Original Article

GSTM1 polymorphism and cataract risk: a systematic review and a meta-analysis

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Abstract: Background: Many studies were conducted to assess the relationship between GSTM1 polymorphism and cataract risk. However, results of these studies remained inconclusive. Thus, we performed this systematic review and meta-analysis to clarify the association between GSTM1 polymorphism and cataract risk. Method: PubMed, EMBASE, and Cochrane databases were searched to find relevant studies by two authors. The data were extracted by these two authors independently. The strength of association between the GSTM1 polymorphism and cataract risk was assessed by calculating OR with 95% CI. Results: A total of 16 studies with 3177 cases and 2217 controls on the association between GSTM1 polymorphism and cataract risk were included for this meta-analysis. GSTM1 null genotype was associated with a significantly increased risk of cataract (OR=1.44; 95% CI, 1.15-1.80; I²=72%). In the race subgroup analysis, both Asians (OR=1.65; 95% CI, 1.16-2.36; I²=68%) and Caucasians (OR=1.44; 95% CI, 1.09-1.90; I²=69%) with GSTM1 null genotype had increased cataract risk. In the subgroup analysis according to gender, both women and men were not associated with risk of cataract (OR=1.06; 95% CI, 0.88-1.27; I²=0% and OR=0.74; 95% CI, 0.49-1.14; I²=68%, respectively). In the subgroup analysis by cataract type, subjects with GSTM1 null genotype did not show increased cortical cataract risk (OR=0.97; 95% CI, 0.74-1.27; I²=64%), nuclear cataract risk (OR=1.19; 95% CI, 0.93-1.52; I²=22%), and posterior subcapsular cataract risk (OR=1.18; 95% CI, 0.83-1.69; I²=54%). Conclusion: This meta-analysis suggested that GSTM1 null genotype may be associated with the risk of cataract.

Keywords: Cataract, GSTM1, meta-analysis, association

Introduction

Cataract is a major cause of visual impairment among senior citizens worldwide [1]. According to the World Health Organization (WHO), cataract is responsible for nearly 50% of blindness across the world [2]. The importance of risk factors identification for cataract is therefore evident.

Genetic variations in the antioxidant genes coding for the glutathione S-transferase (GST) enzymes may lead to decreased or impaired regulation of their enzymatic activity and alter ROS detoxification. Therefore, genetic variations among enzymes that protect the cell against ROS may modulate disease risk [3]. A number of studies investigated the association between GSTM1 polymorphism and cataract risk. However, the results remained inconclusive [4-19]. Thus, we performed a meta-analysis to clarify the association of GSTM1 polymorphism and cataract risk.

Methods

Publication search

Online electronic databases (PubMed, EMBASE, and Cochrane database) was searched using the search terms: Cataract and glutathione S-transferase M or GSTM1. Additional studies were identified by a hand search from reference of original studies or review articles on this topic. There was no language restriction.

Inclusion and exclusion criteria

The following inclusion criteria were used: (1) the study should have evaluated the associa-
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The following data were recorded from each article: first author, years of publication, ethnicity, gender, age, numbers of subjects. The data were extracted by two of the authors independently. Discrepancies between these two authors were resolved by discussion.

**Quality assessment**

The included studies were assessed independently by the two reviewers using the Newcastle-Ottawa Scale (NOS). The NOS employs a star rating system to assess quality from 3 broad perspectives of the study: (1) selection of the study groups, (2) comparability of the groups, and (3) identification of the exposure (for case-control studies) or outcome of interest (for cohort studies). Scores ranged from 0 to 9 stars.

**Statistical analysis**

The strength of association between the GSTM1 polymorphism and cataract risk was assessed by calculating OR with 95% CI. A statistical test for heterogeneity was performed based on the Q statistic. The $P>0.10$ of the Q-test indicated a lack of heterogeneity among studies. The summary OR estimate of each study was calculated by the random-effects model or fixed-effects model. Stratified analysis was performed by race, gender, and cataract type.

Potential publication bias was examined by funnel plot and Egger’s test. All statistical tests
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Table 2. Results of meta-analysis and subgroup analyses

