INTISARI

PENGARUH ASAM KLOROGENAT TERHADAP KADAR KREATININ, CEDERA TUBULUS GINJAL, DAN EKSPRESI mRNA E-CADHERIN PADA MENCIT DENGAN PERIODE KRONIS CEDERA ISKEMIK REPERFUSI GINJAL

Latar Belakang: Cedera iskemik reperfusi (I/R) ginjal menjadi salah satu penyebab terbanyak terjadinya *Acute Kidney Injury* (AKI) yang dapat berprogresi menjadi *Chronic Kidney Disease* (CKD). Asam klorogenat diketahui memiliki efek antioksidan dan antiapoptosis tetapi pengaruhnya terhadap cedera iskemik reperfusi ginjal pada periode kronis belum diketahui secara jelas.

Tujuan: Mengetahui efek asam klorogenat terhadap kadar kreatinin serum, cedera tubulus ginjal, dan ekspresi mRNA E-Cadherin pada mencit dengan periode kronis cedera iskemik reperfusi ginjal.

Metode: Mencit jantan galur *Swiss-Webster* (n=25, usia 3-4 bulan, berat 30-40 g) dibagi dalam 5 kelompok: kontrol (SO), iskemik reperfusi terminasi hari ke-8 (I/R8), iskemik reperfusi terminasi hari ke-12 (I/R12), I/R8 + asam klorogenat 14 mg/kgBB/hari I.P (I/R+CGA8), dan I/R12 + asam klorogenat 14 mg/kgBB/hari I.P (I/R+CGA12). Model cedera I/R dilakukan dengan klem bilateral pediculus renalis selama 30 menit kemudian direperfusi. Kemudian mencit diterminasi pada hari ke-8 dan 12 dan dilakukan pengambilan sampel untuk ekstraksi RNA dan pembuatan blok parafin. Kadar kreatinin serum diuji dan ekspresi mRNA E-Cadherin diukur menggunakan RT-PCR. Dilakukan pula pewarnaan dengan menggunakan Periodic Acid Schiff untuk selanjutnya dilakukan penilaian cedera tubulus menggunakan Skor Cedera Tubulus/ *Tubular Injury Score*.

Hasil: Kadar kreatinin serum dan Skor Cedera Tubulus pada kelompok I/R8 dan I/R12 lebih tinggi dibandingkan SO ($p<0,05$). Sedangkan, ekspresi mRNA E-Cadherin pada kelompok I/R8 dan I/R12 tidak memiliki perbedaan yang signifikan dibandingkan SO ($p>0,05$). Kelompok I/R+CGA8 memiliki kadar kreatinin serum dan Skor Cedera Tubulus yang lebih rendah dibandingkan I/R8, walaupun tidak signifikan ($p>0,05$). Sama halnya dengan ekspresi mRNA E-Cadherin pada kelompok I/R+CGA8 tidak memiliki perbedaan yang signifikan dibandingkan I/R8 ($p>0,05$). Pada kelompok I/R+CGA12 memiliki kadar kreatinin serum dan Skor Cedera Tubulus yang lebih rendah dibandingkan I/R12 ($p<0,05$). Sedangkan, ekspresi mRNA E-Cadherin pada kelompok I/R+CGA12 memiliki nilai yang lebih rendah dibandingkan I/R12, walaupun tidak signifikan ($p>0,05$).

Kesimpulan: Asam klorogenat berpotensi mengurangi perburukan fungsi, cedera tubulus ginjal, dan kerusakan integritas antarsel epitel pada periode kronis cedera iskemik reperfusi ginjal.

Kata Kunci: Iskemik reperfusi ginjal, AKI, asam klorogenat, kreatinin serum, cedera tubulus ginjal, E-Cadherin.

ABSTRACT

THE EFFECT OF CHLOROGENIC ACID TO CREATININE LEVEL, KIDNEY TUBULAR INJURY, AND E-CADHERIN mRNA EXPRESSION IN MICE WITH CHRONIC PERIOD OF KIDNEY ISCHEMIC REPERFUSION INJURY

Background: Kidney ischemic reperfusion injury leads to Acute Kidney Injury (AKI) which will progress to Chronic Kidney Disease (CKD). Chlorogenic acid has been known to have antioxidant and antiapoptotic effects, but its effects in chronic period of kidney ischemic reperfusion injury has to be known yet.

Purpose: The aim of this study is to determine the effect of chlorogenic acid in attenuating the serum creatinine level, kidney tubular injury, and expression of E-Cadherin mRNA in mice with chronic period of kidney ischemic reperfusion injury.

Method: Male Swiss-Webster mice (n=25, 3-4 months, 30-40 gram) were divided into 5 groups: Sham operation/ control (SO), ischemic reperfusion terminated on 8^{th} day (I/R8), ischemic reperfusion terminated on 12^{th} day (I/R12), I/R8 + chlorogenic acid 14 mg/kgBW/day I.P (I/R+CGA8), and I/R12 + chlorogenic acid 14 mg/kgBW/day I.P (I/R+CGA12). The ischemic reperfusion injury model was performed with bilateral renal pedicles clamping for 30 minutes then reperfuse. The mice were terminated on the 8^{th} and 12^{th} day and kidneys were harvested for RNA extraction and paraffin blocks preparation. The serum creatinine level was measured and mRNA expression of E-Cadherin was measured using RT-PCR. Staining using Periodic Acid Schiff was also used for scoring the tubular injury.

Result: Serum creatinine level and tubular injury score of I/R8 and I/R12 group were higher than SO ($p<0,05$). Whereas, E-Cadherin mRNA expression of I/R8 and I/R12 were not significantly different to SO ($p>0,05$). I/R+CGA8 group had lower serum creatinine level and tubular injury score than I/R8 had, although it was not significant ($p>0,05$). E-Cadherin mRNA expression of I/R+CGA8 was not significantly different to I/R8 ($p>0,05$). I/R+CGA12 group had lower serum creatinine level and tubular injury score than I/R12 had ($p<0,05$). Whereas, E-Cadherin mRNA expression of I/R+CGA12 group was lower than I/R12, although it was not significant ($p>0,05$).

Conclusion: Chlorogenic acid may attenuate the deterioration of kidney function, kidney tubular injury, and epithelial integrity in chronic period of kidney ischemic reperfusion injury.

Keywords: Kidney ischemic reperfusion, AKI, chlorogenic acid, serum creatinine, kidney tubular injury, E-Cadherin.