Ethylene oxide allergy in dialysis patients

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Abstract Design of study. Two groups of patients undergoing long-term dialysis were studied in order to evaluate the importance of ethylene oxide (EtO) in causing allergic reactions during dialysis. The first group of 50 subjects had never shown any hypersensitivity reactions related to dialysis, whereas the second group of 20 subjects had previously complained of reactions. All the patients underwent a prick test with a standard kit of aeroallergens in order to assess the presence of atopy (in doubtful cases a RAST test was carried out with the same aeroallergens). A blood sample for the investigation of EtO specific IgE antibodies was taken from all the patients; the immunoenzymatic method was used.

Results. Sensitivity to EtO is significantly higher in the group of patients with previous allergic reactions during dialysis (55 vs 6% in the control group).

Key words: allergic reactions; atopy; dialysis patients; ethylene oxide

Introduction

Ethylene oxide (EtO) is a gas capable of killing microorganisms by the alkylation of the sulphur-containing proteins. As it is a highly inflammable gas, it is used in association with both CO2 (90%) and fluoric hydrocarbons; in such conditions EtO sterilizes at a temperature of 40° and with 40% humidity within 4 h. It is used to sterilize various medical instruments and supplies (such as optical instruments or dialysers) that would not tolerate sterilization by heat.

As EtO gas is genotoxic in a wide variety of biological systems, and carcinogenic in rats and mice, its molecular, cytogenetic and haematological effects on hospital and sterilant workers have been studied [1,2]. It has also been shown that EtO is one of the most important causes of allergic reactions in dialysis patients because of the contact of the patient’s blood with this substance [3,4].

<table>
<thead>
<tr>
<th>Grass mix</th>
<th>Alternaria tenuis</th>
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<tbody>
<tr>
<td>Olea europea</td>
<td>Aspergillus niger</td>
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<tr>
<td>Parietaria judaica</td>
<td>Penicillium</td>
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<tr>
<td>Artemisia vulgaris</td>
<td>Dermatophagoides farinace</td>
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<tr>
<td>Compositae mix</td>
<td>Dermatophagoides pteronyssinus</td>
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<tr>
<td>Betulaceae</td>
<td>Cat</td>
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<tr>
<td>Corylaceae</td>
<td>Dog</td>
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</table>

The aim of this study was to evaluate the incidence of sensitization to EtO and the importance of atopy as a risk factor for sensitization to EtO in two groups of patients maintained by regular dialysis. Group A subjects had a previous hypersensitivity reaction related to dialysis; group B subjects had no history of allergic reactions.

Subjects and methods

In our study two groups of dialysis patients (A and B) were included. Group A: 50 subjects (26 males and 24 females) aged between 41 and 73 years (average age 52.4), with no history for hypersensitivity reactions during dialysis. Group B: 20 subjects (9 males and 11 females), aged between 46 and 68 years (average age 51.1), with hypersensitivity reactions related to dialysis: itching in six cases, urticaria–angioedema in six cases, bronchial asthma in four cases, rhinitis in three cases, anaphylactic shock in one case.

All the patients were dialysed three times weekly, 4 h for each dialytic session, using bicarbonate dialysate (acid composition = mMol/l, Na 80, K+ 2, Ca2+ 1.75, Mg2+ 0.5, Cl− 86.5, acetate 4; basic composition = mMol/l, HCO3− 39, Na+ 59; Cl− 20) and Terumo cuprammonium rayon filters sterilized by autoclaving.

The criteria for including the patients in both groups was based on: (1) frequent dialysis (3 per week) for at least 1 year, (2) no record of therapy with steroids, H1 antagonists or ACEI drugs, (3) good clinical conditions and haemodialytic status which could mask the presence of hypersensitivity reactions.

All the patients underwent a prick test with a standard panel of aeroallergen extracts (Table 1) in order to evaluate the presence of atopy (in doubtful cases a RAST with the same aeroallergens was also performed).

A blood sample for the identification of EtO specific IgE antibodies was also taken from all the patients and from 30 hospital and sterilant workers who agreed to be tested.

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non-dialysed controls; the immunoenzymatic method (Pharmacia) was used.

The statistical analysis was performed by the Fisher Excel test.

Results

In group A only three of 50 patients (6%) were positive for specific EtO IgE antibodies; while in group B 11 of 20 patients (55%) were positive (Fisher Excel test, \( P < 0.0001 \)).

In group A 11 patients (22%) were positive to prick test and/or RAST for at least one aeroallergen, and two of these were positive for EtO specific IgE antibodies.

In group B 10 patients (50%) tested positive for at least one aeroallergen at the prick test and/or RAST; seven of them were also positive for EtO specific IgE antibodies.

None of the 30 non-dialysed controls had detectable levels of anti-EtO IgE.

Discussion

The more frequent use of dialysis has triggered an increase in the number of hypersensitivity reactions [5,6]; EtO, a gas used for the cold sterilization of dialysers, is certainly the substance most frequently reported in literature as causing this kind of reaction [3–11].

Data exists which clearly demonstrate that EtO is capable of binding plasma proteins (mostly seroalbumin), to form an allergen that can trigger an IgE-mediated reaction [3].

The use of EtO during dialysis can give rise to a range of clinical features including itching, rhinitis, bronchial asthma, urticaria, angioedema, or an extremely rare severe reaction such as anaphylactic shock. These clinical features are found with varying frequency in literature [8,12–14]; this is probably due to the different criteria applied in enrolling patients for the various clinical trials.

Furthermore EtO may often cause allergic reactions when associated with other substances, such as latex or formaldehyde, used in surgery (particularly in the case of spina bifida patients) [12,15–19].

The first fact to emerge from our study is that the percentage of positivity for EtO-specific IgE antibodies was higher in the atopic patients (7 patients of 10: 70%) than in the non-atopic subjects (4 patients of 10: 40%) in group B, even if these data are not statistically significant. The second important point to emerge is the marked difference in the percentage of positivity for EtO-specific IgE antibodies between groups A and B (6 and 55% respectively), which shows a strict correlation between sensitization to ethylene oxide and the consequent hypersensitivity reactions.

Our data suggest that patients in dialysis, especially those with a positive history of allergic reactions, should be tested more frequently for EtO IgE specific antibodies.

In our opinion, this kind of investigation should be extended to include long-term dialysis patients with a negative history of allergic reactions so that if sensitivity to EtO is diagnosed steps can be taken to avoid allergic reactions in the future which may be so severe as to put the patient’s life at risk.

Since at present it is impossible to use sterilization by heat it has been suggested that catheters should be washed in a physiological solution and then left in a well-ventilated place in order to remove all trace of the EtO used during sterilization procedures; unfortunately this procedure greatly prolongs the time needed for sterilization and so it is not always feasible [20].

In conclusion, allergic reactions to EtO during dialysis are an issue of increasing interest and worth investigating further.

References


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