

Occupational allergy due to inhalation of ipecacuanha dust

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Summary

A number of workers packing ipecacuanha tablets were complaining of allergic symptoms. Skin-prick tests, RAST and an assessment of clinical history by interview were used to confirm the presence of work-related allergy. Specific IgE antibodies to ipecacuanha were detected and the occurrence of antibodies correlated with the incidence of allergic symptoms. The individuals with positive RAST scores had been employed, on average, longer than those with negative scores. It was found that atopy did not predispose the workers to work-related allergy and that there was no correlation between smoking and respiratory symptoms in this population.

Introduction

Ipecacuanha is prepared from the roots of *Cephaelis ipecacuanha*, known in commerce as Rio or Brazilian ipecacuanha, or the roots of *C. acuminata* known as Cartagena, Nicaragua or Panama ipecacuanha, or from a mixture of both. Prepared ipecacuanha is the root material reduced to a fine powder and containing 2% of total alkaloids. In small doses, ipecacuanha is an expectorant but large doses produce vomiting and diarrhoea. It is employed as an expectorant in children with cough or whooping cough. For an emetic action, ipecacuanha is usually given as a syrup or tincture. It can be given, in powder form, as a diaphoretic in the early stages of febrile affections (Martindale's Pharmacopoeia, 1982).

On a factory visit, it was drawn to our attention that employees handling and packing ipecacuanha tablets were complaining of allergic symptoms, including rhinitis and chest tightness. Sensitization to ipecacuanha has not previously been described, but was considered to be a possibility as cases of allergy to vegetable protein materials, such as dried mushroom powder (Symington, Kerr & McLean, 1981) and garlic dust

(Lybarger *et al.*, 1982), have recently been described. The prevalence of occupational allergy to ipecacuanha was assessed by interviewing the subjects to obtain a clinical history. Skin-prick tests and RAST were also carried out. The relationship between cigarette smoking and allergy was also investigated, following the report of Zetterstrom *et al.* (1981) that sensitization to occupational allergens was more common in smokers.

Materials and methods

Subjects

All the workforce (42 employees) were interviewed to assess those that were experiencing symptoms of work-related allergy. In this study, work-related allergic symptoms were rhinitis, conjunctivitis and chest tightness. Blood samples were obtained from thirty-two subjects, and it was possible to carry out skin-prick tests on thirty-nine subjects.

Preparation of ipecacuanha extract

A 5% w/v extract was prepared by mixing ground ipecacuanha tablets with phosphate-buffered saline (pbs) overnight at 4°C. Insoluble material was removed by centrifugation and the supernatant was dialysed against 10 volumes of pbs overnight. The extract was stored at -20°C.

Radioallergosorbent test (RAST) assay

Ipecacuanha-allergen particles were prepared by coupling the extract to cyanogen-bromide-activated cellulose particles, as described by Merrett & Merrett (1980). The concentration of allergen-specific IgE in serum samples was determined by incubating 200 µl of a 1:5 dilution of sera with 50 µl allergen particles for 18 hr at room temperature. After washing the particles, bound IgE was detected by incubating overnight with 50 µl of ¹²⁵I-labelled anti-human IgE (Pharmacia, Uppsala, Sweden), and after removal of the unbound ¹²⁵I by washing, the ¹²⁵I bound to the particles was measured with an LKB rackgamma II counter. All assays were performed in duplicate. The results were expressed as RAST scores, defined as:

$$\frac{\text{cpm bound to particles incubated with test serum}}{\text{cpm bound to particles incubated with known negative serum}}$$

A score of two or more has been found to be greater than three standard deviations (s.d.) above the mean control serum count, and was, therefore, taken as indicative of the presence of allergen-specific IgE.

Skin-prick tests

To prepare ipecacuanha material for skin-prick testing, the 5% ipecacuanha extract was dialysed against 0.02 M ammonium bicarbonate and then lyophilized. The lyophilized material was reconstituted with Coca's solution (Coca, 1922) to 0.25 of the original volume. One millilitre of the solution was then filtered through a Millex 0.22 µm filter (Millipore Ltd) into 1 ml of sterile glycerol containing 0.4% phenol to give a solution of 10%. Prick-test solutions to B2 grass pollens, cat fur and *D. pteronyssinus* were purchased from Bencard (Brentford, England). Prick tests were performed and a

wheel of diameter 2 mm or greater was regarded as positive. A control of Coca's solution with 50% glycerol was included. Subjects with a positive prick test to one or more of grass pollen, cat fur or house-dust mite were defined as atopic.

Results

Clinical features

The employees were interviewed and twenty were found to have a clinical history of work-related allergy. Of the thirty-nine people who were prick tested, nine (23%) gave a positive response to one or more of grass pollen, cat fur or house-dust mite and were classified as atopic. Using the χ^2 test, it was found that atopy did not predispose to work-related symptoms. There was, similarly, no correlation between smoking habit and the incidence of work-related symptoms in this population.

