

Treatment of KC patients with CyA for approximately 6 months reduced tear MMP9 levels and led to local reduction in corneal curvatures as determined by corneal topography maps.

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Elevated expression of matrix metalloproteinase-9 and inflammatory cytokines in keratoconus patients is inhibited by cyclosporine a.

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Abstract

PURPOSE:

The present study was designed to understand the role of inflammatory cytokines secreted by corneal epithelial cells in keratoconus (KC) and the response to treatment with cyclosporine A (CyA).

METHODS:

The study involved 129 Indian KC patients clinically graded according to Amsler-Krumeich classification and 20 healthy, nonectatic subjects as controls. Tear levels of matrix metalloproteinase-9 (MMP9), interleukin-6 (IL6), and tumor necrosis factor- α (TNF α) were

measured using ELISA kits. Gene expression was measured by qPCR in corneal epithelial cells obtained by debridement from subjects undergoing ocular surface surgeries. In addition, epithelial cells were stimulated with TNF α and treated with CyA to study its role on MMP9 expression. Finally, 20 KC patients (27 eyes) with inflammatory symptoms were treated with topical CyA application.

RESULTS:

We observed that MMP9, TNF α , and IL6 levels were strongly upregulated at the mRNA level in KC patient epithelia. **Similarly, tears collected from KC patients exhibited high levels of MMP9 and IL6 protein.** Cyclosporine A treatment significantly reduced the mRNA expression levels of IL6 and TNF α in both short- and long-term treatments; however, **it reduced MMP9 levels only in long-term treatment in cultured corneal epithelial cells. Subsequent treatment of KC patients with CyA for approximately 6 months reduced tear MMP9 levels and led to local reduction in corneal curvatures as determined by corneal topography maps.**

CONCLUSIONS:

- **The data indicate that corneal epithelium contributes to elevated MMP9 and inflammatory cytokine expression in tears of KC patients.**
- **Cyclosporine A treatment reduced MMP9 and inflammatory cytokine levels in an in vitro inflammation model system. In KC patients, CyA treatment reduced MMP9 levels measured in tears with concomitant arrest of disease progression.**
- **Therefore, CyA might be a novel treatment strategy in KC patients but requires additional evaluation in larger cohorts.**