



Meta-Analysis

Angiotensin-converting enzyme (ACE) I/D polymorphism is a risk factor of allergic rhinitis

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Abstract: Some previous studies and meta-analysis investigated the association between ACE I/D polymorphism and allergic rhinitis risk. However, the results were conflicting. This meta-analysis, therefore, was performed to evaluate the association between ACE I/D polymorphism and allergic rhinitis risk. Online electronic databases (PubMed and EMBASE) were searched. The strength was evaluated by calculating the OR and 95% CI. Five studies were finally included in this meta-analysis. These studies included 681 cases and 629 controls. ACE I/D polymorphism was significantly associated with allergic rhinitis risk (OR = 1.17; 95% CI 1.07 – 1.29; $P = 0.001$). In the subgroup analysis of race, Asians showed the increased allergic rhinitis risk (OR = 1.15; 95% CI 1.02 – 1.30; $P = 0.03$). In a stratified analysis by age, adults with ACE I/D polymorphism showed the increased allergic rhinitis risk (OR = 1.16; 95% CI 1.04 – 1.29; $P = 0.006$). However, children did not have the significantly increased allergic rhinitis risk (OR = 1.24; 95% CI 0.99 – 1.56; $P = 0.06$). In conclusion, this meta-analysis indicated that ACE I/D polymorphism was significantly associated with allergic rhinitis risk.

Key words: Allergic rhinitis; ACE; Risk.

Introduction

Allergic rhinitis is a chronic disease. The worldwide prevalence of this disease is increasing. It is a global health problem which could have a significantly detrimental effect on quality of life. Previous report suggested that allergic rhinitis may affect up to 40% of the general population (1). Therefore, understanding the risk factors of allergic rhinitis is quite critical. Angiotensin-converting enzyme (ACE) is one components of the renin-angiotensin system (RAS) that converts angiotensin (Ang) I to Ang II. Additionally, ACE could metabolize bradykinin to form inactive bradykinin 1–5 (2,3). Gawlik et al. found that allergen-specific immunotherapy could decrease the level of bradykinin in the nasal fluid (4). Shirasaki et al. revealed that epithelial cells, submucosal glands, fibroblast, vascular smooth muscle, vascular endothelial cells, and macrophages showed immunoreactivity for both bradykinin B1 and B2 receptors (5). Some previous studies investigated the association between ACE I/D polymorphism and allergic rhinitis risk (6-10). However, the results were conflicting. Furthermore, three recent meta-analysis also reported inconsistent results (11-13). This meta-analysis, therefore, was performed to evaluate the association between ACE I/D polymorphism and allergic rhinitis risk.

Materials and Methods

Publication search Online electronic databases (PubMed and EMBASE) were searched. These key words were used: “allergic rhinitis” and “angiotensin-

converting enzyme”. Additional articles were identified through references cited in retrieved articles. There was no language restriction.

Inclusion and exclusion criteria Studies were included if the following conditions were met: (1) any study described the association of ACE I/D polymorphism and allergic rhinitis risk; (2) any study reported the numbers of both cases and controls; (3) results were expressed as odds ratio (OR) with 95% confidence intervals (CI); and (4) case-control study. Study that the genotype distributions in the controls were significantly deviated from Hardy-Weinberg equilibrium (HWE) was excluded.

Data extraction Two investigators extracted data independently. Disagreement was resolved by consensus. The following data were extracted: the first author's name, year of publication, ethnicity, age, gender, number of cases, number of controls, and HWE.

Quality assessment The studies were evaluated by the two investigators using the Newcastle-Ottawa Scale (NOS). Scores ranged from 0 to 9 stars.

Statistical analysis We evaluated the allele contrast model. The strength was evaluated by calculating the OR and 95% CI. We conducted the Z test and we regarded it as significant difference when P value less than 0.05 was detected. The heterogeneity was tested by the Q-statistics with P -values < 0.1 . The random-effects was used to calculate the OR. We did subgroup analyses stratified by ethnicity and age. Publication bias was assessed by asymmetry of funnel plots. Cochrane Review Manager Version 5 (Cochrane Library, UK) was used to calculate the available data from each investigation. P value less than 0.05 was considered statistically

Table 1. Characteristics of the included studies.

| First author | Year | Case | | | number (n) | Control number (n) | HWE Result | NOS Score |
|--------------|------|-----------|----------|--------|------------|--------------------|------------|-----------|
| | | Ethnicity | Age | Gender | | | | |
| Holla | 1998 | Caucasian | Adults | Both | 189 | 141 | Yes | 7 |
| Kim | 2004 | Asian | Adults | Both | 137 | 219 | Yes | 7 |
| Wang | 2005 | Asian | Adults | Both | 69 | 101 | Yes | 6 |
| Ku | 2006 | Asian | Children | Both | 75 | 66 | Yes | 6 |
| Lue | 2006 | Asian | Children | Both | 211 | 102 | Yes | 8 |

HWE, Hardy-Weinberg equilibrium; NOS, Newcastle-Ottawa Scale.

significant.

Results

Study characteristics Characteristics of studies included in the current meta-analysis are presented in Table 1. Five studies were finally included in this meta-analysis. These studies included 681 cases and 629 controls. One study included Caucasians and four studies included Asians. Three studies included adults and two studies included children.

Meta-analysis When all eligible studies were pooled into one dataset for the meta-analysis, we found ACE I/D polymorphism was significantly associated with allergic rhinitis risk (OR = 1.17; 95% CI 1.07 – 1.29; *P* = 0.001; Figure 1). In the subgroup analysis of race, Asians showed the increased allergic rhinitis risk (OR = 1.15; 95% CI 1.02 – 1.30; *P* = 0.03; Figure 2). In a stratified analysis by age, adults with ACE I/D polymorphism showed the increased allergic rhinitis risk (OR = 1.16; 95% CI 1.04 – 1.29; *P* = 0.006; Figure 3). However, children did not have the significantly increased allergic rhinitis risk (OR = 1.24; 95% CI 0.99 – 1.56; *P* = 0.06; Figure 3). The shape of the funnel plot showed symmetry (Figure 4).

