Allergol Immunopathol (Madr). 2013;41(5):288–291

Allergologia et immunopathologia

www.elsevier.es/ai

ORIGINAL ARTICLE

May T1 diabetes mellitus protect from asthma?

Maria Angela Tosca[a], Michela Silòvestri[a], Giuseppe D'Annunzio[b], Renata Lorini[b], Giovanni Arturo Rossi[a], Giorgio Ciprandi[c,*]

[a] *Pediatric Pulmonology and Allergy Unit, Istituto Giannina Gaslini, Genoa, Italy*
[b] *Pediatric Clinic, University of Genoa – Istituto Giannini Gaslini, Genoa, Italy*
[c] *Allergy and Respiratory Diseases Clinic, IRCCS – Azienda Ospedaliera Universitaria San Martino, Genoa, Italy*

Received 10 July 2012; accepted 8 October 2012
Available online 21 December 2012

KEYWORDS
Diabetes;
Asthma;
Allergic rhinitis;
Bronchodilation;
FEF25-75%

Abstract
Background: Type 1 diabetes mellitus (T1DM) may be associated with allergy. It was previously reported that >20% of children with T1DM had allergic rhinitis (AR), but none was asthmatic. This finding was surprising as allergic rhinitis is frequently associated with asthma and asthma prevalence is about 10% of the general paediatric population. Thus, it was hypothesized that T1DM could protect from asthma.
Objectives: The aim of this preliminary study was to evaluate the pulmonary function and the response to bronchodilation testing in children, suffering from T1DM with associated AR, comparing them with a control group of children with AR alone.
Methods: Twenty children with T1DM and AR were compared with 59 children with AR alone; spirometry and bronchodilation testing were performed in all patients.
Results: There were no statistically significant differences in both ''at baseline'' and after bronchodilation testing about FVC, FEV_1, and FEF_{25-75} values. However, changes in ''post-bronchodilator'' values of FEF_{25-75} (ΔFEF_{25-75}) were significantly higher in children with AR alone than in children with T1DM and AR ($p = 0.04$).
Conclusions: This preliminary study could sustain the hypothesis that T1DM in children suffering also from AR might exert a protective effect of preventing the possible evolution in asthma.

Introduction

Asthma and Type 1 diabetes mellitus (T1DM) are complex disorders, sustained by an immune dysregulation.[1] T1DM is commonly considered a Th1-mediated autoimmune disorder, whereas asthma, specifically when associated to allergic sensitisation,[2] is typically characterised by a Th2-dependent inflammation.[3] However, the paradigm based on the assumption that Th1 and Th2 diseases should be mutually exclusive has to be substantially revised considering not only the relevant role of T regulatory cells (Tregs) played in both types of disorders[4] but also the epidemiological data showing a frequent association between them.[5] Indeed, T1DM does not

* Corresponding author.
E-mail address: gio.cip@libero.it (G. Ciprandi).

0301-0546/$ - see front matter © 2012 SEICAP. Published by Elsevier España, S.L. All rights reserved.
http://dx.doi.org/10.1016/j.aller.2012.10.009

seem to play a down-regulating role on the development of allergic sensitisation, but might lower the frequency or the severity of its clinical manifestations at respiratory level. In this regard, we previously reported that in a cohort of 112 T1DM teenagers nobody had current asthma even though 49 of them were sensitised to aeroallergens and 25 had allergic rhinitis.[6] This finding was surprising for two reasons: (i) asthma affects about 10% of the general paediatric population, and (ii) allergic rhinitis is frequently associated with asthma. Therefore, the absence of asthma in all these T1DM children could support the idea that diabetes might protect from asthma. To further analyse this hypothesis, a preliminary study was designed to evaluate the pulmonary function and the response to bronchodilation testing in 20 consecutive children, suffering from T1DM with associated allergic rhinitis, comparing them with a control group of 59 consecutive children with allergic rhinitis alone.

