NOVEL CROSS-LINKED HYALURONIC ACID POLYMER MAY IMPROVE OCULAR SURFACE INJURY REPAIR

Extensive experience in veterinary applications already exists.

BY BARBARA WIROSTKO, MD

Representing up to 18% of all emergency room traumas, ocular injuries are highly prevalent.[1] Corneal abrasions account for up to 4% of all US occupational injuries, and approximately 20% of patients with facial burns also exhibit ocular injuries.[1]

For the military, war-related ocular trauma has increased significantly due to advances in combat technology and the indiscriminate use of improvised explosive devices.[2] Eye injuries represent approximately 13% to 16% of the overall injury rate among military personnel who have served in recent wars.[3] Direct injuries to the ocular surface and cornea include blast and burn trauma as well as chemical exposure, and secondary damage, such as inflammation, adhesions, and infections, can also limit vision and healing.[3]

THE LONG-TERM EFFECTS OF OCULAR INJURIES

As with battlefield trauma, occupational injury to the cornea can lead to epithelial defects, which in turn lead to secondary ocular infections, inflammation, corneal neovascularization, and vision loss if not treated promptly and healed rapidly. In addition, infectious keratitis (corneal infections and ulcers) that results from an exposed corneal surface can be a major cause of vision loss in both military personnel and civilians; the annual occurrence of corneal ulcers is roughly 1.5 to 2 million, and studies indicate that more than half of these cases in the United States are due to bacteria.[4]

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The World Health Organization estimates that corneal opacities, including corneal ulceration, are the fourth leading cause of blindness in the world.[5] If corneal epithelial defects could be healed faster, the resulting infections, scars, pain, and associated blindness could be likely reduced and overall patient outcomes improved.

A HEALING POLYMER

I helped found a startup company, Jade Therapeutics, with a mission to develop locally administered polymer technologies—either on a standalone basis or as a medium to deliver

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drugs and biologics in a sustained-release manner—for the treatment and/or prevention of ophthalmic diseases, conditions, and injuries. Jade's lead polymer is a novel, patented, biodegradable, cross-linked thiolated carboxymethylated hyaluronic acid (CMHA-S) that can be formulated as a topical repair eyedrop.

Invented at the University of Utah by Glenn Prestwich, PhD, this polymer has been demonstrated in rabbit studies conducted at the John A. Moran Eye Center of the University of Utah to promote regeneration of damaged corneal epithelial cells following various types of ocular corneal trauma.[6] CMHA-S has also been shown to be safe and efficacious for dermal healing in both large and small animals globally as a marketed product in the veterinary space.[7]

Jade's HA polymer has the ability to bind to CD44 receptors and the receptor for hyaluron-mediated motility (RHAMM), thus stimulating epithelial cells to migrate and heal corneal defects.[8] In addition, by binding to intracellular adhesion molecule 1 (ICAM-1), tumor necrosis factor, and lymphocyte modulators, hyaluronan is known to effectively downregulate local inflammation during corneal wound-healing, thus helping to reduce scar tissue.[9]

One version of the CMHA-S polymer is being manufactured as Remend (SentrX Animal Care) and sold globally in the veterinary market by BayerDVM in two concentrations as either a topical dry eye lubricant or a corneal repair agent. This bioadherent and biodegradable hyaluronic-acid–based eye drop can effectively promote corneal tissue repair and healing while preventing adhesions and scar formation, as demonstrated in thousands of animals around the world. In a randomized double-masked controlled study, this CMHA-S polymer was capable of treating dry eye (keratoconjunctivitis sicca) in dogs resistant to topical cyclosporine.[10]

Jade recently conducted a 28-day rabbit safety and tolerability study comparing the two CMHA-S concentrations dosed six times per day (exaggerated dosing) in each eye versus vehicle.[11] This study, designed in preparation for a planned investigational new drug filing with the US Food and Drug Administration, confirmed excellent safety and ocular biocompatibility. Nick Mamalis, MD, a professor of ophthalmology at the Moran Eye Center, performed the histopathology for the study.[11]

CMHA-S has great potential to fulfill an unmet need in humans, given the excellent safety and tolerability of this formulation and the enormous amount of efficacy data that exist with this CMHA-S as a corneal repair agent and a dry eye lubricating drop in animal models and in real-world settings. All of this preclinical and veterinary experience serves to reduce the risk for the human clinical development path.

CONCLUSION

Jade Therapeutics, with myself as principal investigator, has been awarded phase 1 and phase 2 Small Business Innovation Research grants from both the National Science Foundation and the US Department of Defense to help develop this polymer as a standalone corneal healing agent and as an anterior segment drug delivery platform. In particular, the Department of Defense sees the value of having a topical agent that can be immediately applied to the ocular surface on the battlefield that would significantly hasten the time to corneal healing, decrease complications such as infections and scarring, more rapidly restore vision, and improve the return-to-duty rate. ■

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