Dexamethasone testing in Southwestern Indians

Louis J. Rosenbaum, Ellen Alton, and Bernard Becker

Indians of the Southwestern United States demonstrated prevalences of primary open-angle glaucoma and responsiveness to topical dexamethasone which were comparable to nonIndian St. Louis populations. In both populations plasma cortisol suppression by oral dexamethasone was decreased in individuals in the group most responsive to topical dexamethasone. Indians demonstrated very high prevalences of phenylthiourea tasters and positive oral glucose tolerance tests but, contrary to the St. Louis populations, these two parameters did not correlate with the topical dexamethasone response.

Key words: dexamethasone, North American Indian, intraocular pressure increase, phenylthiourea taste test, glucose tolerance test, local drug administration, hydrocortisone, open-angle glaucoma.

Primary open-angle glaucoma has been reported to occur rarely in Indians of the Southwestern United States.1 In addition, phenylthiourea nontasters were found to be common among patients with primary open-angle glaucoma,2 but were reported to be extremely rare in Indians.3 However, an impressive number of patients with primary open-angle glaucoma have been seen in the Eye Clinic of the Phoenix Indian Hospital. Furthermore, diabetes mellitus has been reported to be especially frequent in Indian populations.1,4-6 Since there is an increased prevalence of response to topical corticosteroids in diabetic patients as well as in patients with primary open-angle glaucoma,7-10 we evaluated topical corticosteroid testing in a group of Indian volunteers.

Method

Patient selection. All patients had been hospitalized at Osbrin Hospital for treatment of tuberculosis and were on therapy for at least 2 weeks prior to the study. In such a "captive population," medications could be administered reliably by nurses.

Topical corticosteroid testing. The unselected hospitalized volunteers ranged in age from the third to the ninth decade (Fig. 1). They came from 11 different tribes, but most were Papago or Apache. All had base-line examinations which included visual acuity, manifest refraction, external examination (especially for trachoma), pupillary and motility examinations, ophthalmos-
copy for evaluation of the optic disc and diabetic retinopathy, slit lamp examination, applanation tonometry, tonography, and gonioscopy. Dexamethasone,* 0.1 per cent ophthalmic solution, was instilled into one eye 4 times a day for 6 weeks by a registered nurse. Intraocular pressure was checked weekly, and the entire examination was repeated at the end of 6 weeks.

**Plasma cortisol suppression test.** Fasting blood was drawn into heparinized tubes at 8 A.M. for base-line plasma cortisol values. At 11 P.M., 1 mg. of dexamethasone was given orally, and fasting blood was obtained at 8 A.M. the following morning for plasma cortisol levels. Plasma cortisol was measured by the method of Mattingly.11

**Oral glucose tolerance test.** Fasting blood for glucose was obtained. A 75 Gm. load of glucose was given orally, and 

1/2, 1 hour, and 2 hour blood specimens were drawn. Patients who demonstrated diabetic curves had repeat tests.

**Phenylthiourea taste testing.** Solutions of phenylthiourea were prepared in the manner described by Harris and Kalms,12 and administered as described by Becker and Morton.2 Patients who failed to taste 8 mg. per cent were considered nontasters.

**Results**

**Intraocular pressure response to topical dexamethasone.** The intraocular pressure in control eyes presented a normal distribution curve prior to and following topical dexamethasone administered to the opposite eye (Fig. 2). The experimental eyes, which also behaved as a single population prior to topical dexametha-
Fig. 3. Intraocular pressure before and after 6 weeks of topical dexamethasone 0.1 per cent four times daily to test eye.

Fig. 4. Cumulative frequency plot of intraocular pressure in experimental eye before and after 6 weeks of topical dexamethasone 0.1 per cent four times daily. Note single population before and more than one population after 6 weeks.
sone, appeared to be distributed as 3 populations following 6 weeks of topical dexamethasone. The populations could be separated into poor responders (intraocular pressure rose to less than 23 mm. Hg), intermediate responders (23 to 33 mm. Hg), and high responders (greater than 33 mm. Hg) (Figs. 3 and 4). By these criteria, there were 27 (57 per cent) poor responders, 15 (32 per cent) intermediate responders, and 5 (11 per cent) high responders. For direct comparison with intraocular pressure values used in prior studies on St. Louis populations, 23 patients (49 per cent) had intraocular pressure rises to less than 20 mm. Hg (nn group), 17 (36 per cent) rose to 20 to 31 mm. Hg (ng group), and 7 (15 per cent) rose to greater than 31 mm. Hg (gg group) after 6 weeks of topical dexamethasone (Table I).

Plasma cortisol suppression. The mean suppression ratio (plasma cortisol 24 hours/plasma cortisol 0 hours) following 1 mg. of oral dexamethasone for the nn group was 20 per cent of base line with a standard deviation of 10 per cent (Fig. 5). There was no significant difference between the 23 patients whose intraocular pressure rose to less than 20 and the 27 whose intraocular pressure rose to less than 23 mm. Hg. There were 7 patients who had plasma cortisol levels greater than 40 per cent of their base-line value. None of these were classified as low responders, 3 were intermediate responders, and 4 were high responders to topical dexamethasone. Thus in the gg group, 4 (57 per cent) of 7 and in the ng group 3 (17 per cent) of 17 had ratios greater than 40 per cent (Table II).

Glucose tolerance. A plasma glucose level greater than 160 mg. per cent two hours after 75 Gm. of oral glucose was considered positive. On this basis, 22 patients had positive glucose tolerance tests. These were classified as 11 nn, 7 ng, and 4 gg individuals (Table III and IV). In contrast to the St. Louis populations, diabetic and nondiabetic Indians demonstrated no significant difference in response to topical corticosteroids. Only one patient had nonproliferative diabetic retinopathy and he was in the nn group.

