



THE OCULAR IMMUNOLOGY
AND UVEITIS FOUNDATION

Dedicated to Eye Disease Cure and Education

Corneal Wound Healing in an Alkali Burn Model

C. Stephen Foster, MD

Alkali burns of the cornea frequently lead to persistent epithelial defects which result in ulceration and perforation. The problems of ulceration and recurrent corneal erosions lead to failure of conventional medical treatment and corneal grafting. In an effort to preserve epithelial integrity and prevent stromal ulceration, multiple therapeutic modalities have been tried, including hypertonic lubricants, steroids, collagenase inhibitors, ascorbate, citrate, fibronectin, heparin, epidermal growth factor, bandage soft contact lenses, conjunctival transplantation, limbal stem cell grafting, and keratoplasty, but none has been completely successful. Using an alkali burn model of corneal ulceration in rabbits, we studied the effects and efficacy of application of a topical model protease on a model corneal wound healing and stromal ulceration.

PHM-101, a serine protease naturally extracted from a species of Antarctic Krill, was developed as a wound healing agent and in an earlier study suggested efficacy in healing decubitus wounds. We produced corneal ulcers in New Zealand white rabbits using four normal sodium hydroxide, and studied the effects of vehicle placebo or of vehicle containing the protease which we expected to help degrade collagenase responsible for cleavage of corneal collagen. The study was performed in a randomized, double-masked way, with multiple observers participating in the study. All of the studies conformed to good practice procedures regarding animal experimentation. Epithelial defects and stromal ulcers were graded by masked observers daily, and the results were analyzed 5 weeks after the study began.

At post burn day 28, re-epithelialization had occurred in 62% of the protease-treated eyes, and in 59% of the placebo-treated eyes. By day 35, however, recurrent erosion and reproduction of epithelial defects occurred in 53% of placebo treated eyes, whereas only 12% of protease-treated eyes developed recurrent erosion. More importantly, corneal stromal ulceration was present in only 2 of the protease-treated eyes, whereas 46% of the placebo-treated eyes exhibited significant corneal ulceration. Indeed, calculation of the volume of these ulcers disclosed strikingly statistically significant differences in not only the incidence of ulceration, but also in the severity of the ulcer. Thus, the "proxy volume" of the 2-day 35 ulcers in the protease-treated group was 3 units, whereas the "proxy volume" of the 6 ulcers in the placebo-treated eyes was 17.76 units.

These preliminary results from these pilot studies suggest that, in addition to ant-collagenolytic therapy (for example with citrate and with medroxyprogesterone and with tetracycline), enhanced degradation of collagenase through the use of krill protease may be additionally beneficial in limiting the progression of alkali burn-induced corneal stromal degradation and ulceration.

Additional studies in progress will further investigate this possibility.