

INTISARI

PENGARUH PEMBERIAN KALSITRIOL TERHADAP FRAKSI AREA MYOFIBROBLAST DAN EKSPRESI *MONOCYTE CHEMOATTRACTANT PROTEIN-1* (MCP-1) PADA GINJAL MENCIT DENGAN MODEL *UNILATERAL URETERAL OBSTRUCTION*

Latar Belakang: Gagal ginjal kronis memiliki progresivitas yang dapat berujung pada *end-stage renal disease*. Fibrosis interstisial merupakan ciri utama yang ditemukan pada gagal ginjal kronis. Pada gagal ginjal kronis, terjadi aktivasi NF- κ B, yang dapat menginduksi kemokin MCP-1 sehingga meningkatkan infiltrasi makrofag. Aktivasi NF- κ B juga meningkatkan ekspresi Snail1 yang dapat menginisiasi proses *epithelial-mesenchymal transition*. Vitamin D aktif (kalsitriol) memiliki efek renoprotektif. Penelitian mengenai pengaruh vitamin D pada kondisi UUU (*unilateral ureteral obstruction*) telah banyak dilakukan, namun mekanisme pengaruhnya terhadap ekspresi MCP-1 dan fraksi area myofibroblast masih perlu dikaji lebih dalam.

Tujuan: Mengetahui pengaruh pemberian kalsitriol terhadap fraksi area myofibroblast dan ekspresi MCP-1 pada ginjal mencit dengan model *unilateral ureteral obstruction*.

Metode Penelitian: Lima belas ekor mencit galur *Swiss* yang berusia 3-4 bulan dengan berat badan 30-50 gram dibagi ke dalam tiga kelompok yaitu mencit dengan *Sham Operation* (SO, n=5), mencit dengan UUU selama 14 hari (UUU, n=5), dan mencit dengan UUU yang diberi kalsitriol 0,125 μ g/kgBB/hari i.p. selama 14 hari (UUU-D, n=5). UUU dilakukan dengan meligasi ureter kanan mencit pada bagian proksimal dan distal dengan memotong ureter di antara kedua ligasi. Fraksi area myofibroblast diperoleh dari sediaan histologis dengan pewarnaan imunohistokimia dengan antibodi monoklonal anti α -SMA. Ekspresi MCP-1 diperoleh dengan menggunakan metode RT-PCR. Data dianalisis menggunakan *software* ImageJ dan diuji statistiknya menggunakan uji *One-way ANOVA* atau *Kruskal Wallis* pada SPSS versi 16.0.

Hasil Penelitian: Pemberian kalsitriol pada mencit model UUU selama 14 hari secara signifikan menurunkan fraksi area myofibroblast ($p=0,014$) dan ekspresi MCP-1 ($p=0,048$). Ekspresi MCP-1 berkorelasi positif kuat secara signifikan terhadap fraksi area myofibroblast ($p=0,001$; $r=0,832$).

Kesimpulan: Pemberian kalsitriol mampu menurunkan fraksi area myofibroblast dan ekspresi MCP-1 pada fibrosis interstisial ginjal.

Kata kunci: Gagal ginjal kronis, fibrosis interstisial ginjal, *unilateral ureteral obstruction*, myofibroblast, MCP-1, kalsitriol

ABSTRACT

THE EFFECTS OF CALCITRIOL TO MYOFIBROBLAST AREA FRACTION AND MONOCYTE CHEMOATTRACTANT PROTEIN-1 (MCP-1) EXPRESSION IN MICE KIDNEY WITH UNILATERAL URETERAL OBSTRUCTION MODEL

Background: Chronic kidney disease can progress to end-stage renal disease. Renal interstitial fibrosis is the main characteristic of chronic kidney disease. In chronic kidney disease, there is activation of NF- κ B, which later can induce MCP-1 expression, and increases macrophages infiltration. NF- κ B activation also induces the expression of Snail1 which can initiate *epithelial-mesenchymal transition*. Active vitamin D (calcitriol) has renoprotective effect. Several studies of vitamin D effects in UUO have been conducted, but the exact mechanism of vitamin D effects to MCP-1 expression dan myofibroblast area fraction should be elucidated more.

Objective: This study is aimed to elucidate the effects of calcitriol to myofibroblast area fraction and MCP-1 expression in mice kidney with unilateral ureteral obstruction model.

Methods: Fifteen (3-4 months old; 30-50 g) Swiss background mice were divided into 3 groups: *Sham Operation* (SO, n=5), mice with UUO in 14 days (UUO, n=5), and mice with UUO plus intraperitoneal calcitriol injection 0,125 μ g/kgBB/day in 14 days (UUO-D, n=5). Animals underwent right side ureter ligation on proximal and distal part and continued with ureteral cutting between both parts. Myofibroblast area fraction were assessed by immunohistochemistry staining with monoclonal antibody anti α -SMA. Expression of MCP-1 were assessed by RT-PCR. Both were analyzed by ImageJ and are statistically tested by One-way ANOVA and Kruskal Wallis on SPSS 16.0 software.

Results: Calcitriol decreased myofibroblast area fraction ($p=0,014$) and MCP-1 expression ($p=0,048$) significantly in mice with UUO model in 14 days. Expression of MCP-1 has strong positive correlation with myofibroblast area fraction ($p=0,001$; $r=0,832$).

Conclusion: Calcitriol decreases myofibroblast area fraction and MCP-1 expression in renal interstitial fibrosis.

Keywords: Chronic kidney disease, renal interstitial fibrosis, unilateral ureteral obstruction, myofibroblast, MCP-1, calcitriol