Dry eye: Two experimental rodent models for drug development.

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Methods

Dry eye syndrome is a relatively common disease with multifactorial causes and can afflict anyone of any age. It is thus necessary to have an experimental model to test and select therapeutic candidates for this disease. The classification1 differentiates dry eye by hyposecretion syndromes and dry eye with tear film instability. In recent years, many discoveries have significantly changed the understanding of dry eye. The important roles played by inflammation of the ocular surface and lacrimal as well as hormonal factors3 or anomalous lacrimal and meibomian gland function are studied in animal models and patients.

Here we describe two experimental models of dry eye in which scopolamine, a tropane alkaloid drug with muscarinic antagonist effects, is employed to suppress lacrimation and induce dry eye symptoms.

Purpose

Experimental dry eye was induced by applying a transdermal and two induced groups, one treated by oral administration of cyclosporine A (20mg/kg/day) and the other one by instillations of 0.9% NaCl three times daily.

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

The rats induced with scopolamine and treated with saline solution showed a rapid and significant decrease of the lacrimation and an increase in the tear volumes in the group, the tear volumes were close to the baseline values except on D14. The rats induced with scopolamine and treated with saline solution showed a rapid and significant decrease of the lacrimation and an increase in the tear volumes in the group, the tear volumes were close to the baseline values except on D14.

Results

Cotton Test Tear production was measured with the cotton thread test (Zone Quick, FCI Ophthalmics, USA) in the lateral canthus of the conjunctival fornix for 30 seconds.

Corneal defects were examined by slit-lamp observation using blue light after instillation of 2µl of 0.5% sodium fluorescein for rat evaluation. Punctate staining was measured using a grading system (National Eye Institute) giving a score to each of 5 areas of a divided cornea for a maximum score of 15.

Statistical analysis

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

Clinical Evaluations

The mice housed in the CEC and exposed to scopolamine showed a rapid and significant decrease of lacrimation by D2. Oral administration of cyclosporine A did not show a significant increase of the tear volumes.

Conclusions

Scopolamine is a good inducer for a dry eye model in rodents. The data show a rapid and significant decrease of the lacrimation and an increase of the corneal defects visible by slit-lamp evaluation. As in human disease, cyclosporine reduces clinical signs of dry eye by increasing lacrimation or decreasing corneal defects.

The two models could be used to test and select treatments for dry eye.

References


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