Allergol Immunopathol (Madr). 2017;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

Allergy is associated with reduced risk of glioma: A meta-analysis

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Received 25 October 2016; accepted 3 December 2016

KEYWORDS
Glioma;
Allergy;
Asthma;
Eczema;
Meta-analysis

Abstract
Background: Increasing evidences suggest that allergy may reduce the risk of glioma, so it is necessary to perform an up-to-data literature search and investigate this relationship by meta-analysis.
Methods: We identified the included studies by searching PubMed and Web of Science and excluding irrelevant or ineligible articles. Nineteen studies from 15 articles, including 8435 cases and 118,719 controls, were selected for data extraction and synthesis.
Results: Pooled outcomes showed that there was an inverse association between allergy and risk of glioma (OR = 0.64, 95% CI = 0.52–0.78, $P < 0.001$). Meanwhile, asthma and eczema would reduce the risk of glioma by 33% and 23% (OR = 0.67, 95% CI = 0.59–0.75, $P < 0.001$; OR = 0.77, 95% CI = 0.68–0.86, $P < 0.001$), respectively. Sensitivity analyses confirmed the stability of these findings. Besides, no publication biases were detected regarding all the investigations.
Conclusions: Overall or specific allergy is protective against glioma. More prospective cohort studies or molecular laboratory experiments are warranted to elucidate the causation and key mechanism.

Introduction

Glioma is the most common primary brain tumour and remains incurable. The most aggressive form, glioblastoma multiforme (GBM), has an overall 15–17-month survival time.[1] Like other neoplasms, glioma develops and progresses as a result of genetic and molecular alterations.[2] Besides, immune system may have an impact on the pathogenesis of this cancer,[3] although the traditional assumption has been that immune responses in the central nervous system (CNS) are limited. Allergic diseases are on the rise, with increasing interest in their long-term health effects. These disorders, including asthma and eczema, have been consistently related to lower risk of glioma in epidemiolog-

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http://dx.doi.org/10.1016/j.aller.2016.12.005
0301-0546/

Please cite this article in press as: Zhang C, Zhu Q-X. Allergy is associated with reduced risk of glioma: A meta-analysis. Allergol Immunopathol (Madr). 2017. http://dx.doi.org/10.1016/j.aller.2016.12.005

ical studies.[4–8] The latest meta-analysis conducted in 2013 concluded that allergic conditions were reversely related to the risk of glioma.[9] Apart from this meta-analysis, recently an unprecedented study with 14 recruitment sites across five countries, the Glioma International Case-Control Study (GICC), has reported that respiratory allergies, asthma and eczema have been significantly protective against glioma.[10]

Due to inclusion of overlapping populations, update of the cohorts that have been published previously[8,11,12] and the emergence of a new study,[6] we conducted an up-to-date literature search, excluded duplicated populations and pooled outcomes of the eligible trails, which aimed to confirm the already existing relationship between allergy and glioma.

Methods and materials

Literature search and selection

A comprehensive literature search was carried out in PubMed and Web of Science databases to identify the relevant articles published from Jan 1979 to Oct 2016. The search terms were ''glioma'', ''brain tumour'', ''allergy'', ''asthma'' and ''eczema''. No special restrictions were imposed regarding type of publication. The irrelevant records were initially discarded according to titles and abstracts. The remaining articles were examined carefully to check if they met the inclusion criteria as follows: (1) case–control or cohort study with special interest on the relationship between allergy and glioma; (2) provided odds ratios (ORs) and 95% confidence intervals (95% CIs) or had enough data to calculate them; (3) reported the newest data of the recruited populations; (4) reported the largest sample of the populations during the same period. The eligible studies were ultimately included in the data synthesis.

Data extraction

The detailed information and data were recorded by two authors independently. The extracted items were: study name, study period, numbers of cases and controls, ORs, 95% CIs and adjusted confounders. ORs were calculated if they were not provided by the original articles. Disagreements on data extraction and calculation were solved after consultation.

Data synthesis

The heterogeneity within studies was assessed by *Q*-statistic.[13] It was measured by I^2 value, which indicated the percent of the total variance across studies due to heterogeneity rather by chance. Heterogeneity was categorised into high, medium or low when $I^2 \geq 50\%$, $50\% > I^2 \geq 25\%$ or $25\% > I^2$, respectively.[14] If no heterogeneity existed, Mantel–Haenszel's method in fixed effect was used to pool outcomes. Otherwise they were accumulated by Dersimonian and Laird method in random effect model.[15] Publication bias was evaluated by the symmetry of funnel plot and by Egger's linear regression test statistically.[13] Sensitivity analysis was performed by omitting each study and checking whether the pooled result changed significantly. All statistical analyses were conducted by Stata 9.0 (Stata Crop LP, College station, TX, USA). All *P* values were two-sided and identified as significant if less than 0.05.

Results

Characteristics of the eligible studies

As shown in Fig. 1, nineteen studies from 15 articles,[4–8,11,12,16–23] including 8435 cases and 118,719 controls, were finally included in this meta-analysis. Fifteen of the included studies[4–8,11,12,16–18,21] reported the ORs of

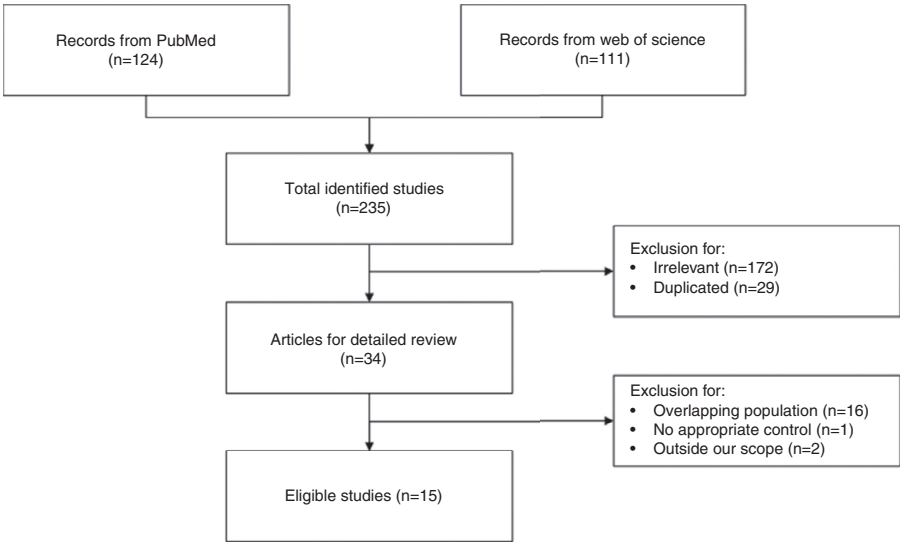

Figure 1 Flow diagram of study selection.

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