
Plasma 8-Isoprostane Concentrations in Patients with Age-Related Cataracts, Bin Wang,1* Huaijun Zhu,1 Hong Sun,2 Jinping Pan,1 Zhilan Yuan,2 and Rongbin Yu3 (1 Department of Pharmacology, School of Basic Medical Science, Nanjing Medical University, Nanjing, China; 2 Department of Ophthalmology, First Affiliated Hospital of Nanjing Medical University, Nanjing, China; 3 Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, China; * address correspondence to this author at: Department of Pharmacology, School of Basic Medical Science, Nanjing Medical University, 140 Hanzhong Road, Nanjing 210029, China; fax 86-25-86862884, e-mail binwang@nmju.edu.cn)

Cataracts are the most common cause of blindness and visual dysfunction in the world. Cataractogenesis is a highly complex, multifactorial process. Epidemiologic studies have shown that potential risk factors include age, sex female, exposure to ultraviolet light, smoking, diabetees, and oxidative stress (1–4). Opacification of the ocular lens may be initiated or promoted by oxidative damage, and data in the literature support an important role of oxidative damage in cataract formation (5, 6). Although animal experiments show evidence for a protective role of antioxidants (7, 8), the association between low concentrations of antioxidants and increased risk of cataracts remains controversial. Whereas some studies have demonstrated such associations, others have not (9, 10).

Isoprostanes are a complex family of compounds produced from arachidonic acid. One of the isoprostanes, 8-isoprostaglandin F2α (8-iso-PGF2α), belongs to a family of eicosanoids of nonenzymatic origin (11). 8-ISO-PGF2α has been widely used as a valid marker of oxidative stress (12, 13). Several methods are currently used to quantify 8-ISO-PGF2α, including gas chromatography–mass spectrometry, gas chromatography–tandem mass spectrometry, and liquid chromatography–tandem mass spectrometry (14, 15), but their cost and technologic requirements limit their routine use. Recently, immunoassays have also been developed to measure 8-iso-PGF2α (16, 17).

Koliakos et al. (18) found that the mean concentration of 8-iso-PGF2α in the aqueous humor from cataract patients with exfoliation syndrome was higher than in patients with cataracts only. However, no study has evaluated plasma 8-iso-PGF2α concentrations in cataract patients. In this study, we used an enzyme immunoassay to measure the plasma concentrations of 8-iso-PGF2α in patients with age-related cataracts and in age/sex frequency-matched controls to explore the potential role of systemic oxidative status in the development of cataracts. Unrelated patients older than 50 years of Chinese nationality with age-related cataracts were recruited at the Nanjing Medical University Affiliated Hospital. Control patients were frequency-matched for age and gender. For each case, a control was matched within the same 5-year age group. All participants had a complete ophthalmologic examination. Cataract status was determined by lens examination with a biomicroscope and ophthal-
moscope, and opacities were categorized into nuclear, cortical, posterior capsular, and mixed type (any combination of the above). Controls had no evidence of lens opacity. Patients with other ocular diseases were not included. Individuals with a systemic disease that may cause complicated cataracts were also excluded. Smoking was defined as ≥5 cigarettes/day. The study was approved by the Nanjing Medical University Ethics Committee, and informed consent was obtained from all participants.

Blood samples were obtained in a fasting state between 0800 and 1000 in a quiet, air-conditioned room with the temperature maintained at 22–24 °C and were anticoagulated with EDTA. Plasma samples were separated by centrifugation immediately after blood collection and stored at −80 °C until analysis. 8-Isoprostane was measured by an enzyme immunoassay (Cayman Chemicals) after purification according to the manufacturer’s specifications. The limit of quantification was 5 ng/L. The intra- and interassay CVs were 7.6% and 8.8%, respectively.

The Kolmogorov–Smirnov test of normality was used to test whether the distribution of variables followed a Gaussian pattern. Nonskewed continuous variables are reported as the mean (SD) and compared by means of paired (between cases and controls) or unpaired (between patients with mixed cataracts and patients with pure cataracts) t-tests. Discrete variables are represented as frequencies and were evaluated by the Pearson χ² test. Any differences among 3 or more groups were evaluated by ANOVA with the Scheffe test for continuous variables. The Pearson correlation test was used to assess correlations between the continuous variables. A P value <0.05 was considered to be statistically significant.

A total of 102 cases and 102 controls, frequency-matched on sex and age, were selected. The 2 groups were comparable on the 2 matching variables with similar age distributions and same gender proportions. Males had higher 8-isoprostane concentrations than females in both the cataract and control groups. We found a significant difference between the 8-isoprostane concentrations in patients with cataracts and controls [274.3 (90.4) ng/L vs 135.5 (24.0) ng/L; P <0.001; Table 1]. 8-Isoprostane was ≤160 ng/L in 10.8% of patients with cataracts, whereas 80.4% of the controls without cataracts had 8-isoprostane concentrations ≥160 ng/L (P <0.001). Sixty percent of patients received topical ofloxacin, but there was no significant difference in 8-isoprostane concentrations between patients receiving or not receiving ofloxacin.

Analysis of the total population revealed a positive correlation between age and 8-isoprostane concentration (r = 0.24; P < 0.01). After the exclusion of controls, the 8-isoprostane concentrations correlated better with age in the case group (r = 0.41; P <0.001; Fig. 1A).

