INTISARI

Latar Belakang: Hiperurisemia merupakan faktor independen dari penyakit kardiovaskular-ginjal, termasuk penyakit ginjal kronis (PGK). Hiperurisemia menyebabkan *nephropath*i hiperurisemi yang ditandai dengan inflamasi, cedera oksidatif, cedera tubulus dan fibrosis. Beberapa faktor mempengaruhi mortalitas PGK, salah satunya vitamin D, tetapi hubungan antara hiperurisemia dan vitamin D belum diteliti secara lebih dalam, terutama aspek biomedisnya.

Tujuan: Penelitian ini bertujuan untuk mengkaji efek pemberian vitamin D setelah induksi asam urat pada model mencit hiperurisemia dengan memeriksa cedera tubulus, remodeling vaskular, inflamasi dan fibrosis.

Material dan Metode: Model hiperurisemia dibuat dengan suntikan intraperitoneal asam urat 125 mg/Kg BB setiap hari selama 7 (UA7, n=7) dan 14 hari (UA14, n=7). Vitamin D diberikan dengan suntikan calcitriol 0.5 ng/Kg BB secara intraperitoneal selama 7 hari setelah induksi asam urat 14 hari (UA14VD7 n=7). Injeksi NaCl dilakukan selama 21 hari pada kelompok kontrol (n=7). Pewarnaan Periodic Acid Schiff (PAS) and Sirius Red digunakan untuk kuantifikasi cedera tubulus dan fibrosis. Reverse Transcriptase and Real Time-PCR (RT-PCR) dilakukan untuk kuantifikasi ekspresi mRNA SOD-1, E-cadherin, ppET-1, ETAR, eNOS, TLR-4, NFkB, MCP-1, TGF-β1 dan Collagen-1. Sedangkan IHC dilakukan untuk lokalisasi ekspresi SOD-1.

Hasil: Hiperurisemia terjadi pada kelompok UA7 dan UA14 ditandai dengan lebih tingginya kadar asam urat dan kreatinin, dengan ekspresi E-cadherin yang lebih rendah. UA14VD7 memperlihatkan perbaikan cedera tubulus dengan ekspresi E-Cadherin yang lebih tinggi. Kelompok dengan induksi asam urat mempunyai ekspresi mRNA TGF-β1, Collagen-1, TLR-4, NF-κB, ppET-1 yang lebih tinggi dengan penurunan ekspresi mRNA SOD-1 and eNOS, yang menunjukkan fibrosis, inflamasi dan remodeling vaskular. Pemberian Calcitriol menurunkan fibrosis, inflamasi, and remodeling vaskular. Hasil ini berhubungan dengan ekspresi mRNA eNOS and SOD-1 yang lebih tinggi. IHC menunjukkan perbaikan ekspresi SOD-1 di sel epithelial.

Kesimpulan: Pemberian Vitamin D setelah induksi asam urat memulihkan gangguan ginjal dengan berkurangnya cedera tubulus, remodeling vascular, inflamasi dan fibrosis.

Kata kunci: vitamin D, hiperurisemia, cedera tubulus, remodeling vaskular, inflamasi, fibrosis

ABSTRACT

Background: Hyperuricemia is the independent factor of cardiovascular and kidney diseases, including of chronic kidney disease (CKD). Hyperuricemia induces hyperuricemia nephropathy with inflammation, tubular injury and fibrosis. Furthermore, CKD mortality is affected by many factors, includes vitamin D status as a non-conventional factor. Association between hyperuricemia and vitamin D need to be studied experimentally to elucidate its biomedical bases.
Objective: This study aimed to know the effect of vitamin D administration to hyperuricemia mice model, especially in kidney injury with elucidating tubular injury, vascular remodeling, inflammation and fibrosis.
Materials and Methods: Hyperuricemia condition was performed by daily intraperitoneal injection of uric acid 125 mg/Kg BW for 7 (UA7 group, n=7) and 14 days (UA14 group, n=7). Vitamin treatment ws carried-out with calcitriol 0.5 ng/Kg BW for 7 days after 14 days of uric acid treatment (UA14VD7 group, n=7). NaCl injection was performed for 21 days in control group (n=7). Periodic Acid Schiff (PAS) and Sirius Red staining were done for tubular injury and fibrosis quantification. Reverse Transcriptase and Real Time-PCR (RT-PCR) were performed for mRNA expression of SOD-1, E-cadherin, ppET-1, ETAR, eNOS, TLR-4, NFkB, MCP-1, TGFbeta and Collagen-1. Meanwhile, immunostaining (IHC) was performed for SOD-1 expression localization in kidney tissue.
Results: Hyperuricemia condition occurred in UA14 group with higher uric acid and creatinine level compared to control group, which associated with higher tubular injury and lower E-Cadherin mRNA expression. UA14VD7 demonstrated attenuation of tubular injury with E-Cadherin mRNA upregulation. Uric acid treated groups also had higher TGF-β1, Collagen-1, TLR-4, NF-κB, ppET-1 with downregulation of SOD-1 and eNOS mRNA expression showing inflammation and vascular remodeling. Calcitriol treatment induced attenuation of fibrosis, inflammation, and vascular remodeling. These findings associated with higher eNOS and SOD-1 mRNA expression. Immunostaining demonstrated preservation of SOD-1 in epithelial cells.
Conclusion: Vitamin D treatment after uric acid induction attenuates the kidney by reducing tubular injury, vascular remodeling, inflammation and fibrosis.

Keywords: vitamin D, hyperuricemia, tubular injury, vascular remodeling, inflammation, fibrosis