Increased Homocysteine Levels in Tear Fluid of Patients with Primary Open-Angle Glaucoma

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Introduction

The pathogenesis of primary open-angle glaucoma (POAG) is still not fully understood. There is accumulating evidence that vascular [1], extracellular matrix [2], and neurotoxic [3] changes contribute to the development of POAG besides increased intraocular pressure (IOP). Extracellular matrix and proinflammatory changes are also involved in ocular surface disorders seen in POAG including fibrosis of the filtering bleb after trabeculectomy [4, 5] and dry eye syndrome [6, 7].

Homocysteine (Hcy) is a highly reactive amino acid that can induce typical pathological changes found in POAG including apoptotic death of retinal ganglion cells [3], vascular [8–10], extracellular matrix [8, 11, 12], and proinflammatory alterations [13]. In POAG and pseudoexfoliation glaucoma (PEXG), elevated plasma Hcy levels were observed in previous studies of our group [14–17]. Hyperhomocysteinemia was also shown to be a risk factor for various other ocular diseases [21–23]. However, there are in-
consistent results in the literature regarding plasma Hcy levels of POAG patients [14, 17, 24–27], possibly due to different assessments of critical determinants of Hcy, such as nutritional and B vitamin status of enrolled subjects. In order to illuminate the role of Hcy in glaucomatous neuropathy and its possible implication in ocular surface disorders associated with POAG, we evaluated associations between Hcy in plasma, Hcy in tear fluid, and blood B vitamins.

Materials and Methods

Patients and Design

In this investigation, 36 consecutive Caucasian German patients with POAG and 36 healthy controls without glaucoma, but concurrent diagnosis of cataract were enrolled. All subjects underwent glaucoma or cataract surgery at the Department of Ophthalmology at the University of Erlangen-Nuremberg, Germany. Patients of the present clinical trial were not enrolled in any of our previous studies [14–17]. Informed consent was obtained from all participants after detailed explanation of the purpose and methods of the trial. The University of Erlangen-Nuremberg Human Subjects Committee approved all protocols of this prospective case-control study, and the methods described adhered to the tenets of the Declaration of Helsinki. All controls and patients were thoroughly examined by slit lamp inspection, applanation tonometry, fundoscopy, gonioscopy, pupillometry, and perimetry (Octopus 101, program G1). All POAG patients had open angles on gonioscopy, characteristic glaucomatous optic disk damage (excavation, presence of neuroretinal rim thinning, notching, or retinal nerve fiber layer defects), and pathological cumulative perimetric defect curves, that is, local as well as diffuse visual field loss in white-on-white perimetry. In POAG patients, the mean duration of disease was 11.2 ± 5.2 years, the mean IOP was 18.3 ± 2.7 mm Hg, and the global indices mean defect was 11.7 ± 2.5 dB. Control subjects had no history of ocular disease (except refractive error, strabismus, or cataracts), normal IOP values (<21 mm Hg), and normal eye examination, including open angles, normal appearance of the optic disks and normal visual fields. Each patient was evaluated for dry eye syndrome based on three criteria which had been used in previous studies [28, 29]: (1) history of, treatment of, or symptoms of dry eye syndrome defined according to the Ocular Surface Disease Index [30] questionnaire; (2) tear dynamics which were assessed by the Schirmer I test and tear breakup time; if one of those two tests was positive (Schirmer I test <10 mm, or breakup time <10 s), the tear dynamics were considered abnormal; (3) ocular surface abnormalities which were identified by positive vital staining with fluorescein. Patients with positive results in all three criteria were considered to have definite dry eye, whereas patients with abnormalities in only two of the three criteria were defined to have probable dry eye disease [28]. Exclusion criteria for controls and POAG patients were: medical history of disorders associated with increased Hcy levels such as thromboembolic, renal, hepatic, gastrointestinal or neurologic disease, as well as prior ocular surgery, a history of ocular inflammation, age-related macular degeneration, diabetic retinopathy, myopia, retinal occlusive disease, ruberosis iris and glaucoma other than POAG. Patients taking hormone substitution and medications known to affect Hcy measurements were excluded.

