Accelerated corneal cross-linking with photoactivated chromophore (PACK-CXL) for moderate therapy-resistant infectious keratitis

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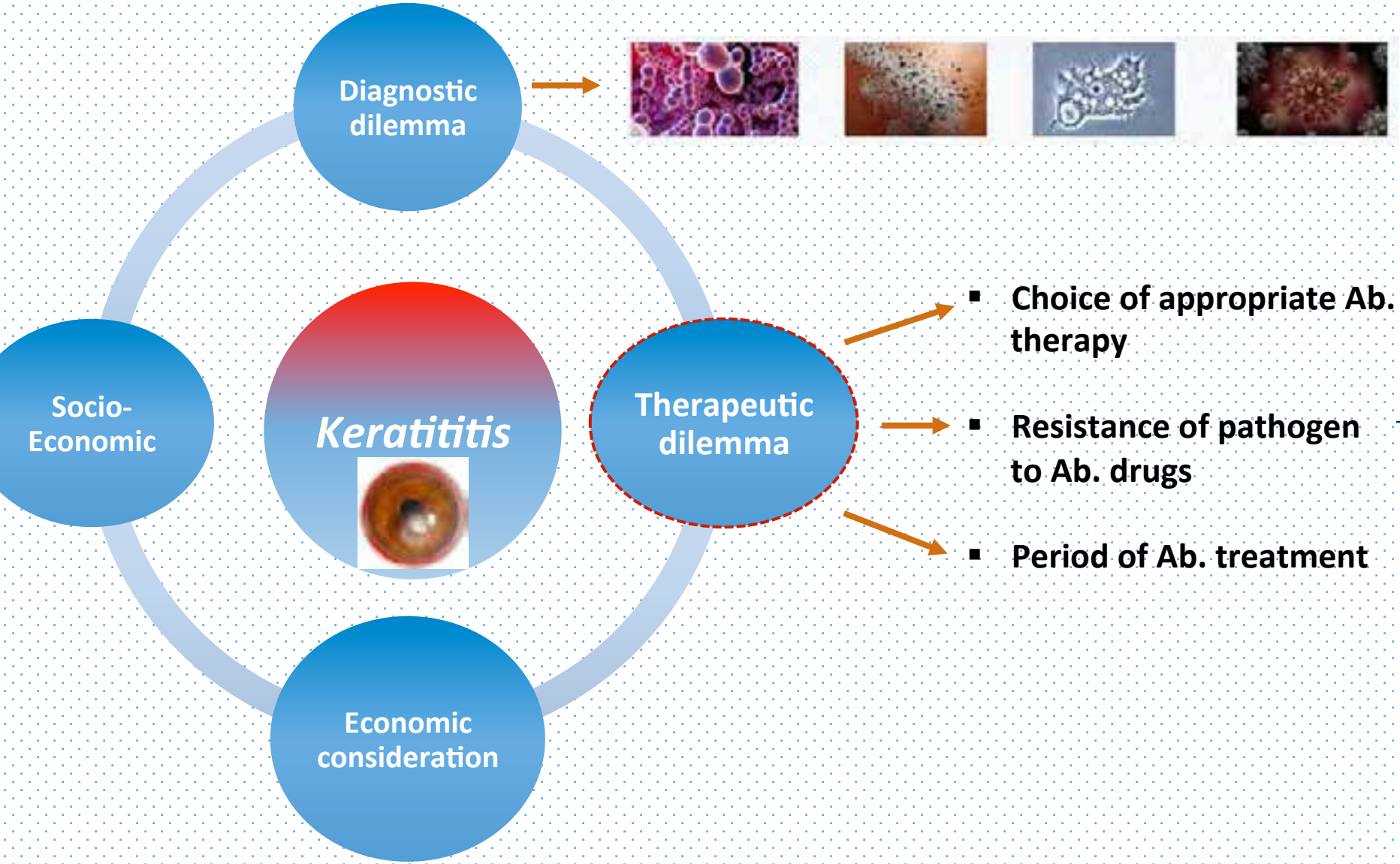
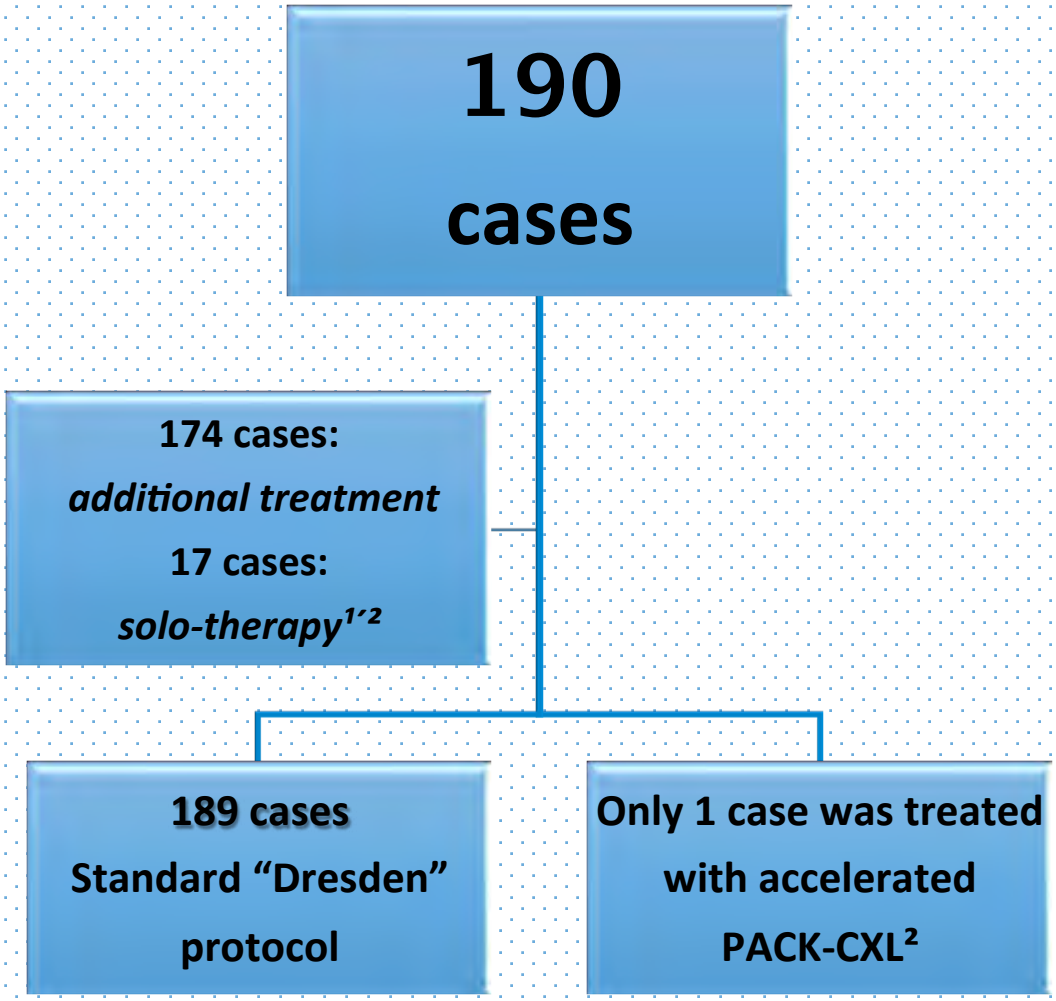
- FH: holds a patent on a UV light source
- All others: none

