CASE REPORT

Type I allergic hypersensitivity reactions due to ethylene oxide sterilised leucocyte filters in patients with thalassaemia: report of four cases

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SUMMARY

Ethylene oxide (EO) is a highly reactive gas used in sterilisation of heat sensitive medical devices, such as infusion sets, cannulae, intubation materials, ventriculoperitoneal shunts, dialysis catheters and stents. Allergic reactions due to EO have been reported in haemodialysis patients, patients undergoing extracorporeal photopheresis and donors of plasmapheresis. Clinical manifestations vary considerably and generally do not allow differentiation between IgE-mediated anaphylaxis and anaphylactoid reactions. We report four patients with thalassaemia who experienced anaphylaxis during transfusion due to ethylene oxide sterilised leucocyte filters. The aim of this report is to highlight the fact that frequently transfused patients can have allergic reactions due to EO particles left in leucocyte filters.

BACKGROUND

Ethylene oxide (EO) is a potent alkylating compound of high chemical reactivity widely used for gas sterilisation of biomedical devices that do not tolerate heat sterilisation.¹ Poothullil *et al*² first described a patient who experienced typical systemic allergic reactions to EO via EO specific IgE in a chronic haemodialysis patient. Allergic reactions caused by EO have been reported in haemodialysis patients, patients undergoing extracorporeal photopheresis and plasmapheresis donors.^{3–6} We report four patients with thalassaemia with anaphylaxis due to EO sterilised leucocyte filters.

CASE PRESENTATION

Four patients with thalassaemia aged 6–15 years (1 girl, 3 boys) were followed up in Gaziantep Childrens' Hospital, Turkey, and admitted on different days for monthly blood transfusion. They were hospitalised and red blood cell (RBC) suspensions matched for blood group and subgroup were ordered. Following filtering of RBC suspensions with a leucocyte filter, approximately 5 min after the start of the transfusion, symptoms of shortness of breath, chest pain and cyanosis occurred in all the patients. Vital signs of the four patients were consistent with anaphylaxis (hypotension, tachycardia and tachypnoea, adjusted for age).

INVESTIGATIONS

The blood samples of the patients and samples from the blood products (RBCs) were sent back to the blood bank and retested for blood group, subgroup and cross-match compatibility. No mismatch

was detected in any of the transfusions. The patients were tested for IgA deficiency and IgA levels were found to be normal in all patients. Mild eosinophilia (2.2–5%) and increased serum IgE levels were shown in all four patients.

DIFFERENTIAL DIAGNOSIS

IgA deficiency was ruled out by normal IgA levels. Differential diagnosis of acute haemolytic transfusion reaction was performed with control of blood groups and cross-match.

TREATMENT

Transfusion was stopped immediately and the patients were treated with oxygen, epinephrine, methylprednisolone, diphenhydramine and salbutamol.

OUTCOME AND FOLLOW-UP

Two days later, one of the patients (a 15-year-old boy) was hospitalised for transfusion. Precautions were taken to prevent the anaphylactic reaction, and the patient was premedicated with steroid and diphenhydramine before transfusion. After filtering of RBCs with the same type of filter, wheezing and difficulty in breathing were observed 6 min after starting of the transfusion. One day later the patient was premedicated with steroid and diphenhydramine and was transfused without leucoreduction. No allergic reaction was observed. EO specific IgE RAST (radioallergosorbent test) was found to be normal (<0.1 kU/L) in all four participants (Specific IgE Assay-ImmunoCAP PHADIA, Laboratoire Cerba, France). The patients were consulted to the paediatric allergy department. It was concluded that the reactions could be attributed to type I hypersensitivity reaction to EO as shown by provocation and elimination tests, even though RAST was negative. EO sterilised leucocyte filters were replaced with γ irradiated sterilised filters and no allergic reaction was seen in any patient for the past 6 months.

DISCUSSION

EO is a potent alkylating agent that is used in gas sterilisation of biomedical devices and, although rarely, can cause severe allergic reactions.⁴ Toxicity caused by EO is fully documented. At the same time EO can cause itching, rhinitis, angio-oedema, asthma, urticaria and anaphylaxis by means of IgE-mediated allergic sensitisation.^{7 8} EO acts as an allergen, especially when it is bound to human albumin. Microparticles left in a dialyser or filter can cause sensitisation. Anaphylaxis occurs due to

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interaction of effector cells, such as the mast cell, and basophils with IgE bound to the IgE receptor (FcεRI).⁷ Diagnosis is based on history, RAST tests, basophil activation and skin tests.^{7 8} In a study by Opstrup *et al*,⁷ EO specific IgE levels were shown to have increased 4–6 weeks after an allergic reaction. After elimination of EO for 8 weeks, specific IgE levels were found to be undetectable and increased again after 4 weeks of re-exposure to EO (7). We could only test EO specific IgE levels, for which we found negative results, at the time of anaphylaxis. A similar relationship between IgE levels and chlorhexidine is previously reported.⁹ Although there is clinical sensitisation to chlorhexidine, specific IgE can be at undetectable levels with RAST.¹⁰ The low IgE levels may be attributable to lack of serial samples after the event. After excluding IgA deficiency and other transfusion reactions, these reactions were attributed to EO particles left in the leucocyte filters with the help of the elimination and provocation test conducted for the leucocyte filter.

After the change in sterilisation technique of the same type of filter (γ irradiation), no further allergic reactions were observed.

Learning points

- ▶ The ethylene oxide used in sterilisation of leucocyte filters can cause anaphylaxis in frequently transfused patients.
- ▶ Allergic reactions in frequently transfused patients should be kept in mind in differential diagnosis of haemolytic reactions.
- ▶ Clinical findings and IgE specific RAST (radioallergosorbent test) is used in diagnosis of ethylene oxide-related allergic reactions.

This finding supported our view that the allergic reactions were caused by EO particles and not other materials used in the filters. As a result, we want to emphasise that EO used in sterilisation of leucocyte filters should be kept in mind as a cause of allergic reactions in frequently transfused patients.

Contributors BB followed the patients and wrote the manuscript. MP revised the manuscript and gave immunological opinion.

Competing interests None.

Patient consent Obtained.

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