CAN CLINICAL ANAPHYLAXIS TO ANAESTHETIC DRUGS BE PREDICTED FROM ALLERGIC HISTORY?

M. McD. FISHER, A. OUTHRED AND C. J. BOWEY

All studies which have compared the incidence of a history of allergy, atopy or asthma in patients experiencing severe clinical anaphylaxis during anaesthesia, with the incidence in non-reacting patients have shown a statistically significant increase in the incidence of these disorders in the reacting patients (Dundee et al., 1978; LaForest, More and Fisher, 1980; Laxenaire et al., 1982; Galletly and Treuren, 1985). This has led some authors to postulate that, in such patients, the selection of drugs for anaesthesia should be altered in the light of the patient's history (Clarke, Fee and Dundee, 1978; Watkins, Clarke and Fee, 1981), or that the patient should be pre-treated with an antihistamine (Lorenz, 1985)—with the implication that such management will reduce the risk of adverse reactions.

These hypotheses appear to have taken on medico-legal significance and it is a common item of complaint, when patients seek legal redress against the anaesthetist who has administered the drug which caused a severe reaction, that inappropriate drugs were given or that inappropriate investigations were performed before operation in the light of the patient's history of allergy, atopy or asthma.

If a history of these diseases indicates that action by the anaesthetist could reduce the recurrence of severe clinical anaphylaxis, then these diseases can be considered as predictive tests and their value as such assessed.

PATIENTS AND METHODS

One thousand patients who underwent uneventful anaesthetics at the Royal North Shore Hospital of Sydney were questioned before operation, by the anaesthetist, as to the presence of allergy, atopy or asthma. The results have been published previously (LaForest, More and Fisher, 1980). Two hundred and twenty-seven patients who had life-threatening clinical anaphylaxis during anaesthesia—as judged by previously published criteria (Fisher and Munro, 1983)—were questioned following the reaction for a history of allergy, atopy or asthma before the reaction. In the case of seven non-survivors their hospital records were perused.

The methodologies of Galen and Gambino (1975) and of Cox (1984) were used to evaluate the indices of a history of allergy, atopy or asthma as diagnostic tests for their likelihood of predicting a life-threatening clinical anaphylactic reaction. The reported incidence of such reactions is between 1:600 (Vervloet, 1985) and 1:20000 (Fisher and Baldo, 1984). The Boston Collaborative Drug Surveillance Survey estimated the rate of reactions as 1:4395 anaesthetics with 90% confidence limits of 1:980-1:20000 (Beard and Jick, 1985). The indices were evaluated using a population constructed for incidence of 1:500-1:20000 using the reacting and non-reacting populations.

The methodology (Galen and Gambino, 1975;
ANAPHYLAXIS AND ALLERGIC HISTORY

TABLE I. Percent of reactors and non-reactors with history of allergy, atopy and asthma in selected populations

<table>
<thead>
<tr>
<th></th>
<th>Australia</th>
<th>New Zealand</th>
<th>France</th>
<th>United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reactor</td>
<td>Non-reactor</td>
<td>Reactor</td>
<td>Non-reactor</td>
</tr>
<tr>
<td>n</td>
<td>227</td>
<td>1000</td>
<td>42</td>
<td>200</td>
</tr>
<tr>
<td>Allergy (%)</td>
<td>45</td>
<td>14.9</td>
<td>53</td>
<td>14</td>
</tr>
<tr>
<td>Atopy (%)</td>
<td>33</td>
<td>8.5</td>
<td>26</td>
<td>7</td>
</tr>
<tr>
<td>Both (%)</td>
<td>23.8</td>
<td>6.2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>18.9</td>
<td>4.1</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Cox, 1984) involves calculating the probabilities that the test (allergy, atopy or asthma) is significantly related to the disease. A \(2 \times 2\) table is constructed, setting out whether the test is positive or negative in patients with or without the disease:

\[
\begin{array}{c|c|c|c}
\text{Test positive} & \text{Disease present} & \text{Disease absent} \\
\hline
a & b & c \\
\end{array}
\]

The following may then be derived:

Sensitivity (true positive rate) = \(\frac{a}{a+b}\)
Specificity (true negative rate) = \(\frac{c}{c+d}\)
Positive predictive value = \(\frac{a}{a+b+c}\)
Negative predictive value = \(\frac{d}{c+d}\)
False alarm rate = \(\frac{b}{b+c}\)
False reassurance rate = \(\frac{c}{c+d}\)

We constructed populations from the Australian data to give a prevalence of severe anaphylactoid reactions of 1:500 and 1:20000 and evaluated allergy, atopy and asthma as predictive tests for life-threatening reactions.

