Impact of the routes of administration on the effects of cyclosporine in an experimental rat model of dry eye.

Nicolas Cimbolini, Sophie Grillo-Antonelli, Laurence Feraillle, Philippe Margaron, Pierre-Paul Elena. Iris Pharma, La Gaude, France.

Background

Dry eye syndrome is with cataract and AMD, the main eye pathology in the elderly population. It is considered that 15 to 25% of the population aged over 65 is treated by tear substitute. The causes of dry eye syndrome are varied and include pathologies involving lacrimal hyposecretion or hypersecretion. The classification1 differentiates dry eye by hyposecretion syndromes and syndromes involving lacrimal hyposecretion or hypersecretion. The important roles played by inflammation in the elderly population. It is considered that 15 to 25% of the population aged over 65 is treated by tear substitute.

Material and method

Animals

Fifteen female Lewis albino rats (180-200g) were randomized in three groups of five animals. Animals were handled 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 topical administrations on this dry eye models in rats. Lacrimal substitution have been the basis of the treatment of moderate dry eye. But new treatments targeting immunological, inflammatory and hormonal causes are under development.

Cyclosporine A (CsA) is the main representative of this new generation of treatments. It has been shown that rodent models of dry eye experimentally induced by scopolamine4, a tropine alkaloid drug with muscarinic antagonist effects, could be helpful to test and select therapeutic candidates in the disease.

Here we propose to compare the action of cyclosporine A, an inhibitor of T-cell activation and inflammatory cytokine production, after oral and topical administrations on this dry eye models in rats.

Clinical Evaluations

Tear production was measured with the cotton thread test (Zone Quick, FC1 Ophthalmics, USA) in the lateral canthus of the conjunctival fornix for 30 seconds. Tear break-up time and corneal defects were examined by slit-lamp observation using blue light after instillation of 2µl of 0.5% sodium fluorescein. Punctuate staining was measured with grading system (National Eye Institute) giving a 0-3 score to each of 5 areas of a divided cornea for a maximum score of 15.

Statistical analysis

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

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 CsA. tBUT values for this latter were not modified in the time of experiment.

Fluorescein Staining

Instillations of saline solution and CsA (Restasis®) did not affect the quality of tears in contrast to oral CsA. tBUT values for this latter were not modified in the time of experiment.

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


Visit us on www.iris-pharma.com