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ORIGINAL ARTICLE

Allergic rhinitis and allergy are risk factors for otitis media with effusion: A meta-analysis

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Abstract
Objective/Hypothesis: We systematically reviewed the associations between allergic rhinitis or allergy and otitis media with effusion, by reference to published data.
Study design: A meta-analysis of case-controlled studies.
Data source: Five databases (Pubmed, Highwire, Medline, Wanfang, and China National Knowledge Infrastructure) were searched for relevant studies in the English language published prior to November 12, 2015.
Studies chosen: Studies with clearly defined experimental and control groups, in which the experimental groups had otitis media with effusion together with allergic rhinitis or allergy, were selected.
Methods: We performed a meta-analysis on data from the identified cross-sectional and case-controlled studies using fixed- or random-effects models (depending on heterogeneity). We used Reviewer Manager 5.3 software to this end.
Results: Seven studies met the inclusion criteria. The prevalence of allergic rhinitis in patients with otitis media with effusion and the control groups differed significantly in three studies ($P < 0.00001$), as did the prevalence of allergy (in six studies; $P = 0.003$).
Conclusion: Allergic rhinitis and allergy appear to be risk factors for otitis media with effusion.

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Introduction

Otitis media with effusion (OME) is globally common, with a prevalence of 8.7% in primary school children (152/1740).[1] In children under six years of age visiting outpatient clinics, the prevalence of OME, Eustachian tube dysfunction (ETD), or tympanic membrane retraction (TMR) is 1.4%.[2] The incidence of otitis media during the first two years of life does not differ between Caucasian and African American infants.[3,4]

The symptoms of OME are problematic, especially the decline in hearing level and the sensation of aural fullness. Children with OME suffer more than adults do.[5,6] However, insertion of a pressure-equalising tube (PET) does not always cure OME.[7] Identification of risk factors would be helpful to prevent OME in children. Many such risk factors have in fact been identified; these include genetic predisposition[8]; gastro-oesophageal reflux (in adult patients)[9,10]; rhinitis[2]; chronic rhinosinusitis[2]; adenoidal problems and adenoiditis[11]; allergic rhinitis (AR; 12, 13); asthma[14]; and allergies,[14,15] *etc*. The middle ear connects with the respiratory tract, and we thus presumed that AR or allergy may be mutually associated with OME.

We thus performed a meta-analysis to systematically explore whether AR or allergy correlates significantly with OME.

Methods

Search strategy

We used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) checklist.[16,17] Two authors independently (and manually) searched for papers on OME and AR or allergy.

Five databases (Pubmed, Highwire, Medline, Wanfang, and CNKI [China National Knowledge Infrastructure]) were searched within the overall term ''AR *vs*. OME'' for all relevant papers published from March 1973 to November 12, 2015. The search subterms emphasised the possible relationship between AR and OME, and included ''allergic rhinitis and otitis media with effusion;'' ''risk factors for otitis media with effusion;'' and ''allergic rhinitis comorbidity'' (indicating that AR was a risk factor for OME). Within the general search term ''allergy *vs*. OME'' (indicating that allergy or atopy was a risk factor for OME), we used the subterms ''allergy and otitis media with effusion'' and ''atopy and otitis media with effusion'' to retrieve citations published from April 1956 to November 12, 2015. All related articles were retrieved. In addition, the two authors screened the reference lists of retrieved papers to further identify potentially relevant publications.

Definition and clinical criteria of OME, AR and allergy

OME is characterised by the presence of mucoid effusion in the middle ear causing decreased mobility of the tympanic membrane and conductive hearing loss.[1,5,6] Allergic rhinitis is defined when patients are allergic to at least one allergen resulting in nasal obstruction or congestion, rhinorrhoea, rhinocnesmus and sneezing.[12,13] Allergy is defined as IgE-mediated allergic diseases.[14,15] The diagnosis criteria of OME, AR and allergy were described in individual studies, which included case history, symptoms, physical examination and other examinations such as tympanogram, microscopic otoscopy or tympanostomy tube insertions, SPT or serum IgE test, *etc*. (Table 1).

Study identification

All selected papers were carefully checked. The eligibility criteria for inclusion were: (a) case–control studies in which all experimental group (EG) members had OME; (b) the control groups (CGs) in all studies retrieved using the ''AR *vs*. OME'' and ''allergy *vs*. OME'' terms were fully or largely healthy (controls with preauricular fistulas, or [only] extremely severe sensorineural hearing loss, were acceptable); and (c) the studies were restricted to humans, published in English, and appeared in either full-text or abstract form.

We excluded studies using outpatients lacking OME as controls. All experimental groups had clearly defined OME (either unilateral or bilateral). Patients with eosinophilic otitis media, otitis media, chronic otitis media with cholesteatoma, or chronic refractory otitis media were excluded. Studies lacking adequate data, immunological or genetic analyses of associations between OME and AR, and studies on participants that had been included in prior works were excluded.

We set two further prerequisites. First, the full text clearly defined the experimental and control groups and, second, the numbers of group members and observational data were available. These allowed us to determine the odds ratios (ORs) with 95% confidence intervals (CIs).

Study quality and data analysis

All studies were case-controlled and cross-sectional in nature. In line with a suggestion of the Agency for Healthcare Research and Quality (AHRQ), we used the Newcastle-Ottawa Scale (NOS) to assess individual study quality and the risk of bias.[18] Review Manager 5.3 software was used to create Forest maps and funnel plots (these are principal summary measures). Either a fixed- or random-effects model was applied, depending on the *P*-value of the chi-squared statistic (a fixed-effects model when P was >0.05; a random-effects model when P was <0.05). An I^2 value <25% was taken to indicate low heterogeneity and an I^2 value >50% high heterogeneity.[19] In the random-effects model used to analyse ''allergy *vs*. OME,'' we sought to perform a meta-regression using Stata12 software to determine the sources of heterogeneity. This was because the I^2 value was >50% for the six relevant studies. However, meta-regression is not reliable if data from fewer than 10 studies are available; we thus do not present our data.

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