CORNEAL COLLAGEN CROSS-LINKING - CLINICAL OUTCOMES AND THE EVOLUTION OF FIVE YEARS OF PUBLIC SERVICE IN AUCKLAND

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Akilesh Gokul, PhD, Bptom (Hons) TPA
Post-Doctoral Clinical Research Fellow
Department of Ophthalmology
University of Auckland
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KERATOCONUS VS. NORMAL

© Dr Hans Vellara, Department of Ophthalmology, University of Auckland

- Deformation amplitude higher in keratoconus

KERATOCONUS

Simulation of what someone with keratoconus perceives

Basic treatment algorithm as disease progresses:
spectacles ↔ contact lenses ↔ transplantation

2009-2012

- Dr Charlotte Jordan’s PhD
- Randomised control trial
- Traditional CXL protocol
- 39 patients
  - Traditional CXL safe and effective

TRADITIONAL CORNEAL CROSS-LINKING

Stroma soaked in riboflavin (vitamin B2) for 30 minutes
Exposure to continuous/uninterrupted ultraviolet light of 3mW/cm² for 30 minutes = total energy of 5.4 J/cm²
Corneal collagen cross-linking

2014-2016

- Dr Akilesh Gokul’s PhD
- High intensity, high energy, continuous vs. pulsed UV-A CXL
- High energy accelerated col
- Randomised intervention study
- 80 eyes with 2 year follow-up
  - 40 eyes/group

CORNEAL CROSS-LINKING
HIGH-INTENSITY (ACCELERATED), HIGH-ENERGY
- CONTINUOUS

Stroma soaked in modified riboflavin (vitamin B2) for 10 minutes
(30 minutes in traditional protocol)
Expose to continuous/uninterrupted ultraviolet light of 30 mW/cm² for
4 minutes = total energy of 7.2 J/cm²
(vs. 3 mW/cm² for 30 minutes = 5.4 J/cm²)

WHY CONTINUOUS VS. PULSED?

- Cross-linking: UV-A + Riboflavin = Reactive Oxygen (O₂) Species
  - Reactive O₂ species = covalent bonds
- Type I and II photodynamic reaction
  - Type II more efficient but oxygen dependent
- O₂ in cornea depleted rapidly on UV-A initiation
  - 30mW/cm² zero in 1s, 3 mW/cm² takes 15s
- O₂ concentration rapidly increases once UV-A stopped
  - Theoretically pulsing UV-A = Type II reaction = covalent bonds

SUMMARY OF KEY RESULTS

- At 24 months follow-up compared to baseline:
  - No significant difference in UVA, K_max, and CTP in both p-ACXL
    and c-ACXL
  - CDVA improved significantly in both p-ACXL and c-ACXL
  - MRSE improved significantly and K_max decreased significantly
    in the c-ACXL group only
  - No complications encountered in either group

CONCLUSION

- Both pulsed-ACXL and continuous-ACXL safe and effective at
  halting the progression of keratoconus at 24 month follow-up
- Continuous-ACXL may offer superior refractive and tomographic
  outcomes but may not translate into better visual outcomes
- Continuous possibly the superior method due to shorter
  procedure time i.e. more efficient – 5 pulsed = 6 continuous
2016-2020

- ADHB service
- Continuous UV-A Accelerated CXL
  - Different protocol to Dr Jordan’s and Dr Gokul’s PhDs
  - 10 minute riboflavin soak
  - 3 minute continuous UV-A exposure
    - 30mW/cm² for 3 minutes = total energy of 5.4 J/cm²
  - High intensity, traditional energy
- Weekly list
  - ~160 procedures per year

POST-OP CARE

- Bandage CL placed
- Ciloxan QID for 1 week, Fluoromethalone QID for 1 month
- Review 3 days post
  - Remove bandage CL – most epithelial defects almost fully healed
- Review 6 weeks, 3 months, 6 months and 1 year post-op
  - Then on case-by-case basis -> 3-12 monthly
- Encouraged to see optometrist for spectacle and/or CL review after 3 month post-op visit

WHO IS UNDERGOING CXL?

- Total number procedures = 573 eyes of 426 patients
  - 500 epi-off
  - 73 transepithelial
    - 2014-2016 = 53 (72.6%)
    - 2017-2020 = 20 (27.4%)
- Gender
  - Male 59%
  - Female 41%

WHO IS UNDERGOING CXL?

Mean age on the day of CXL - 22.41 ± 6.75 years (range 7-48)

- 20-30 years old 40%
- <20 years old 31%
- 20-30 years old 25%

WHO IS UNDERGOING CXL?

Auckland Region*

- European 49%
- Asian 26%
- Māori 10%
- Pacific Peoples 14%

CXL - ADHB

- European 22%
- Pacific Peoples 32%
- Māori 30%
- African 10%
- Middle Eastern 3%
CRITERIA FOR PROGRESSION

- At least 6 months of visual/refractive/tomographic data available
- Progression defined as ≥one of:
  - Increase in maximal keratometry of ≥0.75D
  - Change in refractive astigmatism of ≥0.75D
  - Decrease in thinnest corneal thickness of ≥15μm
  - Progression measured indirectly by using rigid contact lenses; a change of >0.2mm in base curve
  - Loss of 2 or more lines of best spectacle corrected visual acuity
  - Clinician judgement

SAFETY LIMITATIONS

- Corneal thickness
  - Thinnest point >400 μm
- Corneal clarity
  - No significant corneal scarring -> from KC or otherwise
- Inflammatory disease under control -> non-healing epithelial defects
  - E.g. allergic eye disease (VKC, AKC, SAC)
  - No limitation on keratometry values
  - As long as above criteria are met

CLINICAL OUTCOMES SINCE 2014

- 5 (1%) infections
  - All admitted for fortified topical antibiotics
  - No loss of BCVA
- 8 (1.4%) repeat CXL procedures
  - 3 initially had transepithelial CXL
- Zero eyes that have had epi-off CXL progressed to transplant
  - 1 patient that had transepithelial CXL progressed to hydrops
- Many patients change in spec and CL Rx

SO WHAT ARE THE RISKS?

- 0.5-1% infection risk
- ~1% failure – require repeat procedure (if possible)
- Possible spectacle or CL Rx will change
  - Even without complication
  - Advised to not update for at least 3 months post-op
  - Unaided vision can change even without complication
  - Depending on what happens to spec/CL Rx

SUMMARY

- CXL has evolved substantially over the last decade in Auckland
  - Current protocol is accelerated CXL with continuous UV-A
  - Procedure routinely carried out
  - Weekly list
  - Main risk is infection (0.5-1%)
  - Early disease detection remains a challenge
    - Mostly individuals aged 20-30 (~50%) undergoing CXL
  - Very large ethnic bias
    - 30% Māori
    - 32% Pacific Peoples
    - 22% European

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