Matching of controls and POAG patients was performed by demographic, common clinical, and lifestyle factors known to cause increased Hcy levels (table 1) [31].

Nutritional and lifestyle status was assessed using the Subjective Global Nutritional Assessment test [32]. Since all participants and controls were classified as well nourished, we used 11.7 μmol/l as the primary cutoff value to define hyperhomocysteinemia as in previous investigations [14, 16]. Additionally, we performed statistical analysis with 15.0 μmol/l as the threshold. Twenty-nine of the 36 patients in the POAG group were on topical antiglaucomatous therapy: 53% (19/36) of the POAG patients were on beta-blocker, 47% (17/36) on prostaglandin analog, 36% (13/36) on carbonic anhydrase inhibitor, 19% (7/36) on alpha-agonist, 3% (1/36) on cholinergic, and 3% (1/36) on adrenergic topical medication. In order to avoid the possible influence of eyedrops on Hcy measurements, topical therapy was stopped in all patients at least 12 h prior to sampling of reflex tears.

Table 1. Characteristics of POAG patients and controls

<table>
<thead>
<tr>
<th>Nongenetic determinants of Hcy</th>
<th>Controls (n = 36)</th>
<th>POAG (n = 36)</th>
<th>p value (differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD), years</td>
<td>68.5 ± 9.8</td>
<td>67.3 ± 8.2</td>
<td>0.59&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Male sex</td>
<td>17 (48)</td>
<td>15 (42)</td>
<td>0.81&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Caffeinated beverages (&gt;3 per day)</td>
<td>13 (36)</td>
<td>12 (33)</td>
<td>1.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alcoholic drinks (&gt;1 per day)</td>
<td>5 (14)</td>
<td>7 (20)</td>
<td>0.54&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (17)</td>
<td>8 (22)</td>
<td>0.77&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>12 (33)</td>
<td>14 (39)</td>
<td>0.81&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (11)</td>
<td>5 (14)</td>
<td>1.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>6 (17)</td>
<td>4 (11)</td>
<td>0.74&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Atherosclerotic vascular disease</td>
<td>4 (11)</td>
<td>3 (8)</td>
<td>1.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Figures in parentheses are percentages.  
<sup>a</sup> t test;  
<sup>b</sup> Fisher’s exact test.
Laboratory Analyses

All patients underwent blood and tear fluid collection at the day of ocular surgery, ensuring that the patients were fasting. Secretion of reflex tears was incited by the yawn reflex and by stimulation of the trigeminal nerve with a nasal alcohol stimulus. A disposable glass capillary was placed near the cul-de-sac of the eye and 100 µl of tear fluid were collected according to Choy et al. [33]. Reflex tear collection with the capillary tube was shown to be the method of choice in the study by Choy et al. [33]. They compared basal tears with reflex tears as sources of tear fluid, and Schirmer strips with capillary tubes as collection methods. The Schirmer strips have the disadvantage that they are associated with direct conjunctival contact and therefore risk of vascular transudation and cell damage with leakage of plasma and intracellular constituents [34, 35]. Hcy is found both in plasma and in cells and Schirmer strips might therefore lead to spuriously high levels of Hcy in tears. The use of a capillary tube for tear collection is much less invasive [34], allows collection of larger volumes of tear fluid than with the Schirmer strip [35], and is therefore the suggested method of choice for tear collection. There is currently no suitable method available for collection of basal tears for biochemical analysis [33].

Probes were immediately placed on ice, promptly centrifuged (2,000 g, 10 min) within 30 min after collection and stored at −20°C until biochemical analysis was performed.

