

Original articles

IS THE PREVALENCE OF SPECIFIC IgE TO CLASSICAL INHALANT AEROALLERGENS AMONG PATIENTS WITH RESPIRATORY ALLERGY CHANGING? EVIDENCE FROM TWO SURVEYS 15 YEARS APART

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ABSTRACT

Objective: The aim of this study was to evaluate the relative frequencies of sensitisation to four common inhalant allergens in two atopic populations suffering from asthma and/or rhinitis. One had been studied in the period of 1975 till 1979, and a second population was evaluated between 1992 and 1995.

Data sources: At both time periods patients with inhalant allergy and visiting our outpatient clinic were included. Quantification of IgE to *Dermatophagoides pteronyssinus*, birch, timothy grass, and mugwort was performed via the Phadebas RAST technique (Pharmacia, Brussels, Belgium).

Results: In patients suffering from respiratory allergy the frequency of birch pollen sensitisation significantly increased from 13 % in the period 1975-1979 to 34 % in the period 1992-1995. In contrast, the frequency of house dust mite, timothy grass pollen, and mugwort pollen sensitisation remained almost unchanged. The increase was not associated with an increase in the birch pollen count.

Conclusion: Birch pollen hypersensitivity has almost tripled among atopic subjects during the last 2 decades. The exact mechanisms for this increase remain to be evaluated.

INTRODUCTION

During the past three decades, a two- to threefold increase in the prevalence of major atopic diseases, i.e., atopic dermatitis, allergic rhino-conjunctivitis, and allergic asthma, has been reported (1-7). Most of these epidemiological surveys are based on questionnaires and compare the prevalence of the different allergic diseases in a certain population in two time periods. In contrast, little is known about eventual changes in the prevalence of allergen-specific IgE in atopic patients. Nakagawa *et al.* (8) studying 312 Japanese schoolgirls (13-14 years), observed an increase of house dust mite specific IgE from 15% in 1981 to 23% in 1991. Gassner *et al.* (9), in children (15 years) measured serum specific IgE for house dust mite and grass pollen and observed an increase from 6% to 29% and from 13 to 36% respec-

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tively between 1983 and 1992. Using skin-prick tests, Grigoreas *et al.* (10) observed an increase in *Parietaria* pollinosis in Athens (Greece). Furthermore, Rabusin *et al.* (11) reported a rise in cat sensitisation in a selected population of asthmatics living in Trieste (Italy).

In this study we evaluated two populations of atopic patients, presenting with asthma and/or rhinitis, and compared the prevalence of house dust mite, birch, timothy grass and mugwort-specific IgE at two different time points.

MATERIALS AND METHODS

Patients

In order to specify the complaints and causes of asthma and/or rhinitis, evaluation included a standardised questionnaire and a clinical examination at the department of Immunology (University of Antwerp, Belgium). This questionnaire was used for all patients, attending our outpatient clinic with complaints of asthma and/or rhinitis. A venous blood sample was drawn to determine total serum IgE and specific IgE to the following classical inhalant allergens: *Dermatophagoides pteronyssinus*, birch (*Betula verrucosa*), timothy grass (*Phleum pratense*), and mugwort (*Artemisia vulgaris*). All patients were tested with the above-mentioned allergens at their first visit to the clinic. Because not all patients were tested for animal dander (dog or cat) and mould allergens, these allergens will not be discussed. Since we wanted to evaluate changes in frequencies of specific IgE antibodies, at both time points, only patients suffering from asthma and/or rhinitis who had one or more positive relevant allergen-specific IgE were enrolled. The first population (n=299) was examined in a period between 1975 and 1979, the second population (n=283) between 1992 and 1995. The populations were stratified for sex, age and diagnosis.

Methods

Total and allergen-specific IgE antibodies were determined via the Phadebas RAST or CAP technique using a radio isotopic method (Pharmacia, Brussels, Belgium). Since the results of the patients studied at the first time period were expressed as Phadebas RAST classes, varying from 0 to 4, all samples of the second period, recorded in kU/L, were converted to the RAST classes, according to the conversion factor provided rou-

tinely by the company at that time. For both time periods, values exceeding the upper limit of class 1 were considered as positive.

