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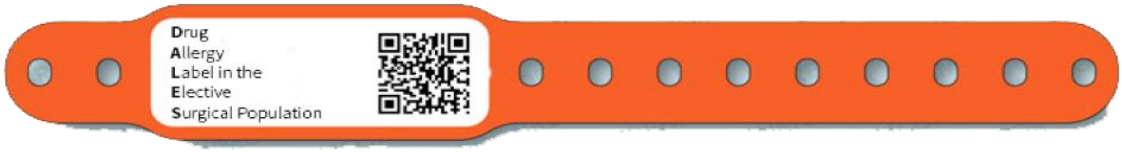

Drug Allergy Labels in the Elective Surgical population (DALES)

Study Protocol Version 3.4

Title

Drug Allergy Labels in the Elective Surgical population (DALES)

A multi-centre patient and anaesthetist questionnaire conducted by the Research and Audit Federation of Trainees (RAFT). DALES will determine the prevalence of drug allergy labels in elective surgical patients, the nature of the reaction(s) described and anaesthetist's attitudes to and knowledge of allergy label.

Introduction

Many patients report drug allergies during their pre-operative anaesthetic assessment. The nature of these reaction(s) are interpreted by the anaesthetist on the day of surgery to determine whether it is true allergic reaction or a side effect, which in turn influences pharmacological management during the perioperative period. Details of such reactions are often not well documented in the patient notes. Incorrect drug allergy labels can be harmful, both through unnecessary avoidance of drugs which may be important for a patient's treatment, or through use of alternatives which may be more toxic and less effective.

An example of a potentially harmful drug allergy label is beta-lactam (penicillin allergy). This label is the commonest of all drug allergy labels on admission to hospital but is often incorrect,

with fewer than 1 in 10 patients demonstrating allergy when tested. A beta-lactam allergy label leads to the use of alternative antibiotics for surgical prophylaxis or treatment; these alternatives tend to be broader spectrum, more toxic, and more expensive. The allergy label is consistently associated with increased length of hospital stay; increased rates of 'superbugs' such as methicillin-resistant staph aureus (MRSA), and increased rates of readmission to hospital, compared to those without the label.

This study will involve asking adult patients questions about their drug allergies on the morning of planned surgery, plus a survey of knowledge and attitudes around drug allergy amongst UK anaesthetists.

Study aims and objectives

We aim to:

1) Determine incidence of drug allergy label in the adult UK elective surgical population
2) Classify the nature of these reaction(s) into high or low probability of true allergy
3) Analyse the effect of drug allergy labels on prescribing by the anaesthetist during the perioperative period
4) Analyse attitudes and knowledge of UK anaesthetists to allergy label

Beta-lactam allergy label patient follow up aims:

1) To demonstrate whether a beta-lactam allergy label results in the anaesthetist administering a second line antibiotic as prophylaxis (where penicillin was the first line choice)
2) To determine whether, if beta-lactam given despite allergy label, this is accompanied by any documentation on the anaesthetic chart.

3) To determine whether any episode of unexpected patient instability took place in the peri-operative period as defined by unanticipated use of chlorpheniramine, hydrocortisone, adrenaline or unanticipated critical care admission.

Opioid allergy label patient follow up aims:

1)To demonstrate which opioids (if any) the patient received in theatre

2) To determine whether, if opioids are given despite the allergy label, this is accompanied by any documentation on the anaesthetic chart.

3) To determine whether any episode of unexpected patient instability took place in the peri-operative period as defined by unanticipated use of chlorpheniramine, hydrocortisone, adrenaline or unanticipated critical care admission.

Background/Rationale

Drug allergy labels are of particular interest to anaesthetists, given the wide range of drugs which a patient may require or be exposed to during the perioperative period.

It is widely accepted that many allergy labels are incorrect, with side effects incorrectly labelled as allergy, and that these incorrect labels can themselves cause harm through avoidance of drugs and use of alternatives. Beta-lactam allergy labels are an example of this: 90-98% of labels are incorrect, and the label associated with increased risk of Clostridium difficile, MRSA, longer hospital stay and other poor outcomes[1]. Work in other countries has investigated the incidence of drug allergy labels and the nature of the reaction described, however this has not been looked at in the UK elective surgical population.

Current Literature

The prevalence of drug allergy label from studies in other countries varies widely depending on the study design and population.

In Canada, of 1818 adult and paediatric patients interviewed, 28.1% claimed to have one or more drug allergies. More women than men claimed to have drug allergies (60.3% vs 39.7%) and there was a positive correlation between age, number of medications and reported drug allergies. Antibiotics (50%), opioids (27%), non-steroidal anti-inflammatory agents (10%), and sedatives (5%) accounted for 92% of all claimed drug allergies. Overall, 50% of claimed allergies had a high probability of true allergic reactions[2].

