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Clinical Investigation

CLINICAL INVESTIGATION

Outcome of repeat anaesthesia after investigation for perioperative anaphylaxis

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Data were presented in part at the British Society for Allergy and Clinical Immunology Annual Meeting, 2014.[1]

Abstract

Background: Perioperative anaphylaxis (POA) is infrequent, but remains an important and potentially life-threatening complication of general anaesthesia. The diagnostic uncertainty surrounding the investigation of anaesthetic allergy poses numerous challenges. We aimed to inform practice by auditing the outcomes of repeat anaesthesia, after an investigation for previous POA.

Methods: One-hundred and seventy-four subjects were investigated after suspected POA between December 2002 and August 2015. Outcome data were obtained for a total of 70 patients who underwent repeat anaesthesia after investigation in the drug-allergy clinic.

Results: Sixty-seven out of the 70 patients studied underwent repeat anaesthesia without further complications. Three individuals experienced a further episode of anaphylaxis. In two cases, incomplete referral information led to the offending drugs being omitted from initial testing. The third was found to have underlying systemic mastocytosis (SM).

Conclusions: In our cohort, the incidence of repeat anaphylaxis after a comprehensive assessment in the drug-allergy clinic for suspected POA was 4%. Important risk factors include the completeness of referral information provided to the assessor and the role of exacerbating disorders, particularly SM.

Keywords: anaesthetic allergy; mast cells; perioperative anaphylaxis

Anaphylaxis is a rare but serious complication of general anaesthesia (GA). Anaphylactic reactions associated with anaesthesia have the potential to cause significant morbidity (with 2% of cases suffering from long-term neurological sequelae) or mortality (3–6% of cases[2,3]).

Whilst the true incidence of perioperative anaphylaxis (POA) is largely unknown, previous studies have reported rates of between 1 in 3000 and 1 in 20,000.[2,4–7] By extrapolating these data, it is estimated that, in the UK, between 175 and 1000 episodes of anaphylaxis occur in relation to anaesthesia each year.[8,9] However, this figure is likely to under-represent the true incidence of anaesthetic-related anaphylaxis. Indeed, data collected from 4595 anaesthetics, performed over 12 hospitals in a large region of the UK, found that as many as 1 in 353 cases met referral criteria for further investigation of suspected POA.[10]

The recognition of POA, followed by the subsequent identification and avoidance of the offending drug trigger, is

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Editor's key points

- General anaesthesia for patients with a history of perioperative anaphylaxis may be problematic, partly because of the limitations of allergy testing.
- In this retrospective study, general anaesthesia was uneventful in 67 out of 70 patients investigated previously for perioperative anaphylaxis.
- In two cases where further anaphylaxis occurred, testing was incomplete because referral information was lacking.
- A further case of repeat anaphylaxis occurred in a patient with systemic mastocytosis.
- These data emphasise the importance of good communication between anaesthetists and allergy specialists.

essential in preventing recurrence during future anaesthetics. However, the investigation of suspected POA is complex, owing to the concurrent administration of both anaesthetic and non-anaesthetic agents during the induction phase, coupled with the lack of reliable and validated tests available for drug-allergy testing.[3] Skin prick and intradermal tests remain the mainstay of allergy testing in this area, but are imperfect for diagnostic purposes because of their limited sensitivity and specificity. Indeed, the consequences of both false-positive and false-negative results are apparent, ranging from the unnecessary avoidance of a drug to erroneous administration of a potentially life-threatening agent.[3] Furthermore, the timing of skin tests may be critical. False negatives may occur if performed too early because of temporary depletion of immunoglobulin E (IgE) antibodies. Conversely, the sensitivity of skin tests may decline over time should testing be delayed.[3] Contrary to other areas of allergic disease, where *in vitro* diagnostic tests are under constant development, the range of drugs that can be tested for in routine laboratory assays is limited. Tests capable of measuring specific IgE (sIgE) to neuromuscular blocking agents (NMBAs), which account for 60–70% of all anaesthetic allergy, remain largely unavailable.[3,11] In other areas of allergic disease, establishing tolerance through double-blind placebo-controlled challenges is fundamental to the diagnostic process. However, sequential drug challenges are impractical and risky for most patients with POA.

Despite these pitfalls, the expert and timely investigation of anaesthetic allergy is essential, particularly in those in whom surgery has been abandoned, in order to ensure safe and satisfactory outcomes from repeat anaesthesia. The aim of this study was to audit outcomes after repeat anaesthesia in a cohort of patients previously investigated for POA in order to quantify risk and improve anaesthetic outcomes for individuals with suspected drug allergy. Data were presented in part at the British Society for Allergy and Clinical Immunology annual meeting in 2014.

Methods

Procedure for allergy assessment

The investigation in the drug-allergy clinic is based on a detailed referral letter, completion of the referral *pro forma* of the Association of Anaesthetists of Great Britain and Ireland (AAGBI), and analysis of anaesthetic charts[9] Patients are skin tested, as appropriate, against the anaesthetic drugs they received at induction alongside any antibiotics, colloidal fluids, antiseptic solutions, and latex to which they were exposed. One or more alternative NMBAs are tested alongside the index NMBA administered before anaphylaxis, to enable the establishment of a safe alternative. Skin prick testing (SPT) is performed with a 1:10 dilution of each drug in solution, followed by a 1:1 dilution if the former is negative. Intradermal testing (IDT) with 1:10 solutions (or recommended non-irritant concentrations) is carried out if SPT is negative. Drug-specific IgE is requested where available. If skin/intradermal tests and sIgE are negative, the advice for avoidance of a particular drug is based on a careful analysis of the temporal relationship of the drugs administered in relation to the onset of anaphylaxis along with consideration of the propensity of certain drugs to cause such reactions.

Study design

This is a retrospective cohort analysis of all patients attending the drug-allergy clinic for investigation of suspected POA between the periods of December 2002 and August 2015. Because this study focused on the outcome of a recognised investigatory pathway, it constituted a service evaluation, and hence, formal ethics approval was not sought. The notes of patients whose surgery was abandoned after POA were reviewed to determine whether the recommendations set out by the drug-allergy clinic had been followed and the outcome of any further anaesthetic encounters. In those in whom notes were not available, information was sought via written correspondence with the referring anaesthetist.

Data collection

Information relating to the initial episode of anaphylaxis was recorded for all patients investigated for suspected POA, and included the name of the surgical procedure, World Allergy Organization (WAO) grade of anaphylaxis, timing of serum tryptase concentrations, interval between reaction and allergy assessment, results of skin prick and IDT plus sIgE where available, and the advice given to the referring anaesthetist regarding future anaesthetics. Follow-up data for repeat anaesthesia included name of surgical procedure, anaesthetic agents administered, and whether or not the patient had repeat anaphylaxis.

Sample size

As this was a retrospective observational study in a random group of patients referred for investigation of suspected POA, we were not intending to generate or test a hypothesis. Consequently, power calculations would not be possible or appropriate.

Results

Study cohort

One-hundred and seventy-four individuals were investigated for suspected POA in the drug-allergy clinic between December 2002 and August 2015. Surgery had been abandoned as a result of anaphylaxis in 86 of these patients. Follow-up data relating to repeat anaesthesia were obtained for 59 of the 86 patients in whom surgery was abandoned, plus an