INTISARI

PENGARUH INDUKSI ASAM URAT TERHADAP EKSPRESI GEN TLR4 DAN MCP-1 SERTA APOPTOSIS HEPATOSIT PADA MENCIT

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Latar Belakang: Hiperurisemia dapat menginduksi terjadinya kerusakan hepar karena asam urat merupakan salah satu zat hepatotoksik. Asam urat termasuk salah satu *damage-associated molecular patterns* (DAMPs) pro-inflamasi yang dikenali oleh *Toll-Like Reseptor* (TLR) dan memicu terjadinya reaksi inflamasi. Kerusakan hepatosit akan menginduksi pelepasan kemokin *monocyte chemoattractant protein-1* (MCP-1). Kematian sel hepatosit merupakan hal yang umum terjadi pada penyakit hepar akibat inflamasi.
Tujuan Penelitian: Penelitian ini bertujuan untuk mengkaji pengaruh induksi asam urat terhadap kadar serum asam urat, SGOT dan SGPT, ekspresi gen TLR4 dan MCP-1 dan juga jumlah hepatosit yang mengalami apoptosis pada mencit.
Metode: 25 ekor mencit jantan galur Swiss umur 3 bulan diinduksi asam urat selama 28 hari. Hewan coba dibagi dalam 5 kelompok perlakuan, yaitu kelompok kontrol (n=5), AU7 (n=5), AU14 (n=5), AU21 (n=5) dan AU28 (n=5). Pada hari yang telah ditentukan diterminasi dan diambil organ hepar. *Tunnel Assay* digunakan untuk menilai jumlah hepatosit yang mengalami apoptosis. Pemeriksaan ekspresi gen TLR4 dan MCP-1 digunakan RT-PCR. Kadar serum asam urat, SGOT dan SGPT diperiksa dari darah vena retroorbita.
Hasil Penelitian: Induksi asam urat menyebabkan terjadi peningkatan kadar serum asam urat, SGOT dan SGPT ($p<0,05$). Terjadi peningkatan ekspresi gen TLR4 dan MCP-1 menunjukkan adanya reaksi inflamasi. serta peningkatan jumlah apoptosis hepatosit seiring lamanya pemberian induksi asam urat ($p<0,05$).
Kesimpulan: Efek dari peningkatan kadar serum asam urat adalah terjadinya respon inflamasi dengan adanya peningkatan ekspresi gen TLR4 dan MCP-1. Terjadi peningkatan jumlah hepatosit yang mengalami apoptosis kemungkinan akibat reaksi inflamasi yang terus terjadi selama induksi asam urat.

Kata kunci: asam urat, hepar, TLR4, MCP-1, apoptosis hepatosit

ABSTRACT

The Effects of Uric Acid Induction toward TLR4 and MCP-1 Gene Expression and Hepatocytes Apoptosis in Mice

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Background: Hyperuricemia may induce liver damage. Uric acid is a hepatotoxic substance causing tissue damage. Uric acid is one of the damage-associated molecular patterns (DAMPs) pro-inflammatory which is recognized by Toll-Like Receptors (TLR) and triggering an inflammatory reaction. Hepatocyte damage induces the release of the monocyte chemoattractant protein-1 (MCP-1) chemokine. Hepatocyte cell death is common in liver disease due to inflammation.
Objective: This study is aimed to assess the effects of hyperuricemia on liver function which can be seen from the serum levels of SGOT and SGPT, the inflammatory response demonstrated by gene expression of TLR4 and MCP-1 and also the number of apoptotic hepatocytes in the liver of mice.
Methods: A total of 25 Swiss male mice with the age of 3 months and weight 30-40 grams received induction of uric acid for 28 days. Animals were divided into five treatment groups: control group (n=5), AU7 (n=5), AU14 (n=5), AU21 (n=5) and AU28 (n=5). On the appointed day, mice would be terminated and the liver would be taken. Tunnel assay was used to assess the number of apoptotic hepatocytes. RT-PCR was used to examine the gene expressions of TLR4 and MCP-1 then densitometry analysis was performed using ImageJ software. Serum uric acid levels, SGOT, and SGPT were examined from retroorbital venous blood. The data were statistically analyzed by One Way ANOVA and Kruskal-Wallis tests ($p<0.05$).
Results: Induction of uric acid caused hyperuricemia, increased expression of TLR4 and MCP-1 gene that showed an inflammatory reaction. Increased levels of SGOT and SGPT ($p<0.05$) as well as an increase in the number of hepatocyte apoptosis induction as the duration of the induction of uric acid ($p<0.05$).
Conclusion: Hyperuricemia affected the inflammatory response by increasing the expression of TLR4 and MCP-1 gene. An increased number of apoptotic hepatocytes was likely caused by the ongoing inflammatory reaction during the induction of uric acid.

Keywords: hyperuricemia, liver, TLR4, MCP-1, hepatocyte apoptosis