

**SAFETY AND EFFICACY OF CORNEAL COLLAGEN CROSSLINKING
WITH RIBOFLAVIN AND ULTRAVIOLET-A IN THE TREATMENT OF
PROGRESSIVE KERATOCONUS**

KEYWORDS

Keratoconus, collagen crosslinking, riboflavin, ultraviolet A, corneal ectasia

INTRODUCTION

Keratoconus is a non-inflammatory progressive corneal thinning of unknown etiology in which the cornea assumes a conical shape, resulting in mild to marked impairment of visual acuity due to irregular astigmatism, progressive myopia and central corneal scarring. A reduced number of collagen cross-links and a pepsin digestion higher than normal induce an overall structural weakness of the corneal tissue, resulting in a stiffness that is only 60% of normal cornea. Changes in corneal collagen structure, organization and intercellular matrix as well as apoptosis and necrosis of keratinocytes, prevalently or exclusively involving the central anterior stroma and Bowman's lamina are documented in literature. Corneal collagen cross-linking (C3R) is a new approach to increase the mechanical and biochemical strength of corneal tissue.

BASIC PRINCIPLE-The aim of this treatment is to create additional chemical bonds inside the corneal stroma by means of highly localised photopolymerisation while minimising exposure to surrounding ocular structures.

Using UVA at 370nm and the photosensitizer riboflavin, the photosensitizer is excited into its triplet state generating the reactive oxygen species (ROS). These are

mainly in the form of singlet oxygen and to a much less degree, they may be in the form of superoxide anion radicals. The ROS then reacts with various molecules, including chemical covalent bonds, bridging amino groups of collagen fibrils (type 2 photochemical reaction). The wavelength of 370nm was chosen because of an absorption peak of riboflavin at this wavelength.

AIMS AND OBJECTIVES

-To evaluate the safety of C3R as measured by intra operative and postoperative complications

-To measure the efficacy of C3R in bringing progressive keratoconus to a halt

MATERIALS AND METHODS

TYPE OF STUDY

Prospective interventional clinical trial

CASE COLLECTION PERIOD - 1 year

FOLLOW UP PERIOD - 1 year

SAMPLE SIZE - 50 patients

SELECTION CRITERIA

Inclusion criteria

Progressive keratoconus

Age between 12 to 30 years

Corneal pachymetry > 400 microns at thinnest point

Normal corneal endothelium

Maximum corneal curvature < 60 D

Willing for follow up

Exclusion criteria

Corneal thickness < 400 microns at thinnest point

H/O herpetic keratitis

Central or paracentral opacities

Prior corneal surgery

Severe dry eye and ocular surface disorders

Concurrent corneal infections

Concomitant autoimmune diseases

Pregnant/nursing women

Hormone therapy

EVALUATION PARAMETERS

- UDVA
- CDVA
- CLVA
- Refraction
- Slit lamp biomicroscopy
- Fundus evaluation
- Non contact tonometry
- Tear Film break up time
- OrbscanIIz (Bausch & Lomb)
- Specular microscopy (Topcon SP 3000 P)
- Clinical Photograph (Haag Streit)

SAFETY PARAMETERS

Post operative complications: -

- Non healing/Persistent Epithelial Defect
 - (a) <2mm (b) 2-5 mm (c) >5 mm
- Permanent stromal Haze
 - (a) mild (b) moderate (c) severe
- Corneal Scarring
 - (a) nebular (b) macular (c) leucomatous
- Infective keratitis
- Corneal melting
- Corneal Infiltrate-
 1. Number (a) single (b) multiple
 2. Size (a) <2mm (b) 2-5 mm (c) >5 mm
 3. Type (a) bacterial (b) fungal (c) sterile
- Endothelial cell loss
- Cataract formation
- Retinal pathology
- Loss of 2 or more lines in BCVA

EFFICACY PARAMETERS

- Best corrected distance visual acuity-
 1. Spectacle corrected
 2. Contact lens corrected
- Refraction-
 1. Spherical
 2. Cylindrical with axis

3. Mean spherical equivalent
- ORBSCAN IIz
 1. Sim K
 2. K max
 3. Thinnest pachymetry
 4. Anterior float BFS difference
 5. Posterior float BFS difference
 6. 3mm zone irregularities
 7. 5mm zone irregularities

METHODOLOGY

-All patients with documented progression of keratoconus(more than 0.5 diopter increase in the past 1 year) were included.

-Preoperative measurements included uncorrected visual acuity,best corrected and contact lens visual acuity,refraction, intra ocular tension (Non contact tonometry), keratometry, specular microscopy and ORBSCAN IIzreadings.

-The eye with advanced keratoconus was treated with C3R while the other eye served as the control.

-The patients were called for follow-up at 1 week,1 month,3 months,6 months and 12 months postoperatively. All necessary investigations were done at each visit.

-The progression of keratoconus (if any) was documented and was compared with the fellow control eye.

-Intraoperative and postoperative complications (if any) were documented.

RESULTS

DEMOGRAPHICS

The mean age of presentation was 17.72 years (SD= 2.98) with a range of 12 to 26 years. A total of 50 patients were enrolled in the study, with 31 males (62%) and 19 females (38%)

VISUAL ACUITY

In our study, we found a significant improvement in uncorrected visual acuity (UDVA) at 12 months follow up visit by 0.11 log MAR units which was significant with respect to the controls where no significant change was observed.

In the corrected distance visual acuity, no significant improvement was observed at 6 months and 12 months in both the case and the control group.

REFRACTION

In our study, a mean decrease in refractive cylinder by 0.44D was observed at 6 months and 0.50D at 1 year, which however was not significant with respect to the control group. The spherical equivalent showed no significant change in the cases but a significant increase in the control group at 6 months and 12 months. There was no significant change in refractive sphere in either group

ORBSCAN IIz

There was a significant reduction in simulated keratometry, maximum keratometry, anterior float, posterior float, 3mm and 5 mm zone irregularities in the cases with respect to preoperative values and values at 6 months and 12 months. The thinnest pachymetry underwent significant reduction from one-month postoperative followup.

COMPLICATIONS

There was no significant change the intraocular pressure at follow up visits in either group. We also observed transient stromal haze in a majority of our patients, which persisted beyond 3 months in 30 patients (60%). Mild scarring was seen in 13(26%) of our patients. No cases of keratitis, infiltrate or corneal melting were seen. We observed no lens changes or induced retinal pathologies in our study.

CONCLUSION

Collagen crosslinking is a safe and effective procedure to halt the progression of disease in cases of mild to moderate keratoconus.