he problem in corneal infections are multipl



Summary of PACK-CXL in the literature.



1. Makdoumi K. UVA-Riboflawin photochemical therapy of bacterial keratits: a pilot study. Graefs Arch Clin Exp Ophthalmol. 2012;250:95-102.
2. Tabibian D. Accelerated PACK-CXL as a First-line and Sole Treatment in Early Fungal Keratitis. JRS. 2014: 30:855-857

Accelerated PACK-CXL ?

- Accelerated UVA irradiation at 365 nm and 9 mW/cm2 for 10 minutes was reported in a single case report by Tabibian in 2014 as a successful first-line and sole treatment in early fungal keratitis

REPORT

Accelerated Photoactivated Chromophore for Keratitis–Corneal Collagen Cross-linking as a First-line and Sole Treatment in Early Fungal Keratitis

David Tabibian, MD; Olivier Richoz, MD; Arnaud Riat, MS; Jacques Schrenzel, MD; Farhad Hafezi, MD, PhD

ABSTRACT

PURPOSE: To report the use of accelerated photoactivated chromophore for keratitis–corneal collagen cross-linking (PACK-CXL) as a first-line treatment in a patient with an atypical fungal keratitis.

METHODS: Case report and literature review.

RESULTS: A patient who presented with a painful peripheral corneal infiltrate underwent PACK-CXL with a local limited abrasion and accelerated ultraviolet-A irradiation at 365 μm and 9 mW/cm² for 10 minutes. Cultures grew *Aureobasidium pullulans*. The corneal epithelium closed completely within 3 days and the infiltrate was completely eradicated without administration of antibiotics.

CONCLUSIONS: Accelerated PACK-CXL was successfully used as a first-line and sole treatment in a case of early fungal keratitis caused by *Aureobasidium pullulans*. Further characterization of the antifungal effect of PACK-CXL is needed in prospective studies.

[*J Refract Surg.* 2014;30(12):855-857.]

Besides the established indication of corneal ectatic disorders, corneal collagen cross-linking (CXL) has more recently been used as photoc-

Iseli et al. published the first report on the PACK-CXL as a treatment in microbial ulcers r in conventional therapy in 2008. Two of the fiv presented were of fungal origin.[1] In 2012, Mal et al. observed 16 eyes of 16 patients with k keratitis that received PACK-CXL as first-lin ment. Postoperatively, only 2 of the 16 eyes r additional topical antibiotic treatment and ep healing occurred within a mean of 7.1 days i the 16 cases.[2] These promising results enco others to explore PACK-CXL as a treatment fo keratitis, both clinically[3-5] and experimentally mal models.[6]

We report successful PACK-CXL as a first-li sole treatment in a patient with an atypical k caused by *Aureobasidium pullulans*, a fungu ence occurrence in corneal infections.

