


Risk of Acute Angle-Closure Glaucoma After Diagnostic Mydriasis in Nonselected Subjects: The Rotterdam Study

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Purpose. To report the prevalence of narrow anterior chamber angles on slit-lamp examination and the incidence of acute angle-closure glaucoma (AACG) after diagnostic mydriasis in nonselected white subjects aged 55 years and over.

Methods. Of all subjects in the population-based Rotterdam Study (n = 7983), 6760 participated in the ophthalmologic examination and received both tropicamide 0.5% and phenylephrine 5% eye drops for diagnostic mydriasis. No exclusion criteria (e.g., level of intraocular pressure, presence of narrow anterior chamber angles, history of or treatment for glaucoma) were used. After the ophthalmologic examination, all participants received thymoxamine 0.5% drops in both eyes and were warned about the symptoms of AACG.

Results. The prevalence of narrow angles was 2.2% and was twice as high in women. In two subjects (0.03%), an attack of AACG developed in one eye after diagnostic mydriasis. After medical therapy, peripheral iridotomies were made with a Nd:YAG laser, and both eyes healed without loss of visual acuity or visual field.

Conclusions. In nonselected white subjects of 55 years of age or older, the 2% prevalence of narrow anterior chamber angles is similar to that in a mixed black and white population in the United States. According to our protocol, 3 in 10,000 subjects are likely to develop AACG after diagnostic mydriasis followed by miotic drops. Invest Ophthalmol Vis Sci. 1997;38:2683–2687.

Diagnostic mydriatic drops are widely used in ophthalmologic clinical practice; in most cases they are essential for an adequate examination of the ocular media and fundus. However, the use of mydriatic agents can provoke an attack of acute angle-closure glaucoma (AACG), with an increase in intraocular pressure (IOP) of up to 80 mm Hg within a few hours and a risk of permanent damage to the optic nerve. Only early recognition of the elevated (in most cases substantially) IOP and subsequent reduction of the pressure can save the visual capacity of the eye involved.

The risk of precipitating an AACG attack might be a reason why many general practitioners, internists, and other nonophthalmologic physicians are reluctant to dilate pupils for ocular examination. Also, when an ophthalmic epidemiologic study is started, the question arises as to whether it is safe to use mydriatics in all participants. In epidemiologic studies, a selection may be made based on, for example, the width of the chamber angle by penlight or slit-lamp examination. No exact data could be obtained from the literature on the risk of AACG when, with or without prior examination, all subjects in a white, population-based study would receive mydriatic drops. Thus,
in the Rotterdam Study, so as not to create bias, all participants were scheduled to receive mydriatic eye drops for fundus examination and photography.

The purpose of this paper is to report the prevalence of narrow anterior chamber angles and the incidence of AACG after diagnostic mydriasis in nonselected subjects in a white population aged 55 years and over.

METHODS. The Rotterdam Study is a large population-based follow-up study in which 7983 subjects from the suburb Ommoord participated. 6,7 Of these, 97% were white. The purpose of the study was to investigate chronic disabling ophthalmologic, cardiovascular, neurogeriatric, and locomotor diseases in subjects aged 55 years and over. 6 The ophthalmologic part focussed on primary open-angle glaucoma and age-related macular degeneration. The study was approved by the Institutional Human Experimentation Committee (Medical Ethics Committee) of Erasmus University, Rotterdam, and was conducted in accord with the Declaration of Helsinki. Written informed consent was obtained from all participants.

The baseline phase (1990 to 1993) consisted of an extensive home interview, followed by a medical and complete ophthalmologic examination in the research center. 6 The ophthalmologic examination included an estimation of the width of the anterior chamber angle by comparing, using the narrowest possible slit-lamp beam perpendicular to the corneal surface at the limbus, the thickness of the cornea and the distance between Descemet’s membrane and the iris surface. 4 The anterior chamber angles were divided into open angles (angle width >25% of corneal thickness) or narrow angles. 4 All participants received both tropicamide 0.5% and phenylephrine 5% mydriatic eye drops, regardless of the level of intraocular pressure, the presence of a narrow anterior chamber angle, or a history of angle-closure or primary open-angle glaucoma. After the examination, all subjects received as a miotic one drop of thymoxamine 0.5% in each eye. Participants were warned to notify the investigator immediately if their vision became more blurred than during mydriasis or if they became nauseated or noted pain or redness around the eye. In those cases, the IOP was remeasured. If the symptoms started later on, at home, participants were told to alert the investigator or their general practitioner.