Materials and methods

Study population

A total of 20 children (11 males, median age 14.6 years) consecutively referred as outpatients to the Regional Childhood Diabetes Centre of the G. Gaslini Institute for T1DM management completed the study. The inclusion criteria were: diagnosis of both T1DM and allergic rhinitis. The exclusion criteria were: previous or current allergen-specific immunotherapy, and use of drugs that could interfere with the study. A control group of 59 consecutive children (31 males, median age 10.3 years) referring to the Allergy Centre of the same institution for allergic rhinitis management were enrolled. The inclusion criterion was the diagnosis of allergic rhinitis. The exclusion criteria were the same as for the study group.

The Institutional Ethical Committee of the G. Gaslini Institute approved the protocol. Signed informed parental consent and the child's assent (if the child was $\geq$10 years old) were obtained. Diabetes diagnosis was based on standardised and validated criteria, such as: (a) positive pancreatic β-cells autoantibodies; (b) signs and symptoms of diabetes mellitus; (c) insulin-dependence.[7,8] Allergic rhinitis diagnosis was performed using validated criteria, such as: (a) presence of typical symptoms, (b) sensitisation to airborne allergens, and (c) symptom occurrence after exposure to the sensitising allergens.[9]

Data collection

Information on demography, metabolic parameters, and presence of respiratory disorders (such as allergic rhinitis and asthma) was collected at the time of the survey. A questionnaire, a slightly modified version of International Study of Asthma and Allergies in Childhood (ISAAC),[10] was used to investigate the frequency of asthma and allergic rhinitis. The questionnaire was administered to parents of all children enrolled in the study and the demographic and clinical data were collected by the physicians involved in the study. Information on current rhinitis symptoms (itchy and/or runny and/or blocked nose) and asthma-related symptoms (dyspnoea, wheezing, recurrent dry cough or exercise-related symptoms) was collected.

Skin prick test

Skin prick tests were performed according to the methodology and criteria proposed by the European Academy of Allergy and Clinical Immunology (EAACI).[11] The test uses a panel of allergens extracts, histamine solution (10 mg/ml) as positive control and glycerol buffer diluents of allergenic preparations as negative control. Wheals at least 3 mm $\times$ 3 mm greater than wheals at the site of negative control are regarded as positive.

Lung function measurement

Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and forced expiratory flows at 25–75% of vital capacity ($FEF_{25-75\%}$) were measured by spirometry (Med Graphics, Pulmonary Function System 1070 series 2, Med Graphics Corp., St. Paul, MN), according to the guidelines provided by the American Thoracic Society.[12] All the children were able to obtain at least three technically acceptable breathing manoeuvres with the spirometer. After the ''at baseline'' evaluation, spirometry was repeated 15 min after two inhalations of a salbutamol metered dose inhaler (100 mg/actuation) via a spacer device, and post-bronchodilation FVC, FEV_1, FEF_{25-75}, and FEV_1/FVC ratio were recorded. Three forced expiratory manoeuvres were obtained, and the best values were retained. The results were expressed as percentage of the predicted and compared with reference values obtained from a well-defined population, identified by the American Thoracic Society, of healthy subjects comparable for gender, height, weight and then expressed as a percentage.[13]

Statistical methods

Descriptive statistics were firstly performed and qualitative data were reported in terms of absolute frequencies and percentages; means and standard deviations (SD), or medians and lower and upper quartiles (LQ-UQ) were reported for quantitative variables (age, BMI, pulmonary function test parameters, etc.) when appropriate. Comparison of qualitative data between groups was made by the chi-square test or by the Fisher's Exact test whenever expected frequencies were less than five. All tests were two sided and a *P* value less than 0.05 was considered statistically significant. The statistical package used was the ''Statistica release 6'' (StatSoft Corp., Tulsa, OK, U.S.A.) for all the analyses.

Results

The median age (with lower and upper quartiles) of the whole study population was 9.0 (12.2, 13.8). The Table shows the demographic and clinical characteristics of studied children (Table 1).

In the group of T1DM patients, Hb A1 C levels (%) were 8.34 (7.4, 9.4). Children with T1DM were older than control group.