

INTISARI

Pengaruh *Unilateral Ureteral Obstruction* (Uuo) Terhadap Proliferasi, Penuaan Seluler, dan Apoptosis Pada Fibrosis Ginjal

Latar Belakang: Fibrosis ginjal merupakan manifestasi akhir semua penyakit ginjal kronis yang ditandai dengan inflamasi, apoptosis sel epitel, proliferasi dan ekspansi fibroblas. Penuaan seluler juga berperan dalam perkembangan fibrosis ginjal. Akan tetapi, keterkaitan penuaan seluler dengan apoptosis dan proliferasi pada fibrosis ginjal belum dapat dijelaskan.

Tujuan: Penelitian ini bertujuan untuk mengetahui pengaruh *unilateral ureteral obstruction* (UUO) terhadap proliferasi, penuaan seluler, dan apoptosis pada fibrosis ginjal.

Metode: Prosedur *unilateral ureteral obstruction* (UUO) dilakukan untuk menginduksi fibrosis ginjal pada 24 ekor mencit galur Swiss berumur 3 bulan dengan berat 30-40gr. Mencit diterminasi pada hari ke-3 (UUO3, n=6), hari ke-7 (UUO7, n=6) dan hari ke-14 (UUO14, n=6). Prosedur *Sham Operation* (SO, n=6) dilakukan pada kelompok kontrol. Ekspresi mRNA Bcl-2 sebagai penanda proliferasi, p16 sebagai penanda penuaan seluler dan Bax sebagai penanda apoptosis diperiksa dengan RT-PCR kemudian dianalisis densitometri dengan *software ImageJ*. Pewarnaan IHC dengan antibodi anti Bcl-2 dan p53 dilakukan untuk mengetahui lokalisasi proliferasi dan apoptosis. Data dianalisis dengan uji statistik *One-way ANOVA* dan *LSD* ($p < 0,05$).

Hasil Penelitian: Analisis RT-PCR menunjukkan ekspresi mRNA Bcl-2, p16 dan Bax lebih tinggi pada kelompok UUO dibandingkan dengan kelompok SO ($p < 0,05$). Lokalisasi ekspresi protein Bcl-2 pada kelompok UUO3 dan UUO7 terdapat di epitel tubulus sedangkan pada UUO14 terdapat di area interstisial. Lokalisasi ekspresi protein p53 pada kelompok UUO3, UUO7 dan UUO14 terdapat di epitel tubulus ginjal.

Kesimpulan: *Unilateral ureteral obstruction* (UUO) menyebabkan peningkatan proliferasi, penuaan seluler, dan apoptosis pada fibrosis ginjal.

Kata Kunci: UUO, fibrosis ginjal, proliferasi, penuaan seluler, apoptosis, Bcl-2, p16, Bax.

ABSTRACT

Effect of Unilateral Ureteral Obstruction (UUO) on Proliferation, Senescence, and Apoptosis in Renal Fibrosis

Background: Kidney fibrosis is a final common pathway of chronic kidney disease (CKD), which is characterized by inflammation, epithelial cells apoptosis, fibroblast expansion and proliferation. Cellular senescence may play role in the development of kidney fibrosis, however its spesific correlation with apoptosis or proliferation has not been elucidated yet.

Objective: The aims of this study is to determine the effect of unilateral ureteral obstruction (UUO) on proliferation, cellular aging, and apoptosis in renal fibrosis.

Methods: Unilateral ureteral obstruction (UUO) procedure was performed to induce kidney fibrosis in 24 Swiss Background mice (3 months-old, 30-40 gr). Mice were terminated on day 3 (UUO3, n=6), day 7 (UUO7, n=6) and day 14 (UUO14, n=6). Sham Operation (SO) procedure was performed in the control group. The expression of Bcl-2, p16 and Bax mRNA was examined by RT-PCR and the results were analyzed using ImageJ software. IHC staining with anti Bcl-2 and p53 antibodies was performed to determine the localization of proliferation and apoptosis. Data were analyzed by One-way ANOVA and followed by post hoc LSD test ($p < 0.05$)

Result: RT-PCR analysis revealed higher mRNA expression of Bcl-2, p16 and Bax in the UUO group compared to the SO group ($p < 0.05$). Immunostaning demonstrated localization of Bcl-2 protein expression in the UUO3 and UUO7 groups was found in the tubular epithelium, whereas in UUO14 there were in the interstitial area. On the other hand, localization of p53 protein expression in the UUO3, UUO7 and UUO14 groups was found in the renal tubular epithelium.

Conclusion: Unilateral ureteral obstruction (UUO) causes increased proliferation, cellular aging, and apoptosis in renal fibrosis.

Keywords: UUO, renal fibrosis, proliferation, senescence cellular, apoptosis, Bcl-2, p16, Bax.