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Allergic asthma is associated with increased risk of infections requiring antibiotics

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ABSTRACT

Background: Viral infection and allergy have been identified as major risk factors for exacerbation in asthma, especially in the presence of both. However, whether patients with allergic asthma are more susceptible to respiratory infections requiring antibiotics remains unknown.
Objective: To investigate allergy as a risk factor for respiratory infections requiring antibiotics based on register data from a nationwide population of patients with asthma.
Methods: A register-based prospective follow-up study was performed using the Danish prescription database. In the inclusion period from 2010 through 2011, we identified patients with allergic asthma 18 to 44 years old. Patients were investigated during the follow-up period from 2012 through 2013, depending on their prescription drug use of antiallergic medication and antibiotics. Odds ratios were adjusted for age, sex, asthma severity, education, and urban vs rural residence.
Results: In a nationwide population we identified 60,415 patients with asthma. Based on prescriptions fillings for antiallergic medication, patients were subdivided into (1) nonallergic asthma (n = 35,334, 51.5%) and (2) allergic asthma (n = 25,081, 48.5%). Allergic asthma was associated with an increased risk of filling at least 2 antibiotic prescriptions per year compared with nonallergic asthma (odds ratio 1.28, 95% confidence interval 1.24–1.33, $P < .0001$). Interestingly, a subgroup analysis showed a protective effect of immunotherapy against the risk of requiring antibiotics (odds ratio 0.76, 95% confidence interval 0.66–0.87, $P = .0001$).
Conclusion: Patients with allergic asthma have an increased risk of being prescribed antibiotics for respiratory infections compared with those with nonallergic asthma. Treatment with allergen immunotherapy appears to have a protective effect against this risk.

Introduction

Respiratory infections are common triggers of asthma exacerbations and the main cause of asthma-related hospitalizations.[1–3] Viral infections[2,4] and allergy[5,6] have been identified as major risk factors for asthma exacerbations, especially in the presence of both.[7–10] However, the association between allergic sensitization and risk of bacterial respiratory infections in patients with asthma is sparsely investigated, particularly in epidemiologic studies.[11] Hence, there is a need for representative population studies describing this relation.

In vivo studies of mice have shown that T-helper cell type (T_H) 2-driven airway inflammation is associated with a suppressed antimicrobial host defense.[12] In humans, evidence has suggested that patients with asthma could have impaired innate immunity against bacteria through altered regulation of Toll-like receptors, leading to increased risk of colonization and infection in the airways.[13] A recent systematic review has concluded that asthma is associated with an increased susceptibility to invasive pneumococcal disease.[14] Furthermore, the risk of severe invasive pneumococcal disease is increased in patients with atopic conditions with or without asthma.[15] Thus, pneumococcal vaccine (PPSV23) is recommended in patients 19 to 64 years old with asthma in the United States.[16]

Although the link between allergy and susceptibility to infection-related exacerbations is acknowledged,[1,2,5,6] surprisingly little evidence exists on the effect of interventions targeting allergy. A potential biological mechanism for a relation between antiallergic treatment and immune defense against pathogens was described in studies of anti-immunoglobulin E (IgE) in children; treatment decreased the seasonal variation in asthma exacerbations[17] and improved the antiviral interferon-α response.[18] Increased interferon-α was associated with fewer exacerbations in the anti-IgE–treated children, which has been interpreted as a possible

