Comparing Ocular Therapies to Improve Corneal Mustard-Induced Injuries

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Sulfur mustard, a chemical weapon used in World War I, the Iraq-Iran War, and in the Syrian conflict, is a vesicant that injures the eyes, lungs and skin. Ocular exposure leads to corneal microblistering, neovascularization, scarring, and loss of vision from separation of the corneal epithelium from its stroma. No drugs are FDA approved for ocular mustard injury. Here two FDA-approved drugs, oxytetracycline and Restasis, were tested as therapies for ocular mustard injury. Corneal organ cultures were exposed to nitrogen mustard (NM) for 2 hr, followed by recovery for 22 hr. Controls included unexposed corneas receiving no therapy, and unexposed corneas receiving Restasis or oxytetracycline. These showed no adverse effects. Test corneas included those exposed to NM for 2 hr without treatment, and NM-exposed eyes followed by Restasis treatment (one drop at 12 hr, one at 24 hr). A duplicate set of NM-exposed corneas was treated 3 times in 24 hr with 0.2 mg oxytetracycline (in 40 µL). After the exposures and treatments, corneas were collected and sectioned to examine the injury by viewing their histology. The images with either drug showed a reduction in NM-induced ocular damage compared to eyes receiving no drug after exposure, as assessed by the degree of epithelial-stromal separation. These data supported proceeding to an in vivo rabbit ocular exposure using sulfur mustard (SM), followed by testing the therapies over the course of 24 hr after a 2 hr SM exposure. Analogous ocular tests were assessed. Restasis was applied as in the organ cultures, but the in vivo oxytetracycline experiment included only 2 applications per day. Both the histology of organ cultured corneas and in vivo exposed corneas indicated that Restasis was more effective for attenuating ocular injury from nitrogen and sulfur mustard. Future work includes adding an antiangiogenic to Restasis to reduce neovascularization. Supported by NIH U54AR055073, P30ES005022, and R25ES020721.