Is Inflammation Driving Keratoconus?
A Holistic Study of The Molecular Pathways

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Keratoconus (KC) is a corneal disorder characterized by progressive corneal thinning leading to astigmatism and visual loss often affecting young adults. The disease is currently treated by various modalities in an attempt to retard KC progression. Despite evolving knowledge about the nature of KC, the molecular factors driving this loss of corneal structural integrity are poorly understood.

Recently, various inflammatory factors such as IL6, TNFα, MMP9, cathepsins, etc. have been shown to be elevated in the tears of KC patients suggesting a deregulation of underlying inflammatory molecular pathways.1-4

1. Investigate whether the corneal epithelium has a functional role in KC progression by engaging in deregulated gene expression profile of a select group of genes suggested to be critically involved.

2. Whether gene expression of LOX and collagen isoforms 1 and 4 in the corneal epithelium corresponds to disease severity.

MATERIALS AND METHODS

Corneal epithelium from 90 KC eyes undergoing surgery (topo-guided photorefractive keratectomy (TOPO-PRK) or corneal crosslinking were included in the study. 52 subjects with normal corneal topography, undergoing surgery (photorefractive keratectomy) for unrelated conditions were used as controls for the corneal epithelium samples.

Surgical procedures for all patients and controls were performed under topical anesthesia with proparacaine 0.5% ophthalmic solution. Debrided epithelial cells were immediately transferred to - 80C for storage till processing for RNA extraction.

Study End Points

The experimental endpoints were analysis of mRNA levels of LOX, MMP9, IL6, Collagen IV and Collagen I in patient derived samples and correlation with disease severity.

RESULTS

An increase in the level of MMP9 and IL6 was noticed across increasing
grades of KC. However a reducing trend for LOX mRNA levels across the grades of KC was observed, suggesting that it may have a role in disease progression.

CONCLUSION

• Increased levels of relative gene expression of MMP9 and IL6 is suggestive of a possible inflammatory pathway which can be a potential target in the treatment of KC.

• mRNA expression levels of corneal structure related genes collagens I and IV and LOX are reduced in KC and may correlate with disease severity.

• There could be a role of LOX on disease pathogenesis since LOX activity and protein levels are decreased.

• LOX could serve as a potential biomarker for disease screening in future.

REFERENCES

