Crosslinking for Infectious Keratitis

A proposed therapy with potential to treat a global problem.

BY FARHAD HAFEZI, MD, PHD

Infectious keratitis is a leading cause of global blindness, with an estimated 5 million new cases occurring every year in developing countries.[1,2] Whereas contact lens wear is often responsible for ulcers in developed countries, minor corneal injuries along with insufficient access to ophthalmologic care and medication are the main reasons for vision loss attributable to severe corneal infections in developing nations. Corneal infections, which are most often caused by bacteria, fungi, or mixed infections, are a diagnostic and therapeutic clinical challenge.

BIOCHEMICAL EFFECTS OF CXL

Corneal collagen crosslinking (CXL) with riboflavin and ultraviolet-A (UV-A) light has been in clinical use since 1999. The proven effect of CXL is an induced increase in the biomechanical stiffness of the corneal stroma. The main indications for CXL are progressive keratoconus, pellucid marginal degeneration, and postoperative ectasia.

CXL also has an indirect biochemical effect. The enormous quantity of reactive oxygen species generated during CXL may directly damage the cell walls of pathogens.[3] Additionally, a change occurs in the tertiary structure of the collagen fibers, making it harder for collagenases to dock to the cleavage sites and exert their digestive function during corneal melting.[3]

Photoactivated riboflavin has been used to reduce the microbial load of liquids for many years. An excellent example can be found in the field of transfusion medicine, where platelet concentrates are routinely treated with UV-A light and riboflavin.[4] These biochemical characteristics have been studied in the cornea in vitro and in animals,[5] and a proof-of-concept study was conducted in a series of five patients in 2008.[6] The term *photoactivated chromophore for infectious keratitis-CXL* (PACK-CXL) has been created to differentiate this form of treatment from conventional CXL.

Weigh in on this topic now!

https://www.surveymonkey.com/s/CRSTEuro34

1. Have you performed PACK-CXL on eyes with corneal infections?
   - ☐ Yes
   - ☐ No

2. If large clinical trials validate PACK-CXL as a safe and effective therapy, would you incorporate this therapeutic modality into your daily practice for the treatment of corneal infections?
   - ☐ Yes
   - ☐ No
   - ☐ Unsure

CLINICAL EXPERIENCE

In a phase 1 clinical study, all 16 eyes treated with PACK-CXL responded with improvement in symptoms and signs of reduced inflammation.[7] Epithelial healing was achieved in all eyes, and only two required additional antimicrobial treatment. In a study of 40 eyes of 40 patients with advanced infectious keratitis and corneal melting, 21 received PACK-CXL plus antimicrobial medication and 19 received antimicrobial medication alone (control group).[8] Although healing times were comparable between both groups, the rate of complications (perforation, recurrence of infection) was 23% in the control group and 0% in the PACK-CXL group.

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FUTURE THERAPY

PACK-CXL is a promising approach for treating infectious keratitis in the presence or absence of corneal melting. If the safety and efficacy of PACK-CXL is validated in large clinical studies, this therapy could be a solution to a global problem. Ideally, PACK-CXL would enable comprehensive ophthalmologists to treat corneal infiltrates and ulcers at early stages.

Unpublished data from my laboratory indicate that novel activated chromophores might be able to kill more than 99% of bacterial and fungal pathogens in 150 seconds; a treatment at the slit lamp might be possible once miniaturized technology is available.

The questions I pose are these:

1. Have you performed PACK-CXL on eyes with corneal infections?
2. If large clinical trials validate PACK-CXL as a safe and effective therapy, would you incorporate this therapeutic modality into your daily practice for the treatment of corneal infections? ■

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