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Efek Asam Klorogenat terhadap Stres Oksidatif dan Apoptosis pada Lobus Frontalis Tikus dengan Diabetes Mellitus
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INTISARI

Latar Belakang: Diabetes mellitus (DM) dengan hiperglikemia menyebabkan berbagai macam komplikasi, salah satunya adalah disfungsi memori. Lobus frontalis diketahui bertanggung jawab terhadap disfungsi memori akibat hiperglikemia dan sering dikaitkan dengan apoptosis sel neuron yang dimediasi stres oksidatif. Asam klorogenat (CGA) dilaporkan memiliki efek neuroprotektif, namun pengaruhnya terhadap lobus frontalis pada tikus DM belum banyak diketahui.

Tujuan: Mengkaji pengaruh pemberian asam klorogenat terhadap ekspresi mRNA SOD1, SOD2, p53, Bax dan Bcl-2 pada lobus frontalis tikus dengan DM.

Metode: Sebanyak 30 tikus jantan galur *Wistar* (umur 2 bulan, berat badan 150-200 gram) dibagi menjadi 6 kelompok (n=5): C (kontrol), DM1,5 (DM 1,5 bulan), DM2 (DM 2 bulan), CGA12,5, CGA25 dan CGA50 (DM+CGA dosis 12,5, 25 dan 50 mg/kgBB secara berturut-turut). Injeksi dosis tunggal streptozotocin (STZ) 60 mg/kgBB intraperitoneal diberikan untuk menginduksi DM. Injeksi CGA intraperitoneal diberikan pada bulan ke-1,5 setelah induksi DM, setiap hari selama 14 hari. Jarak uji *probe* Morris *water maze* (MWM) diukur pada setiap tikus satu hari sebelum terminasi. Setelah terminasi, lobus frontalis tikus dikeluarkan untuk ekstraksi RNA. *Reverse transcriptase* PCR dilakukan untuk mengukur ekspresi mRNA SOD1, SOD2, p53, Bax dan Bcl-2.

Hasil: Kelompok DM2 menunjukkan jarak uji *probe* MWM yang signifikan lebih pendek dan ekspresi mRNA SOD1 dan Bcl-2 yang signifikan lebih rendah secara statistik daripada kelompok C. Setelah pemberian CGA, jarak uji *probe* MWM kelompok CGA25 signifikan lebih panjang daripada kelompok C, tetapi kelompok CGA12,5 dan CGA50 tidak berbeda dibandingkan dengan kelompok C. Ekspresi mRNA SOD1 kelompok CGA12,5 dan CGA25 signifikan lebih tinggi daripada kelompok DM1,5. Ekspresi mRNA SOD2 kelompok CGA12,5, CGA25 dan CGA50 lebih tinggi daripada kelompok DM1,5 dan DM2. Ekspresi mRNA Bcl-2 CGA12,5 dan CGA 50 signifikan lebih tinggi daripada kelompok DM2.

Kesimpulan: Asam klorogenat memiliki kecenderungan fungsi memori melalui peningkatan ekspresi mRNA SOD1 dan Bcl-2 pada tikus diabetes mellitus.

Kata Kunci: *chlorogenic acid, oxidative stress, apoptosis, diabetes, frontal lobe*

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ABSTRACT

Background: Diabetes mellitus (DM), characterized with hyperglycemia, causes various complications, one of which is memory dysfunction. The frontal lobe is known to be responsible for impaired memory function due to hyperglycemia and is often associated with oxidative stress-mediated neuronal cell apoptosis. Chlorogenic acid (CGA) is reported to have neuroprotective effect. However, its effect on the frontal lobe in DM rats is not widely known.

Objective: To elucidate the effect of chlorogenic acid administration on the expression of mRNA SOD1, SOD2, p53, Bax and Bcl-2 in the frontal lobe of DM rats.

Methods: Thirty male rat Wistar background (2-month-old, 150-200 gBW) were randomly divided into six groups: C (control), DM1,5 (1,5-month DM), DM2 (1,5 month), CGA12,5, CGA25 dan CGA50 (DM+CGA 12,5, 25 dan 50 mg/kgBW, respectively). Single dose streptozotocin (STZ) 60 mg/kgBW was intraperitoneally injected for DM induction. Intraperitoneal CGA injection was given at 1,5-month after DM induction, daily for 14 days. Path length was measured on probe test of Morris water maze (MWM) test one day before termination. After sacrificed, frontal lobes were carefully harvested for RNA extraction. Reverse transcriptase PCR was performed to examine mRNA expression of SOD1, SOD2, p53, Bax and Bcl-2.

Results: DM2 group demonstrated significant shorter path length on probe test of MWM and significant lower mRNA expression of SOD1 and Bcl-2, compared to C group. After CGA administration, CGA25 group showed significant longer path length than C group. However, no differences of path length were found between CGA12,5 and CGA50 groups and C group. CGA12,5 and CGA25 had significant higher mRNA expression of SOD1 than DM1,5 group. Compared to DM1,5 and DM2 groups, mRNA expression of SOD2 of the administration of all three CGA doses were markedly increased. Furthermore, mRNA expression of Bcl-2 was significantly upregulated on CGA12,5 and CGA50 groups, compared to DM2 group.

Conclusion: Chlorogenic acid might improve memory function through upregulation of frontal lobes' SOD1 and Bcl-2 mRNA expression in DM rats.

Keywords: chlorogenic acid, oxidative stress, apoptosis, diabetes, frontal lobe