

Allergen-specific conjunctival challenge in children with allergic asthma: a clinical tool

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It is well known that asthma can be considered to be a combination of three pathophysiologic features: 1) airways obstruction with spontaneous and/or pharmacologic reversibility, 2) nonspecific hyperresponsiveness, and 3) airways inflammation (3). Nonspecific hyperresponsiveness broadly correlates with clinical status as well as inflammatory events consequent to allergic reaction (4). A widely employed method to investigate these events is allergen-specific bronchial challenge. On the other hand, bronchial challenge with allergen may be complicated and possibly hazardous in children. For this reason, we evaluated the possible evidence of clinical response to allergen-specific conjunctival challenge in asthmatic children, since it is a common tool in the management of allergic conjunctivitis and rhinitis (2).

Material and methods

Ten healthy volunteers (six boys and four girls, aged 6–13 years, mean 8.4), with no history of allergy and negative skin prick tests and serum specific IgE to a common panel of allergens, were included as control subjects.

Twenty symptom-free children (12 boys and 8 girls, aged 4–14 years, mean 7.2) with a previously documented diagnosis of allergic asthma (10 subjects) or asthma associated with rhinitis (10 subjects) caused only by mite allergy (i.e., *Dermatophagoides pteronyssinus*) were enrolled. The diagnosis of respiratory allergy was based on concordance of his-

tory, positive skin prick test and serum specific IgE for *D. pteronyssinus*, and functional evaluation (i.e., spirometry).

On admission, no subject exhibited asymptomatic conjunctival hyperemia, as determined by ophthalmologic examination. All subjects were free of ocular disease and did not wear contact lenses. No topical or systemic drug was allowed for 2 weeks before the study.

All parents of subjects gave informed consent, and the study was performed according to ethical guidelines (i.e., Helsinki Declaration).

Allergen-specific conjunctival challenge was performed according to our previous reports (2). Briefly, 10 µl of increasing doses of allergen (i.e., extract of *D. pteronyssinus* kindly provided by Bayropharm DHS, Milan, Italy) was instilled into the lower conjunctival sac in each subject's right eye (doses ranged from 20 to 2000 AUR/ml (allergen unit by RAST) diluted in saline albumin solution 0.03%) at 10-min intervals, until provocation dose (PD) was reached. The PD was arbitrarily defined as the minimal allergen dilution able to elicit a clinical response expressed by conjunctival hyperemia intensity equal to +2, according to Abelson et al.'s classification (1). In the left eye, 10 µl saline albumin solution (0.03%) was instilled as control at the same intervals. The clinical reaction to the stimulus was assessed in blinded fashion by two investigators using penlight examination.

Statistical analysis of results was performed by the Mann-Whitney test.

Results

No healthy volunteer showed a clinical reaction after conjunctival challenge at the higher allergen dose (i.e., 2000 AUR/ml) established by previous reports (2). As expected, all allergic subjects with rhinitis showed a clinical reaction after conjunctival challenge. All patients with only allergic asthma also showed a clinical reaction after conjunctival challenge.

The PD ranged from 250 to 2000 AUR/ml (Fig. 1). The PD able to elicit conjunctival hyperemia was significantly lower in patients with asthma associated with rhinitis than in patients with only asthma ($P < 0.025$).

No ocular reaction appeared in the contralateral eye challenged with diluent (saline albumin solution).

Discussion

The present study shows the positivity of allergen-specific conjunctival challenge in patients with allergic asthma, even in the absence of ocular involvement. An explanation of this phenomenon may be offered by the consideration that IgE is always present. In fact, skin prick test and RAST are com-

mon diagnostic tools in allergic subjects. On the other hand, asthmatic patients with associated rhinitis show a lower PD, because nasal mucosa is contiguous to the eye: in fact, conjunctival challenge is commonly used in the diagnosis of allergic rhinitis (2).