In this age-related cataract group, 8-isoprostane concentrations increased stepwise, depending on the age decade: 217.0 (83.2) ng/L in patients 51–60 years, 249.7 (78.4) ng/L in patients 61–70 years, 283.6 (75.8) ng/L in patients 71–80 years, and 360.5 (107.9) ng/L in patients older than 80 years (P <0.001). Patients older than 80 years had the significantly highest 8-isoprostane concentrations (Fig. 1B).

8-Isoprostane concentrations differed significantly between the different clinical types of opacification. Patients with mixed cataracts, compared with patients with pure (cortical, nuclear, or posterior capsular) cataracts, had higher 8-isoprostane concentrations [290.9 (97.2) vs 246.3 (70.2) ng/L; P <0.05; Fig. 1C].

Oxidative stress plays a role in the development of many ocular diseases (19, 20). We have already reported that hypoxia-induced retinopathy and production of angiogenic factors in the retina are inhibited by antioxidant (21–23). Recent data in the literature support an important role of oxidative damage in promoting cataract formation. Kao et al. (24) demonstrated that nitric oxide concentrations in the aqueous humor increased with age in patients with cataracts. Tarwadi et al. (25) reported that plasma thiobarbituric acid–reactive substances were higher in cataract patients than in controls. The activity of erythrocyte catalase was lower and the malondialdehyde concentration in plasma was higher in cataract patients than in controls (26). The association between low antioxidant concentrations and increased risk of cataracts remains controversial. Valero et al. (10) indicated a protective role for vitamin C on the aging lens in a Mediterranean population, and Chasan-Taber et al. (27) reported that dietary carotenoids decrease the risk of cataracts severe enough to require extraction, whereas the Age-Related Eye Disease Study showed no effect of antioxidant formulation on the 7-year risk of development or progression of age-related lens opacities (28). Again, although the Roche European American Cataract Trial demonstrated that daily use of antioxidant micronutrients for 2 years produced a deceleration in progression of age-related cataracts for US patients and for both subgroups (US and UK) after 3 years, there was no significant benefit of treatment in UK patients alone (9).

Isoprostanes are generated by the free radical–mediated peroxidation of arachidonic acid, and 8-isoprostane has been widely used as a valid marker of oxidative stress (11–13). Koliakos et al. (18) reported that the mean concentration of 8-isoprostane in aqueous humor from patients with exfoliation syndrome and cataracts was

### Table 1. 8-Isoprostane concentrations in cases and controls and in males vs females.

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>70.5 (8.4)</td>
<td>70.1 (8.1)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Gender (male), n (%)</td>
<td>45 (44%)</td>
<td>45 (44%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mean (SD) BMI, kg/m²</td>
<td>23.1 (3.3)</td>
<td>22.8 (3.2)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>19 (18.6%)</td>
<td>17 (16.7%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mean (SD) 8-Isoprostane, ng/L</td>
<td>299.9 (102.0) b</td>
<td>144.3 (21.6) b</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Males</td>
<td>254.1 (75.0)</td>
<td>128.6 (23.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Females</td>
<td>274.3 (90.4)</td>
<td>135.5 (24.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
| a BMI, body mass index. | b P <0.05 vs females.
approximately 5 times higher than that measured in the aqueous humor from control cataract patients. However, that study did not evaluate 8-iso-PGF$_{2\alpha}$ between cataract patients and controls without cataracts. To our knowledge, there are no studies examining the plasma 8-iso-PGF$_{2\alpha}$ concentration in cataract patients.

Epidemiologic studies have shown that age and female sex are risk factors for cataracts (9,28). In the present study, cases with cataracts and age/sex frequency-matched controls were selected. The plasma concentrations of 8-iso-PGF$_{2\alpha}$ were higher in patients with age-related cataracts compared with controls, suggesting that systemic oxidative status may play a role in the development of cataracts. In the age-related cataract group, 8-iso-PGF$_{2\alpha}$ concentrations were found to correlate well with age. There is a balance between free radical production and antioxidant capacity, but this balance may be destroyed by certain risk factors of cataracts, such as advanced age.

The present study also revealed that 8-iso-PGF$_{2\alpha}$ concentrations were higher in patients with mixed cataracts than in those with pure cataracts. Different mechanisms may be implicated during development of different types of cataract. Distribution of the glutathione S-transferase genotypes in patients with pure and mixed cataracts are different (29). The nitric oxide concentrations in aqueous humor varied between the clinical types of opacification (24), which can be explained in two ways: (a), in many cases a pure cataract progresses to a mixed cataract involving more than one lens region and becomes more visually disabling, and (b), different processes lead to the formation of pure and mixed opacities.

The vast majority of cataracts are found in developing countries and often result from poverty and poor diet (1, 9, 10). With the population aging, gerontal diseases are becoming a significant social problem in China. Further studies in the Chinese population are needed because of the increasing prevalence of age-related cataracts.

In summary, the present study demonstrates that plasma concentrations of 8-iso-PGF$_{2\alpha}$ may be a risk factor for cataractogenesis in the Chinese population. These findings may have important implications for understanding the role of systemic oxidative status in the development of cataracts.

This project was supported by the National Natural Science Foundation of China (No. 30000207), the Natural Science Foundation of Education Department, Jiangsu Province (No. KJB310001), Commercialization of Science and Technology Foundation of Education Department, Jiangsu Province (JH01-050), and a Nanjing Medical University grant (CX2001003). We are grateful to Dr. Ji-Gao Xiao for expert advice and useful discussions throughout this study.

References