Immunological results

Twelve out of eighteen (67%) individuals with work-related symptoms had positive RAST scores to ipecacuanha, and twelve out of fourteen (86%) individuals with no symptoms consequently were found to have negative RAST scores (Fig. 1). A χ^2 test carried out on these results showed that the RAST score reflected the incidence of work-related allergy ($\chi^2 = 6.78$, $P < 0.01$).

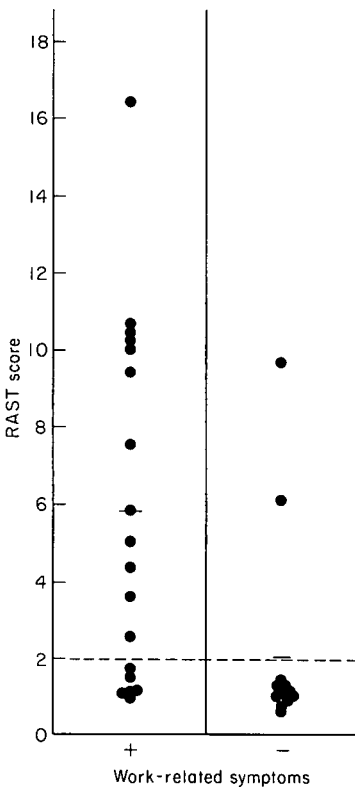


Fig. 1. RAST scores to ipecacuanha of individuals with and without work-related allergic symptoms

Skin-prick tests

Ten out of the nineteen employees (53%) with work-related symptoms gave a wheal and flare reaction to a skin-prick test with 10% ipecacuanha, with three cases where a 'false positive' was obtained, in individuals without symptoms. A χ^2 test was significant at 5% and therefore there was some correlation between skin-prick tests and work-related symptoms.

The relationship between skin-prick tests and RAST scores can be seen in Fig. 2. The mean of the RAST scores of individuals with positive skin-prick test was significantly higher than the mean of the RAST scores of those with negative prick tests ($t=7.33$, $P<0.0005$). There is only one individual in each case with either a 'false positive' RAST or skin-prick test, and the χ^2 value of 18.8 ($P<0.001$) shows a better correlation than that with work-related symptoms. This would be expected as it eliminates any possible bias towards occupational (or other) allergy in the assessment of 'work-related symptoms'.

The relationship between work-related symptoms, RAST scores and skin-prick tests to ipecacuanha for the thirty subjects for whom these data were available is most clearly summarized in the form of a Venn diagram (Fig. 3). All three factors were positive for ten individuals but six did not have their work-related symptoms confirmed by RAST or skin-prick test.

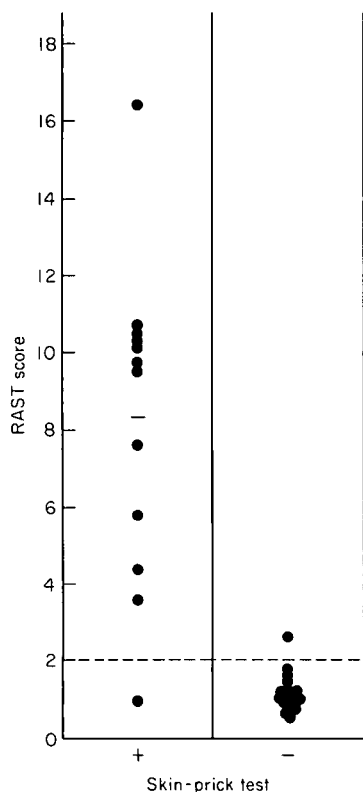


Fig. 2. RAST scores to ipecacuanha of individuals with positive and negative skin-prick tests.

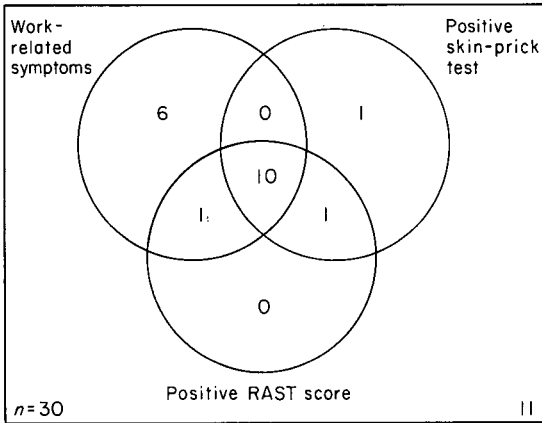


Fig. 3. The relationship between work-related symptoms, positive prick test and positive RAST in the thirty workers for whom complete data is available. (Note eleven of the thirty had no work-related symptoms and negative skin-prick and RAST results.)