CASE REPORT

A 27-year-old woman presented to our ment in June 2014 complaining about a red, and tearing right eye since the morning. The had worn daily soft contact lenses since 7 y age and had no other relevant medical and history. Corrected distance visual acuity (CDV 0.1 logMAR (6/7.5 Snellen) in the right ey -3.50 -0.25 × 9) and 0.0 logMAR (6/6.0 Snellen left eye (with -3.50 -0.75 × 174). Slit-lamp ex tion showed a marked conjunctival hyperem a round corneal stromal infiltrate with a diam 1 mm at the 2-o'clock position in the periphe nea, surrounded by a mild localized corneal (Figure 1A). Minimum corneal thickness was

Accelerated PACK-CXL ?

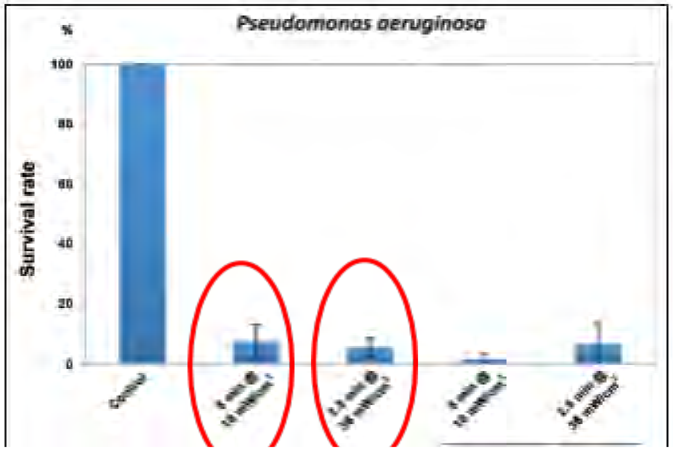
- Richotz O., Hafezi F. Antibacterial efficacy of accelerated corneal cross-linking with photoactivated chromophore (PACK-CXL) .

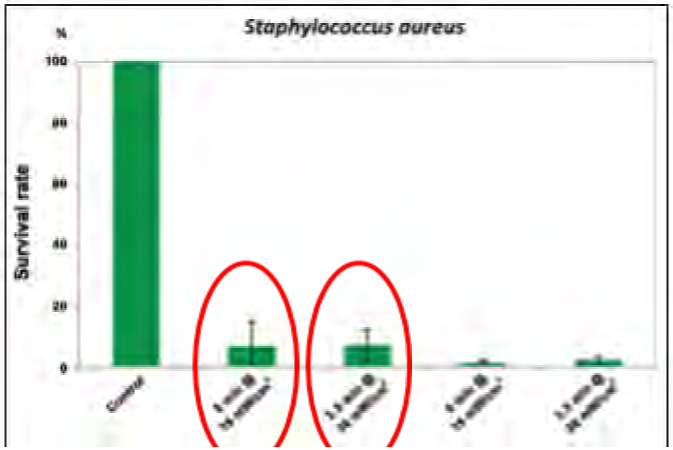
J Refract Surg. 2014;30 :850-854.

TABLE 1
Mean Bacterial Killing Rate at Various Irradiance Settings in the Presence and Absence of BAC

cteria	Control	5 min @ 18 mW/cm²	2.5 min @ 36 mW/cm²	5 min @ 18 mW/cm² with BAC	2.5 min @ 36 mW/cm² with BAC
...udomonas aeruginosa (PA01)	100%	92.5% ± 5.5%	94.4% ± 2.0%	98.5% ± 1.6%	93.3% ± 6.8%
...phylococcus aureus (SA564)	100%	93.2% ± 8.3%	92.9% ± 5.0%	98.5% ± 0.8%	97.7% ± 1.2%

... = *benzalkonium chloride*






ORIGINAL ARTICLE

Antibacterial Efficacy of Accelerated Photoactivated Chromophore for Kerati... Corneal Collagen Cross-linking (PACK-C...

Olivier Richoz, MD; Sabine Kling, PhD; Florence Hoogewoud, MD; Arthur Hammer, MD; David Tabibian, MD; Patrice Francois, PhD; Jacques Schrenzel, MD; Farhad Hafezi, MD

ABSTRACT

Purpose

To evaluate the effect of accelerated PACK-CXL (corneal cross-linking with photoactivated chromophore) as an additional treatment for therapy-resistant infectious keratitis.

Patients and Methods

- A retrospective, interventional, cohort study (may 2015-oct. 2016).

Inclusion criteria:

- Corneal ulcer of suspected bacterial origin >2mm
-No response to conventional Ab. treatment (Vancomycine+ Fortum)
- Signed informed consent

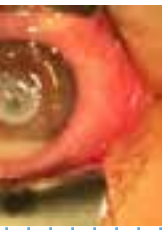
Exclusion criteria:

- Pregnancy or breast feeding
- Descemetocele
- Corneal perforation
- Suspicion of non-infectious keratitis
- Endophtalmitis

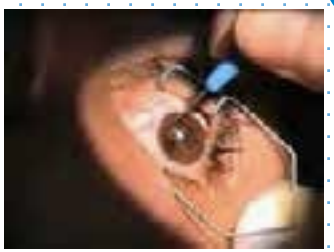
Treatment endpoints:

- Final UDCVA
- Day of re-epitaliza
- Rate of emergency PKP

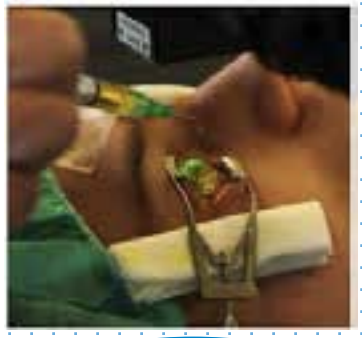
Accelerated PACK-CXL



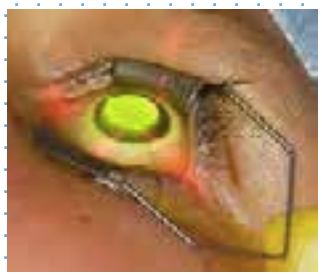
Abrasion of epithelium. (1mm around the borders)



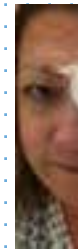
Corneal scraping for culture



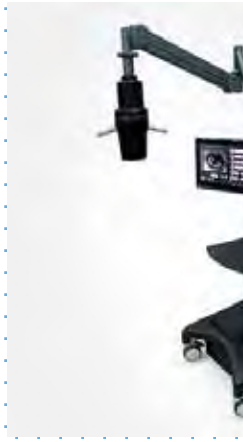
Medio-cross hypo-osmolaric 0.1%, riboflavin (each 2 min for 20 min)



UV-A radiation (30mW/cm² For 3 min, Lightmed Ltd.)



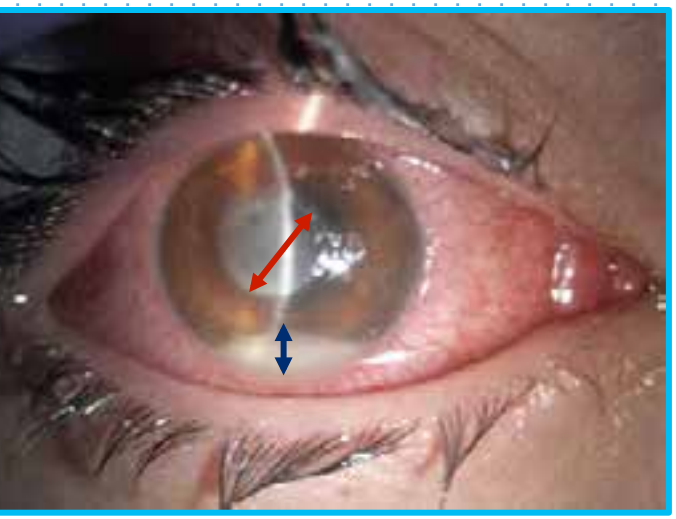
Rinsing a patching with Ab. ointment



LightLink-CXL lamp, LIGH

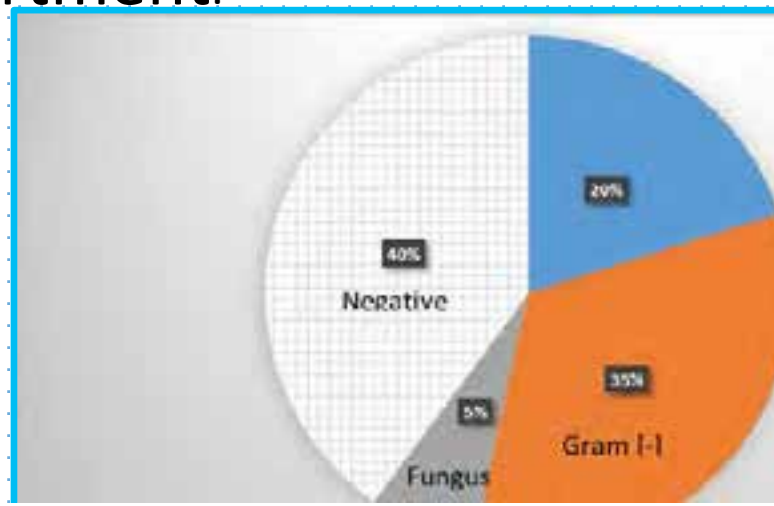
Results

Twenty eyes from **20 patients** (11 males/ 9 females) with an average age 54.5 ± 27.9 years have been included in study.



- The initial mean ulcer diameter was 3.5± 1.3mm
- Five patients (25%) presented with a hypopyon admission to our department.

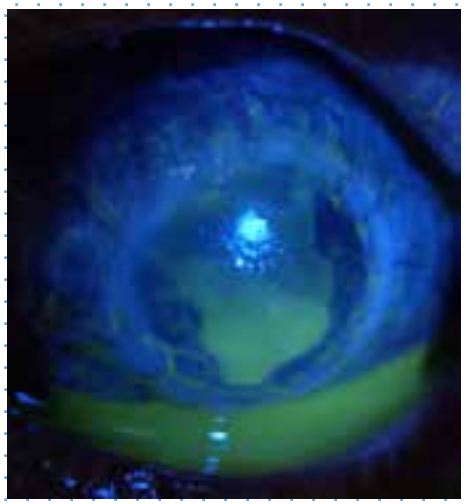
The pathogens were identified in 12 (60%) patients of study population.

