

Short Report

Allergic children have more numerous and severe respiratory infections than non-allergic children

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Allergic disorders are characterized by Th2-polarization, and hence physiological Th1-dependent mechanisms for fighting respiratory infections (RI) may be defective. This study aimed at evaluating the number and duration of RI in allergic and non-allergic children suffering from recurrent RI. One hundred seventeen children (4.02 ± 1.0 yr, 72 males and 45 females) were studied during the spring, 46 were allergic. Allergic children showed a significantly higher number (mean 1.26 ± 0.73) and longer duration of RI (8.92 days) in comparison with non-allergic group (0.94 ± 1.37 and 4.85 days) ($p = 0.0001$ and $p = 0.009$, respectively). In conclusion, this study provides the evidence that allergic children have more numerous and severe RI than non-allergic children.

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Allergic disorders show increasing worldwide prevalence (1). Allergic rhinitis and asthma share common immunological mechanisms characterized by Th2-dependent inflammation (2). As a consequence, atopic subject has typically Th2-polarization and reduced Th1-response (2). Interferon-gamma, typical Th1-derived cytokine, is deputized for fighting infections. Thus, it has been pointed out that allergic children could present higher susceptibility to contract respiratory infections (RI) than non-allergic subjects (3). This hypothesis could be reinforced by the evidence that rhinovirus infections are commonest in childhood (4). The main receptor for rhinovirus is intercellular adhesion molecule-1 (ICAM1) (4). ICAM1 expression in nasal epithelial cells is strictly related to allergen exposure in allergic subjects (5). Thus, there is a clear link between allergen exposure, ICAM1 expression, allergic inflammation, and RI. In addition, treatments with drugs those are able to reduce ICAM1 expression diminish both the number and severity of RI in allergic children (6).

Recurrent RI are frequent in children and constitute a demanding challenge for the pediatrician (7). Recurrent RI (RRI) is diagnosed based on at least any one of the following criteria: (i) >6 annual RI; (ii) >1 monthly RI involving the upper airways from September to April; (iii) >3 annual RI involving the lower airways (8). Moreover, RRI represents a social problem both concerning the pharma-economy and the impact on the family and social milieu of the child. However, there is no data concerning the different impact of RRI on allergic and non-allergic children. Therefore, this study was performed to evaluate the number and duration of RI in allergic and non-allergic children suffering from RRI.

Methods

Population and eligibility criteria

Children with RRI were enrolled in this study. Inclusion criteria were: out-patients of both

sexes, aged 3–6 yr, attending a nursery or primary school, positive history for RRI in the last 12 months (> 6 episodes), and good general conditions; written informed consent of at least one parent was obtained. Exclusion criteria were: primary or acquired immunodeficiency, previous (last three months) or concomitant administration of drugs able to interfere with the study (e.g., immunomodulants, specific immunotherapy, homeopathic therapy, or systemic corticosteroids for at least two consecutive weeks), history of chronic diseases, such as cancer, or congenital malformation of the airways.

Study design

Children with RRI were prospectively and consecutively evaluated. All of them were referred to the Istituto Giannina Gaslini for consultation. Children were subdivided into two groups according to the presence of allergy. Allergy was diagnosed on the basis of positive history and skin prick test (9).

This study was performed during the spring. This season was chosen for two reasons: to evaluate RI in a period with low incidence of infections and to consider the impact of pollen season.

This study was approved by the ethics committee (EC) of the Istituto Giannina Gaslini of Genoa.

Study procedures

The children were examined at study entry and every month for 3 months. At each visit, a history of infections between two visits was achieved and clinical examination was done.

The investigator diagnosed RI on the basis of the symptoms recorded by the parent in the study diary and counted the number of episodes. The diagnosis of RI was made when at least two symptoms or fever (axillary temperature $\geq 38^{\circ}\text{C}$) were present for at least 48 h besides another symptom. The symptoms taken into consideration for diagnostic purposes were: mucopurulent rhinorrhea (stuffy and/or dripping nose), sore throat, cough (dry or productive), otalgia (ear ache), fever, dyspnea, and mucopurulent secretion.

