Sequential versus Simultaneous Photorefractive Keratectomy and Corneal Collagen Cross Linking in Keratoconus Treatment

Essay

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Abstract

Background: Keratoconus is a chronic non-inflammatory, bilateral cornea degeneration,usually characterized by localized corneal thinning, visual distortion, corneal steepening, and central corneal scarring.

Photorefractive keratectomy (PRK) is a laser eye surgery procedure intended to correct refractive error of the human eye. The technique permanently changes the shape of the anterior central cornea using an excimer laser to ablate a small amount of tissue from the corneal stroma.

Several combinations of PRK and CXL have been done, sequential approach has been compared with simultaneous approach in form of same day customized PRK immediately followed by CXL. This comparison will be discussed in this literature.

Aims: The aim of the essay was to sequential versus Simultaneous Photorefractive Keratectomy and Corneal Collagen Cross Linking in Keratoconus Treatment.

Methodology: Keratoconus is a chronic non-inflammatory, usually bilateral cornea degeneration, characterized by localized corneal thinning, visual distortion. It is a multifactorial disease involving complex interaction of both genetic and environmental factors that contribute to the disease manifestation.

Conclusion: Sameday simultaneous topography-guided PRK and collagen cross-linking for treatment of keratoconus give better results on visual acuity, keratometry, topography and central corneal thickness than that given by sequential approach.

Keywords: Sequential versus, Simultaneous Photorefractive Keratectomy, Corneal Collagen Cross Linking, Keratoconus Treatment.

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Abbreviations

mμ	Micron
BV	Blood vessel
KC	Keratoconus
UV	Ultraviolet
ROS	Reactive Oxygen Species
MMP	Matrix Metalloproteinases
IL	Interleukin
TNF	Tumor Necrosis Factor
GWAS	Genome-wide association studies
SNPs	Single nucleotide polymorphisms
CCT	Central corneal thickness
VSX	Visual system homeobox
SOD	Superoxide dismutase
PPCD	Posterior polymorphous corneal dystrophy
ALS	Amyotrophic lateral sclerosis
FCD	Fuch's corneal dystrophy
D	Diopter
DM	Descemet membrane
Sim-K	Simulated keratometry
RGP	Rigid gas permeable
MM	Millimeter
ICRS	Intrastromal corneal ring segments
SK	Sever keratoconus

UCVA	Uncorrected visual acuity
BCVA	Best corrected visual acuity
IOL	Intraocular lens
CXL	Collagen crosslinking
PK	Penetrating keratoplasty
DALK	Deep anterior lamellar keratoplasty
nm	Nanometer
BAK	Benzalkonium chloride
HSV	Herpes simplex virus
PRK	Photorefractive keratectomy
ArF	Argon and Fluorine
LASIK	Laser Assisted in situ Keratomileusis
HOA	High Order Aberration
LASEK	Laser Assisted Sub-epithelial Keratomileusis
PTK	Photo Therapeutic Keratectomy
TGF	Transforming Growth Factor
CTFG	Connective Tissue Growth Factor
BSS	Balanced Salt Solution
DCVA	Distance Corrected Visual acuity
PMC	PolymorphonuclearCells
MMC	Mitomycin C
DNA	Deoxyribonucleic acid
ECM	Extracellular Matrix

IOP	Intraocular Pressure
NSAIDs	Non-Steroidal Anti-inflammatory Drugs
Cox	Cyclo-oxygenase
AMD	Age-Related Macular Degeneration
T-CAT	Topography guided Custom Ablation Treatment
T-PRK	Topography guided Photorefractive Keratectomy
RMS	Root Mean Square

Keratoconus is a chronic non-inflammatory, bilateral cornea degeneration,usually characterized by localized corneal thinning, visual distortion, corneal steepening, and central corneal scarring(1).

The biomechanical strength of the keratoconic cornea is reduced with the central and inferior regions commonly affected, resulting in cone formation (2).

In addition keratoconic patients will suffer from severe visual deterioration due to irregular astigmatism, myopia, corneal scarring (3).

Corneal cross linking is one of the available treatments directed at the underlying pathology in keratoconic corneas in which stromal biomechanical and structural instability leads to progressive ectasia. Corneal cross linking induces covalent inter- and intrafibrillar collagen cross-links creating an increase in biomechanical rigidity of the human cornea(4).

