SHORT REPORT

Occupational sunlight exposure, polymorphism of glutathione S-transferase M1, and senile cataract risk

M Saadat, M Farvardin-Jahromi

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Background: The pathogenesis of cataract is influenced by a number of factors including oxidative stress. Glutathione S-transferase (GST) catalyses the nucleophilic addition of the thiol of GST to electrophilic acceptors. It is important for detoxification of xenobiotics in order to protect tissues from oxidative damage.

Objectives: To examine whether the interaction of polymorphism of GSTM1 gene and occupational sunlight exposure modulate the risk of cataract.

Methods: Blood samples from 95 subjects with cataract and 95 age and sex matched healthy persons were collected. The genotypes of GSTM1 were determined using PCR.

Results: The null genotype of GSTM1 was associated with an increase in cataract risk in the indoor workplace, but this association was not significant in the outdoor subjects.

Conclusion: The active genotype of GSTM1 has lost its protective role in persons who work outdoors. It is suggested that activity of the GST μ enzyme may be inhibited in the human lens after occupational exposure to UV light.

Age related cataract is the leading cause of blindness and visual impairment throughout the world. It has been reported that regular exposure to sunlight during occupational activities increases the risk of cataract, which is consistent with a causal association between chronic ultraviolet exposure and cataract formation.¹

The human cytosolic GST supergene family currently comprises eight families of genes (μ , π , θ , α , σ , κ , ζ , and ω) encoding enzymes involved in the detoxification of a variety of compounds.² GST isozymes are considered to be key enzymes involved in scavenging systems to protect lens clarity.³ Although genetic polymorphism in many of these genes has been identified, GSTM1 (a member of class μ) has been studied in most detail. The GSTM1 has a null allele resulting from gene deletion.⁴ Homozygosity for the null allele results in no production of enzymes; these individuals may therefore be at a greater risk of diseases having an association with oxidative stress, such as several types of malignancies and asthma.^{4–6}

GSTM1 catalyses metabolic pathways for the excretion of reactive oxygen species which may be generated by cellular oxidative stress induced by ultraviolet radiation in sunlight.⁷ Based on published articles there is no consistent association between GSTM1 polymorphism and cataract formation.^{8–12} UV-B radiation in sunlight has been shown to increase the risk of cataract formation.¹ Taken together, we hypothesised that risk of cataract associated with occupational sun exposure might be modulated by the polymorphism of GSTM1.

METHODS

Subjects

The eligible cases with senile cataract were randomly selected patients at Khalili Hospital Ophthalmic Clinic in Shiraz, Iran from March 1999 to June 2001. All subjects with cataract (44 males, 51 females) had severe visual disturbance and their corrected visual acuities were under 0.1. We excluded patients with secondary cataract due to diabetes, trauma, steroid administration, and other causes. Using frequency matching, the sex and age (± 5 years) matched control subjects were collected from patients newly diagnosed with diseases other than cataract and open angle glaucoma in the same clinic. Both groups belong to the same ethnic/religious group. As the genetic polymorphism of GSTM1 is associated with several multifactorial diseases such as asthma and several types of cancer, we tried to select study subjects who had no history of cancer, asthma, and cigarette smoking. The study subjects were divided into two groups: outdoor (farmers, drivers, etc) and indoor (housewives, teachers, etc) according to their job titles. The indoor and outdoor patients were occupationally exposed to sunlight and not exposed to sunlight, respectively. The mean age of the cataract patients and the controls was 62.4 ± 11.2 and 65.4 ± 9.4 years, respectively. Informed consent was obtained from each subject before the study.

DNA extraction and determination of genotypes

Blood samples were obtained from patient and control groups. Immediately after collection, whole blood was stored at -20°C until use. Genomic DNA for PCR was isolated from whole blood using the thawed blood samples. PCR conditions for determining GSTM1 genotypes were as reported previously.⁵ The absence of amplified product was consistent with the null genotype.⁴ Successful amplification by β -globin specific primers confirmed the correct function of the PCR reaction. To test for contamination, negative controls (tubes containing the PCR mixture without the DNA template) were included in every run. To ensure laboratory quality control, two independent readers interpreted the gel photographs. Any sample with ambiguous results (generally due to low PCR yield) was retested, and a random selection of 15% of all samples was repeated. No discrepancies were discovered on replicate testing.

Statistical analysis

The relative associations between the genotypes and cataract were assessed by calculating odds ratios (OR) and 95% confidence intervals (CIs) using SPSS (version 11.5).

RESULTS AND DISCUSSION

A cross-tabulation by workplace (indoor and outdoor) and GSTM1 genotypes (null and positive genotypes) of the cases and controls is presented in table 1. The null genotype of

Table 1 Distribution of study participants by workplace and GSTM1 genotypes

Workplace	GSTM1 genotypes	Controls	Cases	OR	95% CI
Indoor	Positive	42	22	1.00	Reference
	Null	25	40	3.06	1.49–6.26
Outdoor	Positive	17	17	1.00	Reference
	Null	11	16	1.46	0.52–4.04

GSTM1 was associated with an increase in cataract risk in indoor the workplace (OR = 3.06, 95% CI 1.49 to 6.26), but this association was not statistically significant in the outdoor subjects (OR = 1.46, 95% CI 0.52 to 4.04). The active genotype of GSTM1 therefore has no protective role in persons who work outdoors. This finding has not been reported in previous studies.

Based on studies describing GST enzyme activity in the skin tissue of hairless mice¹³ and in Tubifex, an aquatic organism,¹⁴ it might be suggested that GST activity is inhibited after UV-B irradiation. Class mu of GST is expressed in the human lens¹⁵ and GSTM1 contributes approximately 80% of the GST μ activity in the lens.¹⁶ It might therefore be suggested that in persons working outdoors, the activity of GST μ is inhibited, and hence the active GSTM1 genotype loses its ability to prevent cataract development. Further studies of the precise mechanisms by which genetic polymorphism of metabolising enzymes influences the nature history of cataract formation are merited.

Finally it should be mentioned that one limitation of our study is the measurement of sunlight exposure. Only sunlight exposure during occupational activities was taken into account, and we used the dichotomous variable (indoor versus outdoor). We assumed that non-occupational exposures are similar for indoor and outdoor subjects. It is recommended that in future studies, using large sample sizes, sunlight exposure is measured as a variable with more categories or as a continuous variable.

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Authors' affiliations

M Saadat, Department of Biology, College of Sciences, Shiraz University, Shiraz, Iran

M Farvardin-Jahromi, Department of Ophthalmology, Shiraz University of Medical Sciences, Shiraz, Iran

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Correspondence to: Dr M Saadat, Department of Biology, College of Sciences, Shiraz University, Shiraz 71454, Iran; saadat@susc.ac.ir

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