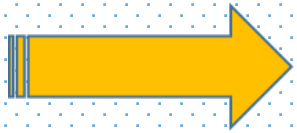


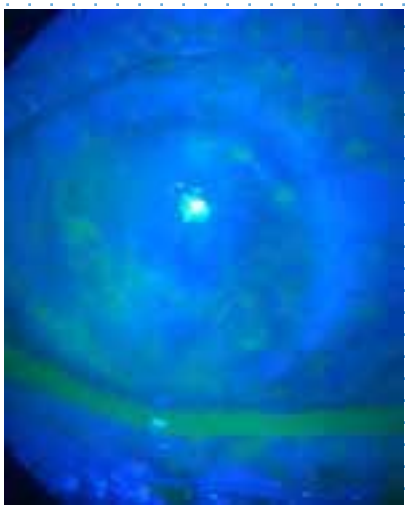
Results

- **Initial UDVA** was 2.1±0.96 **(HM)** and **finally UCVA** 1.26±0.83 (**6/120m**)

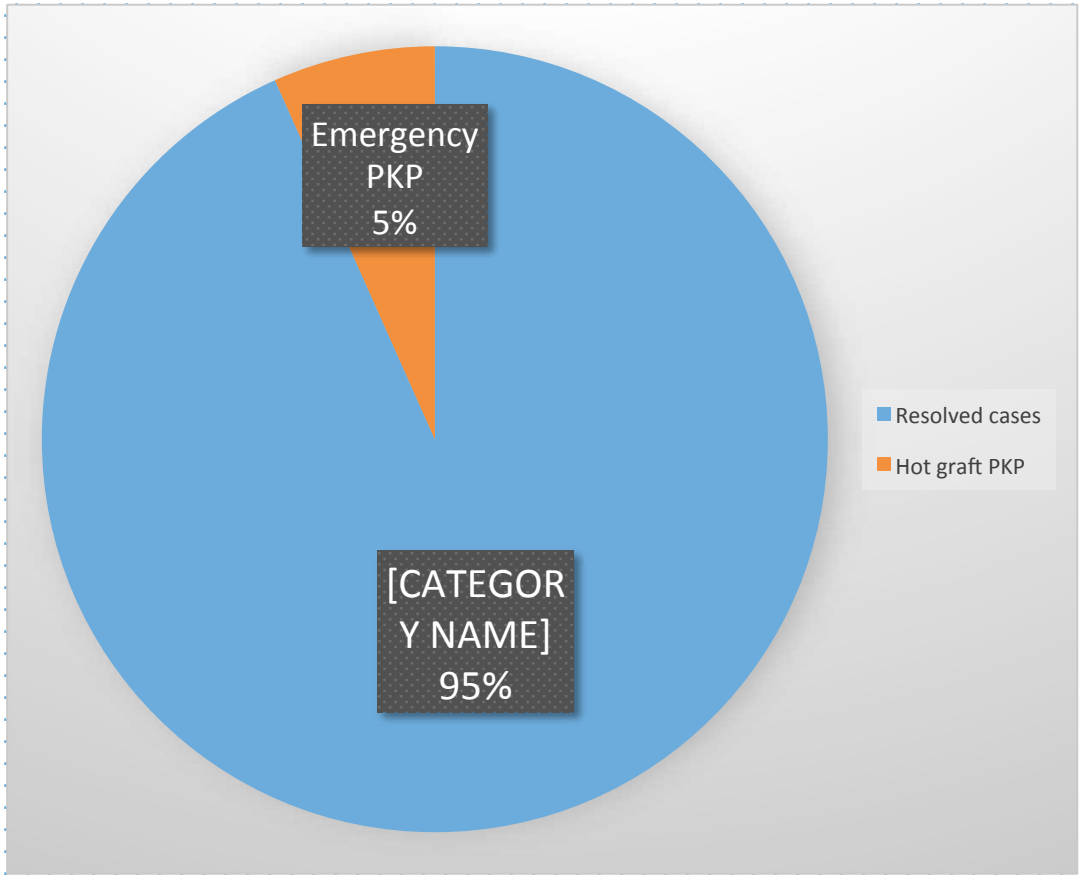
- The mean duration to **complete re-epithelization** was **11.3 ± 7.7** days