Statistical methods

Odds ratios and confidence intervals were calculated according to Morris *et al.* (12).

RESULTS

Demographic data of the patients are presented in table 1. The patients were comparable according to age and sex between both periods. Figure 1 shows the overall prevalence of the four distinctive specific IgE antibodies at both time points. In 1975-79, the prevalence of a positive allergen-specific IgE was, in decreasing order: house dust mite (67%), timothy grass (66%), mugwort (17%) and finally birch (13%), compared to respectively 71%, 65%, 16% and 34% in 1992-95. The frequency of house dust mite, timothy grass pollen, and mugwort pollen sensitisation remained almost unchanged (house dust mite: odds ratio 1.21 (0.85-1.72), timothy grass: odds ratio 0.96 (0.68-1.35) and mugwort: odds ratio 0.87 (0.56-1.36)). In contrast, frequency of birch pollen sensitisation significantly increased from 13 % in the period 1975-1979 to 34 % (odds ratio and confidence interval 3.53, 2.31-5.37) in the period 1992-1995. Figure 2 shows the odds ratios and confidence interval for the different allergen-specific IgE antibodies and age groups. The increased prevalence of birch-specific IgE was statistically significant for all age groups, except for the group aged 0 - 5 years. When the patients are divided according to the symptoms (asthma alone, rhinitis alone, rhinitis and asthma), significant

Table I: Demographic data of the patients

	1975-1979	1992-1995
Sex:		
Male (296)	155 (51.8%)	141 (49.8%)
Female (286)	144 (48.2%)	142 (50.2%)
Diagnosis:		
Asthma only (78)	41 (13.7%)	37 (13.0%)
Rhinitis only (301)	152 (50.8%)	149 (52.7%)
Asthma + rhinitis (203)	106 (35.5%)	97 (34.3%)

Figure 1: Overall prevalence of specific IgE antibodies for house dust mite, birch-, timothy grass-, and mugwort pollen.

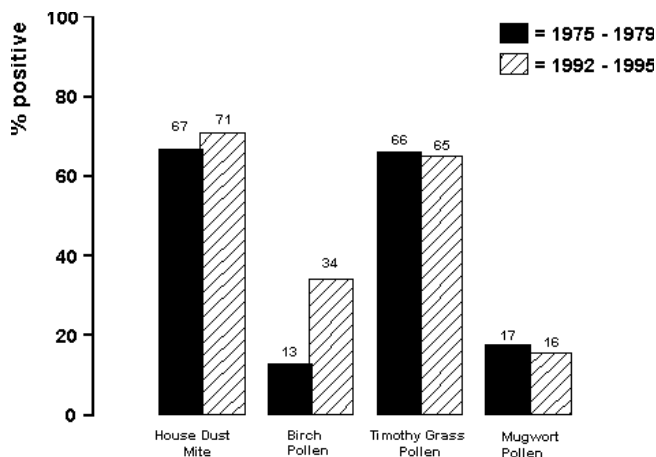
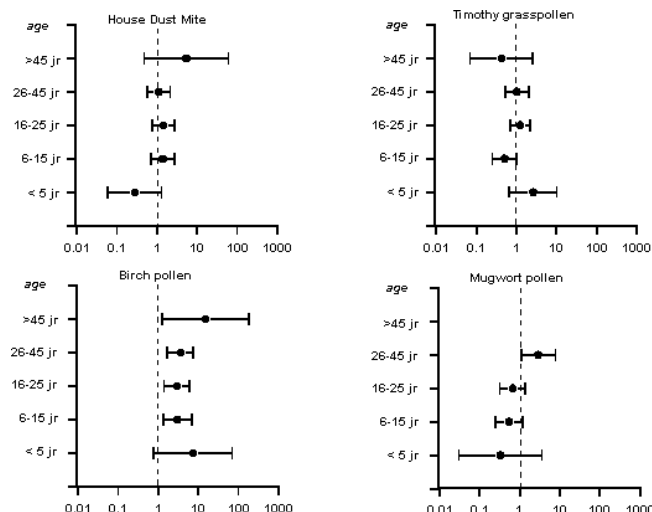
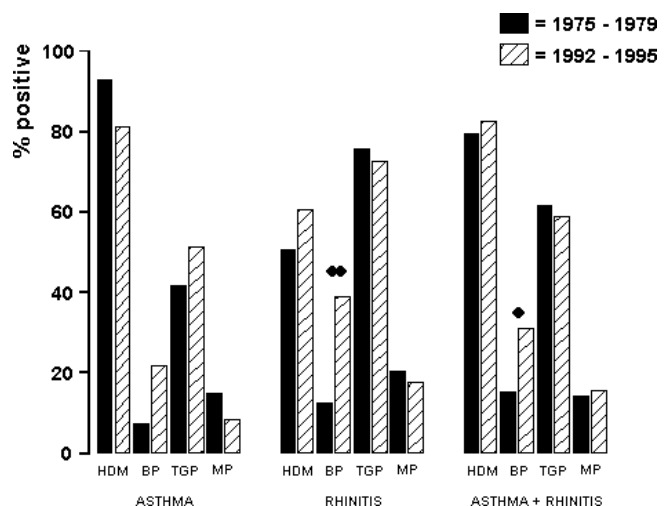