However, these results are important since they show the positivity of allergen-specific conjunctival challenge also in allergic patients with only asthmatic symptoms. In particular, the employment of allergen-specific conjunctival challenge may be envisaged as an auxiliary diagnostic tool in the management of allergic asthmatic subjects to determine the allergen specificity and the specific hyperresponsiveness (i.e., allergen PD) which may be influenced by pharmacologic treatment, specific immunotherapy, and avoidance measures.

A possible further study would be to correlate allergen-specific conjunctival challenge with bronchial nonspecific hyperresponsiveness (i.e., methacholine challenge). In fact, bronchial challenge with allergen may even be hazardous in children; moreover, allergen-specific conjunctival challenge may yield related data on the inflammatory response in comparison with the allergic reaction because cytologic evaluation by scraping (i.e., cytologic evaluation, adhesion molecule expression, etc.) can be easily obtained and comfortably repeated several times in the same patient, as we have reported in a study of late-phase phenomena (2). But this is not true of bronchial challenge.

Thus, it is possible to relate specific changes (i.e., cytologic variables of inflammatory events consequent on allergic reaction) to nonspecific hyperreactivity status (i.e., evolution of methacholine PD_{20}). In addition, allergen-specific conjunctival challenge may be envisaged as an additional tool for the diagnosis of patients with negative or doubtful skin prick tests and/or specific IgE, but a suggestive history of allergy. Finally, conjunctival challenge may be employed to establish the most important causal allergen in polysensitized patients, especially children.

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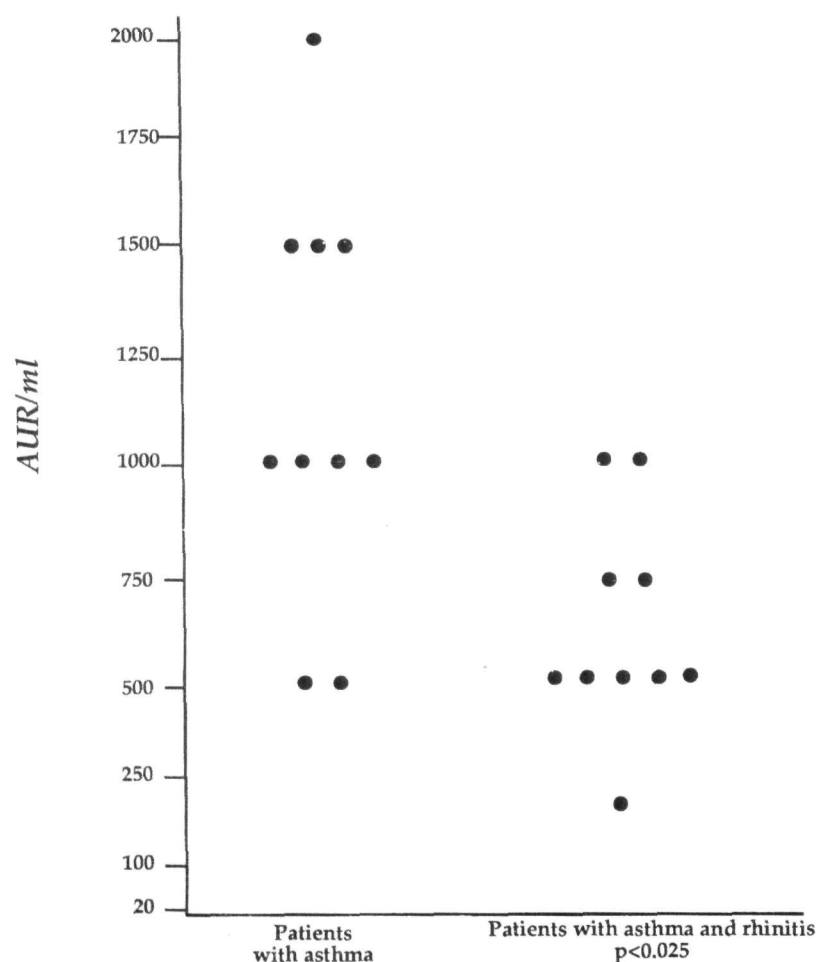


Fig. 1. Allergen provocation dose in allergic patients at conjunctival level (AUR/ml).

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