

ABSTRACT

EFFECT OF TNF- α -1031 T>C (rs1799964) GENE POLYMORPHISM ON CHANGE IN CENTRAL MACULAR THICKNESS AFTER INTRAVITREAL ANTI-VEGF BEVACIZUMAB INJECTION THERAPY IN PATIENTS WITH NEOVASCULAR AMD

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Background: The success of anti-VEGF treatment as standard therapy in neovascular AMD patients is still variable, presumably due to differences in genetic profiles between individuals. Pharmacogenetic studies are important to achieve the hope of personalized therapy application, but they are still rarely carried out.

Objective: This study aims to determine the effect of TNF- α gene polymorphism at -1031 T>C on changes in central macular thickness after intravitreal anti-VEGF bevacizumab injection therapy in patients with neovascular AMD.

Methods: This study was a prospective cohort with a consecutive sampling method. Neovascular AMD patients were classified based on TNF- α genetic profiling at -1031 point, which were polymorphism and without polymorphism, then underwent anti-VEGF Bevacizumab injection therapy. CMT before and after 1 month post-injection was assessed using OCT. OCT decline was assessed based on the difference between baseline CMT and 1-month post-injection CMT.

Results: A total of 92 eyes were included in the study, 2 of which dropped out because they did not attend the CMT examination at 1 month post injection. Median CMT reduction in the polymorphism and non-polymorphism group were 35.674 ± 117.94 and 5.00 ± 108.00 μ m respectively, with no statistically significant difference ($p = 0.292$). Based on dichotomous analysis, there were 21 (51%) subjects in the polymorphism group and 30 (61%) subjects in the non polymorphism group with poor therapeutic response to intravitreal anti-VEGF Bevacizumab injection. Meanwhile, 20 (49%) subjects in the polymorphism group and 19 (39%) subjects in the non-polymorphism group showed a good therapeutic response. The difference in proportion between the two was not statistically significant ($p = 0.340$).

Conclusion: In this study, there is no significant difference in CMT reduction after 1 month of Bevacizumab anti-VEGF injection, both statistically and clinically, between nAMD patients with TNF- α -1031 T>C gene polymorphism and without.

Keywords: Neovascular AMD, TNF- α -1031 T>C Gene Polymorphism, Anti-VEGF, Bevacizumab.

INTISARI

PENGARUH POLIMORFISME GEN TNF- α -1031 T>C (rs1799964) TERHADAP PERUBAHAN KETEBALAN MAKULA SENTRAL PASCA TERAPI INJEKSI ANTI-VEGF BEVACIZUMAB INTRAVITREAL PADA PASIEN DENGAN AMD NEOVASKULAR

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Latar Belakang: Keberhasilan pengobatan Anti-VEGF sebagai terapi standard pada pasien AMD neovaskular masih bervariasi, diduga disebabkan oleh perbedaan profil genetik antar individu. Studi farmakogenetik penting dilakukan guna mencapai harapan aplikasi terapi personalisasi, namun masih jarang dilakukan.

Tujuan: Penelitian ini bertujuan untuk mengetahui pengaruh polimorfisme gen TNF- α pada -1031 T>C terhadap perubahan ketebalan makula sentral pasca terapi injeksi anti-VEGF bevacizumab intravitreal pada pasien dengan AMD neovaskular

Metode: Penelitian ini menggunakan rancangan cohort prospektif dengan pengambilan sampel secara konsekutif. Pasien AMD neovaskular diklasifikasikan berdasarkan profil genetik TNF- α pada titik -1031, yaitu polimorfisme dan tanpa polimorfisme, kemudian menjalani terapi injeksi anti-VEGF Bevacizumab. CMT sebelum dan setelah 1 bulan pasca injeksi dinilai menggunakan OCT. Penurunan OCT dinilai berdasarkan selisih antara CMT awal dan CMT 1 bulan pasca injeksi.

Hasil: Sebanyak 92 mata dilibatkan dalam penelitian, 2 diantaranya mengalami *drop out* karena tidak hadir pada pemeriksaan CMT 1 bulan pasca injeksi. Median penurunan CMT pada kelompok polimorfisme dan non polimorfisme masing-masing adalah $35,674 \pm 117,94 \mu\text{m}$ dan $5,00 \pm 108,00 \mu\text{m}$, secara berurutan, dengan tidak ada perbedaan yang signifikan secara statistik ($p = 0.292$). Berdasarkan analisis dikotomi, terdapat 21 (51%) subjek pada kelompok polimorfisme dan 30 (61%) subjek pada kelompok non polimorfisme yang memiliki respons terapi yang buruk terhadap injeksi anti-VEGF Bevacizumab intravitreal. Sementara itu, 20 (49%) subjek pada kelompok polimorfisme dan 19 (39%) subjek pada kelompok non polimorfisme menunjukkan respons terapi yang baik. Perbedaan proporsi antara kedua kelompok tidak signifikan secara statistik ($p = 0,340$).

Kesimpulan: Pada penelitian ini, tidak didapatkan perbedaan signifikan penurunan CMT pasca 1 bulan injeksi anti-VEGF Bevacizumab, baik secara statistik maupun klinis antara pasien nAMD dengan polimorfisme dan tanpa polimorfisme gen TNF- α -1031 T>C.

Kata Kunci: AMD neovaskular, Polimorfisme gen TNF- α -1031 T>C, Anti-VEGF, Bevacizumab.