CXL in Keratoconus

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Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study

• „CLEK Study subjects with keratoconus exhibited a slow but clear decrease in BCVA during follow-up, with low-contrast acuity deteriorating more rapidly than high-contrast.“

• „The 5-year incidence of scarring is 13,7% for the overall sample and 38,0% for those eyes with corneal curvature greater than 52 D that wore contact lenses.“

Davis LJ, Schechtman KB, Wilson BS et al. Longitudinal changes in visual acuity in keratoconus. IOVS 2006; 47: 489-500
Lifetime economic burden of keratoconus

- compared to the expected cost of the treatment of myopia:
  - included costs of clinic visits, fitting fees, contact lenses, surgical procedures and complications: 25 168 US$
  - the factors that most influenced the lifetime cost were the probability of initial corneal transplant and a subsequent regraft
  - the average annual cost for individual routine vision care is 200 US$, but for patients with keratoconus, it is 653 US$
  - combined with the significantly impaired vision-related quality of life and the relatively young onset of disease, the economic burden of the treatment of keratoconus represents a significant public health concern

Management

- Glasses
- Contact lenses
- Collagen Cross-linking with Riboflavin/UVA
- Intracorneal rings
- Corneal transplant
Indication for CXL

- **PROGRESSION !:**
  - K-Values
  - Astigmatism
  - Pachymetry
  - ORA
  - (Visual acuity)
PROGRESSION

• $\uparrow K_{\text{max- apex}} \geq 1.0 \text{D in 1 y.}, \downarrow \text{VA, } \uparrow \text{CL fitting frequency}$

• $\uparrow \text{Dsph and/or Dcyl} \geq 3 \text{D in 6 mo.}, \text{ or }$
  $\uparrow K_{\text{max}} \geq 1.5 \text{D, or mean } \downarrow \text{CT} \geq 5\% \text{ in 3 consecutive measurements in 6 mo.}$

• $\uparrow K_{\text{max}} \geq 1 \text{D, or } \uparrow \text{Dcyl} \geq 1 \text{D, or } \uparrow \text{Dsph} \geq 0.5 \text{D in 24 mo.} \text{ (FDA study)}$

Indication for CXL:
Medical history

- Age, gender
- Sport: body-building, weight-lifting, yoga (upside down standing, pressure breathing)
- Playing wind-instrument
- Pregnancy
- Hormonal therapy (contraceptives, anabolics)
- Thyroid gland dysfunction
- Allergy (Neurodermitis, Steroids)
- Smoking
- Diabetes mellitus
Keratoconus in children

- rapid progression (high risk group)
- Age: 10-18 y.
- Incidence M:F = 4:1
- prompt indication for CXL!

Progression (F/U 6 mo.)
After CXL (F/U 1 y.)
CXL: Riboflavin + UVA

- Topical anaesthesia
- Epithelium removal
- Pachymetry
- 0.1% Riboflavin: 2 Min for 30 Min, Ø Speculum
- Pachymetry
- UVA (370nm): 3mW/cm² (5.4J/cm²) for 30 Min.
- CL, ATB, lubricants till epithelialisation
- Steroid drops
Epi-off

• prospective, unmasked, randomized controlled trial
• 94 eyes: 48 eyes – control group, 46 eyes – treatment group
• Age: between 16 and 50 years
CONCLUSIONS: At 36 months, there was a sustained improvement in Kmax, UCVA, and BSCVA after CXL, whereas eyes in the control group demonstrated further progression.
• 49 papers included: 8 reported 4 RCTs, 29 prospective, 12 retrospective studies

• the majority of evidence graded as „low“ (trial design, no comparator, large drop-out rate, incomplete reporting)

• „…uncertainty remains about duration of benefit…“

CXL in Dresden: long-term results

- retrospective, non-randomized
- 34 eyes/24 pat.
- ♀:6, ♂:18
- Age: 28.4 ± 7.3y.
- F/U: 131.91 ± 20.13 mo.
- Statistics: linear mixed models with repeated measures (Version 21, SPSS, GmbH Software, Munich, Germany).

JCRS 2014: in press
10-year-results
High-intensity devices
(second generation of cross-linking devices)

18 mW/cm² 5 min
KXL (Avedro)
USA

18 mW/cm² 5 min
CCL-365 HE (Peschke)
Switzerland

9 mW/cm² 10 min
UV-X 2000 (IROC)
Switzerland
Accelerated CXL

- shortens the illumination time by increasing the illumination intensity (Bunsen-Roscoe law of reciprocity)
- reduces the overall treatment time
• The ex vivo results in porcine corneas show that the Bunsen-Roscoe reciprocity law is only valid for illumination intensities up to 40 to 50mW/cm² and illumination times of more than 2 min. (Wernli J, Schumacher S, Spoerl E, Mrochen M. The efficacy of corneal cross-linking shows a sudden decrease with a very high intensity UL light and short treatment time. IOVS 2013; 54: 1176-1180)
Accelerated CXL

• The biomechanical effect of CXL decreased significantly when using high irradiance/short irradiation time settings. Intrastromal oxygen diffusion capacity and increased oxygen consumption associated with higher irradiances may be a limiting factor leading to reduced treatment efficiency. (Hammer A, Richoz O, Mosquera SA et al. Corneal biomechanical properties at different corneal CXL irradiances. IOVS 2014; 55: 2881-2884)
Accelerated CXL


Iontophoresis

- no riboflavin-dextran was detected in the corneal stroma after transepithelial Coulomb-controlled iontophoresis (CCI)

- riboflavin-phosphate was detected throughout the full thickness of the stroma in the eyes of rats

Iontophoresis

- 45% less riboflavin concentration was observed in rabbit corneas treated by iontophoresis compared to corneas soaked with the conventional application.
- There were no significant toxic changes on corneal epithelium after iontophoresis compared to untreated corneas.
- Similar results were achieved in both groups in the stress-strain measurements regarding the stiffness of corneas and increased resistance against corneal collagenase digestion treated by iontophoresis compared to conventional riboflavin application.

Iontophoresis

• Conclusion: Corneal cross-linking transepithelial iontophoresis imbibition yielded greater and deeper riboflavin saturation with respect to pharmacological epi-on, while maintaining the advantages of avoiding epithelial removal and shorter procedure time, but did not reach concentrations obtained with standard epi-off.

Iontophoresis


• Vinciguerra P. et al. Transepithelial iontophoresis corneal collagen cross-linking for progressive keratoconus: Initial clinical outcomes. J Refract Surg 2014; 30(11): 746-753. prospective non-randomized clinical study: „All topographic parameters were stable during the follow-up, but exhibited a positive non-significant trend toward improvement…however, the relative efficacy of this technique compared to standard epithelium-off techniques remains to be determined.”
Iontophoresis
What is evidence-based?

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