For analysis of Hcy in tears, 50 µl of undiluted tear fluid were mixed with 14 µl of reduction agent (1.43 mol/l sodium borohydride). The samples were then gently vortex-mixed and incubated for 5 min at room temperature. We added 50 µl of precipitation agent (1.50 mol/l perchloric acid) and vortex mixed the samples for 30 s. After removal of protein with centrifugation (12,000 g, 5 min), 40 µl of the probes were mixed with 80 µl of derivatization agent (10.0 mmol/l monobromobimane). The tubes were capped, mixed, and incubated at 42°C. The autosampler (model: Midas, Spark Systems®, Emmen, The Netherlands) injected 50 µl aliquots onto a 4.6 × 150 mm LC8 Supelcosil column (Supelco®, Bellefonte, Pa., USA) with a column temperature of 25°C. For determination of homocysteine-S-bimane, the column was developed at a flow rate of 1.2 ml/min. Homocysteine-bimane adduct was detected fluorometrically with an RF-10AxI high-performance liquid chromatography detector (Shimadzu Corporation®, Kyoto, Japan). The excitation wavelength was set at 385 nm, and the emission wavelength at 515 nm. Standard curves and quality control samples were run with each batch.

For analysis of Hcy in plasma, 20 µl of the diluted plasma probe (1:10) were mixed with 30 µl of water before the reduction agent was added. The following steps of the analysis were identical to the preparation of tear fluid.

Vitamin B_{12} concentrations were analyzed by high-performance liquid chromatography (kit by Chromsystems®, Munich, Germany), and serum vitamin B_{12} and folate concentrations were determined by immunoassay (Immulite, DPC Biermann®, Bad Nauheim, Germany).

Statistical Analysis

All statistical tests were two-sided and a p value less than 0.05 was considered statistically significant. The Kolmogorov-Smirnov test showed that Hcy, B vitamins, and age were normally distributed. Differences between patient groups were evaluated by the Fisher exact, ANOVA, and t tests. Correlation between Hcy in plasma, Hcy in tear fluid, age, and B vitamins was assessed using Pearson’s correlation coefficient. In controls and patients, univariate analysis followed by multiple regression analysis was executed to find nongenetic determinants of Hcy. After adjustment for confounding factors, logistic regression analysis was done to calculate odds ratios for POAG associated with elevated Hcy levels.

Results

Hcy was detected in all tear fluid and plasma samples. Hcy levels in tear fluid and in plasma were significantly higher in patients with POAG than in control patients (fig. 1; table 2). Elevation of Hcy both in tear fluid and in plasma was associated with a higher risk for POAG compared to controls in a logistic regression model (table 2).

In POAG eyes, a significant correlation with a moderate degree of strength could be observed between Hcy in plasma and Hcy in tear fluid (r = 0.459; p = 0.005; fig. 2a) as opposed to control subjects in whom no significant correlation was found (r = 0.068; p = 0.695; fig. 2b). The association between Hcy levels in tear fluid and plasma in POAG patients was further demonstrated in a general linear analysis, in which only the plasma Hcy (p = 0.005) was a significant predictor of tear fluid Hcy, but not age (p = 0.316), sex (p = 0.510), or B vitamin levels (B_{12}: p = 0.144, B_{6}: p = 0.755, folate: p = 0.151). In controls, this as-

Homocysteine in Primary Open-Angle Glaucoma

Ophthalmic Res 2008;40:249–256

Fig. 1. Distribution of Hcy levels in tear fluid (a) and plasma (b) for controls and POAG patients. The box length is the interquartile range with the median represented by the horizontal line. ○ = Case with more than 1.5 box lengths from the upper edge of the box.
The association between tear fluid and plasma Hcy was not significant (p = 0.550).

There was no significant difference in potential confounding factors between POAG patients and controls: levels of B vitamins and creatinine, the most important nongenetic determinants of elevated Hcy, did not differ significantly between POAG patients and controls (Table 3).

We evaluated the relationship between Hcy levels and major nongenetic determinants of Hcy in a general linear model for both groups. In POAG patients, neither Hcy in plasma nor Hcy in lacrimal fluid was significantly related to any of the nongenetic determinants of Hcy. However, in the control group, folate (p = 0.008) demonstrated a significant negative association, whereas age (p = 0.009) and caffeine consumption (p = 0.036) showed a significant negative association between tear fluid and plasma Hcy was not significant (p = 0.550).

