INTISARI

PENGARUH PEMBERIAN ASAM KLOROGENAT TERHADAP EKSPRESI GEN VIMENTIN DAN JUMLAH PROLIFERASI SEL EPITEL TUBULUS GINJAL PADA MENCIT DENGAN CEDERA ISKEMIA REPERFUSI GINJAL

Latar Belakang:
Cedera iskemia reperfusi ginjal adalah salah satu sebab utama cedera ginjal akut yang berakibat pada tingginya angka morbiditas dan mortalitas. Dalam beberapa penelitian, asam klorogenat dapat mengurangi dampak cedera iskemia reperfusi dengan berperan sebagai anti-inflamasi, antioksidan, dan meningkatkan regenerasi ginjal. Namun, penelitian mengenai pengaruh asam klorogenat terhadap proses perbaikan dan regenerasi ginjal masih terbatas.

Tujuan:
Penelitian ini bertujuan untuk menginvestigasi aktivitas renoprotektif asam klorogenat pada mencit dengan cedera iskemia reperfusi ginjal, khususnya pada ekspresi gen vimentin yang merupakan penanda mesenkim pada proses *epithelial-mesenchymal transition* dan jumlah proliferasi sel epitel tubulus pada mencit dengan cedera iskemia reperfusi ginjal.

Metode:
Dua puluh lima mencit galur *Swiss-Webster* jantan (3-4 bulan, 30-40 g) dibagi secara random menjadi 5 kelompok perlakuan: *Sham Operation* (SO), iskemia reperfusi (I/R) yang diinduksi dengan *bilateral renal pedicles clamping*, dan I/R yang diberikan CGA. Asam klorogenat diberikan secara intraperitoneal pada kelompok I/R+CGA (3,5; 7; dan 14mg/kg) satu hari setelah *clamping*. Mencit diobservasi selama 3 hari setelah pemberian perlakuan, lalu diterminasi. Ekspresi vimentin diukur menggunakan *Reverse Transcriptase*-PCR. Sedangkan, jumlah proliferasi sel epitel tubulus dikuantifikasi menggunakan pewarnaan imunohistokimia terhadap PCNA.

Hasil:
Kelompok I/R memiliki ekspresi gen vimentin yang lebih tinggi terhadap kelompok SO. Namun, tidak ada peningkatan proliferasi sel epitel yang signifikan pada kelompok I/R terhadap SO. Ekspresi vimentin pada kelompok I/R+CGA lebih rendah dibandingkan I/R. Jumlah proliferasi sel epitel pada kelompok I/R+CGA2 dan I/R+CGA3 meningkat signifikan dibandingkan kelompok I/R. Penurunan ekspresi vimentin di antara kelompok I/R+CGA tidak signifikan secara statistik. Namun, ada peningkatan yang signifikan terhadap jumlah proliferasi sel epitel pada I/R+CGA3 jika dibanding I/R+CGA1.

Kesimpulan:
Asam klorogenat meningkatkan perbaikan dan regenerasi ginjal dengan menurunkan ekspresi vimentin dan meningkatkan proliferasi sel epitel tubulus.

Kata Kunci:
Asam klorogenat, AKI, cedera iskemia reperfusi, *epithelial-mesenchymal transition*, vimentin, PCNA

ABSTRACT

THE EFFECT OF CHLOROGENIC ACID SUPPLEMENTATION TO VIMENTIN GENE EXPRESSION AND RENAL TUBULAR EPITHELIAL CELL PROLIFERATION IN MICE WITH RENAL ISCHEMIA REPERFUSION INJURY

Background:
Kidney ischemia reperfusion injury is the main cause of AKI that lead to increasing morbidity and mortality. Some studies suggest that chlorogenic acid attenuates the effect of ischemia reperfusion injury by its role as an anti-inflammation, antioxidant, and improving kidney regeneration. Unfortunately, studies about the effect of chlorogenic acid on kidney repair and regeneration are still limited.

Aim:
The aim of this study was to investigate the renoprotective activity of chlorogenic acid (CA) in a murine model of kidney ischemia reperfusion injury particularly its effect on vimentin gene expression as a mesenchymal marker of epithelial-mesenchymal transition and kidney epithelial cell proliferation in mice with renal ischemia reperfusion injury.

Method:
Twenty five male *Swiss-Webster* mice (3-4 months-old, 30-40 g) were randomly divided into 5 treatment groups: *Sham Operation* (SO), Ischemia reperfusion (I/R) induced by bilateral renal pedicles clamping, and I/R with supplementation of CGA groups (I/R+CGA). The mice of I/R+CGA (3.5, 7, and 14mg/kg) groups were intraperitoneally administered of CGA 1 day after clamping. Mice were observed for 3 days after treatment, then euthanized. Expression of vimentin was measured using Reverse Transcriptase-PCR. Meanwhile, the number of tubular epithelial cell proliferation was quantified using immunostaining of PCNA.

Result:
I/R group had higher expression of vimentin gene than SO group. However we did not find that proliferation of epithelial cells on I/R group compared to SO increase significantly. There were significantly lower expression of vimentin gene on I/R+CGA groups than I/R group. Epithelial cell proliferation number was higher on I/R+CGA2 and I/R+CGA3 groups compared to I/R group. There were no significant reduction of vimentin gene expression among I/R+CGA groups. Meanwhile epithelial cell proliferation of I/R+CGA1 was higher than I/R+CGA3.

Conclusion:
Chlorogenic acid improves kidney repair and regeneration by reducing the expression of vimentin gene and improve the the kidney epithelial tubular cell proliferation.

Keywords:
Chlorogenic acid, AKI, ischemia reperfusion injury, epithelial-mesenchymal transition, vimentin, PCNA