

ARVO ABSTRACT:

Correlation of the Controlled Adverse Environment Methodology with a Murine Model of Experimental Dry Eye in Assessing the Ability of Topical Doxycycline to Prevent Corneal Barrier Disruption

Introduction: De Paiva et al. have demonstrated that disruption of the apical corneal barrier in a murine model of experimental dry eye (EDE) can be halted with topical application of low-dose doxycycline eye drops¹. The murine model of EDE involves injecting mice with scopolamine and subjecting them to an environment of tightly controlled temperature, low humidity and airflow over several days². The Controlled Adverse Environment (CAE) model for studying dry eye in humans is an established and proprietary methodology of Ophthalmic Research Associates, North Andover, MA. Because the CAE also involves exposing patients to periods of controlled temperature, humidity and airflow, it was hypothesized that corneal staining from CAE exposure in dry eye patients could be avoided by treatment with doxycycline eye drops.

Methodology: Thirty patients were randomized to receive 0.025% doxycycline eye drops (Leiter's Pharmacy, San Jose, CA) or its vehicle QID in a 28 day double-masked, parallel group trial. Patients were required to demonstrate an increase in corneal staining following CAE exposure at the baseline visit, and were exposed to the CAE at follow-up visits on days 14 and 28. Signs and symptoms of dry eye were assessed before and after exposure to the CAE at each of these visits. Patients applied study meds QID for the 28 day period, and recorded symptom severity measurements in a diary throughout the study.

Results: Utilizing the NEI scale for grading corneal staining, both active and vehicle treated patients exhibited increases in central corneal staining following CAE exposure at the baseline visit. Patients treated with the active drug exhibited no change in central corneal staining following CAE at day 14 and day 28. While the study was not powered to demonstrate statistically significant differences, there was a trend toward significance of this parameter vs. vehicle ($p = 0.099$). This was correlated with numerous instances of statistically significant differences in patient diary symptom improvements favoring the active treatment.

Conclusion: The CAE methodology for studying dry eye correlates well with an established murine model of experimental dry eye when assessing agents capable of maintaining the corneal epithelial barrier. Further study of low-concentration topical doxycycline to treat signs and symptoms of dry eye is warranted.

References:

1. De Paiva et al., *Invest Ophthalmol Vis Sci.* 2006; 47: 2847-2856
2. Luo et al., *Invest Ophthalmol Vis Sci.* 2004; 45: 4293-4301