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ORIGINAL ARTICLE

The relationship between gastro-oesophageal reflux disease and asthma during childhood

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Abstract
Background: The relationship between GERD and asthma is complex. It is not yet clear whether GERD is an accompanying finding or a cause of asthma, or even if it is an aggravating factor. The aim of this study was to determine the frequency of asthma and allergic diseases in patients who underwent 24-h pH monitoring for a suspicion of GERD, including a comparison between subjects with and without GERD.
Method: Subjects who were evaluated by 24 h ambulatory intraoesophageal pH monitoring were investigated for the presence of asthma and allergic disorders. All participants were subjected to a skin prick test and a complete blood count and serum levels of specific IgE.
Results: A total of 204 subjects (49.5% male) with a mean age of 7.8 ± 4.3 years were enrolled. A diagnosis of GERD was made in 78 (38.2%) subjects after 24 h pH monitoring. The frequency of asthma in subjects with GERD was 20.5% compared to 25.4% in subjects without GERD ($p = 0.424$). Subjects with GERD presenting with respiratory symptoms have higher incidence of asthma compared to subjects with GERD presenting with gastrointestinal symptoms (35.3% and 5.3% respectively; $p = 0.001$).
Conclusion: Although, patients with and without GERD had comparable frequencies of asthma, our findings suggest that subjects who present with respiratory symptoms suggestive of GERD should also be evaluated for the presence of an underlying asthma.

Introduction

Gastro-oesophageal reflux disease (GERD) typically presents with oesophageal symptoms such as heartburn and regurgitation, although non-oesophageal symptoms like chronic

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cough, hoarseness and chest pain are not uncommon.[1,2] Furthermore, chronic cough and wheezing can be the sole presenting manifestation of GERD,[3,4] and 24 h oesophageal pH monitoring should be performed in subjects in whom cough is still yet unexplained after a detailed history and physical examination and chest radiograph.[5]

GERD has been shown to play a role in inflammatory diseases of the upper and lower respiratory tract. The relationship between GERD and asthma is particularly complicated. It is not yet clear whether GERD is an accompanying finding or a cause of asthma, or even if it is an aggravating factor.[6] Gastro-oesophageal reflux was identified in asthmatic children even without any gastrointestinal symptoms.[7]

Twenty-four hour pH monitoring is considered the gold standard test for making a diagnosis of GERD.[8] Using this method, different studies have reported a GERD prevalence of between 55–83% in adults and 50–63% in children with asthma.[9–11]

Although numerous studies have evaluated the prevalence GERD in patients with asthma, very few studies have focused on the prevalence of asthma in patients with GERD. In this study, we aimed to evaluate and compare the frequency of asthma and allergic diseases in patients with or without GERD, evaluated by 24-h pH monitoring.

Materials and methods

This study was undertaken in Ankara Children's Health and Diseases Hematology-Oncology Hospital, the third largest tertiary healthy centre in Ankara, with the approval of the local ethics committee and written informed consent was obtained from the participants and from their parents. The study population consisted of children between 6 months to 17 years of age who underwent 24-h ambulatory intra-oesophageal pH monitoring with a suspicion of GERD, between June 2010 and June 2011. Subjects were stratified into two groups based on presenting symptoms (symptoms before pH monitoring); those with respiratory symptoms (cough, wheezing) and gastrointestinal symptoms (nausea, vomiting, acid reflux and abdominal pain) which persisted for at least four weeks. We evaluated all the participants for the presence of allergic disorders, and a family history of physician diagnosed allergic disorders was obtained.

GERD diagnosis

A diagnosis of GERD was made using 24-h ambulatory intra-oesophageal pH monitoring. None of the subjects were on acid suppressive medications before or during the study. This is performed by placing an acid-sensitive probe proximal to the lower oesophageal sphincter which measures and records oesophageal pH over a period of 24 h. Data are then transferred onto a computer and analysed using specific software (MMS, OhmegaR, The Netherlands). A diagnosis of GERD was based on the reflux index, which is the ratio of the time a pH less than 4 was measured, to the total time of pH evaluation. Gastro-oesophageal reflux was defined as a reflux index of more than 10% in infants under two years of age, and more than 5% in children older than two years of age.[12,13] Reflux indices were calculated using a commercial software program (MMS, OhmegaR, The Netherlands).

Allergic evaluation

All participants were evaluated (after pH monitoring) for the presence of asthma and allergic disorders and a detailed family history for allergic disorders was obtained. The diagnosis of asthma was made according to Global Initiative for Asthma guidelines (GINA).[14] Briefly, in subjects who were older than five years asthma diagnosis was made for a history of multiple episodes of wheezing with at least a 12% improvement in forced expiratory volume in one second following bronchodilator therapy, whereas in subjects who were five years old or younger asthma diagnosis was made by history of recurrent respiratory symptoms; a strong family history of asthma in first degree relatives; and/or atopy presenting as atopic dermatitis, food allergy and/or allergic rhinitis. Subjects with an underlying chronic condition other than asthma were excluded from the study. Spirometry was performed (Spirolab 2, Rome, Italy) and analysed in accordance with published recommendations.[15,16] The following variables were obtained from the best of three reproducible forced expiratory manoeuvres: FVC, FEV1 and FEV1/FVC ratio.

A diagnosis of allergic rhinitis was confirmed by a positive skin test or by the presence of specific IgE in subjects whose parents answered in the affirmative to the question ''Since birth, has your child had nasal discharge, nasal congestion, nasal itching or sneezing without the presence of the common cold or a flu-like infection?''. A diagnosis of atopic dermatitis was only accepted if it had previously been made by a physician, with a compatible history.

All subjects underwent skin prick testing for *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Cat and Dog dander*, *Alternaria*, *Cockroach*, *Aspergillus*, *Clodosporium*, *Betulaceae*, *Grass mix*, *Tree mix*, *Artemisia*, *Oleaceae*, *Saliceae*, *Parieteria*, *egg*, *wheat*, *peanut*, *hazelnut*, *milk*, *sesame*, *soya*, *fish*, *histamine*, and *negative controls* (Stallergens, Antony, France). These tests were performed on the volar surface of both forearms, with results recorded after 15 min. Results were considered positive when the mean wheal diameter was at least 3 mm larger than that produced by the control. Blood samples were obtained from all participants for the determination of complete blood counts and serum levels of total IgE as well as specific IgE (Fx5: egg white, milk, fish, wheat, peanut, soybean; Phadiatop: aeroallergens; Pharmacia Diagnostics AB, Uppsala, Sweden).

Subjects with a positive reaction to any of the aeroallergens or food allergens on a skin test, or those who had an elevated specific IgE level of >0.35 kIU/ml were considered to have allergen sensitisation.

Statistical analysis

Statistical analysis was performed using the SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Values were either provided as numbers and percentages, or as mean ± standard deviation, where applicable. Comparisons of the frequency of allergic diseases and other variables between subjects