Provocative testing for primary open-angle glaucoma in “senior citizens”

Norman Ballin* and Bernard Becker

A group of “senior citizens” was studied with respect to applanation pressures, water-provocative tonography, and steroid-provocative testing. The results showed that considerable numbers of elderly individuals demonstrate applanation pressures greater than or equal to 20 mm. Hg and Po/C ratios after water greater than 100, and yet have normal disks and normal fields. It was concluded that such testing should be interpreted with caution in the elderly individual. However, comparable percentages of responders to topical corticosteroids were found in these same elderly individuals as in younger age groups. In the older age groups, the homozygous nonresponders and the heterozygous responders to topical corticosteroids differed significantly as to their applanation pressures before steroids and their Po/C ratios after water.

The problem of the glaucoma suspect continues to be a perplexing one both to the practicing ophthalmologist and to his colleagues in investigational work. The recent studies of Armaly1 provide surprisingly high estimates of the number of asymptomatic individuals in this country with at least borderline abnormal intraocular pressures. Such estimates, based on the 1960 census, are that 15.5 million individuals in this country have intraocular pressures of 20 mm. Hg or more and over 3 million have pressures of 23 or more.

Since the usual natural history of glaucoma is that of pressure elevations preceding changes in disk and field, it would be ideal to be able to predict which individuals with borderline pressures are likely to develop overt open-angle glaucoma. To this end, certain provocative tests have been advocated. Among these, the water-provocative test combined with tonography has shown an excellent separation of glaucomatous and selected normal eyes. In addition, investigations of the phenomenon of ocular hypertension induced by topical steroids have suggested that individuals with a genetic predisposition for glaucoma might be identified by the magnitude of their response to steroids.

An invitation to perform a glaucoma survey among a small group of “senior citizens” in the city of St. Louis provided us with the opportunity of studying the above tests in an age group where one might reasonably expect a better correlation between positive provocative testing and evidence of spontaneous pressure elevation. The results showed a rather high

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*Present address: Department of Ophthalmology, University of Florida School of Medicine, Gainesville, Fla.
prevalence of individuals with elevated applanation pressures and positive water-provocative tests in spite of clinically non-glaucomatous eyes. However, when the steroid provocative data were analyzed as to absolute applanation pressure \((A)\) after four weeks of topical corticosteroids, the percentage of steroid responders was similar to that found in younger age groups. Comparison of heterozygous responders \((A \geq 20\) after steroids) with homozygous nonresponders \((A < 20\) after steroids) in the older age group showed significant differences between these phenotypes in their presteroid applanation pressures and water-provocative tonograms.

Material and methods

A free survey for glaucoma was publicized among the Senior Citizen group sponsored by the Soroptimist Club in St. Louis. Individuals with known glaucoma were not to report. Approximately 100 individuals, age 60 and above, reported and were subjected to a relatively complete eye examination including the following specific tests:

1. Goldmann fields, peripheral and central, using appropriate corrections based on the glasses worn and the patient's age. The smallest isopter which just encompassed the blind spot was used for central fields. Fields were classified as normal, suspect, or pathologic: small enlargements of the blind spot were considered to be normal, marked enlargement (greater than 45 degrees) of the blind spot was considered suspect, and a Bjerrum scotoma was considered pathologic.

2. Applanation pressures done with the Goldmann tonometer followed by tonography. The subject then drank one liter of water in five minutes. A repeat applanation pressure and repeat tonography were performed 40 minutes later.

3. Ophthalmoscopy for appearance of the disk and any other abnormality. All disks were examined by one observer and were graded according to the examiner's impression. Normal disks included those without any suspicion of glaucomatous cupping. If even slightly suspicious of glaucoma, the disk was classified as suspicious. More advanced cupping was classified as probably or definitely pathologic. These disks were graded as far as possible without knowledge of the pressure, tonography, or field results.

