

Korelasi Ekspansi Sel Interstitial Ginjal Dengan Konsentrasi Hemoglobin Dan Ekspresi Eritropoietin Pada Ginjal Sebagai Efek Akut Dan Kronis Cedera Iskemia/Reperfusion Tunggal Dan Berulang Pada Mencit

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INTISARI

Latar belakang : Cedera iskemia/reperfusion ginjal diketahui merupakan penyebab utama gagal ginjal akut yang dapat berkembang menjadi penyakit ginjal kronis. Progresifitas penyakit ginjal kronis ditandai oleh fibrosis tubulointerstitial dan anemia. Mengetahui efek kronis dari cedera I/R tunggal dan berulang terhadap ekspansi sel interstitial ginjal dan korelasinya terhadap eritropoietin dan hemoglobin dapat membantu pencarian alternatif diagnosis dan terapi penyakit ginjal kronis.

Tujuan Penelitian : Penelitian ini bertujuan mengetahui korelasi ekspansi sel interstitial ginjal terhadap ekspresi eritropoietin dan konsentrasi hemoglobin pada ginjal sebagai efek akut dan kronis cedera I/R tunggal dan berulang pada mencit.

Metode : Dua puluh empat ekor mencit jantan galur Swiss umur 3-4 bulan menjalani prosedur penjepitan pedikel ginjal selama 30 menit sebagai model cedera I/R. Hewan coba dikelompokkan menjadi 4 kelompok secara acak, yakni kelompok *Sham Operation* (SO, n=6), IR1 (n=6), IR12 (n=6), dan IR7-12 (n=6). Pewarnaan PAS digunakan untuk menilai skor cedera tubulus. Ekspansi sel interstitial ginjal diperiksa dengan pemeriksaan imunohistokimia menggunakan antibody PDGFR β , sedangkan ekspresi eritropoietin diperiksa dengan PCR, dianalisis dengan software ImageJ. Hemoglobin dan kreatinin diperiksa dari darah vena retroorbita. Data dianalisis dengan uji statistik *one way ANOVA* dan uji korelasi Pearson ($p < 0,001$).

Hasil Penelitian : Cedera I/R tunggal dan berulang menyebabkan peningkatan skor cedera tubulus, jumlah sel positif PDGFR β , dan ekspresi eritropoietin, sedangkan konsentrasi hemoglobin mengalami penurunan ($p < 0,001$). Ekspansi sel interstitial ginjal berkorelasi positif dengan ekspresi eritropoietin, namun berkorelasi negatif dengan konsentrasi hemoglobin ($p < 0,001$).

Kesimpulan : Efek kronis cedera I/R tunggal dan berulang adalah ekspansi sel interstitial ginjal dan peningkatan ekspresi eritropoietin. Penurunan konsentrasi hemoglobin dimungkinkan karena inflamasi kronis yang menghambat efektivitas eritropoietin.

Kata Kunci : cedera I/R, eritropoietin, fibrosis, anemia, penyakit ginjal kronis

Correlation of Kidney Interstitial Cells Expansion with Hemoglobin Concentration and Erythropoietin Expression on Kidney as Acute and Chronic Effect of Single and Repeated Ischemic/Reperfusion Injury in Mice

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ABSTRACT

Background : Kidney ischemia/reperfusion injury (I/R) is the most frequent cause of acute kidney injury (AKI) that lead to Chronic Kidney Disease (CKD). Progression of CKD are characterized by tubulointerstitial fibrosis and anemia. Elucidate the chronic effect of single and repeated kidney I/R injury to interstitial cells expansion and associate it with erythropoietin expression and hemoglobin could be used as alternative for diagnosis and therapy of CKD.

Objective : This study is to elucidate the association between interstitial kidney expansion and erythropoietin expression and hemoglobin concentration on kidney as the acute and chronic effect of single and repeated kidney I/R injury on mice.

Methods : Twenty four (3-4 months old) male Swiss mice were undergo bilateral pedicle renal clamping as kidney I/R injury model. Animals were divided into 4 groups : *Sham Operation* (SO, n=6), IR1 (n=6), IR12 (n=6), and IR7-12 (n=6). PAS staining was used to quantify tubular injury score. Kidney interstitial cells expansion assessed by immunostaining PDGFR β , whereas erythropoietin expression assessed by PCR, both analyzed using ImageJ. Hemoglobin and creatinine was measured from retroorbital venous. Data were analyzed using one way ANOVA and Pearson correlation test ($p < 0,001$).

Results : Single and repeated kidney I/R injury caused elevation of tubular injury score, number of PDGFR β positive cells, and erythropoietin expression, but caused decrease of hemoglobin concentration ($p < 0,001$). Kidney interstitial cells expansion positively correlate with erythropoietin expression, but negatively correlate with hemoglobin concentration ($p < 0,001$).

Conclusion : Chronic effect of single and repeated kidney I/R injury are interstitial cells expansion and increase of erythropoietin expression. The decrease of hemoglobin concentration could be due to chronic inflammation which inhibit erythropoietin effectiveness.

Keywords : I/R Injury, erythropoietin, fibrosis, anemia, chronic kidney disease