ABSTRACT

Background: Liver is affected due to chronic hyperglycemia in Diabetes mellitus (DM) cases. Hyperglycemia causes oxidative stress, mitochondrial electron transport disruptions thus produce ROS. Excessive ROS degrades antioxidant enzyme SOD2 and induces apoptosis by disrupting p53, Bax, and Bcl-2 signaling.

Objective: This study determines effect of non-enzymatic antioxidant chlorogenic acid (CGA) in association with antioxidant SOD2 and apoptotic regulatory genes Bax, Bcl-2, and p53 in diabetic rats.

Methods: Male Wistar rats divided into six groups: control, DM 1.5 months, DM 2 months, DM with CGA 12.5 mg/kgBW (CGA1), DM with CGA 25 mg/kgBW (CGA2), DM with CGA 50 mg /kgBW (CGA3). Blood examination was carried out to measure SGOT and SGPT levels. Liver tissue was harvested for mRNA analysis of SOD2, Bax, and Bcl-2 using RT-PCR. Difference test statistics were performed on average electrophoresis band density of each group. Immunohistochemical staining was performed to see positive signals of p53 in liver cells. Difference test statistics were performed on average percentage of p53 positive signals in each group.

Results: Liver disfunction occured in DM2 group through higher levels of SGPT and SGOT, higher expression of Bax, higher signal on p53 immunostaining, and lower expression of Bcl-2 compared to control group. Administration of CGA 12.5 mg/kgBW showed lower levels of SGPT (p=0.023) and SGOT (p=0.021), lower expression of Bax (p=0.014), lower positive signal of p53 immunostaining (p=0.001), and higher expression of Bcl-2 (p=0,043) compared to DM2 group. Expression of SOD2 in DM2 group was higher than control, administration of CGA 50 mg/kgBW showed higher SOD2 expression than DM2 group but not significant.

Conclusion: Giving CGA 12.5 mg/kgBW ameliorated liver function of diabetic rats through downregulation of Bax and p53, and upregulation of Bcl-2. Administration of CGA had no effect on SOD2 expression in diabetic rats.

Keywords: Chlorogenic acid, Diebetes mellitus, liver, Bax, Bcl-2, p53

INTISARI

Latar belakang: Hati mengalami gangguan akibat hiperglikemi kronis pada Diabetes mellitus (DM). Hiperglikemi menyebabkan stres oksidatif, menggangu transpor elektron mitokondria, dan menghasilkan ROS. ROS menurunkan enzim antioksidan SOD2 dan mencetuskan apoptosis melalui gangguan persinyalan p53, Bax, dan Bcl-2.

Tujuan: Mengetahui efek pemberian antioksidan non-enzimatik asam klorogenat (CGA) dalam kaitannya dengan ekspresi SOD2 dan gen regulator apoptosis Bax, Bcl-2 dan p53 pada tikus DM.

Metode: Tikus Wistar jantan dibagi menjadi enam kelompok: kontrol, DM 1,5 bulan, DM 2 bulan, DM dengan CGA 12.5 mg/kgBB (CGA1), DM dengan CGA 25 mg/kgBB (CGA2), dan DM dengan CGA 50 mg/kgBB (CGA3). Darah diambil untuk pemeriksaan enzimatik kadar SGOT dan SGPT. Jaringan hati diambil untuk analisis ekspresi mRNA SOD2, Bax, dan Bcl-2 menggunakan RT-PCR. Uji beda dilakukan terhadap rerata densitas pita hasil elektroforesis setiap kelompok. Pengecatan imunohistokimia dilakukan untuk melihat sinyal positif ekspresi p53 sel hati. Uji beda dilakukan terhadap rerata persentase sinyal positif ekspresi p53 setiap kelompok.

Hasil: Gangguan hati terjadi pada kelompok DM2 berupa kadar SGPT dan SGOT lebih tinggi, ekspresi Bax dan sinyal positif p53 lebih tinggi, dan ekspresi Bcl-2 lebih rendah dibandingkan kontrol. Pemberian CGA 12,5 mg/kgBB menunjukkan perbaikan hati berupa kadar SGPT (p=0,023) dan SGOT (p=0,021) lebih rendah, ekspresi Bax (p=0,014) dan sinyal positif p53 (p=0,001) lebih rendah, serta ekspresi Bcl-2 (p=0,043) lebih tinggi dibandingkan kelompok DM2. Kelompok DM2 menunjukkan ekspresi SOD2 lebih tinggi dari kontrol. Pemberian CGA 50mg/kgBB menunjukkan ekspresi SOD2 lebih tinggi dibanding kelompok DM2, namun tidak signifikan.

Simpulan: Pemberian CGA 12,5 mg/kgBB berpengaruh pada perbaikan fungsi hati tikus DM melalui ekspresi Bax dan p53 yang lebih rendah, serta ekspresi Bcl-2 yang lebih tinggi. Pemberian CGA tidak berpengaruh pada ekspresi SOD2 hati tikus DM.

Kata kunci: Asam klorogenat, Diabetes mellitus, hati, Bax, Bcl-2, p53