
Corticosteroid provocative testing

Raymond P. LeBlanc,* R. H. Stewart,** and Bernard Becker

Topical corticosteroid provocative testing for three to eight weeks was carried out on three groups of patients in order to evaluate effects on aqueous dynamics and visual fields. All changes were reversible and no long-term effects were noted.

Key words: corticosteroid provocative testing, intraocular pressure, open-angle glaucoma, aqueous dynamics, visual field.

Increased intraocular pressure as a response to topically applied corticosteroids has been the subject of many clinical and experimental investigations. Furthermore, the corticosteroid provocative test has become an important parameter of investigation in the study of the genetics of primary open-angle glaucoma.¹⁻¹² In such studies, and more significantly with the increased use of topical corticosteroids, questions have been raised as to the possible irreversible intraocular pressure and visual field changes induced by short-term medication.⁵ Therefore, a controlled prospective study has been carried out of aqueous dynamics and visual field studies during and follow-

ing short-term topical corticosteroid provocative testing.

Materials and methods

Selection of patients.

Group I: Effects on aqueous dynamics. Five hundred patients, including normal volunteers, subjects with ocular hypertension, siblings and offspring of glaucoma patients, and patients with secondary or primary open-angle glaucomas, were subjected to provocative testing with topical dexamethasone, 0.1 per cent every other day to one eye only for six weeks.

Group II: Effects on visual fields. Seventy patients with no evidence of field loss were selected on the basis of an applanation pressure response after six weeks of topical corticosteroids to levels over 30 mm. Hg.

Group III: Long-term follow-up. Seventy-five siblings and offspring of glaucoma patients were selected for this part of the study. Complete eye examinations were performed on each patient at yearly intervals for a minimum of three consecutive years prior to steroid testing. In 1965 each patient received topical corticosteroid testing to one eye only with the use of 0.1 per cent betamethasone. Weekly evaluations were made to monitor the response of intraocular pressure and the period of testing was extended from three to eight weeks. Four yearly follow-up studies were available on each of these patients. None has had further topical corticosteroid testing or any other eye medication.

Method of testing. For all groups, the testing protocol included a general medical history;

From the Glaucoma Center, Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo.

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*Dr. LeBlanc is a Fellow of the McLaughlin Foundation, Toronto, Ontario, Canada.

**Dr. Stewart is a Fellow of the Heed Foundation.

ocular history; and complete ocular examination, including visual acuity, refraction, perimetry (Goldmann-kinetic), applanation tensions, tonography, gonioscopy, and fundus examination. These parameters were repeated as indicated in the course of testing and again in the follow-up visits.

For patients in Group II, additional visual testing was done with the use of static circular technics on the Goldmann perimeter. This was carried out for baseline values, at the height of the intraocular pressure rise, and at the conclusion of the provocative test period.

Statistical method. The long-term follow-up of topical corticosteroid provocative testing for three to eight weeks upon aqueous dynamics (Group III) was evaluated by statistical analysis, in which a factor (value of test eye minus the value of control eye) was determined. This factor was then compared (paired t test) for the periods before and after the corticosteroid test.

Results

Group I: Effects on aqueous dynamics.

In the group of 500 consecutive provocative tests with topical corticosteroids, all elevations of intraocular pressure were completely reversible. In each case, applanation tensions and facility of outflow values obtained upon cessation of the test were the same as the baseline values. Some of the patients (25 per cent) were subjected to a repeat provocative test on the same eye, and again demonstrated a return to baseline values upon completion of the test. The return to baseline values occurred within ten days in 98 per cent of patients; all eyes were back to normal by 21 days.

Group II: Effects on visual fields. The 70 selected patients in this group seemed most likely to demonstrate changes in their visual fields because of pronounced elevations in intraocular pressure. The careful evaluation of visual fields was made by five independent observers, none of whom knew which eye had been subjected to topical corticosteroids or which fields were "before" or "after" the test. Glaucomatous-type field loss in the Bjerrum area was recorded in 14 (20 per cent) of the 70 eyes and always was confined to the eye with the induced elevation of intraocular pressure. In all instances these changes were

Table I. Long-term follow-up of topical corticosteroid testing: statistical analysis; tested vs nontested

	Mean*	S.E.M.	P value
<i>Applanation intraocular pressure</i>			
Baseline	0.195	0.61	p > 0.7 < 0.8
After H ₂ O provocative	-0.730	0.495	p > 0.1 < 0.2
Change after H ₂ O provocative	-0.006	0.008	p > 0.4 < 0.5
<i>Facility of outflow</i>			
Baseline	-0.002	0.006	p > 0.7 < 0.8
After H ₂ O provocative	-0.426	0.108	p > 0.2 < 0.3
Change after H ₂ O provocative	0.004	0.009	p > 0.6 < 0.7

*Mean of difference (before test minus after test) value for each patient.

completely and promptly reversible when topical corticosteroids were discontinued.