4. Gonioscopy: individuals with synechiae or closed angles were excluded from the study.

5. Steroid testing: 59 individuals volunteered for further testing which was done with topical steroids. This consisted of the application by the patient of topical dexamethasone suspension, 0.1 per cent,* to the right eye, three times daily, for a period of four weeks. At the end of four weeks, applanation pressures and tonography were performed and steroids were discontinued. One individual had a spontaneous applanation pressure of 30 in one eye and was eliminated from steroid testing on that basis. Other eliminations included a failure to volunteer for this testing, angles which were felt to be quite narrow and possibly occludable by slight dilation of the pupil, and a history or evidence of previous herpetic corneal disease.

Results and discussion

The results of this study will be discussed from two stand-points: (1) attributes of the normal population, and (2) results of steroid-provocative testing.

Normal population. In order to present the attributes of the normal population, only patients with normal disks and normal fields in both eyes are considered. The distributions of applanation pressures and Po/C after water are presented. The group consisted of 72 patients; 41 were between the ages of 60 and 70, the remainder were 70 and above. Fig. 1 shows the distribution of applanation pressures in this age group. Because a few patients were unable to cooperate for complete testing, 140 eyes were tested; applanation pressures of 20 mm. Hg or greater were found in 17 per cent of eyes, and 23 mm. Hg or more in 5 per cent. The results of the water provocative tonography are shown in Fig. 2. This distribution is plotted as log Po/C, as this method of plotting has been shown to result in a normal distribution of this function. The results show a rather high prevalence of Po/C greater than 100 after water in this group of eyes. The curve is skewed to the right: Po/C greater than 100 occurred in 30 per cent of eyes in this group, and Po/C greater than 138 in 16 per cent. If

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*Maxidex 0.1% kindly supplied by Alcon Laboratories, Fort Worth, Texas.
one examines the group of patients, $P_o/C$ greater than 100 in either eye occurred in 43 per cent of patients. These results were found in patients who from all objective criteria do not have glaucoma. It must be concluded that applanation pressures, and particularly water-provocative tonography, which might be considered abnormal in younger individuals should be interpreted with caution as indications of glaucoma in the older age groups (see Table 1).

**Steroid-provocative testing.** The results of the steroid-provocative testing are shown as a cumulative frequency plot of pressures after steroids in Fig. 3. For this analysis, the entire group of patients tested with steroids to the right eye was used, regardless of the disk and field findings. Previous studies of steroid responsiveness have characterized the homozygous non-responder ($A < 20$ mm. Hg after steroids), the heterozygous responder ($A 20$ to $31$ mm. Hg), and the homozygous responder ($A > 31$ mm. Hg). Applanation pressures of 20 or higher were found in 41 per cent of our steroid-tested patients, a figure

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**Fig. 1.** Applanation pressures in both eyes of individuals aged 60 and over with normal disks and fields.

**Fig. 2.** Log $P_o/C$ after water in both eyes of individuals aged 60 and over with normal disks and fields.
Table I. Applanation pressures and water provocative tonography in patients 60 and over with normal disks and fields

<table>
<thead>
<tr>
<th>Per cent</th>
<th>Applanation pressure</th>
<th>Po/C after water</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 20</td>
<td>&gt; 100</td>
</tr>
<tr>
<td></td>
<td>≥ 23</td>
<td>&gt; 138</td>
</tr>
</tbody>
</table>

Fig. 3. Applanation pressures after steroids (right eye only).

slightly higher than but quite similar to that found in younger age groups. No patients tested with steroids demonstrated applanation pressures greater than 31 mm. The applanation pressures in the right eyes before steroids are shown for all patients, for the heterozygous responders (ng), and for the homozygous nonresponders (nn) in Fig. 4. Statistically significant differences are noted ($t = 2.9$) between the mean applanation pressures before steroids of the ng and of the nn groups. Po/C after water is shown for the same groups in Fig. 5.

Fig. 4. Applanation pressures before steroids (right eye only).