Figure 2: Odds ratios and confidence interval for the distinctive allergen-specific IgE antibodies stratified for age. No mugwort-specific IgE reactivity in patients older than 45 years was observed.



differences in prevalence of birch-specific IgE are observed in the latter two groups. In the rhinitis group the prevalence of birch pollen specific IgE rose from 13% to 39% (odds ratio (confidence interval) 4.46 (2.44-7.99); $p=0.0001$), whilst in the asthma-rhinitis combination group this prevalence rose from 15 to 31% (odds ratio (confidence interval) 2.52 (1.27-4.99) $p=0.01$) (Figure 3). The distribution of the distinctive specific IgE antibodies showed no difference between men and women.

Figure 3: Prevalence of specific IgE antibodies for house dust mite, birch-, timothy grass-, and mugwort pollen according to the clinical presentation of atopy. HDM: house dust mite; BP: birch pollen; TGP: timothy grass pollen; MP: mugwort pollen.
◆ $p < 0.01$ ◆◆ $p < 0.0001$



DISCUSSION

Data on the changes in time of the distribution of specific IgE to common aeroallergens in atopic populations are rare. We evaluated the prevalence of allergen-specific IgE for house dust mite, birch, timothy grass and mugwort in two geographically and demographically comparable atopic populations suffering from respiratory allergy, this 15 years apart. At both time points, specific IgE antibodies for house dust mite and for timothy grass were observed to be the most frequent, showing a considerable overlap. The distribution of these specific IgE antibodies is consistent with prior observations (13-15). Obviously, the far most important finding in this survey is the extreme increase of the birch pollen-specific IgE that almost tripled over the investigated time period. This increase was significant for all age groups, except for the youngest one; probably reflecting the fact that it generally needs several seasons before sensitisation for pollens takes place. It should be acknowledged that methodological issues such as the retrospective character of the study and changes in the RAST assay, can have influenced the outcome of the study. Nevertheless, in both time periods patients were investigated with the same diagnostic procedure. The changes in the RAST technique were addressed by using or converting the results to RAST classes and per-

forming categorical analysis. For the time being, the cause of the increase in birch pollen sensitisation remains unclear. One could hypothesise that our observations might be mirroring an increased allergen load, as recent experimental data are in support that an increase in the atmospheric CO₂, the so-called "green-house effect", leads to an increase in the pollen production by ragweed (16). Atmospheric pollen counts, including birch pollen, however, available from 1982 until 1997 and performed in 10 Belgian measuring stations, failed to demonstrate significant changes (17).