In Spain, a prospective study of 1439 patients undergoing a surgical intervention were asked about drug allergy. The prevalence of self-reported drug allergies was 8.3% (119/1439). 3.6% considered themselves allergic to β-lactams and 2.4% to non-steroidal anti-inflammatory drugs[3].

In Serbia, 1126 surgical patients were questioned. 434 (38.5%) reported drug reactions. The most common allergy claim was to antibiotics (68%), nonsteroidal anti-inflammatory drugs (16.4%) and iodine (3.9%). Women, urban residents and herbal drug consumers were more likely to state an allergy. The majority of reported reactions were cutaneous (72%) and respiratory (34%), while anaphylaxis was reported by 3.2% of patients. Only 38 (8.7%) patients had previously undergone any formal allergy testing. Retrospective chart review revealed that 26 (6%) patients were administered the drug to which they had reported allergic reaction in the past, with no adverse effects[4].

In this study we aim to identify the prevalence of drug allergy labels, and to categorise these reactions on the basis of history into high or low risk of true allergy (as opposed to recognised side effect).

References

1. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study. *J Allergy Clin Immunol* 2014; **133** (3): 790-6.
2. Hung OR, Bands C, Laney G et al. Drug allergies in the surgical population. *Can J Anaesth* 1994; **41**(12):1149-55.
3. Tamayo E et al. Self-reported drug allergies and the diagnostic work-up in the surgical population. *J Eval Clin Pract* 2010; **16** (5): 902–4.
4. Velicković J, Palibrk I, Miljković B et al. Self-reported drug allergies in the surgical population in Serbia. *Acta Clin Croat* 2015; **54**(4): 492-9.

Methods

Study Design

A study administering questionnaires/interviews for quantitative analysis. This is a cross sectional, observational and descriptive study design.

Patient questionnaire

- When the patient attends hospital on the morning of planned surgery, patient consent will be taken by a local investigator (who will typically be an anaesthetic trainee but who may also be a consultant, staff grade or research nurse) for participation in the patient questionnaire about drug allergy.
- This will occur across the country in multiple sites on three locally agreed days in six-week period.
- Patients who consent to the questionnaire will be interviewed by an anaesthetist about the presence of drug allergies, when the reaction took place and the nature of the reaction.
- Local investigators will review documentation on allergy wristbands and interview the patient about their allergy labels if present.
- In the situation where a patient is unable to remember their allergy and the Trust wristbands do not document specific allergies, the local investigator will review the admission document to confirm presence and nature of reactions. We do not ask further review of notes, I.e. local investigators will not review volumes of case notes or the electronic record.
- Some baseline data will be collected from all patients attending for elective surgery, regardless of allergy status.
- All data will be stored securely on password protected NHS premises. The data will be collected electronically at the bedside using the REDCap system.

Targeted patient follow up

- Patients who report allergy to beta-lactam or opioids will be followed up post -op at the end of the day of surgery if a beta-lactam was documented as being first line

prophylaxis for their procedure.

- An anaesthetist will review the anaesthetic and drug charts and note how the drug allergy was documented.
- For patients reporting beta-lactam allergy, the antibiotic required for their surgery will be recorded (according to Trust antibiotic guidelines) and the antibiotic the patient received will be recorded.
- In opioid allergy patients, if opioids have been prescribed this will be recorded.
- Any changes to the documentation of allergy on the anaesthetic chart following surgery, will be recorded.
- It will be recorded whether any episode of unexpected patient instability took place in the peri-operative period as defined by unanticipated use of chlorpheniramine, hydrocortisone, adrenaline or unanticipated critical care admission.

Anaesthetist Survey

- All anaesthetists and prescribing anaesthetic practitioners working during the study period will be invited to take part in a survey about attitudes to drug allergy labels in the elective perioperative setting.

Denominator survey

- A short denominator survey will be sent to all site leads to gather baseline information on each site. This comprises the opioids and non-steroidal anti-inflammatory drugs available at each site, local antibiotic protocols and the type of allergy wristband used at each site.

Setting

Participants will be consenting adult patients presenting for elective surgery in pre-waiting areas (wards or admission lounges) over three locally agreed days in a six-week period across participating sites in the UK. They will be consented and interviewed by a locl investigator on the morning of surgery.