RESULTS

The incidence of a history of allergy, atopy, asthma or both in the Australian population is shown in table I, and the figures for British (Dundee et al., 1978), French (Laxenaire et al., 1982) and New Zealand (Galletly and Treuren, 1985) populations are included for comparison.

In the Australian population there was a statistically significant increase in the incidence of a history of allergy, atopy or asthma in patients who reacted to anaesthetic drugs, compared with patients who underwent uneventful anaesthesia (table II).

Table III shows the sensitivity, specificity, predictive values, false alarm and false reassurance

TABLE II. Difference incidence of allergy, atopy and asthma in reacting and non-reacting populations

<table>
<thead>
<tr>
<th></th>
<th>Reactors</th>
<th>Non-reactors</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>227</td>
<td>1000</td>
</tr>
<tr>
<td>Allergy</td>
<td>101</td>
<td>149</td>
</tr>
<tr>
<td>Atopy</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>Both</td>
<td>54</td>
<td>64</td>
</tr>
<tr>
<td>Asthma</td>
<td>43</td>
<td>41</td>
</tr>
</tbody>
</table>

P > 0.999

We constructed populations from the Australian data to give a prevalence of severe anaphylactoid reactions of 1:500 and 1:20000 and evaluated allergy, atopy and asthma as predictive tests for life-threatening reactions.

TABLE III. Value of a history of allergy, atopy or asthma in prediction of risk of clinical anaphylaxis during anaesthesia

<table>
<thead>
<tr>
<th></th>
<th>Incidence 1:500</th>
<th>Incidence 1:20000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Allergy</td>
<td>Atopy</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>44.9</td>
<td>33.04</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>85.1</td>
<td>91.5</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>0.6</td>
<td>0.77</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>99.9</td>
<td>99.9</td>
</tr>
<tr>
<td>False reassurance rate (%)</td>
<td>0.07</td>
<td>0.07</td>
</tr>
</tbody>
</table>
rates of a history of allergy, atopy and asthma as diagnostic tests for a reaction rate of 1:500 anaesthetics and for a reaction rate of 1:20 000 anaesthetics. The results show that such a history is not a valid predictor of the likelihood of a severe clinical anaphylactic reaction at the reported published incidences of life-threatening clinical anaphylaxis.

**DISCUSSION**

The figures in table III demonstrate that a history of allergy, atopy or asthma is not a reliable predictor of the risk of severe clinical anaphylaxis. Although specificity (the likelihood that a negative finding will occur in a patient without the disease) is high, all other indices of the effectiveness of such a history as a predictor are unacceptable. Prevalence of the disease is probably the most important variable (Cox, 1984) affecting the predictive value of diagnostic tests, and table III shows that the predictive value of an “allergic” history is poor for all published ranges of incidence.

Further, the potential interventions based on such a history have not been validated. Choice of low-risk drugs and pretreatment have both been subject to failure with fatal consequences (Watkins, 1985), and preoperative intradermal testing does not appear a valid predictor in the absence of a past history of a reaction (Fisher, 1985; Wood et al., 1985).

This is not to say that care should not be taken with potent histamine-releasing drugs in patients with an allergic or atopic history, as there is evidence that the direct histamine-releasing effects of drugs may be more pronounced in patients with such a history (Laxenaire et al., 1982), or in patients with cardiovascular disease (Philbin et al., 1981). If these drugs are indicated in such patients, their direct histamine-releasing effects can be reduced by slow injection and blocked by the administration of H1- and H2-receptor blocking drugs (Lorenz, 1985). The situation with respect to a history of asthma is less clear since, although in vitro tests of blood from asthmatic and non-asthmatic patients show greater histamine release in asthmatics (Guldager et al., 1985), and atopic patients are sensitive to histamine (Laxenaire et al., 1982), the only factor proven to be likely to make asthma worse during clinical anaesthesia is the placement of a tracheal tube (Schnider and Papper, 1961). The occurrence of life-threatening clinical anaphylaxis does not appear to be related to the ability of drugs to release histamine (Fisher and Baldo, 1984).

Thus modification in anaesthetic technique based on a history of allergy, atopy or asthma is unlikely to reduce the likelihood of severe clinical anaphylaxis.

**REFERENCES**


