

## INTISARI

### PENGARUH VITAMIN D TERHADAP VASCULAR REMODELING DAN EKSPRESI ENDOTHELIAL NITRIC OXIDE SYNTHASE (ENOS) DAN PREPROENDOTHELIN-1 (PPET-1) PADA MENCIT MODEL UNILATERAL URETERAL OBSTRUCTION

#### Latar Belakang:

Penderita *chronic kidney disease* (CKD) saat ini mengalami peningkatan di Indonesia maupun dunia. ET-1 dan eNOS diduga terlibat dalam progresi CKD dimana keduanya berperan dalam regulasi vasa. Bentuk aktif Vitamin D, calcitriol diduga memiliki efek renoprotektif. Namun, hingga saat ini belum banyak diketahui peran calcitriol dalam regulasi ET-1, eNOS, dan *vascular remodeling*.

#### Tujuan:

Penelitian ini bertujuan untuk mengetahui peran Vitamin D dalam *vascular remodeling* melalui modulasi ET-1 dan eNOS pada mencit dengan *Unilateral Ureteral Obstruction* (UUO).

#### Metode:

Mencit jantan galur *Swiss Webster* (n=15, usia 3-4 bulan, berat 30-40 g) dibagi dalam 3 kelompok: kontrol (SO), UUO 7 hari tanpa Vitamin D (UUO), dan UUO 7 hari dengan Vitamin D (UUOD). Pada hari ke-7, mencit diterminasi kemudian dilakukan pengambilan sampel untuk ekstraksi cDNA dan blok parafin. Remodeling vasa dinilai dengan pengecatan *Sirius Red* dengan parameter area lumen dan *lumen-to-wall area ratio* (LWAR). Ekspresi PPET-1 dan eNOS dinilai menggunakan RT-PCR.

#### Hasil:

Didapatkan penurunan area lumen, LWAR dan peningkatan ekspresi PPET-1 ( $p < 0,05$ ) tanpa perbedaan bermakna pada ekspresi eNOS pada kelompok UUO dibandingkan dengan SO. Sedangkan dibanding UUO, pada kelompok UUOD didapatkan nilai yang lebih tinggi untuk ekspresi eNOS ( $p < 0,05$ ) tanpa perbedaan bermakna pada area lumen, LWAR dan ekspresi ET-1.

#### Kesimpulan:

Vitamin D mempengaruhi *vascular remodeling* melalui modulasi eNOS tanpa melalui jalur ET-1.

#### Kata Kunci:

CKD, calcitriol, *vascular remodeling*, PPET-1, eNOS

## ABSTRACT

### THE EFFECT OF VITAMIN D ON VASCULAR REMODELING, PREPROENDOTHELIN-1 (PPET-1) AND ENDOTHELIAL NITRIC OXIDE SYNTHASE (eNOS) EXPRESSION IN MICE WITH UNILATERAL URETERAL OBSTRUCTION (UO)

#### **Background:**

Increased prevalence of patient with chronic kidney disease (CKD) is happening not only in Indonesia but also globally. ET-1 and eNOS are known to be involved in CKD progression where both have role on vascular regulation. Active form of Vitamin D, calcitriol are suggested to have renoprotective effect. However, the role of calcitriol on ET-1 and eNOS regulation marked by vascular remodeling is not clearly understood.

#### **Aim:**

This study is aimed to elucidate the role of Vitamin D in vascular remodeling through ET-1 and eNOS modulation in mice with unilateral ureteral obstruction (UO).

#### **Method:**

Male Swiss-Webster background mice (n=15, 3-4 months old, weighted 30-40 g) was divided into three groups: sham-operated (SO), 7 days UO without Vitamin D (UO), and 7 days UO with Vitamin D (UOD). Termination was done at day 7, and the obstructed kidney was harvested for paraffin making and cDNA extraction. Vascular remodeling was assessed by measuring lumen area and lumen-to-wall area ratio (LWAR) microscopically with Sirius Red staining. The expression of PPET-1 and eNOS was quantified using RT-PCR.

#### **Results:**

UO7 group demonstrated lower lumen area, LWAR and higher PPET-1 expression ( $p < 0,05$ ), but no significance difference in eNOS expression compared to SO. While compared to UO, UOD group demonstrate higher eNOS expression ( $p < 0,05$ ), but no significance difference in lumen area, LWAR and PPET-1 expression.

#### **Conclusion:**

Vitamin D is suggested to have a role in vascular remodeling via eNOS modulation independent ET-1 pathway.

#### **Keywords:**

CKD, calcitriol, vascular remodeling, PPET-1, eNOS