

Perbandingan Kadar Vascular Endothelial Growth Factor (VEGF) Air Mata Terhadap Neovaskularisasi Kornea Antara Ulkus Kornea Bakteri dan Jamur = Comparison of Tear Fluid Vascular Endothelial Growth Factor and Corneal Neovascularization between Bacterial and Fungal Corneal Ulcers

Dita Permatasari, author

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Abstrak

Latar belakang: Ulkus kornea dapat menyebabkan kebutaan karena sikatriks kornea. Transplantasi kornea sebagai tatalaksana sikatriks kornea berisiko tinggi mengalami kegagalan dengan adanya neovaskular pada kornea resipien. VEGF-A diduga sebagai faktor angiogenik utama dalam terbentuknya neovaskular kornea. Berdasarkan pengamatan klinis, neovaskular kornea pada pasien ulkus kornea bakteri lebih luas dibandingkan ulkus kornea jamur, namun belum pernah dibandingkan secara ilmiah. Tujuan: Studi ini membandingkan VEGF-A air mata dan neovaskularisasi kornea antara ulkus kornea bakteri dan jamur. Korelasi antara VEGF-A dengan luas neovaskular juga dihitung. Metode: Penelitian dilakukan terhadap pasien ulkus kornea bakteri dan jamur dengan sampel foto kornea dan air mata. Pengambilan sampel dilakukan pada hari pertama kedatangan dan diulang pada minggu keempat. Analisis foto kornea menggunakan peranti lunak ImageJ® untuk menilai luas neovaskular kornea dan luas defek kornea. Analisis VEGF-A air mata menggunakan enzyme-linked immunosorbent assay (ELISA). Perbedaan dianggap signifikan jika $p < 0,05$. Hasil: Didapatkan 12 subjek ulkus kornea bakteri dan 10 subjek ulkus kornea jamur dengan rerata usia 37 tahun. Bakteri terbanyak *Pseudomonas aeruginosa*. dan jamur terbanyak *Fusarium sp.* Defek kornea setara pada awal (bakteri 25,6% (1,8-81,5) vs jamur 22,7% (3,0-45,0), $p = 0,644$) dan membaik pada minggu keempat (bakteri 0,04% (0-30,5) vs jamur 2,5% (0-15,1), $p = 0,368$). Luas neovaskular kornea pada hari pertama setara (bakteri 10,3% (2,3-37,5) vs jamur 8,0% (3,7-22,8), $p = 0,262$) namun pada minggu keempat lebih luas pada kelompok bakteri (bakteri 21,6% (2,3-58,0) vs jamur 11,0% (5,4-22,5), $p = 0,033$). VEGF-A air mata setara pada hari pertama (bakteri 215,6 pg/ml (58,0-1111,6) vs jamur 339,3 pg/ml (22,7-1313,0), $p = 0,391$) dan minggu keempat (bakteri 399,7 pg/ml (181,9-1496,3) vs jamur 743,8 pg/ml (78,7-1416,5), $p = 0,792$). Tidak didapatkan korelasi VEGF-A terhadap luas area neovaskular kornea (hari pertama $r = -0,28$, $p = 0,212$, minggu keempat $r = -0,04$ $p = 0,855$). Kesimpulan: Perbedaan luas neovaskular pada minggu keempat diduga karena faktor proangiogenik pada bakteri yang jarasnya melalui VEGF-A serta faktor antiangiogenik pada jamur yang mengalahkan pengaruh VEGF-A. Diperlukan penelitian mendasar yang mencari faktor antiangiogenik tersebut pada jamur.

.....Background: Corneal ulcer can cause blindness due to corneal cicatrix. Corneal transplantation as the treatment of corneal cicatrix had higher risk for rejection or failure if the recipient's cornea possessed neovascularization. VEGF-A was thought to be the major angiogenic factor in corneal neovascularization. Based on clinical observation, corneal neovascularization in bacterial corneal ulcers had more area than in fungal corneal ulcers, however it was never proved scientifically. Objective: This study aimed to compare tear fluid VEGF-A and corneal neovascularization between bacterial and fungal corneal ulcers. The correlation between VEGF-A and neovascular area was also measured. Methods: Corneal photograph and tear fluid samples of bacterial and fungal in corneal ulcer patients were studied. Sample was taken at the first

visit and at the fourth week follow up. Corneal photograph was analyzed using ImageJ® software to measure neovascular area and defect area. Tear fluid VEGF-A was examined using enzyme-linked immunosorbent assay (ELISA). Difference was considered significant if $p < 0,05$. Results: There were 12 bacterial corneal ulcer patients and 10 fungal corneal ulcer patients with mean age 37 years old. Most common bacteria was *Pseudomonas aeruginosa* and most common fungi was *Fusarium* sp. Corneal defect area between the groups was similar at the first visit (bacterial 25,6% (1,8-81,5) vs fungal 22,7% (3,0-45,0), $p = 0,644$) and improved at the fourth week (bacterial 0,04% (0-30,5) vs fungal 2,5% (0-15,1), $p=0,368$). Neovascular area was similar among the groups at the first visit (bacterial 10,3% (2,3-37,5) vs fungal 8,0% (3,7-22,8), $p = 0,262$), however bacterial group showed larger area at the fourth week (bacterial 21,6% (2,3-58,0) vs fungal 11,0% (5,4-22,5), $p=0,033$). Tear fluid VEGF-A was similar at the first visit (bacterial 215,6 pg/ml (58,0-1111,6) vs fungal 339,3 pg/ml (22,7-1313,0), $p=0,391$) and the fourth week (bacterial 399,7 pg/ml (181,9-1496,3) vs fungal 743,8 pg/ml (78,7-1416,5), $p=0,792$). No correlation obtained between VEGF-A and corneal neovascular area (first visit $r -0,28$, $p=0,212$, fourth week $r -0,04$ $p=0,855$).

Conclusion: The difference of neovascular area at the fourth week could be due to proangiogenic factor of bacteria through its effect on VEGF-A and antiangiogenic factor in fungi that may overcome VEGF-A effect. Further study is needed to confirm the antiangiogenic factor that fungi possess.