ABSTRAK

PENGARUH ASAM KLOROGENAT TERHADAP REMODELING VASKULAR ARTERI INTRARENAL PADA MENCIT DENGAN PERIODE KRONIS CEDERA ISKEMIK REPERFUSI GINJAL

Latar Belakang:
Cedera iskemik/reperfusi (I/R) ginjal merupakan penyebab utama gagal ginjal akut yang dapat berlanjut menjadi gagal ginjal kronis. Gangguan hemodinamik dan metabolisme menyebabkan remodeling vaskular arteri intrarenal. Asam klorogenat (CGA) telah diketahui memiliki efek terhadap remodeling vaskular. Tetapi, efek CGA terhadap remodeling vaskular arteri intrarenal pada periode kronis cedera I/R ginjal masih belum diketahui.

Tujuan:
Mengetahui pengaruh pemberian asam klorogenat terhadap remodeling vaskular arteri intrarenal pada mencit galur *Swiss* dengan periode kronis cedera iskemik/reperfusi ginjal.

Metode:
Mencit jantan galur *Swiss-Webster* (n=25, usia 2-3 bulan, berat 30-40 g) dibagi dalam 5 kelompok: kontrol (SO), iskemik/reperfusi 8 hari (IR8), iskemik/reperfusi 12 hari (IR12), iskemik/reperfusi 8 hari + asam klorogenat 14 mg/kgBB per hari (IR8 CGA), dan iskemik/reperfusi 12 hari + asam klorogenat 14 mg/kgBB per hari (IR12 CGA). Pada hari ke-8 dan ke-12, mencit diterminasi kemudian dilakukan pengambilan sampel untuk blok parafin. Ketebalan dinding, luas lumen, dan *lumen/wall area ratio* vasa intrarenal dihitung berdasarkan pewarnaan histologis dengan *Sirius Red*.

Hasil:
Ketebalan dinding vasa intrarenal pada kelompok IR8 lebih tebal dibandingkan kelompok SO ($p<0,05$). Ketebalan dinding vasa pada kelompok IR12 lebih tebal dibandingkan kelompok SO ($p<0,01$). Ketebalan dinding vasa pada kelompok yang diberi CGA (IR8 CGA dan IR12 CGA) lebih sempit daripada kelompok IR (IR8 dan IR12), namun tidak signifkan secara statistik ($p>0,05$). Luas lumen vasa pada kelompok IR lebih kecil dibandingkan kelompok SO ($p<0,01$) dan luas lumen vasa pada kelompok yang diberi CGA lebih besar daripada kelompok IR ($p<0,05$). *lumen/wall area ratio* vasa pada kelompok IR8 lebih rendah dibandingkan kelompok SO ($p<0,05$). *Lumen/wall area ratio* vasa pada kelompok IR12 lebih rendah dibandingkan kelompok SO ($p<0,01$). *Lumen/wall area ratio* vasa pada kelompok yang diberi CGA lebih tinggi daripada kelompok IR, namun tidak signifikan secara statistik ($p>0,05$).

Kesimpulan:
Asam klorogenat (CGA) berpotensi untuk mengurangi dampak cedera iskemik/reperfusi ginjal dengan menurunkan efek vasokonstriksi.

Kata Kunci:
Asam klorogenat, iskemik/reperfusi, periode kronis, remodeling vaskular, ketebalan dinding vasa, luas lumen vasa, *lumen/wall area ratio* vasa.

ABSTRACT

THE EFFECT OF CHLOROGENIC ACID ON INTRARENAL ARTERIES VASCULAR REMODELING IN MICE WITH CHRONIC PERIOD OF RENAL ISCHEMIC/REPERFUSION INJURY

Background:
Renal ischemic/reperfusion (I/R) injury is a major cause of acute kidney injury which can progress to chronic kidney disease. Hemodynamic and metabolic disturbance cause vascular remodeling in the intrarenal arteries. Chlorogenic acid (CGA) has been known to have effect on vascular remodeling. However, the effect of CGA on intrarenal arteries vascular remodeling in the chronic period of renal I/R injury remains unknown.

Aim:
Elucidate the effect of chlorogenic acid supplementation on intrarenal arteries vascular remodeling in Swiss strain mice with a chronic period of renal ischemic/reperfusion injury.

Method:
Male Swiss-Webster mice (n=25, 2-3 months old, 30-40 grams) were divided into five groups: control (SO), renal ischemic/reperfusion injury terminated on 8^{th} day (IR8), renal ischemic/reperfusion injury terminated on 12^{th} day (IR12), IR8 + chlorogenic acid 14 mg/kg/day (IR8 CGA), and IR12 + chlorogenic acid 14 mg/kg/day (IR12 CGA). On the 8^{th} and 12^{th} days, mice were terminated and then samples were taken for paraffin blocks. Wall thickness, lumen area, and lumen/wall area ratio of intrarenal arteries were calculated based on histological staining with Sirius Red.

Results:
Intrarenal arteries wall thickness in IR8 were significantly thicker compared to SO ($p<0,05$). Wall thickness in IR12 were significantly thicker compared to SO ($p<0,01$). Wall thickness in all groups with chlorogenic acid (IR8 CGA and IR12 CGA) were thinner compared to IR group (IR8 and IR12), but were not statistically significant ($p>0,05$). Vascular lumen area in IR group were smaller compared to SO ($p<0,01$) and vascular lumen area in all groups with chlorogenic acid were bigger compared to IR ($p<0,05$). Vascular lumen/wall area ratio in IR8 were lower compared to SO ($p<0,05$). Vascular lumen/wall area ratio in IR12 were lower compared to SO ($p<0,01$). Vascular lumen/wall area ratio in all groups with chlorogenic acid were higher compared to IR, but were not statistically significant ($p>0,05$).

Conclusion:
Chlorogenic acid (CGA) may attenuate renal ischemic/reperfusion injury by reducing vasoconstriction effect.

Keyword:
Chlorogenic acid, ischemic/reperfusion, chronic period, vascular remodeling, vascular wall thickness, vascular lumen area, vascular lumen/wall area ratio.