<table>
<thead>
<tr>
<th></th>
<th>No. of studies</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>Model</th>
<th>I² (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>16</td>
<td>1.44 (1.15-1.80)</td>
<td>0.002</td>
<td>R</td>
<td>72</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>6</td>
<td>1.65 (1.16-2.36)</td>
<td>0.006</td>
<td>R</td>
<td>68</td>
</tr>
<tr>
<td>Caucasian</td>
<td>9</td>
<td>1.44 (1.09-1.90)</td>
<td>0.01</td>
<td>R</td>
<td>69</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>4</td>
<td>1.06 (0.88-1.27)</td>
<td>0.54</td>
<td>F</td>
<td>0</td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>0.74 (0.49-1.14)</td>
<td>0.17</td>
<td>R</td>
<td>68</td>
</tr>
<tr>
<td>Cataract type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortical</td>
<td>4</td>
<td>0.97 (0.74-1.27)</td>
<td>0.83</td>
<td>R</td>
<td>64</td>
</tr>
<tr>
<td>Nuclear</td>
<td>4</td>
<td>1.19 (0.93-1.52)</td>
<td>0.17</td>
<td>F</td>
<td>22</td>
</tr>
<tr>
<td>Posterior subcapsular</td>
<td>3</td>
<td>1.18 (0.83-1.69)</td>
<td>0.36</td>
<td>R</td>
<td>54</td>
</tr>
</tbody>
</table>

R, random-effects model; F, fixed-effects model.

were performed with the software STATA version 11.0 (Stata Corporation, College station, TX, USA). A P value <0.05 was considered statistically significant.

Results

Study characteristics

According to the searching strategy, 332 papers were found. We reviewed the titles, abstracts and the full texts of all retrieved articles through defined criteria. Figure 1 showed the flow diagram. A total of 16 studies with 3177 cases and 2217 controlson the association between GSTM1 polymorphism and cataract risk were included for this meta-analysis. There were 6 studies of Asian population, 9 studies of Caucasian population, and 1 study of African population. The characteristics of each study are presented in Table 1.

Results of meta-analysis

The results of the association between GSTM1 polymorphism and cataract riskier summarized in Table 2. GSTM1 null genotype was associated with a significantly increased risk of cataract (OR=1.44; 95% CI, 1.15-1.80; P=0.002; Figure 2). In the race subgroup analysis, both Asians (OR=1.65; 95% CI, 1.16-2.36; I²=68%) and Caucasians (OR=1.44; 95% CI, 1.09-1.90; P=0.05) with GSTM1 null genotype had increased cataract risk. In the subgroup analysis according to gender, both women and men were not associated with risk of cataract (OR=1.06; 95% CI, 0.88-1.27; P=0.05 and OR=0.74; 95% CI, 0.49-1.14; I²=68%, respectively). In the subgroup analysis by cataract type, subjects with GSTM1 null genotype did not show increased cortical cataract risk (OR=0.97; 95% CI, 0.74-1.27; P=0.45), nuclear cataract risk (OR=1.19; 95% CI, 0.93-1.52; P=0.22), and posterior subcapsular cataract risk (OR=1.18; 95% CI, 0.83-1.69; P=0.54).

The Galbraith plot was used to find the source of the heterogeneity. As shown in Figure 3, five studies were the outliers. After excluding these studies, the heterogeneity decreased significantly (P=0.05). Funnel plot was performed to assess the publication bias of literatures. The shape of the funnel plot showed symmetry (Figure 4). Egger’s test found no evidence of publication bias (P=0.55).
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Discussion

In this meta-analysis, we investigated the association between the GSTM1 polymorphism and cataract risk including 3177 cases and 2217 controls. We found that individuals with GSTM1 null genotype showed an increased risk of cataract in the overall population. In the stratified analysis by ethnicity, the significant association was observed in Asians and Caucasians. Only one study conducted in African population was included in this meta-analysis. Thus, more studies with African are still needed. In the subgroup analysis by gender and cataract type, we did not found any positive results. The possible reason might be the low sample size. Thus, more studies with large sample size should be conducted in the future.

The pathophysiologies of age-related ocular diseases are complex and remain poorly understood. Oxidative stress, associated with cellular damage caused by reactive oxygen intermediates (ROI), has been implicated in the development of cataract [20]. A previous meta-analysis also suggested that GSTM1 null genotype was significantly associated with cataract risk [21]. That study found that GSTM1 null genotype was significantly associated with cataract risk in Caucasians. More studies with Caucasians were reported recently. Thus, our result might be different from that study.

In this meta-analysis, significant heterogeneity was observed. Galbraith plots were applied to explore the sources of heterogeneity. Five studies were spotted as outliers. \( I^2 \) value was decreased significantly after excluding the outliers. However, some limitations should be addressed. First, due to the limited availability of published results, the number of studies included in each meta-analysis was small. Second, the studies investigating genetic associations should be based on a large sample size, similar study designs and standardized case and control definitions. Third, we did not have enough data to conduct any gene-gene interaction analyses. Finally, our results were based on single-factor evaluations without adjustment for other risk factors, including BMI, tobacco, alcohol, environmental factors, or lifestyle.

In conclusion, this meta-analysis suggested that GSTM1 null genotype may be associated with the risk of cataract.
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Disclosure of conflict of interest

None.

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References