INTISARI

Latar belakang: Cedera iskemia-reperfusi (I/R) ginjal menyebabkan cedera ginjal akut yang berpotensi menjadi gagal ginjal kronis. Calcitriol menunjukkan peran renoprotektif, tetapi pengaruhnya terhadap *remodeling* vaskular dan ekspresi zat-zat vasoaktif pada disfungsi endothelial pasca cedera I/R ginjal masih belum jelas.

Tujuan: Mengetahui pengaruh pemberian Calcitriol terhadap ekspresi mRNA ppET-1, ET_AR, eNOS, dan *remodeling* vaskular pada mencit model cedera I/R ginjal fase akut dan kronis.

Metode: Sebanyak 25 mencit jantan galur Swiss (usia 3-4 bulan, berat badan 30-40 gram) dibagi 5 kelompok (n=5): SO (kontrol), IR3 (cedera I/R ginjal 3 hari), IR12 (cedera I/R ginjal 12 hari), IRD3 (cedera I/R ginjal 3 hari + injeksi Calcitriol 0,5 µg/kgBB/hari), IRD12 (cedera I/R ginjal 12 hari + injeksi Calcitriol 0,5 µg/kgBB/hari). Kelompok I/R diberi perlakuan *clamping* pediculus renalis bilateral 30 menit diikuti reperfusi. Setelah terminasi, ginjal bilateral dipreservasi. Pewarnaan Sirius Red untuk kuantifikasi *lumen/wall area ratio* dan ketebalan dinding arteri. RT-PCR untuk mengukur ekspresi mRNA ppET-1, ET_AR, eNOS. Uji statistik menggunakan *one-way ANOVA* diikuti *post-hoc LSD*. Nilai $p<0,05$ dianggap signifikan secara statistik.

Hasil: Kuantifikasi arteri intrarenalis kelompok IRD3 dan IRD12 menunjukkan LWAR lebih tinggi dan ketebalan dinding lebih rendah dibandingkan kelompok I/R tanpa Calcitriol. Ekspresi mRNA ppET-1 kelompok IRD3 lebih tinggi daripada IR3, sedangkan kelompok IRD12 lebih rendah dibandingkan IR12 dan secara statistik bermakna (p=0,037). Kelompok I/R dengan Calcitriol menunjukkan ekspresi mRNA ET_AR lebih rendah secara signifikan pada IRD3 (p=0,000) dan IRD12 (p=0,029). Ekspresi mRNA eNOS kelompok I/R dengan Calcitriol lebih tinggi daripada kelompok I/R tanpa Calcitriol, dengan perbedaan signifikan secara statistik pada IRD12 (p=0,015).

Kesimpulan: Pemberian Calcitriol 0,5 µg/kgBB/hari menunjukkan pencegahan *remodeling* vaskular, ekspresi mRNA ET_AR lebih rendah dan eNOS lebih tinggi pada mencit model cedera I/R ginjal fase akut dan kronis. Setelah pemberian Calcitriol, ekspresi mRNA ppET-1 lebih tinggi pada cedera I/R ginjal fase akut tetapi lebih rendah pada fase kronis.

Kata kunci: *Calcitriol, vascular remodeling, endothelin, ET_AR, eNOS, kidney ischemia-reperfusion injury*

ABSTRACT

Background: Kidney ischemia-reperfusion (I/R) injury causes acute kidney injury which often develops chronic kidney disease. Calcitriol has shown renoprotective effects, but its role in vascular remodeling and vasoactive substances expression in endothelial dysfunction following kidney I/R injury remains unclear.

Objective: To investigate Calcitriol's effects on ppET-1, ET_AR, eNOS mRNA expression and vascular remodeling during acute and chronic phases of kidney I/R injury in mice

Methods: Twenty-five male Swiss background mice (3–4-month-old, 30-40 gBW) were randomly divided into 5 groups (n=5): SO (control), IR3 (3-day kidney I/R injury), IR12 (12-day kidney I/R injury), IRD3 (3-day kidney I/R injury + Calcitriol injection 0,5 µg/kgBB/day), IRD12 (12-day kidney I/R injury + Calcitriol injection 0,5 µg/kgBB/day). Bilateral renal pedicles clamping for 30 minutes was performed on I/R groups followed by reperfusion. After termination, bilateral kidneys were preserved. Sirius Red staining was performed to quantify lumen/wall area ratio and arterial wall thickness. RT-PCR was conducted to measure ppET-1, ET_AR, eNOS mRNA expression. Statistical analysis used one-way ANOVA followed by post-hoc LSD, with $p<0,05$ considered statistically significant.

Results: Intrarenal arteries quantification of IRD3 and IRD12 showed higher LWAR and lower wall thickness than I/R groups without Calcitriol. Group IRD3 had higher ppET-1 mRNA expression than IR3, meanwhile IRD12 was lower than IR12 and statistically significant (p=0,037). The I/R groups receiving Calcitriol had significantly lower ET_AR mRNA expression in IRD3 (p=0,000) and IRD12 (p=0,029). In I/R groups with Calcitriol, eNOS mRNA expression was higher than I/R groups without Calcitriol, with statistically significant difference in IRD12 (p=0,015).

Conclusions: Administration of 0,5 µg/kgBB/day Calcitriol showed vascular remodeling prevention, lower ET_AR, higher eNOS mRNA expression in acute and chronic phases of kidney I/R injury in mice. Following Calcitriol administration, ppET-1 mRNA expression was higher in acute phase, but lower in chronic phase of kidney I/R injury.

Keywords: Calcitriol, vascular remodeling, endothelin, ET_AR, eNOS, kidney ischemia-reperfusion injury