Fig. 5. Po/C after water, before steroids (right eye only).
Table II. Characterization of topical corticosteroid phenotypes in patients 60 and over

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>nn (36 patients)</th>
<th>ng (23 patients)</th>
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<tbody>
<tr>
<td>Applanation before steroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 20</td>
<td>11 (per cent)</td>
<td>35 (per cent)</td>
</tr>
<tr>
<td>Applanation before steroid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 23</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Po/C &gt; 100 after water</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>Po/C &gt; 138 after water</td>
<td>11</td>
<td>31</td>
</tr>
</tbody>
</table>

Table III. Characterization of topical corticosteroid phenotypes in younger and older age groups

<table>
<thead>
<tr>
<th>Phenotypes</th>
<th>nn</th>
<th>ng</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applanation before steroids, age &lt; 60</td>
<td>14.5 ± 2.2</td>
<td>16.0 ± 2.5</td>
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<tr>
<td>Applanation before steroids, age ≥ 60</td>
<td>15.8 ± 3.0</td>
<td>18.0 ± 3.3</td>
</tr>
<tr>
<td>Applanation after steroids, age &lt; 60</td>
<td>16.1 ± 2.4</td>
<td>24.1 ± 4.0</td>
</tr>
<tr>
<td>Applanation after steroids, age ≥ 60</td>
<td>16.0 ± 2.1</td>
<td>23.0 ± 3.0</td>
</tr>
<tr>
<td>Po/C after H₂O &gt; 100 (before steroids), age &lt; 60</td>
<td>5 per cent</td>
<td>32 per cent</td>
</tr>
<tr>
<td>Po/C after H₂O &gt; 100 (before steroids), age ≥ 60</td>
<td>28 per cent</td>
<td>70 per cent</td>
</tr>
</tbody>
</table>

Again, statistically significant differences in the mean Po/C are noted (t = 2.9). Table II summarizes the differences between ng and nn in their presteroid applanation pressures and water-provocative tonograms. Applanation pressures of 20 mm. or higher and Po/C ratios after water of greater than 100 are seen in strikingly higher percentages of ng than in the nn group. Table III compares the steroid provocative data from younger age groups for the nn and ng phenotypes with data derived for the same phenotypes from this study. A general increase due to aging is demonstrated on applanation pressures and Po/C after water for all phenotypes.

We are indebted to Miss Carol Gossin and Mrs. Gay Ackerman for performance of the tonographic and field examinations.

REFERENCES


Discussion

Dr. Becker. There are several factors presented here which should be emphasized. A large number of patients picked up on surveys or on routine examinations do not have glaucoma and never develop glaucoma. Dr. Ballin's work confirms that age is one of the factors that determines the expression of the genetic glaucomatous state. An interesting fact here is that even those who are just carriers of the disease present as they age an increasing prevalence of what we interpret as abnormal pressures, abnormal outflow facilities, and abnormal water tonograms. This means that if one lives long enough the genetic state will reveal itself both in its homozygous and heterozygous aspects by ordinary clinical determinations. The striking thing he pointed out is that the best measure of what we consider the true genetic state, the steroid provocative test, stays constant with age and is not altered by aging per se. I think this presents very exciting possibilities of clinical importance.

Dr. Henkind. I would be interested to know what the blood pressure of these patients was. Is there any vascular basis for glaucoma field defects? It is known that hypertensive individuals with a predisposition to glaucoma may get field defects when their pressures are lower.

Dr. Ballin. We did not measure the blood pressure in this group.

From the floor. I wonder if there can be some comment on the status of the optic nerve in these patients?

Dr. Becker. As I understand it, every patient with any abnormality of the optic nerve or field was eliminated from the study. Therefore, the data presented are entirely from patients who appeared clinically normal. This is a selected normal population and still shows this remarkable number of abnormalities.

From the floor. In this sized group it was a little surprising that you did not get any patients that showed a rise greater than 31 mm. Hg after steroids.
Dr. Ballin. This group was told that no glaucoma patients were to report and so it was somewhat selected. It may well be that, in this older age group, the genetic predisposition for glaucoma should have manifested itself by this time and that group is already selected out by our method of selection.

Dr. Becker. Isn’t it true that in this series there were patients found with glaucoma who, therefore, were not studied? In other words, the glaucoma patient was not included in the series.

Dr. Ballin. Yes. I think there were one or two patients who had pressures over thirty. We did not test them.