Glutathione S-transferase M1 polymorphism and primary open-angle glaucoma (POAG) in a Chinese population.

Jiyun Gao1,2, Dabo Wang3*, Peng Liu2, Xiaojing Pan3, Teng Sun3

1Qingdao University, Qingdao, Shandong, China
2Department of Ophthalmology, the Second People’s Hospital of Huangdao District, Qingdao, Shandong, PR China
3Department of Ophthalmology, the Affiliated Hospital Of Qingdao University, Qingdao, Shandong, PR China

Abstract

Primary Open-Angle Glaucoma (POAG) is a leading cause of irreversible blinding disease. We conducted this case-control study to assess the association between GSTM1 null polymorphism and POAG risk in Chinese. Unrelated 323 adult-onset POAG patients and 295 control subjects were recruited. We found that patients carrying the GSTM1 null genotype had increased risk of POAG (OR=1.80, 95% CI 1.25-2.54, P=0.002). No statistically significantly association was found between GSTM1 polymorphism and smoking status. However, GSTM1 polymorphism was significantly associated with diabetes mellitus in patients. In conclusion, the GSTM1 polymorphism was significantly associated with the risk of POAG.

Keywords: Primary open-angle glaucoma, GSTM1D.

Introduction

Primary Open-Angle Glaucoma (POAG) is a leading cause of irreversible blinding disease [1]. Blindness caused by glaucoma affects 8.4 million people nowadays, and this number is estimated to rise up to 11 million people for the year 2020 [2]. Current treatments are aimed at lowering Intraocular Pressure (IOP) with the goal of slowing or halting the progression of POAG.

Glutathione S Transferases (GSTs) have an essential role in protection of DNA from genotoxic damage by inhibiting the formation of DNA adducts [3]. Glutathione S-transferase M1 (GSTM1) is one of a family of proteins catalysing the conjugation of reduced glutathione to a variety of electrophilic compounds, including metabolites of benzo(a)pyrene (B(a)P) [4]. Lavaris et al. suggested that GSTM1 null genotype might be associated with increased risk of development of POAG in the Greek population [5]. Malik et al. found that GSTM1 polymorphism was not associated with JOAG risk in North Indian population [6]. Rocha et al. demonstrated that GSTM1 null polymorphism is associated with POAG in the Brazilian population [7]. However, the association between GSTM1 null polymorphism and POAG risk in Chinese is not very clear. Thus, we conducted this case-control study.

Methods

Study population

Unrelated 323 adult-onset POAG patients and 295 control subjects were recruited. All subjects were given written informed consents. The research protocol was approved by the Ethics Committee of The Affiliated Hospital of Qingdao University. Diagnosis of POAG was based on exclusion of congenital glaucoma and secondary causes (pseudoexfoliation syndrome, uveitis, trauma, steroid-induced glaucoma), anterior chamber angle open, grade III or IV gonioscopy, optic nerve and visual field changes compatible with glaucomatous damage, and initial IOP (before treatment) above 21 mmHg.

DNA extraction and genotyping

DNA was isolated from peripheral blood samples by standard methods. The polymorphism of the GSTM1 loci arises from the complete deletion. DNA was amplified in a total volume of 20 μl containing 10 pmol of each primer, 0.5 unit of Taq DNA polymerase, 1.5 mM MgCl2 and PCR buffer. Following an initial denaturation step at 94°C for 3 min, 35 cycles of amplification were carried out at 94°C for 45 s, 60°C for 45 s and 72°C for 45 s. Both positive and negative controls were analysed in each experiment. GSTM1 genotypes were not scored unless the PCR product from the internal reference β-globulin was evident.
Statistical analysis

χ² tests were used to examine the differences in the distributions of genotypes between cases and controls. The association between the GSTM1 polymorphism and risk of POAG was estimated by Odds Ratios (ORs) and their 95% Confidence Intervals (CIs), which were calculated by unconditional logistic regression. Statistical analyses were carried out using the SPSS WIN v 16.0 statistical package (SPSS, Chicago, IL).

Results

Relevant characteristics of the study subjects are given in Table 1. The distributions for gender and age among cases and controls were not statistically different. The median age was 62 y for cases and 61 y for controls. The distribution of smokers was higher in cases than in controls. The distribution of diabetes mellitus was not different between cases and controls.

The OR and 95% CI for the GSTM1 polymorphism and the risk of POAG were shown in Table 2. We found that patients carrying the GSTM1 null genotype had increased risk of POAG (OR=1.80, 95% CI 1.25-2.54, P=0.002). The results in Table 3 suggested no statistically significantly association between GSTM1 polymorphism and smoking status. However, GSTM1 polymorphism was significantly associated with diabetes mellitus in patients.

Discussion

In our study, we investigated whether GSTM1 polymorphism could have an impact on risk for developing POAG in the Chinese population. We found that patients carrying the GSTM1 null genotype had increased risk of POAG. Juronen et al. suggests that the GSTM1 polymorphism may be associated with increased risk of development of primary open-angle glaucoma [8]. However, Jansson et al. found no evidence of association between GSTM1 and glaucoma in the Swedish population [9]. Fan et al. suggested that variants in TNF and TP53 are risk factors for POAG [10]. Huang et al. found that dual null genotype of GSTM1/GSTT1 is associated with increased risk of POAG [11]. Safa et al. found that increased frequencies of GSTM1 null in patients with PCAG could be a risk factor for incidence of PCAG in the Iranian population [12].

This study has several limitations. First, we only measured the GSTM1 polymorphism. Second, the presence of other factor may have biased the control group in this study. Finally, the sample size of the study was relatively small, and a larger number of subjects are needed to properly evaluate their characteristics.

In conclusion, the GSTM1 polymorphism was significantly associated with the risk of POAG.

Conflicts of Interest

None

References


*Correspondence to*

Dabo Wang
Department of Ophthalmology
The Affiliated Hospital of Qingdao University
PR China