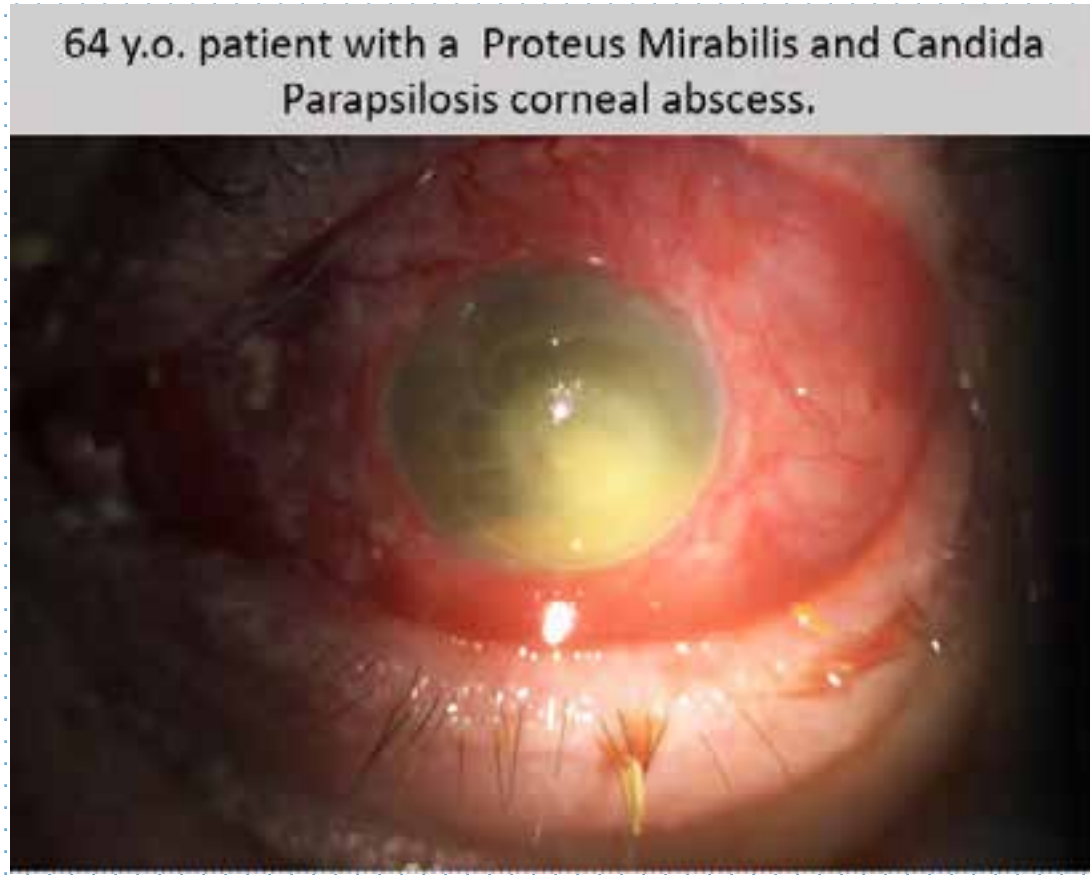




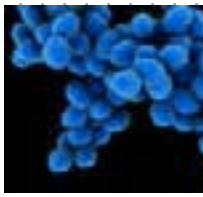


Surgical treatment after PACK-CXL



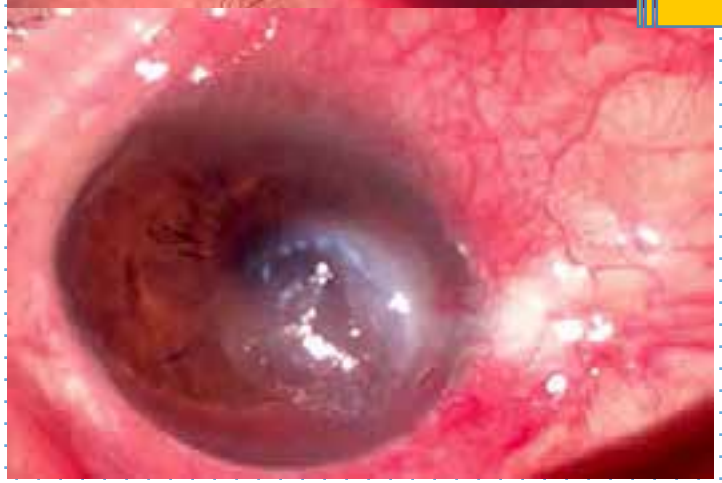


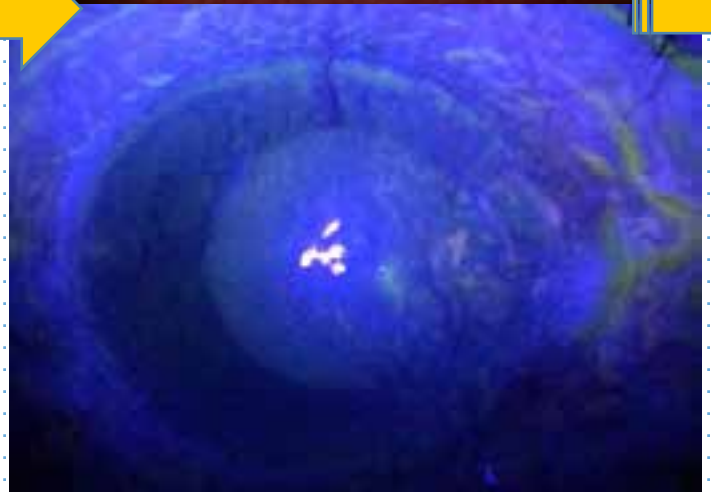
Accelerated PACK-CXL in Gram (+)