Table 2. Hcy levels in tear fluid and plasma were significantly increased in POAG patients using t tests and displayed graded risk factors for POAG in a logistic regression model

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n = 36)</th>
<th>POAG (n = 36)</th>
<th>p value (differences)</th>
<th>Odds ratio (logistic regression)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>130 ± 53</td>
<td>205 ± 84</td>
<td>t = –4.52; p &lt; 0.001</td>
<td>OR = 1.015^a 95% CI = 1.005–1.025 p = 0.003</td>
</tr>
<tr>
<td>Hcy in plasma, µmol/l</td>
<td>10.50 ± 3.33</td>
<td>13.43 ± 3.53</td>
<td>t = –3.63; p = 0.001</td>
<td>OR = 1.356^b 95% CI = 1.131–1.625 p = 0.001</td>
</tr>
<tr>
<td>Hyperhomocysteinemia &gt;11.7 µmol/l</td>
<td>22% (8/36)</td>
<td>64% (23/36)</td>
<td>p = 0.001</td>
<td>OR = 6.72^c 95% CI = 2.25–20.07 p = 0.001</td>
</tr>
<tr>
<td>Hyperhomocysteinemia &gt;15.0 µmol/l</td>
<td>8% (3/36)</td>
<td>39% (14/36)</td>
<td>p = 0.004</td>
<td>OR = 7.80^c 95% CI = 1.93–31.51 p = 0.007</td>
</tr>
</tbody>
</table>

^a Odds ratio for POAG per 1 nmol/l elevation of Hcy in tear fluid after adjustment for age, folate, caffeine, and plasma Hcy.

^b Odds ratio for POAG per 1 µmol/l elevation of Hcy in plasma after adjustment for age, folate, and caffeine. Hyperhomocysteinemia, defined on two different cutoff levels, was more prevalent in POAG using Fisher’s exact tests and was a significant risk factor for POAG compared to controls.

^c Odds ratio for POAG associated with hyperhomocysteinemia.

Table 3. B vitamin and creatinine levels in controls and POAG patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n = 36)</th>
<th>POAG (n = 36)</th>
<th>p value (differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folate in serum, ng/ml</td>
<td>12.54 ± 6.43</td>
<td>11.55 ± 5.58</td>
<td>t = 0.70; p = 0.49</td>
</tr>
<tr>
<td>Vitamin B₁₂ in serum, pg/ml</td>
<td>425 ± 194</td>
<td>438 ± 243</td>
<td>t = –0.27; p = 0.79</td>
</tr>
<tr>
<td>Vitamin B₆ in plasma, ng/ml</td>
<td>13.12 ± 7.61</td>
<td>12.50 ± 7.15</td>
<td>t = 0.35; p = 0.73</td>
</tr>
<tr>
<td>Creatinine in serum, mg/dl</td>
<td>0.83 ± 0.18</td>
<td>0.81 ± 0.16</td>
<td>t = 0.70; p = 0.49</td>
</tr>
</tbody>
</table>

No significant differences were found between controls and POAG patients in the above important confounding factors of hyperhomocysteinemia.
Homocysteine in Primary Open-Angle Glaucoma

Ophthalmic Res 2008;40:249–256

253

cant positive association with plasma Hcy levels in the multiple regression model. Hcy in tear fluid was negatively associated with serum folate \( p = 0.047 \) in the control group.