Analysis

The primary end-point was the number of RI episodes recorded during the 3-month study in the two groups. The secondary efficacy outcomes were: (i) total duration of RI episodes (days) and

(ii) number on the basis of the type of RI severity. RI were considered as mild or severe. Mild RI involved the rhinopharynx (rhinitis, rhinopharyngitis with possible involvement of tonsils), and/or the larynx. Severe RI involved the middle ear, the lower airways, or the paranasal sinuses.

Statistical analysis

The main descriptive statistics was calculated for each variable: mean, median and s.d. for quantitative variables. Absolute and relative frequencies were calculated for qualitative variables. Also the 95% confidence limit was calculated whenever relevant.

The analysis was carried out using non-parametric Mann-Whitney's test for unpaired samples except for the frequency of the type of episodes, which were analyzed using the χ^2 -test.

Results

Population

One hundred and seventeen children with RRI were studied: age 4.02 ± 1.0 yr, 72 males and 45 females. Allergy was diagnosed in 46 children. Allergic children were mainly sensitized to: house dust mites (29), grasses (9), olive tree (9), Parietaria (7), cat (7), dog (4), hazel (4), and birch (4).

Primary outcome

Allergic group showed a significantly higher number (mean 1.26 ± 0.73) of RI in comparison with the non-allergic group (mean 0.94 ± 1.37) ($p = 0.0001$) (Table 1).

Secondary outcomes

Allergic group showed longer duration of RI (8.92 days) in comparison with the non-allergic group (4.85 days) ($p=0.009$) (Table 1). Moreover, in evaluating mild RI, allergic children

Table 1. Weighted mean $\pm$ s.d. of number and duration of respiratory infections (RI) in children with recurrent RI

Total number and forms of RI	Non-allergic children (n = 71)	Allergic children (n = 46)
Total RI number ($p = 0.0001$)	0.94 ± 1.37	1.26 ± 0.73
Mild RI number ($p < 0.00001$)	0.53 ± 0.64	1.02 ± 0.7
Total RI duration (days) ($p = 0.009$)	4.85 ± 5.24	8.92 ± 9.64
Mild RI duration (days) ($p = 0.0007$)	2.99 ± 3.91	7.82 ± 9.87

showed higher number (1.02) and longer duration (7.82 days) than the non-allergic children (0.53 and 2.99, respectively) (Table 1).

Discussion

This study clearly evidences that allergic children have more numerous and severe RI than non-allergic children. This phenomenon appears to be more evident considering mild RI, such as infections involving the rhinopharynx.

These findings seem to be more convincing as the study was performed during a period that was quite unfavorable for RI. In fact, on an average, children suffered from one RI only. Moreover, allergic children have more infections as an allergic reaction is characterized by mucosal inflammation that predisposes to infections. In addition, allergic subjects express ICAM1 – adhesion molecule involved in inflammatory events – as a ligand for LFA1 expressed on leukocytes, but also as a receptor for rhinovirus (5).

It is to be noted that most sensitizations were for pollens, and thus in allergic children exposed to these allergens, inflammatory phenomena were more pronounced.

These findings are reinforced by the concept that anti-allergic treatments may reduce number and severity of RI (6).

On the other hand, allergic children present a typical Th2-polarization with a consequent reduced Th1-response that adequately fights infections mainly by interferon-gamma (IFN γ). In this regard, a previous study reported that allergic children with RRI show characteristic Th2-polarization and a defect in the Th1-activity at the nasal level (10). It is to be noted that probiotic treatment induces a physiological inversion of Th1- and Th2-derived cytokines (10).

In conclusion, this study provides the evidence that allergic children have more numerous and

severe RI than non-allergic children and our result suggests that allergy could have a negative role in RRI, although a further case-control study would be needed to investigate more accurately the cause-effective role of allergy in respiratory infections.

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