Some studies have detected a high rate of progression of keratoconus in younger patients and so have suggested treatment with corneal cross linking on diagnosis, and not waiting for progression (5).

Photorefractive keratectomy (PRK) is a laser eye surgery procedure intended to correct refractive error of the human eye. The technique permanently changes the shape of the anterior central cornea using an excimer laser to ablate a small amount of tissue from the corneal stroma(6).

In an attempt to reverse the impact of KC on vision, corneal collagen crosslinking has been combined with topography-guided photorefractive keratectomy with good results regarding safety and patient satisfaction(7).

Several combinations of PRK and CXL have been done, sequential approach has been compared with simultaneous approach in form of same day customized PRK immediately followed by CXL(8). This comparison will be discussed in this literature.

Keratoconus is a corneal ectatic disease that results in bilateral and asymmetrical corneal distortion, altered refractive powers, and reduced vision. The disease usually manifests itself during the late teens or early twenties and shows a slow progression for the next decade or two(9).

Risk Factors for KC

1. Environmental Factors

It is commonly accepted that the etiology of KC is multifactorial combining environmental and genetic factors (10).

1.1. Eye Rubbing

An association between eye rubbing and KC has long been described and accepted as a risk factor (11). Obviously, there are some variations in this association whether the eye rubbing is gentle or vigorous (12).

The microtrauma caused to the epithelium by rubbing KC corneas generates elevated levels of matrix metalloproteinases MMP-1 and MMP-13 (13), which are secreted by epithelial and stromal cells, and inflammatory

mediators including IL-6 and TNF-α (14). The release of these factors form part of the process that leads to KC and its progression. The processes include apoptosis of keratocytes as a result of increased levels of interleukin IL-1 with subsequent loss of stromal volume (15).

1.2. Atopy

Atopy is a hypersensitivity reaction, which comprises allergy, asthma, and eczema. There are some reports of an association between KC and atopy. (16). Atopy may be associated indirectly because the itch that it induced led to eye rubbing. People with KC and atopy had a steeper and thinner ectatic cornea than age- and sex-matched people with KC but without atopy(16).

1.3. Miscellaneous

Exposure to environmental neurotoxins such as nicotine in the form of cigarette smoking has not been found to be associated with KC,. In fact, there may be a negative correlation between cigarette smoking and KC possibly because the by-products of smoke may lead to cross-linking of collagen in the cornea (17). On the other hand it was indicated

more cases of KC in the urban centers with polluting industries than in the rural areas(18).

2.Genetic Studies of KC

2.1. Traditional Linkage Studies

Genetics plays an important role in the pathogenesis of KC. Relatives of KC patients have an elevated risk compared to those with unaffected relatives. Most of the familial KC is autosomal dominant while autosomal recessive pattern has also been suggested(19).

2.2. Genome-Wide Association Studies

Genome-wide association studies (GWAS) examine a large number of single nucleotide polymorphisms SNPs in thousands of individuals using high DNA genotyping technology (20). GWAS has been shown to be very powerful to identify the genetic factors of many complex traits and diseases, including central corneal thickness (CCT) and KC. A number of GWAS reported the association of CCT with sequence variants near or within many genes(21). Two CCT-associated genomic regions *FOXO1* and *FNDC3B* have been associated with KC risk (22).

2.3. Candidate Genes

A large number of candidate genes have been studied in relation to KC pathogenesis. There are two main candidate genes, visual system homeobox 1 (*VSX1*) and superoxide dismutase 1 (*SOD1*). *VSX1* is located within a linkage locus for a corneal dystrophy called posterior polymorphous corneal dystrophy (PPCD) (23), which has been associated with KC (24). PPCD and KC have similar corneal curvatures and posterior surface involvement, specifically Descemet's membrane. In 2002 *VSX1* mutations were first reported in PPCD and KC patients (25).

SOD1 encodes a major cytoplasmic antioxidant enzyme that metabolizes superoxide radicals and provides a defence against oxygen toxicity (26). Mutations in SOD1 have been implicated in familial amyotrophic lateral sclerosis (ALS) (26). It is widely accepted that oxidative stress plays a critical role in the progression of KC. An accumulation of cytotoxic by-products and high levels of oxidative stress in KC-affected corneas have been reported(27). .