing outpatient prescriptions for amoxycillin/clavulanate to patients with documented penicillin allergies without the first dose being observed in hospital is also of concern. Another Australian study by Fehily found that only 38% of doctors, 87% of nurses, and 66% of pharmacists were aware that their patient had an adverse drug reaction to penicillin.[12] However, the fact that 10 people received the antibiotic they were reportedly allergic to and 8 of these (2 lost to follow up) did not have any allergic reactions, would support the fact that antibiotic allergies may be over reported. It has been shown that most patients with antibiotic allergy labels have negative skin tests and can safely be given the antibiotic in question.[1,2,3] There are several reasons for this including selective side chain allergy, loss of sensitivity over time or that there was never an allergic reaction in the first place (e.g. an antibiotic-virus interaction in childhood or primary disease as cause of rash).[13,14,15]

Anaphylaxis was the documented reaction in more than 11.5% of the presentations with allergies and in 1.1% of the total presentations to ED (95% CI: 0.0089-0.0133). This documented rate is much higher than previous published data where 1-4 episodes of anaphylaxis happen per 10,000 administrations, and is likely to be an over estimate.[13] Another interesting finding was that there was a large gender difference in that over two thirds of the presentations with antibiotic allergies were women (67.4%). It is unclear whether there is a physiological explanation to this gender difference or whether it represents reporting differences, but it is in keeping with findings from other publications.[16]

Skin testing can be used to determine if it is safe to give penicillin to a patient with a previous history of penicillin allergy.[17] Skin testing has been shown to decrease the use of broad spectrum antibiotics and is used to evaluate patients with a history of immediate hypersensitivity to penicillin. A study by Park et al at the Mayo Clinic showed that a perioperative allergy clinic decreased the vancomycin use significantly in patients with previously documented penicillin allergy.[1] Protocols for oral re-challenge in patients with low risk allergy histories has been successfully implemented elsewhere and could be trialled at our hospital.[18,19]

This study highlights a number of areas for improvement in relation to antibiotic allergy management. Documentation of allergies and antibiotic treatment guideline concordance in people with antibiotic allergies can be significantly improved. Feedback sessions to medical and nursing staff regarding the findings of this audit may assist in changing practice. A recent study by Trubiano *et al* identified knowledge gaps in infectious diseases specialists, suggesting that any interventions need to target senior as well as junior staff. More than half of the group overestimated the cross reactivity between penicillins, cephalosporins and carbapenems.[20] The same group also looked into the interaction between antimicrobial stewardship and antibiotic allergy de-labelling finding that de-labelling would lead to less broad spectrum antibiotic use.[21]

This audit has limitations. We relied on the documentation of allergies by health care workers and these may have been under-assessed and reported. This may be why our allergy prevalence was lower than some other studies. We collected data from only one hospital, and we only looked at how allergy labels were handled in the ED, which may not reflect the rest of the hospital. We only looked at the appropriateness of antibiotics given to patients with antibiotic allergies. It would have been useful to compare this with the level of appropriate antibiotics given to non-allergic patients. However, the NAPS audit from 2015 found that 80.2% of antibiotic prescriptions in the same hospital were appropriate.[8] Although this audit and the NAPS dataset cannot be directly compared, this suggests that patients with documented antibiotic allergy are less likely to get appropriate antibiotics than non-allergic patients.

Conclusion

The management of antibiotic allergy labels in our hospital needs to be reviewed. Almost a third of presentations to ED with documented antibiotic allergies received inappropriate antibiotics and details about the allergy were only documented in 62 percent of presentations. Improvement in the documentation of antibiotic allergies and in the choice of antibiotics for people with documented allergies is required. Strategies to safely de-label people with documented allergies who are not truly allergic need to be explored.

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