RESULTS. Of the 7983 participants in the baseline phase, 6760 subjects (84.7%) underwent an ophthalmologic examination, and 6679 (98.8%) of these received mydriatic drops for ophthalmoscopy and fundus photographs (Table 1). A few participants (1.2%) refused the mydriatics. This refusal was significantly dependent only on age and not on gender, presence of narrow chamber angles, or eye-related complaints in the past (Table 2). Subjects with a history of ophthalmologic examinations did not refuse more frequently.

The prevalence of a narrow anterior chamber angle was 2.2%. The prevalence rates in the different age and gender categories are given in Table 3. With increasing age, the chance of having a narrow angle increased by 3% per year (odds ratio 1.03; 95% confidence interval 1.01 to 1.04; P = 0.0043), but after adjustment for refraction, this effect of age disappeared (odds ratio 1.01; 95% confidence interval 0.99 to 1.03; P = 0.32). Women were twice as likely as men to have a narrow anterior chamber angle (odds ratio 2.0, 95% confidence interval 1.4 to 3.0; adjusted for age and refraction).

Of the 6679 subjects who received mydriatic eye drops, 2 participants (0.03%; Table 4) developed an AACG attack after mydriasis. They were initially treated medically (thymoxamine 0.5% eye drops and oral acetazolamide 0.500 mg) and subsequently were referred to the Department of Ophthalmology of the University Hospital, Rotterdam. In both cases, peripheral iridotomies were made with a Nd:YAG laser, and both kept a visual acuity similar to that before the AACG attack. Their visual fields also remained normal.

DISCUSSION. The results of this study show that only about 1 in 3000 unselected white persons aged 55 years and over will develop AACG after the use of tropicamide 0.5% and phenylephrine 5% eye drops. The number of subjects who developed AACG in our study is too low to allow reliable statistical analysis of risk factors for AACG. However, from our figures we can calculate that the positive predictive value of the angle width, estimated using the slit-lamp method of

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TABLE 1. Number of Participants and Those Refusing Mydriatic Drops in the Ophthalmologic Part of the Rotterdam Study

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>% Refusal of Mydriatics</td>
<td>Number</td>
<td>% Refusal of Mydriatics</td>
</tr>
<tr>
<td>55–64</td>
<td>1098</td>
<td>1.1 (n = 12)</td>
<td>1463</td>
</tr>
<tr>
<td>65–74</td>
<td>1051</td>
<td>1.3 (n = 14)</td>
<td>1349</td>
</tr>
<tr>
<td>75–84</td>
<td>503</td>
<td>1.2 (n = 6)</td>
<td>887</td>
</tr>
<tr>
<td>85+</td>
<td>89</td>
<td>3.4 (n = 3)</td>
<td>320</td>
</tr>
<tr>
<td>Total</td>
<td>2741</td>
<td>1.3 (n = 35)</td>
<td>4019</td>
</tr>
</tbody>
</table>

Van Herick et al,4 with regard to the development of AACG after diagnostic mydriasis is < 1% in the general white population. Gonioscopy with the Goldmann three-mirror goniolens was performed only in subjects with persistent visual field loss on Goldmann perimetry; thus, we cannot say much about the association between Van Herick’s method and gonioscopy with a goniolens.

The close communication between general practitioners, examiners, and area ophthalmologists and the fact that our research was done at the primary healthcare center make it extremely unlikely that we would have missed cases with full-blown AAGC within a few days after the diagnostic mydriasis. We received no serious complaints about poorer vision or other symptoms of AACG, but that does not exclude the possibility that some subjects with minor complaints may have escaped our attention.

Narrow anterior chamber angles were present in 149 subjects (2.2%), when estimated using Van Herick’s4 method. Of all subjects with primary open-angle glaucoma in the Rotterdam Study (n = 56; for criteria see Dielemans et al7), none had narrow angles using this method. Thus, our concern at the start of the study about creating bias with regard to the prevalence of primary open-angle glaucoma by omitting these subjects seems to be unfounded.

Eyes with open anterior chamber angles on gonioscopy with a goniolens can still develop AAGC after mydriasis.9 Even an elevation of the IOP after mydriasis is compatible with a normal open anterior chamber angle; also, a gonioscopically closed anterior angle chamber is compatible with no rise in IOP after mydriasis.10 Therefore, gonioscopy seems of limited value in predicting which eyes will develop angle-closure glaucoma in response to pupillary dilatation.