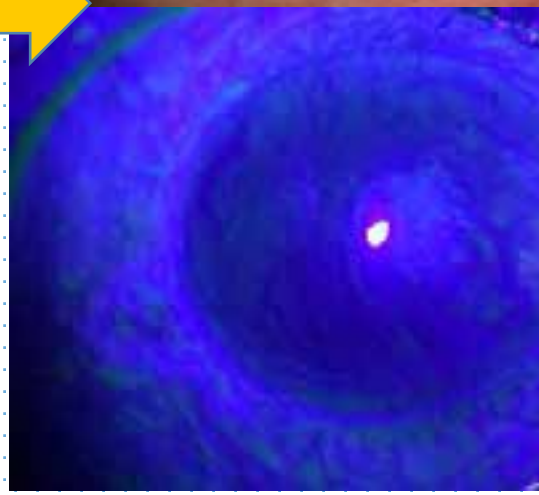


- **Staphylococcus epidermidis.**

before PACK-CXL | **S/P 5 Days** | **S/P 2 weeks**



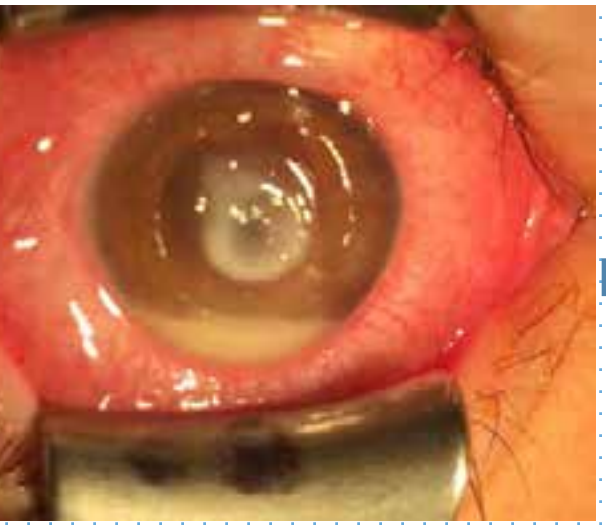




Pre and Post accelerated PACK-CXL in Gram (-)

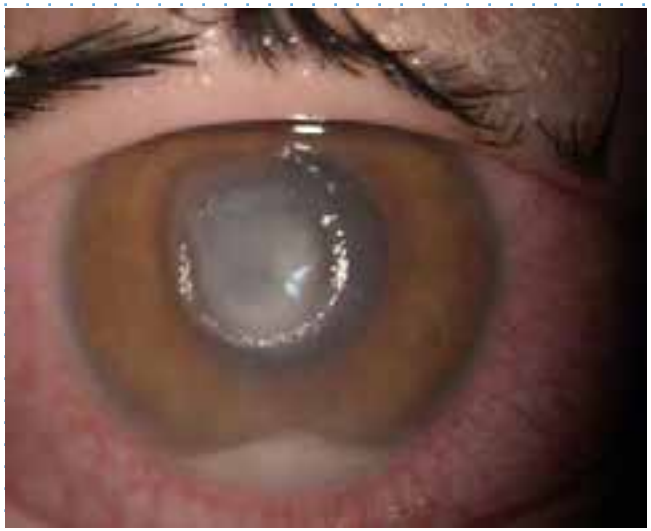
lebsiella pneumoniae, Pseudomonas Aeruginosa and Serratia Morganella