Phenylthiourea taste test. There were no nontasters among the 47 Indians tested (Table V).

Other observations. There were no changes in visual acuity greater than one line on the Snellen chart. No ptosis or mydriasis was noted following administration of topical steroids. There were 22 patients with Stage IV trachoma but no evidence of activation of the disease while on topical steroids.

Table I. Tucson Indian study; topical dexamethasone test

<table>
<thead>
<tr>
<th></th>
<th>Applanation pressure (mm. Hg) after steroids (6 weeks)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 23 (%)</td>
</tr>
<tr>
<td>Indians</td>
<td>47</td>
</tr>
<tr>
<td>St. Louis volunteers</td>
<td>200</td>
</tr>
</tbody>
</table>

Fig. 5. Comparison of suppression ratios (plasma cortisol 24 hours/plasma cortisol 0 hours) following oral dexamethasone (1 mg.) in nn, ng, and gg populations.
Table II. Tucson Indian study; cortisol suppression

<table>
<thead>
<tr>
<th>Group</th>
<th>nn</th>
<th>ng</th>
<th>gg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indians</td>
<td>&gt; 40%*</td>
<td>0/22 (0%)</td>
<td>3/17 (18%)</td>
</tr>
<tr>
<td>St. Louis</td>
<td>≥ 65%*</td>
<td>1/40 (3%)</td>
<td>3/54 (6%)</td>
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</table>

*Two standard deviations from mean in nn population.

Table III. Tucson Indian study; diabetes and topical corticosteroid test

<table>
<thead>
<tr>
<th></th>
<th>Applanation pressure (mm. Hg) after steroids (6 weeks)</th>
<th>No.</th>
<th>&lt;20 (%)</th>
<th>20-31 (%)</th>
<th>&gt; 31 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indian diabetics</td>
<td></td>
<td>22</td>
<td>56</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td>Indian nondiabetics</td>
<td></td>
<td>25</td>
<td>48</td>
<td>40</td>
<td>12</td>
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<tr>
<td>St. Louis diabetics</td>
<td></td>
<td>100</td>
<td>36</td>
<td>47</td>
<td>17</td>
</tr>
<tr>
<td>St. Louis nondiabetics</td>
<td></td>
<td>100</td>
<td>60</td>
<td>34</td>
<td>6</td>
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Table IV. Tucson Indian study positive glucose tolerance*

<table>
<thead>
<tr>
<th></th>
<th>Indians</th>
<th>St. Louis</th>
</tr>
</thead>
<tbody>
<tr>
<td>nn</td>
<td>11/23 (48%)</td>
<td>1/34 (3%)</td>
</tr>
<tr>
<td>ng</td>
<td>7/17 (41%)</td>
<td>2/38 (5%)</td>
</tr>
<tr>
<td>gg</td>
<td>4/7 (57%)</td>
<td>17/97 (17%)</td>
</tr>
<tr>
<td>Total</td>
<td>22/47 (47%)</td>
<td>(63% over 40 yr.)</td>
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*Two hour > 160 mg. per cent.

Table V. Tucson Indian study; phenylthiourea taste test (per cent nontasters)

<table>
<thead>
<tr>
<th></th>
<th>nn (%)</th>
<th>ng (%)</th>
<th>gg (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indians</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>St. Louis (Caucasian)</td>
<td>25</td>
<td>33</td>
<td>52</td>
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Discussion

It appears that Indians of the Southwestern United States have the same or slightly greater gene prevalence for pressure responsiveness to topical corticosteroids as do nonIndian populations (Table I). The small differences between the St. Louis volunteers and the Indians is not significant. Although high responsiveness to topical dexamethasone testing and primary open-angle glaucoma may not be identical, they are certainly closely related. It is therefore of interest to note that a review of adult Indian outpatient visits to the eye clinic of the Phoenix Indian Hospital shows the incidence of open-angle glaucoma to be approximately that found in a nonIndian population.

As found by Levene and Schwartz and confirmed by Becker and Ramsey, a negative correlation exists between the rise in intraocular pressure following topical steroids and the suppression of plasma cortisol by oral dexamethasone. This is also found in an Indian population (Table II).

Many authors have reported a higher prevalence of increased intraocular pressure in diabetic patients. In addition, Becker and associates found more high and intermediate responders to topical steroids among diabetic patients than in a nondiabetic (nonIndian) volunteer population. Conversely, Armaly and Baloglu claim that diabetic adults have a decreased intraocular pressure at various ages and that diabetic patients have no greater frequency of ocular hypertension than control subjects. However Armaly does find a greater frequency of responders to topical corticosteroids in Caucasian juvenile diabetic patients. Indian diabetic patients do not show a higher prevalence of responsiveness to topical corticosteroid testing than do Indian nondiabetes. This
is in marked contrast to non-Indian St. Louis populations (Table III).

In non-Indians there is a significantly greater prevalence of positive oral glucose tolerance tests in the gg responders than in nn and ng populations. However, Indians tested in this study show no significant relationship between responsiveness to topical steroid testing and oral glucose tolerance testing (Table IV).

Another genetic marker which relates to primary open-angle glaucoma is the inability to taste phenylthiourea. Becker and Morton found 53 per cent nontasters in Caucasians with primary open-angle glaucoma as compared with 28 per cent nontasters in non-glaucomatous Caucasians. Thirty-seven per cent of St. Louis Negroes with primary open-angle glaucoma were nontasters, while only 17 per cent of non-glaucomatous Negroes were so classified. However, Indians appear to show no correlation between phenylthiourea taste testing and topical steroid responsiveness (Table V).

REFERENCES