The higher risk for women of having a narrow chamber angle was in agreement with a study using gonioscopy.11 Also, the effect of age on the presence of narrow anterior chamber angles has been described earlier.10,11 However, after adjustment for refraction, the effect of age disappeared in our study.

Recently, the absence of AACG after the use of mydriatic drops in a population-based survey on 4870 subjects was reported.5 The prevalence of 2% narrow angles on penlight examination in that study with 45% blacks was in the same range as our 2.2% and the 1.6% in a clinic-based study of 2185 patients.4 However, the methodology in the Baltimore Eye Survey5 was different in that all subjects who had a shallow anterior

TABLE 2. Relative Risks for Refusal of Mydriatic Drops

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Odds Ratio*</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference: age category 55–64 years.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex: females vs males.</td>
<td></td>
<td></td>
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<tr>
<td>Presence vs absence of narrow chamber angle (method of Van Herick).</td>
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<tr>
<td>Visits vs no visits to ophthalmologist for examination (other than for prescription of glasses) in the past.</td>
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</tbody>
</table>

* Odds ratio from multiple logistic regression with age, gender, presence of narrow chamber angle, and eye complaints in the past in the model.

TABLE 3. Prevalence of Narrow Anterior Chamber Angles (Van Herick Grade 1 and 2; ≥25%) in 6679 Subjects

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>SEM</th>
<th>Women</th>
<th>SEM</th>
<th>Total</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>55–64</td>
<td>1.2</td>
<td>0.33</td>
<td>2.4</td>
<td>0.40</td>
<td>1.9</td>
<td>0.27</td>
</tr>
<tr>
<td>65–74</td>
<td>1.4</td>
<td>0.37</td>
<td>2.4</td>
<td>0.42</td>
<td>2.0</td>
<td>0.29</td>
</tr>
<tr>
<td>75–84</td>
<td>1.4</td>
<td>0.52</td>
<td>2.8</td>
<td>0.55</td>
<td>2.3</td>
<td>0.40</td>
</tr>
<tr>
<td>85+</td>
<td>1.1</td>
<td>1.11</td>
<td>5.7</td>
<td>1.31</td>
<td>4.7</td>
<td>1.05</td>
</tr>
<tr>
<td>Total</td>
<td>1.3</td>
<td>0.22</td>
<td>2.8</td>
<td>0.26</td>
<td>2.2</td>
<td>0.18</td>
</tr>
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</table>
chamber by penlight examination were initially excluded from receiving mydriatic drops. At a later stage, 74% were dilated with 0.5% tropicamide only, hampering comparison with our results; also, different study algorithms were used. Use of three screening factors for AACG with poor predictive value (shallow anterior eye chamber on penlight examination, history of glaucoma, or blindness in at least one eye), and using as a gold standard the diagnosis of potentially occludable angle on four-mirror gonioprism gonioscopy by a glaucoma subspecialist, led to a assessed risk of AACG of 0.3%. This factor is 10 times higher than what we found, and it is not likely that this is due to racial differences. Because many of these screening factors—and even gonioscopy—have a poor predictive value with regard to the risk of developing AACG after diagnostic mydriasis, we might better concentrate on warning subjects about the symptoms of AACG after diagnostic mydriasis than on these elusive risk factors.

Because tropicamide by itself did not result in sufficient mydriasis for our purposes within the time span of the study, we added phenylephrine eye drops. From the literature, we gathered that tropicamide and phenylephrine seemed to have lowest risk of causing AACG. The action of phenylephrine is rapidly reversed by thymoxamine, and the effects of tropicamide can be quickly counteracted by acetazolamide. In mydriasis, the sensitivity of funduscopy in the detection of diabetic retinopathy is considerably improved; the same is true for macular and peripheral retinal disorders. In our view, the advantage of permitting a more sensitive fundus examination in mydriasis outbalances the risk of precipitating AACG. Moreover, in 8% of the subjects at risk, AACG would have occurred within 2 years, usually late in the evening, without the subject having knowledge of the symptoms and without medical supervision. This may lead to a higher chance of permanent loss of visual capacity in the affected eye.

Therefore, we consider diagnostic mydriasis with the mentioned mydriatics and subsequent miotics to be relatively safe, provided that the subject has been thoroughly informed about related complaints and that a physician is available for reexamination. Good contact with eye-care facilities in the neighborhood is necessary to reduce the risk of permanent damage to the eye.

Key Words
acutec angle-closure glaucoma, epidemiology, incidence, mydriasis

References