As an alternative explanation, one might hypothesise that the allergen composition of birch pollen grains has changed. However, as more than 95% of the patients in our regions suffering from tree pollen allergy is sensitised to the major birch pollen allergen Bet v 1, and 60% reacts exclusively to Bet v 1 (18), this seems rather unlikely. In contrast, an enhanced expression of the pathogenesis-related related Bet v 1 protein, e.g., as a consequence of pollution (19), might well have contributed to the augmented prevalence of birch pollen sensitisation. Moreover, an increased expression of Bet v 1 might help to explain the increased prevalence of birch pollen-related food allergy (20), an association that rests on the presence in pollen and vegetable foods of allergens with significant structural homology with Bet v 1 (21). Unfortunately, to our knowledge, there has been no previous longitudinal quantification of particular allergens in pollen grains over prolonged sampling periods, and, therefore, this hypothesis cannot be verified.

Finally, it should be remembered that pollen counts do not per se completely reflect the allergen load in atmosphere. Several potential mechanisms for dispersion of pollen allergen as micro-aerosols have been advocated. Most data describe allergen micro-aerosols emitted during the release of mature pollen grains (anthesis) such as liberation of anther fragments and fluid, i.e., tapetal fluid and orbicules that develop simultaneously with the growing pollen in plants with a secretory tapetum such as pollinosis-causing angiosperms (22, 23). Moreover, several investigators have identified Bet v 1 in aerosol fractions much smaller than pollen grains (24, 25), and this even extra-seasonally. Meteorological conditions might also contribute to the generation of micro-aerosols that contain pollen allergen activity. A scenario matching the dramatic power of thunderstorms to worsen or incite grass-induced asthma (26) has at present not been reported for tree pollen but, Bet v 1, as a consequence of rainfall, has been recorded in respirable fractions smaller than birch pollen grains (27). Quantifica-

tions of these micro-aerosols, however, are not performed routinely.

In conclusion, in patients suffering from rhinitis and/or asthma, the prevalence of birch pollen allergy increased significantly between the two observation periods. Because this rise in birch pollen hypersensitivity was not associated with an increase in the birch pollen counts one can only hypothesise on the underlying mechanism of this phenomenon. It is tempting to speculate on an up-regulated expression of particular birch pollen allergens because this might help to explain the concordant increase of pollen-related food allergy.

SAMENVATTING

Achtergrond: Gedurende de laatste 3 decades is de prevalentie van atopische aandoeningen zoals atopische dermatitis, allergische rhinoconjunctivitis en allergisch astma verdubbeld tot verdrievoudigd. Daartegenover staat dat er weinig gegevens zijn betreffende de eventuele veranderingen van allergeenspecifiek IgE binnen deze atopische populaties.

Doelstelling en methode: Het doel van deze studie is het bepalen van de relatieve frequenties van sensibilisatie ten opzichte van 4 klassieke inhalatieallergenen in 2 populaties lijdend aan astma en/of rhinitis. Een populatie werd bestudeerd in de periode 1975 tot en met 1979, de andere ongeveer 15 jaar later, namelijk tussen 1992 en 1995.

Op beide tijdstippen werden ambulante patiënten ingesloten. Bepaling van specifiek IgE voor huisstofmijt, berkenpollen, timotheegraspollen, en bijvoetpollen geschiedde aan de hand van de Phadebas RAST techniek (Pharmacia, Brussel, België).

Resultaten: In patiënten met een inhalatieallergie bleek de frequentie van sensibilisatie voor berkenpollen significant toegenomen van 13% in de periode 1975-79 tot 34% in de periode 1992-1995. De frequentie van sensibilisatie voor huisstofmijt, timotheegraspollen en bijvoetpollen, daarentegen, bleek ongewijzigd. De stijging van sensibilisatie ten opzichte van berkenpollen was niet vergezeld van een toename van het aantal berkenpollen.

Conclusie: Berkenpollenovergevoeligheid is bijna verdrievoudigd tijdens de laatste 2 decades bij atopische individuen. Het juiste mechanisme voor deze aanzienlijke stijging blijft onduidelijk.

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