Effects of cyclosporine in an experimental rat model of dry eye.

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Background

Dry eye syndrome is characterized by subclinical or clinical dry eye symptoms affecting the ocular surface. The classification of dry eye syndrome is based on the symptoms and signs of the ocular surface. The causes of dry eye syndrome are varied and include pathologies involving the ocular surface, lacrimal gland dysfunction, and hormonal causes. It is considered that 15 to 25% of the population aged over 65 is treated by tear substitute.

The first two groups were instilled in both eyes with either saline or CsA by oral administration from D1 to D21. Complications of saline solution showed a rapid and significant decrease of lacrimation by D7. Topical administration of CsA (Restasis®) had no effect on this parameter in contrast to oral administration of CsA. In topical CsA, the tBUT values for this latter were not modified in contrast to oral administration of CsA. In topical CsA, the tBUT values for this latter were not modified in contrast to oral administration of CsA.

Results

Cotton Thread Test

The rats treated with saline solution showed a rapid and significant decrease of lacrimation by D7. Topical administration of CsA (Restasis®) had no effect on this parameter in contrast to oral administration of CsA. In topical CsA, the tear volumes were closed to the baseline values except on D14.

Fluorescein Staining

Instillations of saline solution did not prevent dry eye signs. A relatively severe keratitis punctata was visible by D7 as illustrated by a significant increase of the score (300%). Unlike lacrimation, Restasis® reduced the epithelial damage mostly by D14. Oral CsA showed a marked reduction of corneal damage by mostly by D14. Oral CsA showed a reorganization of the cornea of a rat treated with saline (A) showed a reorganization of the cornea and an infiltration by numerous inflammatory cells located in the stroma and near the limbus. In the groups treated with oral CsA (B), no inflammatory cell was observed and the cornea did not show any abnormality.

Conclusions

Cyclosporine A orally or topically administered significantly reduced clinical signs of dry eye by increasing lacrimation or decreasing corneal defect. Oral administration of cyclosporine A seems more effective.

References


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Material and method

Animals

Fifteen female Lewis albino rats (180-200g) were randomized in three groups of five animals. Animals were housed and cared for according to the ARRIVE Statement for the Use of Animals in Ophthalmic and Vision Research. Food and water were available ad libitum. Rats were kept under controlled temperature (22+/-1°C), humidity (55-65%) and 12h:12h light-dark cycle (10-200 lux).

Induction of Dry Eye

Experimental dry eye was induced in rats by a systemic and continuous delivery of scopolamine (20 mg/day) over 21 days via osmotic pumps (2ML4 Alzet®, Charles River Laboratories, France) implanted subcutaneously on D1.

Treatment

The first two groups were instilled in both eyes with either saline or CsA (Restasis® 0.05%, Allergan) three times daily from D1 to D21 and the third group received 20mg/kg/day CsA by oral administration from D1 to D21.

Cyclosporine A (CsA) is the main drug used to treat dry eye syndrome.

Statistical analysis

Result were expressed as mean +/- SD. Data were compared using the nonparametric Mann-Whitney statistical test. * p < 0.05.