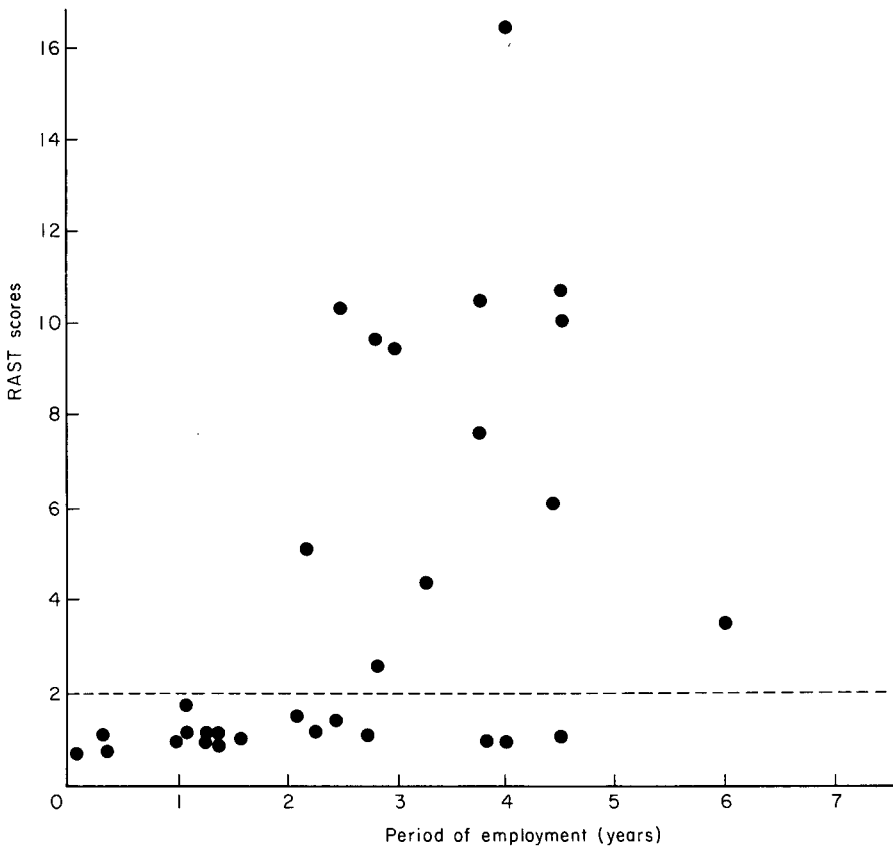


Fig. 4. RAST score to ipecacuanha and length of employment.

Length of time of employment

In Fig. 4, it can be seen that no individuals employed for less than 2 years have positive RAST scores, although there is only little correlation between the length of time of employment and RAST score ($r=0.55$, $P<0.01$).

Discussion

From the results obtained in this investigation, it is apparent that ipecacuanha powder is capable of sensitizing exposed individuals. The clinical symptoms observed were typical of type-I hypersensitivity and were of occupational origin. Their occurrence was unrelated to atopic status or to other environmental factors, such as smoking.

Using the RAST assay we were able to demonstrate specific IgE antibodies to ipecacuanha. Presence of antibodies was found to correlate with the occurrence of work-related symptoms as assessed by interviewing the subject. The wheal and flare reaction to ipecacuanha skin-prick-test solution gave further evidence that occupational allergy was present in these individuals. The results show that RAST and skin-prick tests give confirmation of allergy in symptomatic individuals and can also identify the putative allergen. The occurrence of 'false positives' is low. However, there was a relatively higher number of employees who complained of work-related symptoms but did not have these confirmed by RAST or prick tests. It is possible that they could be sensitized to other pharmaceutical materials to which they are exposed at work, or that their allergy is predominantly of environmental origin. Also they could have been wrongly assessed as symptomatic due to unavoidable bias in the interview in favour of an allergic status.

The observation that no individuals employed within the 2 years prior to the survey have occupational allergy to ipecacuanha could have a number of explanations. It was made known to us that the firm changed their supplier of ipecacuanha 14 months prior to our visit, and it is therefore possible that this new ipecacuanha is less allergenic, so that individuals exposed to only this type do not become sensitized. Another possibility is the lag period of exposure to the allergen seen before an antibody response is evoked. As we do not have detailed information concerning the date of onset of symptoms relative to start of employment we cannot make any definite statements about this as employees working there for longer than 2 years could have developed their symptoms quite recently. However, it is apparent that those individuals that have occupational allergy diagnosed by us have on average been employed at the factory for longer than unsensitized individuals. The proposed follow-up study on recent employees is expected to yield further information on the allergenicity of the new supplies of ipecacuanha. The extent of occupational allergy to ipecacuanha cannot be assessed from one investigation alone as this could merely be a 'survivor population' of individuals whose symptoms are not so distressing so as to cause them to seek alternative employment (Perks *et al.*, 1979). Nevertheless, we conclude that exposure to ipecacuanha dust bears a considerable hazard of sensitization, as does exposure to any vegetable protein, and should be controlled.

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