

PENGARUH DIET RENDAH PROTEIN TERHADAP CEDERA TUBULUS DAN EKSPRESI mRNA E-CADHERIN PADA MENCIT DENGAN UNILATERAL URETERAL OBSTRUCTION

INTISARI

Latar Belakang: Gizi kurang khususnya pada periode perkembangan janin hingga perinatal terbukti berdampak pada proses organogenesis dan fungsi ginjal ketika dewasa. *Unilateral Ureteral Obstruction* (UOO) merupakan metode representatif dari kondisi gagal ginjal kronis. Kekurangan protein dilaporkan memperburuk kondisi cedera, namun efeknya pada ginjal belum diketahui secara mendalam.

Tujuan Penelitian: Untuk mengkaji pengaruh diet rendah protein terhadap ketahanan ginjal dalam kondisi gagal ginjal kronis melalui eksplorasi skor cedera tubulus dan ekspresi mRNA E-cadherin pada mencit dengan UOO.

Metode Penelitian: Penelitian ini merupakan jenis penelitian quasi eksperimental dengan rancangan penelitian *post-test with control group design*. Kondisi gagal ginjal kronis direpresentasikan dengan model *Unilateral Ureteral Obstruction* (UOO) pada 20 mencit jantan galur Swiss Webster berusia 2-3 bulan yang dibagi dalam 4 kelompok, yaitu kelompok SO (*Sham Operation*, n=5), UOO (UOO dengan diet normal sebagai kontrol, kadar protein 20%, n=5), UOO+10% (UOO dengan diet kasein, kadar protein 10% selama 1 bulan sebelum UOO, n=5), dan UOO+12% (UOO dengan diet kasein, kadar protein 12% selama 1 bulan sebelum UOO, n=5). Mencit diterminasi pada hari ke-7 setelah UOO. Skor cedera tubulus diperiksa dengan pewarnaan *Periodic Acid Schiff* (PAS). Ekspresi mRNA E-cadherin diperiksa dengan RT-PCR kemudian dilakukan analisis densitometri dari foto pita hasil elektroforesis. Skor cedera tubulus diuji menggunakan Kruskal-Wallis dan uji *post-hoc* Mann-Whitney untuk analisis komparatif non-parametrik, sedangkan ekspresi mRNA E-cadherin diuji menggunakan ANOVA satu jalur yang dilanjutkan dengan uji *post-hoc* LSD untuk uji parametrik.

Hasil: Analisis komparatif non-parametrik menunjukkan perbedaan skor cedera tubulus yang signifikan antarkelompok. Kelompok dengan perlakuan UOO menunjukkan skor cedera tubulus yang lebih tinggi ($1,70 \pm 0,10$ vs. $0,38 \pm 0,08$; $p < 0,05$) dan ekspresi mRNA E-cadherin yang lebih rendah ($1,13 \pm 0,26$ vs. $1,57 \pm 0,12$; $p < 0,05$) dibandingkan kelompok *sham operation*, sedangkan kelompok dengan diet rendah protein 10% dan 12% menunjukkan skor cedera tubulus yang lebih tinggi ($3,88 \pm 0,08$ vs. $0,38 \pm 0,08$; $3,62 \pm 0,08$ vs. $0,38 \pm 0,08$; $p < 0,05$) dan ekspresi mRNA E-cadherin yang lebih rendah ($1,10 \pm 0,24$ vs. $1,57 \pm 0,12$; $1,12 \pm 0,18$ vs. $1,57 \pm 0,12$; $p > 0,05$) dibandingkan kelompok UOO dengan diet normal.

Kesimpulan: Pemberian diet rendah protein menghasilkan skor cedera tubulus yang lebih tinggi secara signifikan dan ekspresi E-cadherin yang lebih rendah namun tidak signifikan pada mencit dengan *unilateral ureteral obstruction*.

Kata Kunci: diet rendah protein, cedera tubulus, E-cadherin, *unilateral ureteral obstruction* (UOO)

THE EFFECT OF LOW PROTEIN DIET ON TUBULAR INJURY AND E-CADHERIN mRNA EXPRESSION IN MICE WITH UNILATERAL URETERAL OBSTRUCTION

ABSTRACT

Background: Undernutrition is one of the public health problems that still occur in Indonesia. Undernutrition, specifically in the period of fetal development until perinatal, proven to have an impact on organogenesis and adult kidney function. *Unilateral ureteral obstruction* (UUO) is a representative method of chronic kidney failure. Protein deficiency is reported to worsen the condition of injury, but its effects on the kidneys have not been well understood.

Objectives: To explore the effect of low-protein diet on renal resistance in chronic renal failure through tubular injury and E-cadherin mRNA expression in mice with UUO.

Methods: This research was a quasi-experimental research and the research design is post-test with control group design. Condition of chronic kidney failure is represented by unilateral ureteral obstruction (UUO) model on 20 male Swiss Webster strain mice aged 2-3 months divided into 4 groups, namely the SO group (sham operation, n=5), UUO (UUO with normal diet as control group, 20% protein content, n=5), UUO + 10% (UUO with casein diet, 10% protein content for 1 month before UUO, n=5), and UUO + 12% (UUO with casein diet, 12% protein content for 1 month before UUO, n=5). Mice were sacrificed after 7 days of UUO. Tubular injury is scored with Periodic-Acid Schiff (PAS) staining. E-cadherin mRNA expression was examined by RT-PCR then densitometry analysis was carried out from the electrophoresis band photo result. Tubular injury scores were tested using Kruskal-Wallis with post-hoc Mann Whitney for comparative non-parametric analysis, while E-cadherin mRNA expression were tested using one-way ANOVA and post-hoc LSD for parametric test.

Results: Comparative non-parametric analysis showed different tubular injury scores between groups significantly. Group with UUO treatment but with normal diet showed higher tubular injury scores (1.70 ± 0.10 vs. 0.38 ± 0.08 ; $p < 0.05$) and lower E-cadherin mRNA expression (1.13 ± 0.26 vs. 1.57 ± 0.12 ; $p < 0.05$) compared to the sham operation group, while those on the low protein diet of 10% and 12% showed higher tubular injury scores (3.88 ± 0.08 vs. 0.38 ± 0.08 ; 3.62 ± 0.08 vs. 0.38 ± 0.08 ; $p < 0.05$) and lower E-cadherin mRNA expression (1.10 ± 0.24 vs. 1.57 ± 0.12 ; 1.12 ± 0.18 vs. 1.57 ± 0.12 ; $p > 0,05$) than the UUO with normal diet group.

Conclusion: Low protein diet produces higher tubular injury score significantly and lower E-cadherin mRNA expression insignificantly in mice with unilateral ureteral obstruction.

Keywords: low protein diet, tubular injury, E-cadherin, unilateral ureteral obstruction (UUO)