
Tetrahydrotriamcinolone and triamcinolone

II. Effect on xenograft reaction in rabbits

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Triamcinolone (TA) and tetrahydrotriamcinolone (THTA) are similar in structure and ocular penetration capabilities but differ markedly in pressure-elevating potential in susceptible individuals. The present study, using pig-corneal xenografts in rabbits, showed a small effect in preventing rejection using 0.25 per cent THTA, while 0.25 per cent TA and 0.001 per cent dexamethasone phosphate were effective.

Key words: triamcinolone, tetrahydrotriamcinolone, dexamethasone, ocular inflammation, corticosteroid-induced glaucoma, xenograft.

In a previous study¹ we have shown that tetrahydrotriamcinolone acetonide dipotassium phosphate (THTA) and triamcinolone acetonide dipotassium phosphate (TA), which differ structurally only in the degree of saturation of their steroid nucleus but differ markedly in their effects on intraocular pressure in corticosteroid-responsive individuals,²⁻⁴ penetrated the eye with approximately equal facility. In an attempt to further characterize these drugs their relative anti-inflammatory effect has been compared in an animal model.

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Materials and methods

Lamellar corneal pockets were dissected, according to the method of Lorenzetti and Kaufman,⁵ in both eyes of two to three kilogram albino rabbits. The animals were anesthetized with intramuscular chlorpromazine, intravenous sodium thiopental, and topical proparacaine, and clean but not sterile technique was used. Six millimeter, full thickness corneal buttons, including epithelium, were taken from freshly obtained pig eyes and were implanted centrally in these pockets. Both corneal buttons used in each recipient rabbit were obtained from the same donor eye. One 8-0 black silk suture was used to close the corneal wound and was left in place for the duration of the experiment. At the end of the surgical procedure, topical atropine and neomycin-polymixin-bacitracin ointment were instilled in the eyes of each rabbit.*

The rabbits were divided into four treatment groups (Table I). The rabbits in Group I received no topical medication to either eye. The animals in Group II received one drop of 0.001 per cent dexamethasone phosphate topically in one eye,

*Because of high infection rates in the fourth group, corneal buttons were soaked in neomycin-polymixin-bacitracin solution prior to implantation and 300,000 units of procaine penicillin-G was injected intramuscularly at the end of the procedure.

Table I. Effect of topical corticosteroid therapy on xenografts

Group		Number of eyes	Per cent rejected	Average day of rejection
I. Controls	All untreated	21	81.0	10.0
II. Dexamethasone(0.001%)	Treated eyes	16	31.3	12.6
	Untreated eyes	13	92.0	11.4
III. THTA (0.25%)	Treated eyes	15	66.7	10.2
	Untreated eyes	11	90.9	09.9
IV. TA (0.25%)	Treated eyes	15	00.0	—
	Untreated eyes	12	83.3	16.1

three times daily, starting on the third postoperative day. The Group III animals received one drop of 0.25 per cent THTA in one eye, three times daily, and Group IV received one drop of 0.25 per cent TA suspension in one eye, three times daily, starting on the third postoperative day. Topical therapy was continued in all groups until the twenty-first postoperative day. Any animals that died during the experiment, or eyes that became infected before the end of the experimental protocol, were excluded from the study.

All rabbits were evaluated daily for clarity and degree of vascularization, both of the host cornea and of the implanted corneal xenograft. The grading system involved the subjective assignment of a number from zero to 4+ to the evaluated corneas. A reaction of zero denoted that the host and implanted tissues were clear; 1+ and 2+ indicated increasing degrees of cloudiness of implanted tissue; 3+ noted the presence of vascularization of the donor cornea; and 4+ denoted vessels extending into the xenograft. At the end of the evaluation period, zero to 2+ was considered to denote no rejection process, and 4+ was termed "rejected." The day of onset of rejection and the percentage of eyes showing rejection from each group were recorded.

Results

At the end of the treatment period all eyes fell into two groups: Zero to 1+ or 4+. The percentage of xenografts rejecting in each group and the average day of onset of rejection are shown in Table I. In Group I, the control group, 81 per cent of xenografts rejected with the average day of rejection occurring on day ten. In Group II, the animals receiving 0.001 per cent dexamethasone, there was a rejection rate of approximately 31 per cent with the average day of rejection being 12.6 days, while the contralateral untreated eye showed re-

jection in 92 per cent of eyes with the average day of rejection being 11.4 days. In Group III, the animals treated with 0.25 per cent THTA, rejection was decreased to approximately 67 per cent with an average day of onset of rejection of 10.2 days, while 91 per cent of the untreated contralateral eyes showed rejection, on the average, at 9.9 days. The Group IV rabbits, treated with 0.25 per cent TA, demonstrated no rejection in the treated eyes, while 83.3 per cent of the contralateral eyes showed rejection, on the average, at 16.1 days.

Discussion

It is apparent that TA is more effective than THTA in preventing xenograft rejection in this model. The prolongation of xenograft survival in the untreated contralateral eyes in the group receiving TA suggests that there is a systemic effect achieved from the absorption of the TA. Dexamethasone, diluted 100-fold from the common clinical dosage, is also more effective than THTA in preventing the xenograft rejection phenomenon.⁶

THTA has been demonstrated by Kolker and Becker⁷ to be clinically effective in suppressing the allergic reactions of certain patients to topical glaucoma medication. No other clinical or experimental data on THTA in ophthalmic use are available to us. In topical application of TA and THTA to skin, it has been shown that TA is between six and eighteen times as effective as THTA in suppressing pituitary-adrenal function.⁸

The relative inability of THTA to raise

intraocular pressure in susceptible individuals and its relative ineffectiveness as an anti-inflammatory agent when compared to TA,³ despite the similar ocular penetration of these drugs,¹ raises the possibility that the anti-inflammatory potency and ability of a drug to induce rises in intraocular pressure are linked. This hypothesis has been raised before,⁹ and indeed it has been shown that reducing the concentration of effective corticosteroids not only decreases their anti-inflammatory effects but also their pressure-elevating effects in susceptible individuals.^{4, 6, 10} The fact that these great differences occur between two drugs of such similar structure, when used in the same concentration, is of interest.

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