Prevalence of definite dry eye syndrome was significantly higher in POAG patients compared to controls \([28\% (10/36) \text{ vs. } 8\% (3/36), \text{ respectively; } p = 0.035, \text{ Fisher’s exact test}]\), whereas prevalence of probable dry eye disease was not significantly different between both groups \([31\% (11/36) \text{ vs. } 14\% (3/36), \text{ respectively; } p = 0.155, \text{ Fisher’s exact test}]\). POAG patients with probable dry eye disease had significantly higher Hcy levels than subjects without dry eye syndrome both in tear fluid \((252 \pm 67 \text{ nmol/l vs. } 185 \pm 84 \text{ nmol/l}; \ t = -2.33, \ p = 0.026)\) and in plasma \((15.89 \pm 3.08 \mu \text{mol/l vs. } 12.34 \pm 3.20 \mu \text{mol/l}; \ t = -3.09, \ p = 0.004)\). In the control group, patients with a diagnosis of dry eye did not have significantly increased Hcy levels compared to subjects without dry eye disease in tear fluid \((156 \pm 40 \text{ nmol/l vs. } 126 \pm 54 \text{ nmol/l}; \ t = -1.18, \ p = 0.245)\) or plasma \((12.86 \pm 6.01 \mu \text{mol/l vs. } 10.11 \pm 2.65 \mu \text{mol/l}; \ t = -1.77, \ p = 0.368)\). After exclusion of all POAG and control patients with dry eye disease, patients with POAG still had significantly higher Hcy levels compared with control patients both in plasma \((12.34 \pm 3.20 \mu \text{mol/l vs. } 10.11 \pm 2.65 \mu \text{mol/l}; \ t = -2.86, \ p = 0.006)\) and tear fluid \((184 \pm 84 \text{ nmol/l vs. } 126 \pm 54 \text{ nmol/l}; \ t = -3.16, \ p = 0.003)\). Furthermore, POAG patients with dry eye syndrome had higher Hcy levels in tear fluid than control patients with dry eye syndrome \((252 \pm 66 \text{ nmol/l vs. } 156 \pm 40 \text{ nmol/l}; \ t = -3.0, \ p = 0.010)\).

Topical therapy was abandoned 12 h prior to collection of reflex tears, in order to avoid contamination of tear fluid with eyedrops and thus interference of Hcy measurements. Despite these precautions, a possible influence of chronic antiglaucomatous medication on Hcy levels could not be ruled out. Therefore, we additionally evaluated possible associations between topical therapy prior to the 12-hour pause and Hcy levels in tear fluid and dry eye disease.

\( t \) Tests for the various types of antiglaucomatous eyedrops were performed and no significant association between Hcy levels in tear fluid and any topical therapy could be observed \((t \text{ tests; } p > 0.3 \text{ in all types of eye medication; table 4})\). Furthermore, the 29 POAG patients with and the 7 POAG patients without topical antiglaucomatous drugs showed no significant difference in Hcy levels of tear fluid \((201 \pm 77 \text{ nmol/l vs. } 221 \pm 116 \text{ nmol/l}; \ t = 0.559, \ p = 0.580)\). Besides that, Hcy levels in tear fluid and the number of different topical drugs used for glaucoma therapy were not significantly associated \((x = \text{number of different antiglaucomatous eyedrops}; \ n = \text{number of patients}); \ x = 0 (n = 7): 221 \pm 116 \text{ nmol/l}; \ x = 1 (n = 12): 212 \pm 85 \text{ nmol/l}; \ x = 2 (n = 9): 177 \pm 68 \text{ nmol/l}; \ x = 3 (n =

**Fig. 2.** Scatterplot graphs with linear regression lines in POAG patients \((n = 36)\) (a) and controls \((n = 36)\) (b). a Positive correlation between tear fluid and plasma Hcy \((r = 0.459; p = 0.005)\) in POAG patients. \( \bigcirc \) Patients with topical antiglaucomatous therapy; \( \times \) patients without topical antiglaucomatous therapy. b No significant correlation in controls \((r = 0.068; p = 0.695)\).
Table 4. Association between Hcy levels in tear fluid and therapy with different antiglaucomatous eyedrops in POAG patients (n = number of patients)

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Yes</th>
<th>No</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 19)</td>
<td>(n = 17)</td>
<td></td>
</tr>
<tr>
<td>Prostaglandin analogs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 17)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td>Carbonic anhydrase inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 13)</td>
<td>(n = 23)</td>
<td></td>
</tr>
<tr>
<td>Alpha-agonists</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 7 )</td>
<td>(n = 29)</td>
<td></td>
</tr>
<tr>
<td>Cholinergics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 1 )</td>
<td>(n = 35)</td>
<td></td>
</tr>
<tr>
<td>Adrenergics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hcy in tear fluid, nmol/l</td>
<td>(n = 1 )</td>
<td>(n = 35)</td>
<td></td>
</tr>
</tbody>
</table>

Topical therapy was stopped 12 h prior to sampling of reflex tears to avoid contamination of tear fluid. Chronic antiglaucomatous treatment prior to this 12-hour pause was not associated with Hcy levels in tears (t tests; p > 0.5 in all types of topical medication).

