INTISARI

PENGARUH VITAMIN D TERHADAP EKSPRESI TLR-4, MCP-1, DAN JUMLAH MAKROFAG PADA MENCIT DENGAN CEDERA ISKEMIA/REPERFUSI GINJAL

Latar Belakang: Cedera iskemia/reperfusi (I/R) merupakan penyebab utama gagal ginjal akut (*Acute Kidney* Injury / AKI) yang memiliki karakteristik restriksi awal pasokan darah ke organ tertentu yang diikuti restorasi dan reoksigenisasi. Cedera I/R menginisiasi sel epitel tubulus dan sel endotel ginjal menghasilkan sitokin dan kemokin sebagai respon inflamasi, salah satunya adalah TLR-4. Aktivasi dari TLR-4 dapat menginduksi kemokin MCP-1 yang bertanggung jawab pada akumulasi makrofag di ruang interstitial ginjal. Vitamin D diketahui memiliki efek renoprotektif. Telah banyak dilakukan penelitian mengenai vitamin D dan cedera I/R, namun masih sedikit yang mengulas tentang pengaruhnya terhadap ekspresi TLR-4, MCP-1, dan jumlah makrofag.

Tujuan: Meneliti pengaruh vitamin D terhadap ekspresi TLR-4, MCP-1, dan jumlah makrofag pada mencit dengan cedera iskemia/reperfusi ginjal.

Metode Penelitian: Lima belas ekor mencit berlatarbelakang Swiss dengan usia 3-4 bulan dibagi dalam tiga kelompok yaitu mencit dengan hanya melakukan Sham Operation (SO, n=5), mencit dengan cedera I/R selama 7 hari (IR7, n=5), dan mencit dengan cedera I/R yang diberi vitamin D selama 7 hari (IRD7, n=5). Cedera I/R didapatkan dengan *clamping* pedikulus renalis bilateral selama 30 menit dilanjutkan reperfusi. Ekspresi TLR-4 dan MCP-1 diperoleh dari RT-PCR, sedangkan jumlah makrofag diperoleh dari sediaan histologis dengan pewarnaan imunohistokimia dengan antibodi anti-CD68. Data dianalisis menggunakan *software* ImageJ dan diuji statistiknya dengan *one way* ANOVA atau *Kruskal Wallis* pada SPSS versi 16.0.

Hasil Penelitian: Pemberian vitamin D setelah cedera I/R menurunkan ekspresi TLR-4 ($p<0,05$) dan jumlah makrofag ($p<0,001$). Ekspresi MCP-1 menurun secara klinis namun tidak secara statistik ($p>0,05$).

Kesimpulan: Pemberian vitamin D menurunkan ekspresi TLR-4 yang kemungkinan berakibat pada penurunan ekspresi MCP-1 dan jumlah makrofag melalui penghambatan jalur sinyal kaskade inflamasi.

Kata kunci : ischemia/reperfusion injury, inflammation, tlr-4, mcp-1, macrophage

ABSTRACT

VITAMIN D EFFECTS TO EXPRESSION OF TLR-4, MCP-1, AND INTERSTITIAL MACROPHAGES IN MICE WITH KIDNEY ISCHEMIA/REPERFUSION INJURY

Background: Kidney ischemia/reperfusion injury (I/R) is the most frequent cause of acute kidney injury (AKI) which is characterized by initial restriction supply of blood to the organs and is continued with restoration and re-oxygenation. I/R injury initiates tubular epithelial cells and endothelial cells inducing some cytokines and chemokine as an inflammatory response, including TLR-4. Activation of TLR-4 signaling promotes the tubular epithelial cells to produce MCP-1 that is responsible for macrophages accumulation in interstitial space of the kidney. Some researches proved that vitamin D has a renoprotective effect but its effect to expression TLR-4, MCP-1, and interstitial macrophages after I/R injury has not been elucidated.
Objective: This study is to elucidate the effects of vitamin D to expression of TLR-4, MCP-1, and interstitial macrophages in mice with ischemia/reperfusion injury.
Methods: Fifteen (3-4 months old) Swiss mice were divided into 3 groups: *Sham Operation* (SO, n=5), mice with I/R injury (IR7, n=5), and mice with I/R injury plus intraperitoneal vitamin D injection (IRD7, n=5). Animals were undergo bilateral pedicle clamping for 30 minutes and continued with reperfusion as kidney I/R injury model. Expression of TLR-4 and MCP-1 were assessed by RT-PCR, whereas the interstitial macrophages were assessed by immunohistochemistry staining with antibody anti-CD68, both are analyzed by ImageJ and are statistically tested by *one way* ANOVA and Kruskal Wallis on SPSS 16.0 software.
Results: Vitamin D attenuates expression of TLR-4 ($p<0,05$) and interstitial macrophages ($p<0,001$). Expression of MCP-1 is clinically attenuated but it is statistically insignificant ($p>0,05$).
Conclusion: Attenuated expression of TLR-4 ultimately decrease the expression of MCP-1 and interstitial macrophages. It might be due to the inhibition of inflammatory signaling cascade by the vitamin D.
Keywords: ischemia/reperfusion injury, inflammation, tlr-4, mcp-1, macrophage