

## ABSTRACT

### Effect of High Dose Oral Riboflavin and Direct-sun UV-A on Tumor Necrosis

### Factor Alpha (TNF- $\alpha$ ) Concentrations in Tears of Mild-Moderate Keratoconus

#### Patients

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#### Background

To date, keratoconus pathogenesis remains unclear. However, the involvement of inflammatory pathways in disease development is scientifically proven. This study offers a clinical perspective on the evidence and implications of the several inflammatory processes (TNF- $\alpha$ ) that have been identified in the tears. Also, this study evaluated the effect of high dose oral riboflavin and direct sun UV-A exposure as new alternative therapy for keratoconus.

#### Method

The TNF- $\alpha$  from tear of 8 patients (10 eyes) was evaluated before and after therapy. All patients received a high dose of oral riboflavin (800 mg/day) and direct UV-A exposure ( $\geq 15$  minutes/day) for a total of three months of follow-up. The TNF- $\alpha$  expression in tears, visual acuity, keratometry and the risk factors were examined at baseline until three months follow-up.

#### Results

TNF- $\alpha$  levels in tears decreased significantly from baseline ( $6.74 \pm 1.39$  pg/ml) to 1st month ( $5.98 \pm 0.69$  pg/ml;  $p = 0.048$ ). However, in the following months, the levels of TNF- $\alpha$  elevated in the 2nd month ( $6.29 \pm 0.84$ ;  $p = 0.390$ ) and the 3rd month ( $6.20 \pm 0.95$ ;  $p = 0.177$ ). Although re-elevated after two months, TNF- $\alpha$  concentration still decreased from the beginning of the study ( $6.74 \pm 1.39$  to  $6.20 \pm 0.95$  pg/ml). The Uncorrected visual acuity and best corrected visual acuity were significantly improved from baseline to the last follow up ( $p = 0.02$  and  $p = 0.026$  respectively).

#### Conclusion

There was a significant decrease of TNF- $\alpha$  levels in tears of mild-moderate keratoconus patients 1st month after therapy but no significant decrease in the subsequent follow-up. Furthermore, UCVA and BCVA values were improved.

#### Keywords

*TNF- $\alpha$ , Keratoconus, riboflavin, Corneal cross linkage.*

## INTISARI

### **Pengaruh Suplementasi Riboflavin Oral Dosis Tinggi dan Paparan Sinar UV-A Matahari Langsung Terhadap Ekspresi TNF- $\alpha$ pada Air Mata Pasien Keratokonus Derajat Ringan-Sedang**

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#### **Latar Belakang**

Patogenesis keratokonus masih belum jelas penyebabnya. Namun, keterlibatan jalur inflamasi dalam progresivitas penyakit telah terbukti secara ilmiah. Studi ini memberikan perspektif klinis mengenai bukti dan implikasi dari beberapa proses inflamasi (TNF- $\alpha$ ) yang telah diidentifikasi pada air mata. Selain itu, penelitian ini mengevaluasi efek riboflavin oral dosis tinggi dan paparan sinar UV-A matahari langsung sebagai terapi alternatif baru untuk keratokonus.

#### **Metode**

TNF- $\alpha$  dari air mata 8 pasien (10 mata) dievaluasi sebelum dan sesudah terapi. Semua pasien mendapatkan riboflavin oral dosis tinggi (800 mg/hari) dan paparan UV-A langsung ( $\geq 15$  menit/hari) selama total tiga bulan follow up. Ekspresi TNF- $\alpha$  pada air mata, ketajaman penglihatan, keratometri dan faktor risiko diperiksa pada awal hingga tiga bulan *follow up*.

#### **Hasil**

Kadar TNF- $\alpha$  dalam air mata menurun secara signifikan dari awal ( $6.74 \pm 1.39$  pg/ml) hingga bulan pertama ( $5.98 \pm 0.69$  pg/ml;  $p = 0.048$ ). Namun kadar TNF- $\alpha$  meningkat pada bulan ke-2 ( $6.29 \pm 0.84$ ;  $p = 0.390$ ) dan bulan ke-3 ( $6.20 \pm 0.95$ ;  $p = 0.177$ ). Meskipun meningkat kembali setelah dua bulan, konsentrasi TNF- $\alpha$  menurun hingga akhir penelitian ( $6.74 \pm 1.39$  menjadi  $6.20 \pm 0.95$  pg/ml). UCVA dan BCVA meningkat secara signifikan dari awal hingga akhir *follow up* ( $p = 0.02$  dan  $p = 0.026$ ).

#### **Kesimpulan**

Terdapat penurunan signifikan kadar TNF- $\alpha$  pada air mata pasien keratokonus ringan-sedang pada bulan pertama setelah terapi namun tidak ada penurunan signifikan pada follow up berikutnya. Nilai UCVA dan BCVA juga mengalami perbaikan.

#### **Kata Kunci**

*TNF- $\alpha$ , Keratoconus, Riboflavin, Corneal cross linkage.*