4): 225 ± 70 nmol/l; x = 4 (n = 4): 203 ± 94 nmol/l; p = 0.830, F = 0.367, one-way ANOVA. No association was found between any of the antiglaucomatous eye medications and dry eye syndrome (Fisher’s exact test: beta-blockers, p = 1.0; prostaglandin analogs, p = 0.281; carbonic anhydrase inhibitors, p = 0.475; alpha-agonists, p = 1.0; cholinergics, p = 0.306; adrenergics, p = 1.0). Furthermore, the number of different antiglaucomatous drugs was not associated with dry eye syndrome (p = 0.302; χ² test).

Discussion

In the current study, increased Hcy concentrations in both tear fluid and plasma of POAG patients were detected.

The measured mean plasma Hcy levels in POAG patients and controls of the present study were similar to values found in other diseases with Hcy as a risk factor including vascular [9, 10] and ocular [19–23] disorders. However, in the study by Wang et al. [25], who found no significant differences between Hcy levels in POAG and controls, the mean Hcy value of the control subjects was above most thresholds for hyperhomocysteinemia. It was at least 1 μmol/l higher compared to controls of other investigations [9, 19–23] including 27 studies evaluated by Boushey et al. [10] in a meta-analysis. Furthermore, different ethnicities of the enrolled patients and different evaluation of critical nongenetic determinants of Hcy [31], such as assessment of nutritional status, B vitamin and creatinine levels, might be responsible for the inconsistent results in the literature.

Hcy in plasma showed a significant and moderately strong correlation with Hcy in tear fluid in POAG patients, but not in controls. Furthermore, POAG patients with dry eye syndrome had significantly higher Hcy levels in tear fluid and plasma than POAG patients without dry eye disease. Subjects with POAG suffered significantly more often from definite dry eye syndrome than control patients. To our knowledge, this is the first study evaluating the possible clinical role of Hcy in tear fluid.

Hcy can induce deposition of extracellular matrix components, fibrosis [11], oxidative stress, and production of those subtypes of matrix metalloproteinases [8], transforming growth factors, collagens [12], and proinflammatory factors [13], which were found to be increased in dry eye syndrome [7] and insufficient filtering blebs [4, 5]. Therefore, further studies are warranted to investigate whether increased Hcy levels in tear fluid might be implicated in dry eye syndrome or failure of filtering blebs in POAG eyes.

The result of a previous investigation [18], which showed that hyperhomocysteinemia in POAG might be caused by an endogenous genetic variant, is indirectly supported by our finding that elevated Hcy levels in plasma and tear fluid in POAG were not associated with low B vitamin levels or other important nongenetic determinants of Hcy, such as increasing age or caffeine consumption, as opposed to controls. Similar associations were found for Hcy in aqueous humor and nongenetic determinants in a previous study [17].

The study has limitations. Due to the prospective study design and the complex nature of collecting tear fluid, the study population in this investigation was relatively small (n = 72), especially the number of patients with dry eye syndrome (n = 16). Further studies are needed with larger patient numbers to confirm the possible...
association between increased Hcy levels in tear fluid and dry eye syndrome in POAG patients.

In conclusion, our results suggest that elevated Hcy levels in tear fluid and plasma might be potential risk factors for POAG and dry eye disease in patients with glaucoma. Therapy of high Hcy levels by administration of systemic or topical B vitamin preparations would be safe, effective and inexpensive. Thus, further investigations are necessary to elucidate the potential clinical role of Hcy in glaucoma patients, as such the possible association between elevated Hcy values and the higher prevalence of systemic vascular dysregulations or ocular surface disorders in POAG.

References