efore PACK-CXL

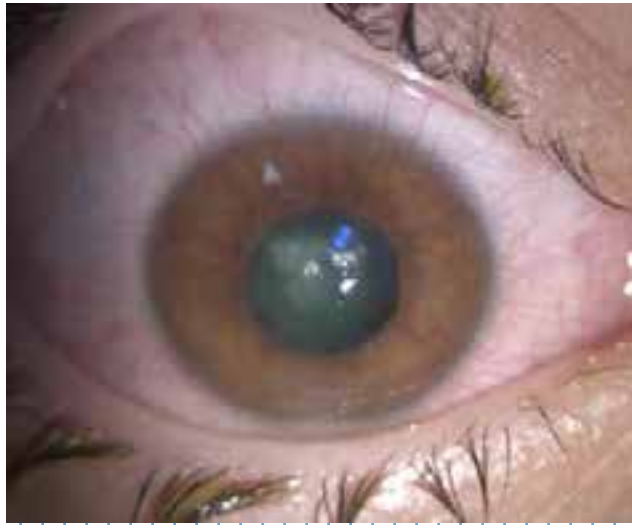


initial UCVA= CF 1 m

S/P 3 Days



S/P 2 weeks

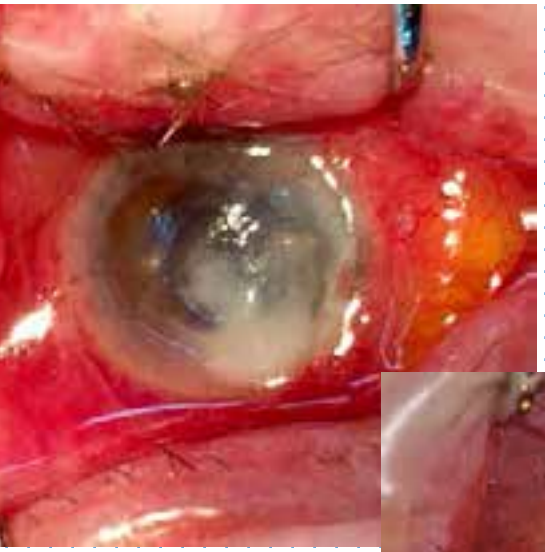


final UCVA= 6/24

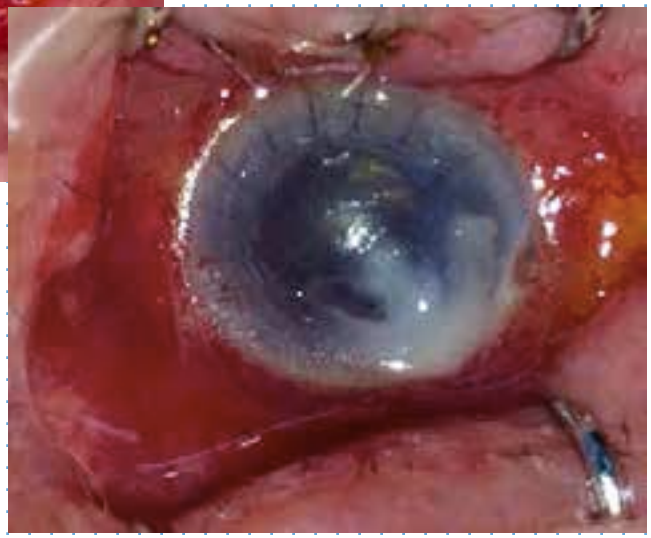
Accelerated PACK-CXL in Gram (-)

Klebsiella Pneumonia

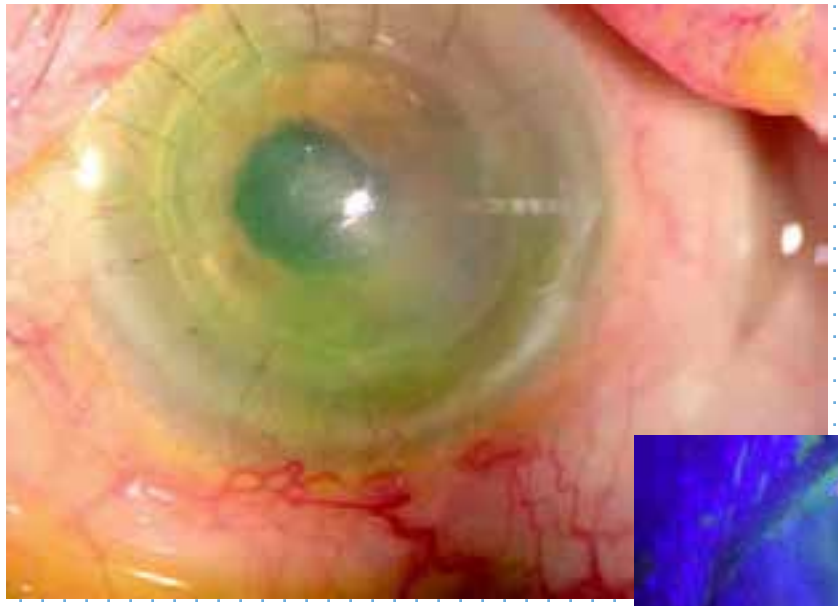
Before PACK



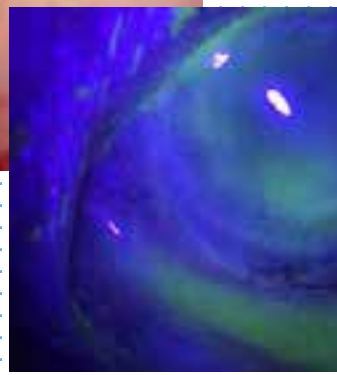
Initial UCVA=HM



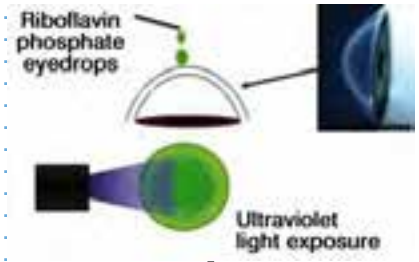
S/P 3 weeks



Final
=6

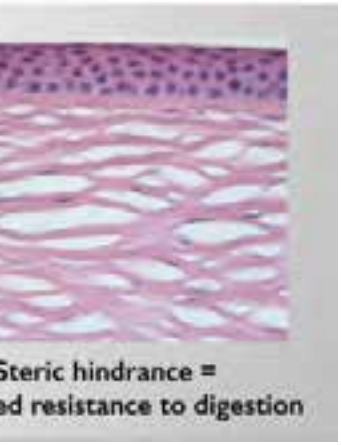


Effects of PACK-CXL in infective keratitis



Cornea

1. Increase the biomechanical strength of cornea



2. Stabilize and increase response of cornea to digestive enzymes of pathogens.

Microorganism

3. Intercalation of the chromophore (riboflavin) with the nucleic acids of the pathogen and inhibition of replication.

4. Damage to the pathogen's cell walls caused by massive amounts of ROS

Conclusion.

- *This is the first study that shows the promising results of therapy with accelerated PACK-CXL protocol.*

- Our results suggest that accelerated PACK-CXL may provide an antimicrobial effect similar to the low intensity slow settings (30 min @ 3 mW/cm2), and may be used as an additional treatment in moderate-sized therapy-resistant infectious keratitis.

- Further research is needed to show the beneficial effect of this accelerated treatment for infective keratitis.


Thank you