Accelerated PACK-CXL as adjuvant treatment in infectious keratitis

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• Disclosure:

NO FINANCIAL INTEREST
Effects of PACK-CXL in infective keratitis

**Cornea**

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

2. Steric hindrance = Increased resistance to digestion

**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.
PACK-CXL: published data

238 cases

183 cases: additional treatment
17 cases: solo-therapy\textsuperscript{1,2}

198 cases
Standard “Dresden” protocol

40 cases were treated with A- PACK-CXL \textsuperscript{2,3}

20 cases-9mW/cm\textsuperscript{2}
20 cases-30mW/cm\textsuperscript{2}

Why to accelerate PACK-CXL?

- Evidence based-
- Save time of the patients and medical staff-
- Save money for the health system-
- Efficacy and Safety-
- More bactericidal features-
Purpose

To evaluate the therapeutic effect of PACK-CXL with riboflavin on therapy-refractory infectious keratitis and compare it to the effect of the standard antibiotic therapy.
Patients and Methods

- A retrospective, single central, interventional, comparative study (may 2013-may 2018).

Inclusion criteria:
Only patients with moderate corneal ulcers with diameters of up to 7 mm.

Exclusion criteria:
suspicion of non-bacterial keratitis, (viral, fungal, Acanthamoeba keratitis)
- descemetocele,
- corneal perforation,
- pregnancy or breast feeding,
- immunosuppressed/immune-compromised patients,
- corneal ulcers that were less than 2.0 mm.

Antimicrobial therapy
- Antimicrobial therapy in both groups consisted of fortified Vancomycin and Ceftazidime eye drops, artificial tears and cyclopedia.
- In both groups, a therapeutic 14-mm diameter soft contact lens (PureVision, Baush&Lomb, USA) was placed after 50% reepithelization was achieved.

Treatment endpoints:
- Day of re-epitelization
- Final UDCVA
- Rate of emergency PKP
- Period of follow up
- # of FU visits
Accelerated PACK-CXL

1. Abrasion of epithelium. (1mm around the borders)
2. Corneal scraping for culture
3. Medio-cross hypo-osmolaric 0.1%, riboflavin (each 2 min for 20 min)
4. UV-A radiation (30mW/cm² For 3 min, Lightmed Ltd.)
5. Rinsing and patching with Ab. ointment

LightLink-CXL lamp, LIGHTMED Ltd.
## Results

<table>
<thead>
<tr>
<th>Variables</th>
<th>PACK+Ab group (n=40 pt.)</th>
<th>Antibiotic group (n=30 pt.)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.9±26.89</td>
<td>68.29±23.59</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>24 (60%)</td>
<td>18 (60%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Origin (Jewish/Bedouin)</td>
<td>28/12 (70/30%)</td>
<td>24/6 (80/20%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>9 (23%)</td>
<td>10 (33.3%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Hypopion</td>
<td>10 (25%)</td>
<td>5 (17%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Initial UCVA (LogMAR)</td>
<td>1.7</td>
<td>1.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Size of corneal ulcer (mm)</td>
<td>3.2±1.3</td>
<td>3.1±1.2</td>
<td>0.7</td>
</tr>
</tbody>
</table>
# Results

- The mean duration to **complete re-epithelization** in days

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration (mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB group</td>
<td>12.0 ± 4.5 days</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>PACK+Ab group</td>
<td>7.0 ± 2.5 days</td>
<td></td>
</tr>
</tbody>
</table>
Emergency PKP

PACK+Ab group

Resolved cases 100%

Antibiotic group

Emergency PKP 20%

Resolved cases 80%

P < 0.001
Outcome results in the study populations

**Treatment endpoints:**
- Final UDCVA
- Day of re-epithalization
- Rate of emergency PKP
- Period of follow up
- # of FU visits

<table>
<thead>
<tr>
<th></th>
<th>PACK+Ab group</th>
<th>Ab group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final UCDVA [LogMAR]</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Long of Stay [days]</td>
<td>6.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Follow Up period [months]</td>
<td>2.6</td>
<td>4.4</td>
</tr>
<tr>
<td># FU Visits</td>
<td>7.3</td>
<td>15.1</td>
</tr>
</tbody>
</table>

P=0.3  P=0.06  P=0.001  P=0.001
Pre and Post accelerated PACK-CXL in Gram (+)

- Staphylococcus epidermidis.

before PACK-CXL

S/P 7 Days

S/P 2 weeks

Initial UCVA 6/60

CXL EXPERTS’ MEETING 2018

Final UCVA 6/15
Pre and Post accelerated PACK-CXL in Gram (-)

- Klebsiella pneumoniae, Pseudomonas Aeruginosa and Serratia Morganella

before PACK-CXL

S/P 3 Days

S/P 2 weeks

initial UCVA= CF 1 m

final UCVA= 6/24
Pre and Post accelerated PACK-CXL in Gram (-)

*Klebsiella Pneumonia*

Before PACK

S/P 10 days
Why the A-PACK-CXL may be better than S-CXL?

**Reaction mechanisms**

**Type I mechanism:**

\[
Rf_3^+ + SH \rightarrow (Rf^- + SH^+) \quad \text{ radicals}
\]

\[
2RfH^+ \rightarrow Rf + RfH \quad \text{ Little oxygen consumption.}
\]

\[
RfH_2 + O_2 \rightarrow Rf + H_2O_2
\]

\[
\text{Little oxygen consumption.}
\]

**Type II mechanism:**

\[
Rf_3^+ + O_2 \rightarrow ^1O_2
\]

\[
SH + ^1O_2 \rightarrow S_{ox}
\]

\[
\text{High oxygen consumption.}
\]

Kamaev P. IOVS 2012
Conclusion.

✓ Promising first results using accelerated PACK-CXL with 30 mW/cm² intensity.

✓ Accelerated PACK-CXL beneficial as an additional treatment in moderate-sized infectious keratitis.

✓ Further research is needed for the optimization of treatment parameters to achieve the maximal antibacteriacidal effect in infectious keratitis.
Thank you