

CHANGES IN THE LEVELS OF INTERLEUKIN-6 (IL-6) IN TEARS AND BLOOD SERUM IN GRAVES ORBITOPATHY BEFORE AND AFTER INTRAVENOUS CORTICOSTEROID ADMINISTRATION.

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Introduction : Interleukin-6 (IL-6) is a key cytokine in initiating and propagating the immune response in the inflammatory process. In Graves' orbitopathy, activated B cells will increase the production of anti-thyrotropin-receptor (TSHR-Ab) antibodies by plasma cells. TSHR-Ab binds to the TSH receptor in orbital fibroblasts to produce IL-6 in tears. Inflammatory T cells that are activated in a negative response to TSHR/IGF1R also circulate in the peripheral to produce IL-6 in serum. The aim of this study is to determine changes in IL-6 levels in tears and blood serum sample in moderate to severe active graves orbitopathy before and after a total of 3 grams intravenous methylprednisolone therapy and its relationship with clinical outcomes.

Method : The study design used is a pre-post design research conducted on 21 patients, including all patients diagnosed with moderate to severe active graves orbitopathy, whom will be receiving a total of 3 grams methylprednisolone therapy among 6 weeks at the ophthalmology clinic of Dr. Sardjito Hospital, Yogyakarta. Tears and serum samples were taken before and after the 7th day of therapy. Tear samples were taken using schirmer paper in a sterile manner, while serum samples were taken from venous blood. Clinical changes in the form of improvements in CAS scores, OSDI, TBUT, and Schimer tests were recorded.

Result : There is no significant decrease in serum IL-6 levels after 6 weeks of a total 3 grams methylprednisolone administered intravenously, with a median of 2.01 (1.5-6.10) pg/ml to 1.84 (1.5-8.39)pg/ml ($p=0.975$). There is no decrease in IL-6 level in tear samples after intravenous administration of 3 grams methylprednisolone, 52.92 (22.74-239) pg/ml to 54.76 (15.61-163.32) pg/ml ($p=0.068$). There are clinical improvements found during post 6 weeks evaluation of 3 grams methylprednisolone therapy with a decrease in CAS score ($p<0.001$), decreased OSDI ($p<0.001$), increased TBUT ($p<0.001$), and an increase in Schimer test result ($p=0.001$). There is no correlation between changes in IL-6 levels in tears with changes in TBUT ($p=0.763$), changes in Schirmer test ($p=0.750$), OSDI (0.804), and CAS score ($p=0.584$). There is no correlation in changes of serum IL-6 level with changes in TBUT ($p=0.603$), OSDI ($p=0.679$), and CAS score ($p=0.274$). There is significant correlation in the changes of serum IL-6 levels with changes in Schirmer test result ($p=0.024$, $r = 0.492$).

Conclusion : IL-6 levels in tears and serum samples in patients with moderate to severe active Graves orbitopathy after administration of 3 gram intravenous methylprednisolone therapy were no different compared to before therapy. Changes in serum IL-6 were negatively correlated with changes in the Schirmer test.

Key words : Active Graves Orbitopathy, Interleukin-6, Methylprednisolone

INTISARI

PERUBAHAN KADAR INTERLEUKIN-6 (IL-6) DI AIR MATA DAN SERUM DARAH PADA GRAVES ORBITOPATI SEBELUM DAN SESUDAH PEMBERIAN KORTIKOSTEROID INTRAVENA

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Pendahuluan : Interleukin-6 (IL-6) merupakan sitokin kunci dalam memulai dan menyebarkan respon imun pada proses inflamasi. Pada Graves Orbitopati, sel B yang teraktivasi akan meningkatkan produksi antibodi anti-thyrotropin-receptor (TSHR-Ab) oleh sel plasma. TSHR-Ab berikatan dengan reseptor TSH di fibroblas orbita sehingga menghasilkan IL-6 pada air mata. Sel T inflamasi yang teraktivasi sebagai respon negatif dari TSHR/IGF1R juga bersirkulasi di perifer sehingga menghasilkan IL-6 pada serum. Penelitian ini bertujuan untuk mengetahui perubahan kadar IL-6 di air mata dan serum darah pada graves orbitopati aktif derajat sedang berat sebelum dan sesudah terapi intravena metylprednisolon total dosis 3 gram dan hubungannya dengan luaran klinis.

Metode : Desain penelitian ini menggunakan rancangan penelitian pre-post design yang dilakukan pada 21 pasien, meliputi semua pasien yang terdiagnosis graves orbitopati aktif derajat sedang-berat dan mendapat terapi metylprednisolon total dosis 3 gram selama 6 minggu di Poliklinik Mata RSUP Dr.Sardjito Yogyakarta. Pengambilan air mata dan serum dilakukan sebelum terapi dan setelah terapi hari ke-7. Sampel air mata diambil menggunakan kertas schimer secara steril, sedangkan sampel serum dilakukan pengambilan melalui darah vena. Perubahan klinis berupa perbaikan CAS skor, OSDI, TBUT, dan Schimer test dilakukan pencatatan.

Hasil : Tidak terdapat penurunan signifikan kadar IL-6 serum sebelum dan sesudah 6 minggu pemberian intravena metylprednisolon 3 gram, yaitu median 2,01 (1,5-6,10) pg/ml menjadi 1,84 (1,5-8,39)pg/ml ($p=0,975$). Tidak didapatkan penurunan kadar IL-6 air mata sebelum dan sesudah pemberian intravena metylprednisolon 3 gram, yaitu 52,92 (22,74-239) pg/ml menjadi 54,76 (15,61-163,32) pg/ml ($p=0,068$). Terdapat perbaikan klinis pada evaluasi setelah 6 minggu terapi Methylprednisolon 3 gram berupa penurunan CAS skor ($p<0,001$), penurunan OSDI ($p<0,001$), peningkatan TBUT ($p<0,001$), dan peningkatan Schimer test ($p=0,001$). Tidak terdapat hubungan antara perubahan IL-6 air mata dengan perubahan TBUT ($p=0,763$), perubahan Schirmer test ($p=0,750$), OSDI (0,804), dan CAS score ($p=0,584$). Tidak terdapat hubungan antara perubahan IL-6 serum dengan perubahan TBUT ($p=0,603$), OSDI ($p=0,679$), dan CAS score ($p=0,274$). Terdapat hubungan yang bermakna antara perubahan IL-6 serum dengan perubahan Schirmer test ($p=0,024$, $r = 0,492$).

Kesimpulan: Kadar IL-6 di air mata dan serum darah pada pasien graves orbitopati aktif derajat sedang berat setelah pemberian terapi metylprednisolon 3 gram intravena tidak ada beda dibandingkan dengan sebelum terapi. Perubahan IL-6 serum berkorelasi negatif dengan perubahan Schirmer test.

Kata Kunci : Graves Orbitopati Aktif, Interleukin-6, Methylprednisolon.