Comparative study of the intraocular pressure effects of fluorometholone 0.1% versus dexamethasone 0.1%

A. O. AKINGBEHIN

From Southport General Infirmary, Scarisbrick New Road, Southport, Merseyside PR8 6PH

SUMMARY The intraocular pressure effect of fluorometholone 0.1% was compared with that of dexamethasone 0.1% by performing corticosteroid provocative tests on 24 matched pairs of eyes. Fifteen of the 24 dexamethasone treated eyes, 62.5%, showed a change in intraocular pressure greater than 5 mmHg, with mean ΔP=8.58 mmHg and range 0 to +20 mmHg. Only 2 of the 24 fluorometholone treated eyes, 8.3%, showed a change in pressure greater than 5 mmHg, with mean ΔP=2.96 mmHg and range -2 to +14 mmHg. There was a highly statistically significant difference between the intraocular pressure effects of topical dexamethasone and fluorometholone (correlated t test, p<0.001). Fluorometholone would appear to be the topical steroid of choice for patients with glaucoma and other known steroid responders when topical steroid treatment is indicated.

The single most important factor which has restricted the use of topical corticosteroids in ophthalmic practice is the failure to eliminate the adverse effects of these drugs. A measure of this restriction can be gained from the immense interest in, firstly, modifying the basic structure of the anti-inflammatory corticosteroid to retain its anti-inflammatory activity without the adverse effects. With regard to systemic corticosteroids, a new class of anti-inflammatory steroids, the glucocorticoid 21-oic acid esters, have been synthesised by modifying the 17-ketol side chain of cortisol and prednisolone with the hope that they retain significant local anti-inflammatory activity but would be hydrolysed to the inactive free acids and hence cause minimal side effects.1 Secondly, there has been much interest in the therapeutic application of the knowledge that some forms of ocular inflammation are entirely or partly mediated by prostaglandin synthesis,2-4 and consequently in the development of nonsteroidal anti-inflammatory drugs.

Manipulation of the basic structure of the anti-inflammatory corticosteroid has produced a variety of synthetic analogues, but only a few of these represent significant therapeutic gains in terms of the ratio of anti-inflammatory potency to unwanted effects. Fluorometholone (21-desoxy-9-fluoro-6 methyl prednisolone) is such a product, an anti-inflammatory steroid with structural characteristics in common with progesterone and found to have anti-inflammatory activity 25 to 50 times that of hydrocortisone5 but without the same propensity to raise intraocular pressure.6-7 This effect is thought to be related to the chemical structure of fluorometholone, specifically, the deoxygenation at the C21 position.

This study was designed to compare the intraocular pressure effect of fluorometholone with that of dexamethasone, a topical steroid with an established high tendency to raise intraocular pressure.

Materials and methods

Twenty-four patients were entered in a comparative study of the intraocular pressure effects of topical dexamethasone and fluorometholone. Twenty-two eyes were provoked with dexamethasone and 6 months later with fluorometholone. The remaining 2 patients were subjected to simultaneous bilateral provocative testing, receiving dexamethasone in the right eyes and fluorometholone in the left eyes.

The corticosteroid provocative testing was performed with eyedrops of either dexamethasone 0.1% or fluorometholone 0.1% 4 times a day for 6 weeks but terminated earlier if the change in intraocular pressure was greater than 15 mmHg. Both preparations are available only in suspension form, and the patients were specifically instructed to shake the container several times before use.
Details of the corticosteroid provocative test were given in an earlier paper.9

Results

The intraocular pressures and outflow facilities (C values) before the dexamethasone and the fluorometholone provocative tests were similar. The 22 eyes subjected to repeat provocative testing were made up as follows: 11 closed-angle glaucoma eyes, 10 fellow eyes, and 1 eye with ocular hypertension. Of the 2 patients who had both eyes provoked simultaneously one had ocular hypertension and the other was referred for exclusion of glaucoma.

Fifteen of the dexamethasone treated eyes, 62.5%, showed a change in intraocular pressure greater than 5 mmHg, with mean ΔP=8.58 mmHg and range 0 to +20 mmHg. Only 2 of the fluorometholone treated eyes, 8.3%, showed a change in pressure greater than 5 mmHg, mean ΔP=2.96 mmHg, range −2 to 14 mmHg.

The mean reduction in outflow facility in the dexamethasone treated eyes was −0.044 μl/min/mmHg compared with −0.019 μl/min/mmHg for the fluorometholone treated eyes. The results are shown in detail in Table 1.

Discussion

There is a highly statistically significant difference between the intraocular pressure effects of topical dexamethasone and fluorometholone (correlated t test, t=4.63, DF=23, p<0.001): mean ΔP of +8.58 mmHg for dexamethasone compared with +2.96 mmHg for fluorometholone. This difference between the 2 groups is also reflected in the percentage of steroid responders in each group—dexamethasone 62.5% compared with fluorometholone 8.3%.

The 2 fluorometholone treated eyes with positive steroid response showed a change in pressure of +8 mmHg and +14 mmHg, compared with +12 mmHg and +20 mmHg respectively when the same eyes were provoked with dexamethasone.

From the results of this study it would appear that fluorometholone has a substantially lower tendency to raise intraocular pressure than dexamethasone. If this significant difference is to be attributed to the chemical structure of fluorometholone, it must be
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shown that the drug can penetrate the cornea and be detected in aqueous in concentrations comparable with those of other steroids. There is evidence to suggest that after a single standard drop of fluorometholone 0.1% measurable levels of the unchanged drug were found in the aqueous.9 10

The prevalence of corticosteroid-induced ocular hypertension in glaucomatous eyes ranges from 65% in closed-angle glaucoma to 92% in open-angle glaucoma.11 12 Other eyes with trabecular damage have also been shown to have a high prevalence of steroid response.13 There is evidence to suggest that up to 25% of glaucomatous eyes following trabeculectomy may develop a significant rise in intraocular pressure in the immediate postoperative period when treated with topical steroids in spite of a successful drainage operation.14 It would therefore appear that there is a need for an effective anti-inflammatory drug with a very low propensity to raise intraocular pressures in the postoperative management of patients with glaucoma and other steroid responders.

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References


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A O Akingbehin

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