

Pengaruh kombinasi recombinant humun Hepatocyte Growth Factor dan vesikel ekstraseluler terhadap fibrosis hati (skor Laennec), penanda cedera hati (AST dan ALT) serta Hepatocyte Growth Factor pada model tikus ligasi duktus bilier = The effect of combination of recombinant human hepatocyte growth factor and extracellular vesicles in liver fibrosis (score Laennec), liver injury markers (AST and ALT), and hepatocyte growth factor un the rat bile duct ligation model

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Abstrak

Latar Belakang: Fibrosis hati disebabkan cedera hati kronis akan menjadi sirosis. Vesikel ekstraseluler (VE) dan Hepatocyte Growth Factor (HGF) banyak dipelajari sebagai terapi fibrosis dan regenerasi hati. Penelitian ini memanfaatkan kombinasi VE dan recombinant human-HGF (rh-HGF) sebagai terapi alternatif fibrosis hati pada model tikus ligasi duktus bilier (LDB).

Metode: Sebelas tikus Sprague Dawley (SD) menjalani LDB, 5 tikus kontrol dan 6 tikus mendapat perlakuan injeksi VE 150 uL dan rh-HGF 0,1 mg intravena sejak 3 minggu pasca LDB, selama 7 hari. Satu tikus kontrol diterminasi 3 minggu pasca LDB sebagai data dasar. Tikus-tikus kelompok kontrol dan perlakuan diterminasi pada 1 hari dan 2 minggu setelah injeksi terakhir. Dilakukan penilaian skor Laennec hati serta kadar HGF, alanine aminotransferase (ALT) dan aspartate aminotransferase (AST).

Hasil: Histopatologi 3 minggu pasca LDB menunjukkan skor Laennec 2. Skor fibrosis kelompok kontrol (KK) dan kelompok perlakuan (KP) 1 minggu dan 2 minggu pasca injeksi VE dan rh-HGF seluruhnya dengan skor 2. Kadar HGF pada KP lebih rendah secara signifikan dibandingkan dengan KK 1 hari pasca injeksi terakhir (1,35+0,06 vs 1,53+0,06; $p<0,001$), semakin menurun setelah 2 minggu pasca injeksi terakhir namun tidak bermakna secara statistik 0,83 (0,73-0,84) vs 0,76 (0,73-0,80) $p=0,248$). Kadar AST 1 hari pasca injeksi terakhir; KK 1,66+0,05 KP 0,91+0,12 dengan $p = 0,001$. Setelah 2 minggu pasca injeksi; kadar AST pada kedua kelompok menurun 1,12 (1,11-1,22) vs (0,96+0,03); $p=0,021$). Kadar ALT pada kelompok perlakuan lebih rendah secara signifikan pada 1 hari pasca injeksi dan 2 minggu pasca injeksi dengan nilai $p<0,001$ dan 0,033a

.....Background: Fibrosis of the liver due to a chronic liver injury will become cirrhosis at the end-stage. The Extracellular Vesicles (EV) and hepatocyte growth factor (HGF) are recently learned as much as fibrosis and liver regeneration therapy. This study aims to know the result of using a combination of EV and recombinant human HGF (rh-HGF) as an alternative therapy due to liver fibrosis on the rat bile duct ligation (BDL) model.

Methods: Eleven BDL Sprague Dawley (SD) were divided into two groups, five mice as the untreated control group and six mice as the treatment group was getting an EV 150 ul and rh-hgf 0.1 mg intravenous injection three weeks after BDL, for seven days. One control rat is expanded three weeks after BDL as baseline data. The control and treatment group mice were projected at day one and two weeks after the final

injection. This study was assessed from liver fibrosis by using Laennec score, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and Hepatocyte Growth Factor (HGF) level.

Results: Scoring of histopathology by using the Laennec score at 3 weeks after BDL was 2. Meanwhile scoring of fibrosis of the control group and treatment group at 1 week and 2 weeks after ve and rh-hgf injection were 2. HGF level of the treatment group was lower significantly than control group at day 1 after last injection ($1,35 \pm 0,06$ vs $1,53 \pm 0,06$; $p < 0,001$), and within 2 weeks, the number of HGF levels decreased but statistically insignificant; $0,83$ ($0,73-0,84$) vs $0,76$ ($0,73-0,80$) $p = 0,248$). AST level at day 1 after last injection; control group vs treatment group ; $1,66 \pm 0,05$ vs $0,91 \pm 0,12$, p value = $0,001$. 2 weeks after injection; AST level for both group were become lower $1,12$ ($1,11-1,22$) vs ($0,96 \pm 0,03$); $p = 0,021$), and ALT level on treatment group was significantly lower at day 1 and 2 weeks after injection with p value $< 0,001$ and $0,033a$