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

M Saadat and M Farvardin-Jahromi


Updated information and services can be found at:
http://oem.bmjournals.com/cgi/content/full/63/7/503

These include:

**References**

This article cites 16 articles, 1 of which can be accessed free at:
http://oem.bmjournals.com/cgi/content/full/63/7/503#BIBL

1 online articles that cite this article can be accessed at:
http://oem.bmjournals.com/cgi/content/full/63/7/503#otherarticles

**Rapid responses**

You can respond to this article at:
http://oem.bmjournals.com/cgi/eletter-submit/63/7/503

**Email alerting service**

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

**Topic collections**

Articles on similar topics can be found in the following collections

- Occupational Health (1231 articles)
- Genetics (3885 articles)
- Other ophthalmology (2317 articles)

Notes

To order reprints of this article go to:
http://www.bmjournals.com/cgi/reprintform

To subscribe to *Occupational and Environmental Medicine* go to:
http://www.bmjournals.com/subscriptions/
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 GSTM enzyme may be inhibited in the human lens after occupational exposure to UV light.

Aging 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 (mu, pi, theta, alpha, sigma, kappa, zeta, and omega) 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 mu) 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.5–7

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.

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.6 The absence of amplified product was consistent with the null genotype.6 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
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 mice and in Tubifex, an aquatic organism, it might be suggested that GST activity is inhibited after UV-B irradiation. Class μ of GST is expressed in the human lens and GSTM1 contributes approximately 80% of the GSTu activity in the lens. It might therefore be suggested that in persons working outdoors, the activity of GSTu 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.

ACKNOWLEDGEMENTS
The authors are indebted to the participants for their close cooperation. This study was supported by Shiraz University.

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

Competing interests: none declared

Table 1 Distribution of study participants by workplace and GSTM1 genotypes

<table>
<thead>
<tr>
<th>Workplace</th>
<th>GSTM1 genotypes</th>
<th>Controls</th>
<th>Cases</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoor</td>
<td>Positive</td>
<td>42</td>
<td>22</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>Indoor</td>
<td>Null</td>
<td>25</td>
<td>40</td>
<td>3.06</td>
<td>1.49–6.26</td>
</tr>
<tr>
<td>Outdoor</td>
<td>Positive</td>
<td>17</td>
<td>17</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>Outdoor</td>
<td>Null</td>
<td>11</td>
<td>16</td>
<td>1.46</td>
<td>0.52–4.04</td>
</tr>
</tbody>
</table>

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

Accepted 10 February 2006
Published Online First 21 March 2006

REFERENCES