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SPECIAL FOCUS

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RESIDENT'S DIARY

PERFORMING SOLO VITRECTOMY:
A TEST OF BODY AND MIND

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PACK-CXL POTENTIAL

Hope on the horizon for meeting the challenges of corneal infection treatment.

Cheryl Guttman Krader reports



hoto-activated chromophore for infectious keratitis corneal crosslinking (PACK-CXL) is showing promise as standalone treatment

for early corneal ulcers and as an adjunct to antimicrobial treatment in more severe cases. However, it should not be used yet as a routine procedure, Farhad Hafezi MD, PhD told attendees at the 5th EuCornea Congress in Barcelona, Spain.

"Our vision is that PACK-CXL may become an early and first-line treatment for infectious keratitis. Perhaps with the development of a shortened treatment protocol, it may even be performed at the slit lamp by comprehensive ophthalmologists in the community," said Dr Hafezi, Professor of Ophthalmology, University of Geneva, Switzerland and University of Southern California, Los Angeles, USA.

However, PACK-CXL is not an established method. Whereas the published literature from 1997 until now includes 880 articles on CXL for keratoconus, there are only 50 articles on PACK-CXL. Additional research is needed in this field, and it is important that further development of PACK-CXL not be hampered by early reports of uncontrolled application leading to preventable complications, he emphasised.

Dalia G Said MD reviewed findings from a prospective clinical trial showing that PACK-CXL may be a safe and effective adjuvant for treating advanced infectious keratitis with corneal melting (*Said DG, et al. Ophthalmology. 2014;121(7):1377-1382*). She also suggested PACK-CXL may be essential treatment for antimicrobial-resistant infectious keratitis, but Dr Said similarly identified a need for more research.

"Further study is needed to develop standardised protocols and to assess the response of different microorganisms in vivo," said Dr Said, Research Institute of Ophthalmology, Cairo, Egypt, and University of Nottingham, UK.

Dr Said also proposed that future research should evaluate whether repeating PACK-CXL can accelerate healing. "In our study of severe ulcers, there was a very rapid response to PACK-CXL, and the eyes improved dramatically during the first two to three weeks. Then, the improvement was more gradual, which raises the question: 'Would an additional PACK-CXL be helpful?'" Dr Said explained.

Swiss PACK-CXL multicenter trial



The participating sites of the Swiss multicentre PACK-CXL trial

17 sites

15 countries

Courtesy of Farhad Hafezi MD, PhD

FIRST-LINE INTERVENTION

The name 'PACK-CXL' was adopted at the 9th CXL Congress in 2013 to replace 'CXL for infectious keratitis'. Dr Hafezi noted the name refers to photo-activated chromophore rather than riboflavin, anticipating the introduction of new compounds that would increase the microbicidal efficacy currently achieved with riboflavin while allowing for a shorter treatment time.

In fact, a multicentre trial using an optimised photo-activator combining riboflavin with a novel chromophore in an accelerated treatment protocol is now under way. The study is being conducted at 17 sites in 15 countries and is comparing PACK-CXL to the current standard of care with antimicrobial therapy. It aims to enrol 252 eyes with an untreated corneal infiltrate or early superficial ulcer (<2mm, <300µm depth). Patients will be evaluated every 24 hours, and if PACK-CXL eyes show evidence of clinical deterioration they will be switched to conventional treatment. Time to re-epithelialisation of the cornea is being analysed as the primary endpoint.

"We are restricting the patients to those with early corneal ulcers, because findings from previous studies suggest that PACK-CXL might be most beneficial before the depth of the ulcer exceeds the penetration possible with our current technical settings for CXL," Dr Hafezi said.

The study aims to show that primary therapy with PACK-CXL will be at least as effective as topical antimicrobial treatment. The results of a recently published animal study (*Tal K et al. Cornea. 2015;34(10):1281-*

1286) that compared the two modalities for the management of corneal ulcers induced by inoculation with methicillin-sensitive *Staphylococcus aureus* in rabbit eyes support that working hypothesis, Dr Hafezi said.

PACK-CXL FOR SEVERE CORNEAL ULCERS

The study presented by Dr Said randomised 40 patients to PACK-CXL and medical treatment with an antimicrobial or to medical treatment alone. Isolated organisms included bacteria, fungi, mixed origin, and *Acanthamoeba*, although there was no growth in 25 per cent of cases.

At entry, the corneal ulcer was significantly larger in both width and length measurements in the PACK-CXL plus medication group compared with the controls. Nevertheless, mean time to healing was not significantly different between the two study groups (40 vs 46 days, respectively), and their final mean logMAR visual acuity was also similar (1.64 vs 1.67, respectively).

Safety was not significantly different in the PACK-CXL plus medication group. Patients in the study returned for daily follow-up until healing was complete, and Dr Said noted that hypopyon size in some eyes transiently increased early after PACK-CXL.

"We believe this represents an inflammatory reaction to the dead microorganisms and the endotoxins and lipoproteins that are released," she stated, similar to the "Jerish Herxheimer" reaction known from internal medicine.

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