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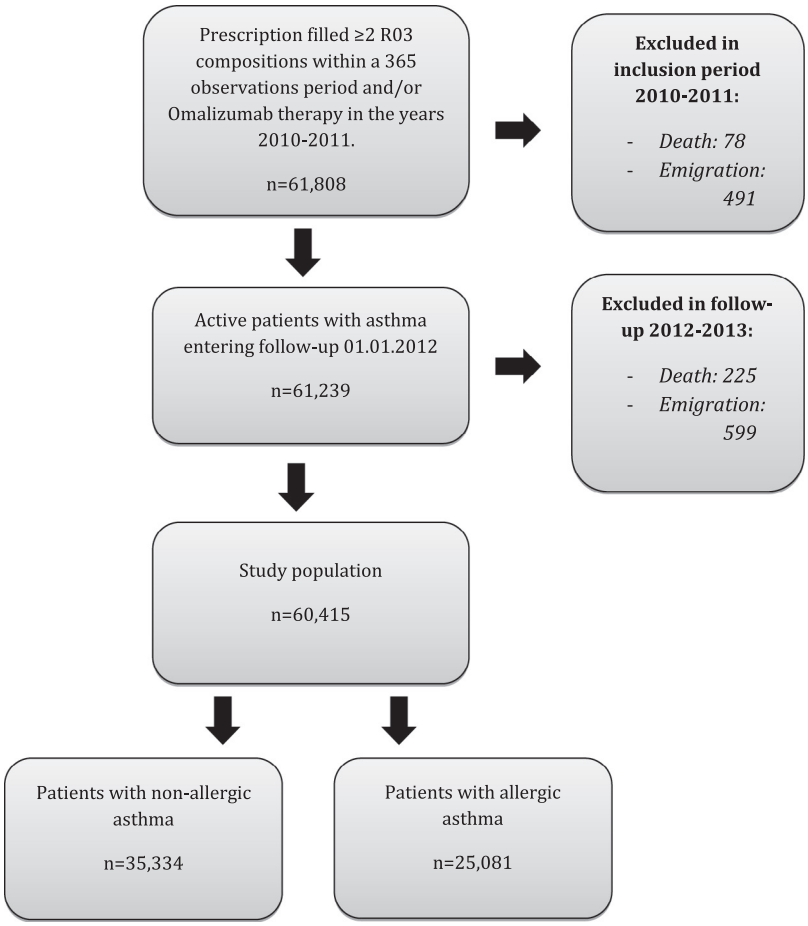

Figure 1. Patient flow.

decrease in virally induced exacerbations.[19] Allergen-specific immunotherapy (AIT) lowers the risk of deterioration of asthma control,[20] but no studies have examined the effect on frequency of bacterial respiratory infections.

We tested the hypothesis that patients with allergic asthma would be more likely to be prescribed antibiotics (AB) targeting respiratory infections compared with patients with nonallergic asthma. Furthermore, we speculated that AIT would lower the risk of developing respiratory infections requiring AB and the risk of asthma exacerbations.

We conducted a nationwide population study of the association between allergy and the risk of being prescribed AB for respiratory infections in adults with asthma.

Methods

Study Design

This was a retrospective register-based cohort study of Danish patients with asthma using data from Statistics Denmark (www.dst.dk). All Danish residents are assigned a unique personal identification number, which enables individual linkage throughout nationwide registers. This study used the Danish prescription database and cross-referenced the data with other health and social and economic registers. It contains detailed information about every dispensed drug to an individual (eg, dose, date, pack size, etc) according to the unique Anatomical Therapeutic Chemical Classification (ATC) code. Patients were included only if they had filled prescriptions for the medicines specified below. The personal identification number also is linked to the Danish National Patient Register, which contains detailed information about hospital admissions (eg, municipality, admission and discharge, duration, hospital, department, treatments, investigations, diagnoses, and operations) according to the *International Statistical Classification of Disease and Related Health Problems, Tenth Revision* (*ICD-10*).

Study Population

Data used in this study originated from registers from 2010 through 2013 and included persons with a Danish social security number 18 to 44 years old within the inclusion period of January 1, 2010 through December 31, 2011 (24 months). All included patients entered the follow-up period of January 1, 2012 through December 31, 2013 (24 months) to avoid seasonal variation in allergen exposure, drug use, and exacerbations. Figure 1 presents the patient flow.

Patients with asthma were identified and included if they fulfilled the following criteria: filled at least 2 prescriptions for a drug with an ATC code starting with R03 (medicine for obstructive airway diseases) within a 365-day observation period.[21] If a patient redeemed an inhaled corticosteroid (ICS) combination device in 2010, then this was selected as the index date; otherwise, the date for the first redemption of an R03 drug was selected.[22]

Patients who filled prescriptions for a specific medicine recommended for the treatment of chronic obstructive pulmonary disease and/or cystic fibrosis (eTable 1) or died or emigrated at any point during the observation period[22] were excluded.