Discussion

The aim of this meta-analysis was to evaluate the association between ACE I/D polymorphism and allergic rhinitis risk. This meta-analysis included five case-control studies with 681 cases and 629 controls. We found ACE I/D polymorphism was significantly associated with allergic rhinitis risk. In the subgroup analysis of race, Asians showed the increased allergic rhinitis risk.

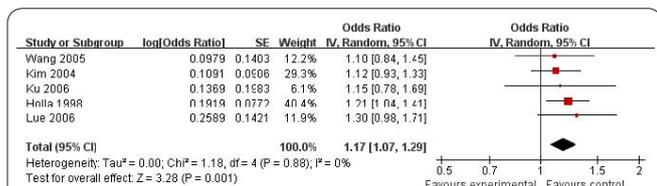


Figure 1. Meta-analysis for the association between ACE I/D polymorphism and allergic rhinitis risk.

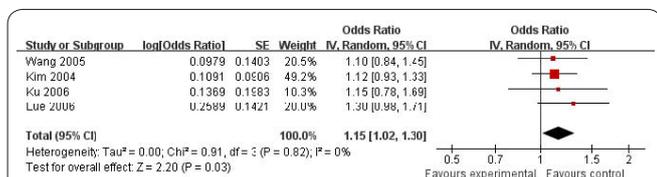


Figure 2. Meta-analysis for the association between ACE I/D polymorphism and allergic rhinitis risk in Asians.

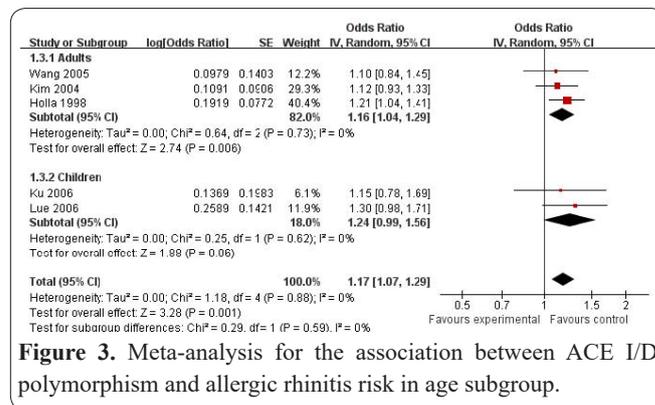


Figure 3. Meta-analysis for the association between ACE I/D polymorphism and allergic rhinitis risk in age subgroup.

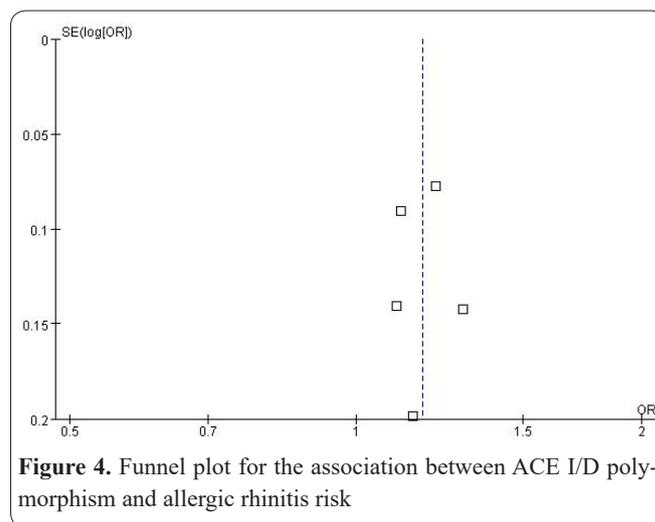


Figure 4. Funnel plot for the association between ACE I/D polymorphism and allergic rhinitis risk

In the subgroup analysis by age, adults with ACE I/D polymorphism showed the increased allergic rhinitis risk. However, children did not have the significantly increased allergic rhinitis risk. Although no significant result was found in the children subgroup, we cannot preclude that children with ACE I/D polymorphism might have high risk of allergic rhinitis. Only two studies used children. Thus, more studies are needed to assess the association between ACE I/D polymorphism and allergic rhinitis risk in children. Many studies suggested that ACE I/D polymorphism had taken part in the onset of some diseases. Yang et al. suggested that the ACE DD genotype correlated with an increased risk of sarcoidosis (14). Ai et al. showed significant association between ACE I/D polymorphism and vesicoureteral reflux risk (15). Miao et al. suggested that the ACE gene I/D polymorphism was associated with coronary restenosis, regardless of age and ethnicity (16). Ma et al. suggested that individuals with the ACE D/D genotype appeared to be at higher risk of atrial fibrillation (17). Wan et al. found that ACE II genotype could exert a protective effect against migraine with aura and without aura

(18). Yang *et al.* suggested that ACE gene I allele might be a protective factor against gastric cancer (19) This meta-analysis study had several limitations. Firstly, the sample size of each included study was small. Thus, the statistical power of this meta-analysis was small. Secondly, meta-analysis remained retrospective research that was subject to the methodological deficiencies of the included studies.

Thirdly, we didn't explore gene-gene and gene-environment interactions because of the insufficient data. Fourthly, the ORs for the individual studies are not adjusted for other covariates. In conclusion, this meta-analysis indicated that ACE I/D polymorphism was significantly associated with allergic rhinitis risk.

Conflicts of interest

None

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