Participants

Patient survey

Inclusion Criteria

- Present for elective surgery during the three-day study period
- ≥18
- Willing to participate
- Patients who have capacity to consent
- Elective surgery

Exclusion Criteria

- Patients lacking capacity to consent
- Not willing to consent
- Non-elective surgery
- Patients admitted from prison

Withdrawal Criteria

- Any patient who removes their consent to the study
- Any patient who no longer has capacity to consent to the study

Anaesthetist survey

Inclusion criteria

- Doctors/prescribing nurse practitioners who are working as an anaesthetist during the three locally-agreed study days, and willing to complete the survey

Exclusion criteria

- Anaesthetists covering intensive care units during the three locally-agreed study days, anaesthetic practitioners without prescribing qualifications.

Recruitment

Patients presenting for elective surgery during the three-day study period will be given a patient information leaflet to read on arrival. Posters advertising the study in the admission areas will be displayed. On the morning of surgery, patients will be offered verbal and written information then verbally asked if they want to participate. Consent will be recorded via the REDCap system.

Data sources and measurement

Data collection will be via the REDCap database (used for the previous RAFT project, iHypE). Local investigators will interview patients in admission lounges/pre-waiting areas on the day of surgery and enter the data into the REDCap system on a mobile device. A secure weblink will be used.

Local investigators who have consented a patient with either beta-lactam or opioid allergy and where the patient would otherwise receive these drugs in the peri-operative period are prompted to enter a pseudoanonymiser code based on theatre suite, theatre number and patient position on list. The REDCap system will prompt the investigator to input this code. This will involve a minority of patients recruited to DALES, i.e. those with the above allergy labels only. The pseudoanonymiser will be sent from the REDCap system to the nhs.net email address of the investigator with details of all follow-up information required. No patient contact is made at this stage; follow-up is completed from theatre and other peri-operative documents. Until data analysis is completed, local sites will either store theatre lists in a securely locked room or they will be only be accessible from password-protected Trust intranet sites. No local investigators have access to the anonymised master dataset and no lead investigators with access to the master dataset have access to the pseudoanonymiser information.

The minimum patient-identifiable data necessary to address the study aims will be collected. We are not recording patient-identifiable data in the patient questionnaire besides surgical specialty, age range, allergy and atopy history and sex. Data for analysis will only be accessed by members of the study steering committee who are fully aware of their Caldicott responsibilities.

As all members of the research team are NHS doctors, the NHS Code of Confidentiality will be followed at all times. All members of RAFT carrying out the study have confidentiality clauses in their staff contract. All staff work to appropriate confidentiality standards and have completed training in Good Clinical Practice.

Pseudoanonymised data will be transferred outside individual Trusts. All data analysis will take place using password protected Trust desktops. All data exported from the REDCap/Anaesthesia.Audit system will be anonymised, i.e. stripped of all pseudoidentifiers and local investigator information. No identifiable patient data will be used in the subsequent write up of results.

Study size

We aim to collect 12,000 patient and 5000 anaesthetist questionnaires, based on the number of participating sites and previous experience of RAFT in carrying out similar snapshot work across the UK. We will be following up an estimated 10-30% patients interviewed.

Quantitative variables

In the patient questionnaire, continuous data is grouped to aid presentation and to simplify analysis (for example age is categorized in to age range). In the case of age it is also used to minimize patient identifiable data collected.

Statistical methods

Statistical analysis will be performed by a University of Leeds statistician, the cost of which is covered by the funding requested and awarded for the study.

Missing data is expected in both questionnaires as questionnaires are not always filled in completely. We limit this through use of mandatory fields. We will report the number of missing values for each variable of interest and for each step in the analysis. Reasons for missing values will be given if possible and we will report how many individuals were excluded because of missing data.

A sensitivity analysis will be performed to investigate whether the main results are consistent with those obtained with alternative analysis strategies or assumptions. Issues that will be examined include the method of handling missing data and possible recall/response bias. Where possible, sensitivity analysis will be used to identify the degree of confounding and selection bias.

Data storage

Theatre lists and rotas used during the study period will either be in paper copy or accessible from password-protected areas of the local Trusts's intranet site. Paper copies of theatre lists and rotas will be stored securely in a locked office on NHS premises for the duration of data analysis.

For the duration of the data analysis period, the master dataset will be stored on the secure Anaesthesia.Audit system, hosted by the NSS SHOW server. When exported for analysis to members of the central study team and to the statistician, this will be anonymous, i.e. no pseudoidentifier information remains at this point. Long term data storage (for 10 years) will be on an NHS desktop computer in a locked office and will be available to members of the central study team and Leeds R and D.

The anaesthetist study data will be collected predominantly in paper form and these will also be stored securely in a locked office on NHS premises for the duration of the data analysis period. After this, paper copies of the anaesthetist survey will be securely archived locally for ten years, after which time they will be destroyed.