

Correlation between vitreous advanced glycation end products, and d-dimer with blood hba1c levels in proliferative diabetic retinopathy

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Abstrak

BACKGROUND:proliferative diabetic retinopathy (DR) is an advanced form of DR that eventually could lead to blindness. Levels of vitreous advanced glycation end products (AGEs) and D-dimer may reflect the pathological changes in the retina, but only few studies have assessed their correlation with blood hemoglobin A1C (HbA1c) levels. This study aimed to find the association between blood HbA1c levels with vitreous AGEs and D-dimer levels in patients with proliferative DR.

METHODS:an analytical cross-sectional study was performed in subjects with proliferative DR who underwent vitrectomy. Subjects were divided into 2 subgroups, i.e. uncontrolled ($HbA1c > 7\%$) and controlled ($HbA1c < 7\%$) groups. Vitreous AGEs and D-dimer levels were assessed; the levels were compared between uncontrolled and controlled hyperglycemic patients. Statistic correlation tests were also performed for evaluating blood HbA1c, vitreous AGEs, and D-dimer levels.

RESULTS:a total of 47 patients were enrolled in this study and 32 (68.1%) of them were women. Median vitreous AGEs level was 11.0 (3.0 - 48.0) $\mu g/mL$; whereas median vitreous D-dimers level was 5,446.0 (44.0 - 37,394.0) ng/mL . The median vitreous AGEs levels was significantly higher in patients with uncontrolled vs. controlled hyperglycemia (14.0 vs. 4.0 mg/mL ; $p<0.001$). There was a significant positive correlation with moderate strength between blood HbA1c level and vitreous AGEs level ($r=0.524$; $r^2=0.130$; $p=0.0001$). Blood HbA1c level could be used to predict vitreous AGEs level by using the following calculation:
vitreous AGEs = $-1.442 + (1.740 \times \text{blood HbA1c})$. Vitreous D-dimer levels were not significantly different between uncontrolled and controlled hyperglycemia (median 4607.5 vs. 5701.6 ng/mL ; $p = 0.458$). There was a positive significant correlation between blood HbA1c and vitreous D-dimer levels ($r = 0.342$; $p = 0.019$); however the correlation was weak. Vitreous AGEs level had a positive significant correlation with vitreous D-dimer levels ($r = 0.292$; $p = 0.046$) and the correlation strength was also weak.

CONCLUSION:median vitreous AGEs levels were significantly higher in proliferative DR patients with uncontrolled than those with controlled hyperglycemia. Blood HbA1c level can be used to assess vitreous AGEs level in patients with proliferative DR by using the following calculation: vitreous AGEs = $-1.442 + (1.740 \times \text{HbA1c})$. However, the blood HbA1c level can not be used to predict vitreous D-dimer level in patients with proliferative DR.

.....Latar belakang: retinopati diabetik (RD) tipe proliferatif merupakan bentuk lanjut RD yang selanjutnya dapat menyebabkan kebutaan. Kadar produk akhir glikasi/advanced glycation end products (AGEs) dan D-dimer cairan vitreus dapat menggambarkan perubahan patologi pada retina, tetapi hanya ada sedikit penelitian yang menilai korelasi antara kedua parameter tersebut dengan kadar HbA1c dalam darah. Tujuan penelitian ini menemukan hubungan antara kadar HbA1c darah dengan kadar AGEs dan D-dimer cairan vitreus pada pasien dengan RD tipe proliferatif. Metode: penelitian bersifat analitik potong lintang pada pasien dengan RD tipe proliferatif yang menjalani vitrektomi. Pasien dibagi dalam 2 kelompok yaitu hiperglikemi tidak terkendali ($HbA1c > 7\%$) dan terkendali ($HbA1c < 7\%$). Kadar AGEs dan D-dmer

cairan vitreus diukur dan kadarnya dibandingkan antara pasien hiperglikemi tidak terkendali dan terkendali. Uji korelasi statistik juga dilakukan antara kadar HbA1c darah dengan kadar AGEs dan D-dimer cairan vitreus.

Hasil: pasien berjumlah 47, dengan 32 (68.1%) pasien adalah wanita. Nilai median kadar AGEs cairan vitreus 11.0 (3.0 – 48.0) g/mL, dan nilai median kadar D-dimer cairan vitreus 5,446.0 (44.0 – 37,394.0) ng/mL. Nilai median kadar AGEs cairan vitreus lebih tinggi bermakna pada pasien dengan hiperglikemia tidak terkendali dibandingkan dengan hiperglikemia terkendali (14.0 vs. 4.0 mg/mL; p<0.001). Terdapat korelasi positif bermakna dengan kekuatan sedang antara kadar HbA1c darah dan kadar AGEs cairan vitreus ($r = 0.524$; $r^2 = 0.130$; $p=0.0001$). Kadar HbA1c darah dapat digunakan untuk memperkirakan kadar AGEs cairan vitreus dengan menggunakan rumus: kadar AGEs cairan vitreus = $-1.442 + (1.740 \times \text{HbA1c darah})$. Kadar D-dimer cairan vitreus pasien dengan hiperglikemia tidak terkendali tidak berbeda bermakna dengan pasien hiperglikemia terkendali (median 4607.5 vs. 5701.6 ng/mL; $p = 0.458$). Terdapat korelasi positif bermakna tetapi dengan kekuatan lemah antara kadar HbA1c darah dengan kadar D-dimer cairan vitreus ($r = 0.342$; $p = 0.019$). Kadar AGEs cairan vitreus memiliki korelasi positif bermakna dengan kekuatan lemah dibandingkan dengan kadar D-dimer cairan vitreus ($r = 0.292$; $p = 0.046$).

Kesimpulan: nilai median kadar AGEs cairan vitreus lebih tinggi bermakna pada pasien RD proliferatif dengan hiperglikemia tidak terkendali dibandingkan hiperglikemia terkendali. Kadar HbA1c darah dapat digunakan untuk memperkirakan kadar AGEs cairan vitreus pada pasien RD proliferatif dengan menggunakan rumus: kadar AGEs cairan vitreus = $-1.442 + (1.740 \times \text{HbA1c darah})$. Kadar HbA1c darah pada pasien RD proliferatif tidak dapat digunakan untuk memperkirakan kadar D-dimer cairan vitreus.