Group III: Long-term follow-up. Statistical analysis of aqueous dynamics parameters in this group of 75 patients who were relatives of glaucoma patients was carried out in order to evaluate any long-term effects of the three to eight weeks of topical corticosteroid provocative testing. The evaluation of intraocular pressure compared the pre-provocative corticosteroid test period to the period after the test and showed no significant difference (p > 0.7). Similarly, in comparing the same periods for intraocular pressure changes induced by water loading (both final applanation values and change of pressure), no significant differences were noted (p > 0.1, p > 0.4). When similarly designated facility of outflow values was compared, again no statistically significant changes were noted (p > 0.7, p > 0.2, p > 0.6) (Table I). The method of analysis used the untested eye as a control and so had a built-in age correction factor.

Discussion

The results of the study confirm that changes in aqueous humor dynamics and

visual fields induced by topical corticosteroid provocative testing are completely reversible. This is true for all ranges of pressure response and in all categories of patients studied. More important, no detectable permanent changes in aqueous dynamics are demonstrated after a four-year follow-up. Most observers note complete reversibility of pressure and field changes induced by topical corticosteroid testing.^{3, 6, 7, 9, 11} Francois et al.,⁵ however, report irreversible elevations of intraocular pressure in six patients out of 876 tested. The question remains unresolved as to whether these high responders had ocular hypertension before the testing. Although we see glaucoma which is aggravated to the point of extensive damage by topical corticosteroids, we also see referred cases of apparent corticosteroid-induced glaucoma with cupping and field loss¹³ in which aqueous dynamic changes are reversible. To describe changes as irreversible, one must have adequate baseline studies of aqueous dynamics and visual fields prior to topical corticosteroids. No lens changes were seen in the present study nor have they been described after short-term testing with topical corticosteroids. However, with more extended use of topical corticosteroids, subcapsular opacities have been reported.¹³

In Group II, a "high risk" population, reversible visual field changes are observed much as described by Kolker and associates,¹⁰ Armaly,⁸ Nordmann and associates,¹¹ and Lobstein.¹² It is of considerable interest that one of Kolker and associates¹⁰ reported cases has diabetes and two others have abnormal glucose tolerance tests. Of the 70 patients of Group II in the present series, 13 (19 per cent) demonstrate diabetes or abnormal glucose tolerance tests (sum plasma glucose at 0, 60, 120, and 180 minutes of 600 mg. per cent or more).¹⁴ However, of the 14 patients showing pressure-induced field changes, eight (57 per cent) have

diabetes or positive glucose tolerance tests. The possible role of abnormal carbohydrate metabolism in glaucomatous field loss needs further evaluation.

REFERENCES

1. Goldmann, H.: Cortisone glaucoma, *Arch. Ophthalmol.* **68**: 621, 1962.
2. Goldmann, H.: Cortisone glaucoma, *Int. Ophthalmol. Clin.* **6**: 991, 1966.
3. Becker, B., and Mills, D. W.: Corticosteroids and intraocular pressure, *Arch. Ophthalmol.* **70**: 500, 1963.
4. Becker, B., and Hahn, K. A.: Topical corticosteroids and heredity in primary open-angle glaucoma, *Arch. Ophthalmol.* **70**: 492, 1963.
5. Francois, J., et al.: The cortisone test and the heredity of primary open angle glaucoma, *Amer. J. Ophthalmol.* **62**: 844, 1966.
6. Armaly, M. F.: Effects of corticosteroids on intraocular pressure and fluid dynamics. I. The effect of dexamethasone in the normal eye, *Arch. Ophthalmol.* **70**: 482, 1963.
7. Armaly, M. F.: Effects of corticosteroids on intraocular pressure and fluid dynamics. II. The effect of dexamethasone in the glaucomatous eye, *Arch. Ophthalmol.* **70**: 492, 1963.
8. Armaly, M. F.: Effects of corticosteroids on intraocular pressure and fluid dynamics. III. Changes in visual function and pupil size during topical dexamethasone application, *Arch. Ophthalmol.* **71**: 636, 1964.
9. Becker, B.: Intraocular pressure response to topical corticosteroids, *INVEST. OPHTHAL.* **4**: 198, 1965.
10. Kolker, A. E., Becker, B., and Mills, D. W.: Intraocular pressure and visual fields: Effect of corticosteroids, *Arch. Ophthalmol.* **72**: 772, 1964.
11. Nordmann, J., Lobstein, A., Gerhard, J. P., and Benck, P.: Le test á la cortisone dans le glaucome simple á champ visuel normal, *Ophthalmologica* **150**: 1965.
12. Lobstein, A.: Factors affecting the susceptibility of the glaucomatous eye to raised intraocular pressure, *Bibl. Ophthalmol.* **74**: 73, 1968.
13. Burde, R., and Becker, B.: Corticosteroid-induced glaucoma and cataracts in contact lens wearers, *J.A.M.A.* **213**: 2075, 1970.
14. Becker, B., and LeBlanc, R. P.: The glucose tolerance test and the response of intraocular pressure to topical corticosteroids, *Diabetes*, **19**: 715, 1970.