INTISARI

Latar belakang: Penuaan pada hepar berhubungan dengan penyakit perlemakan hepar non-alkoholik (NAFLD) dan meningkatkan risiko terjadinya fibrosis. Studi mengenai penuaan pada manusia memiliki hambatan waktu dan etika sehingga diperlukan hewan model, salah satunya dengan induksi D-Galaktosa. Penuaan pada hepar ditandai dengan peningkatan ekspresi protein inhibitor siklus sel (p16), akumulasi lipofuscin akibat kerusakan oksidatif dan peningkatan produksi kolagen interstisial oleh *cellula perisinusoidalis* atau disebut fibrosis. Model penuaan hepar dengan induksi D-Galaktosa telah dilakukan sebelumnya namun studi yang menganalisis korelasi multivariat antara ekspresi p16, akumulasi lipofuscin, ekspresi α-SMA, dan fibrosis belum pernah dilaporkan sebelumnya.

Tujuan: Membandingkan ekspresi p16, persentase area lipofuscin, ekspresi α-SMA, dan skor fibrosis pada hepar tikus yang diinduksi D-Galaktosa dengan tikus kontrol, serta menganalisis korelasi antar variabel tersebut pada hepar tikus yang diinduksi D-Galaktosa.

Metode: Tikus Sprague-Dawley jantan usia 12 minggu dibagi menjadi dua kelompok, kelompok kontrol dan kelompok induksi yang diinjeksi larutan D-Galaktosa 100 mg/kgBB/hari intraperitoneal selama 6 minggu. Kemudian ekspresi protein p16 dan α-SMA dinilai dengan *H-score*, persentase area lipofuscin dinilai dengan perangkat lunak ImageJ, dan skor fibrosis dinilai dengan skor semi kuantitatif.

Hasil: Ekspresi p16 ($p=0,03$) dan persentase area lipofuscin ($p=0,01$) pada kelompok D-Galaktosa lebih tinggi dibandingkan kelompok kontrol. Namun tidak terdapat perbedaan ekspresi α-SMA dan skor fibrosis antara kelompok D-Galaktosa dengan kontrol ($p>0,05$). Tidak terdapat korelasi yang bermakna antar variabel terikat ($p>0,05$).

Kesimpulan: Ekspresi p16 dan persentase area lipofuscin pada tikus induksi D-Galaktosa lebih tinggi dibandingkan tikus kontrol, tetapi tidak terdapat perbedaan ekspresi α-SMA dan skor fibrosis pada kelompok D-Gal dan kontrol. Tidak terdapat korelasi antara keempat variabel tersebut.

Kata kunci: D-Galaktosa, p16, lipofuscin, α-SMA, fibrosis, penuaan seluler.

ABSTRACT

Background: Aging in the liver associated with non-alcoholic fatty liver disease (NAFLD) and liver fibrosis. Due to ethical and time limitations in human aging research, animal models become a necessity. One of the aging models on animals is D-Galactose induction. Aging liver is characterized by an increase of cell cycle inhibitory protein (p16), accumulation of lipofuscin, and enhanced interstitial collagen production by hepatic stellate cells, resulting in fibrosis. While D-Galactose induced liver aging models have been previously established, studies investigating the multivariate correlation between p16 expression, lipofuscin accumulation, α-SMA expression, and fibrosis have not been previously reported.

Objectives: This study aims to compare p16 expression, lipofuscin area percentage, α-SMA expression, and fibrosis score in the livers of D-Galactose-induced rats and control rats. Furthermore, this study seeks to analyze the correlations among these parameters.

Methods: Twelve-week-old male Sprague-Dawley rats were divided into two groups, a control group and an induction group receiving intraperitoneal D-Galactose at 100 mg/kg body weight/day for six weeks. Hepatic p16 and α-SMA protein expression were assessed using H-score method, lipofuscin accumulation was quantified as a percentage area using ImageJ software, while liver fibrosis was evaluated using a semi-quantitative scoring system.

Results: Rats in the D-Galactose group exhibited significantly higher p16 expression ($p=0,03$) and lipofuscin area percentages ($p=0,01$) compared to the control group. However, no significant differences were observed in α-SMA expression and fibrosis score between two groups ($p>0,05$). Additionally, no statistically significant correlations were found among these parameters ($p>0,05$).

Conclusion: The expression of p16 and the percentage of lipofuscin area were higher in D-Galactose-induced rats compared to the control rats; however, there were no differences in α-SMA expression and fibrosis scores between the D-Gal and control groups. No correlations were found among these four parameters.

Key Words: D-Galactose, p16, α-SMA, fibrosis, cellular senescence.