Efek pemberian sel punca mesenkim intrahepatika dan intrasplenika terhadap kadar alanin aminotransferase, apartat aminotransferase, bilirubin, dan fibrosis hati Oryctolagus cuniculus ligasi duktus bilier = The effect of intrahepatic and intrasplenic administration of mesenchymal stem cell to alanine aminotransferase, aspartate aminotransferase, bilirubin level and degree of liver fibrosis in Oryctolagus cuniculus bile duct ligation model

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Abstrak

Latar belakang: Sel punca mesenkim (SPM) telah menjadi salah satu alternatif untuk menghambat proses fibrosis dan memperbaiki fungsi hati. Berbagai jalur dapat digunakan untuk pemberian SPM, namun belum banyak studi yang membandingkan jalur pemberian. Pada studi ini dibandingkan pemberian SPM intrahepatika dan intrasplenika terhadap fungsi hati dan derajat fibrosis hati Oryctolagus cuniculus ligasi duktus bilier.
Metode penelitian: Penelitian ekperimental dengan menggunakan model hewan kelinci (Oryctolagus cuniculus) yang dilakukan ligasi duktus bilier (LDB). Kelinci dibagi ke dalam 4 kelompok, yaitu kelompok sham surgery, LDB, injeksi SPM intrahepatika(LDB + SPM IH) dan injeksi SPM intrasplenika (LDB + SPM IS). Injeksi SPM tali pusat dilakukan pada hari kelima LBD, kemudian kelinci diobservasi sebelum diterminasi seluruhnya pada hari ke-14. Dinilai fungsi hati yang dinilai dengan kadar serum AST, ALT, bilirubin total dan direk, serta derajat fibrosis hati yang dinilai dengan skor Laennec.
Hasil penelitian: Dari total 23 kelinci, dibagi menjadi 4 kelompok, yaitu kelompok sham 2 ekor dan masing-masing 7 ekor untuk kelompok LDB, LDB + SPM IH, dan IS. Didapatkan mortalitas sebesar 57,1% pada kelompok LDB, mortalitas 14,3% pada kelompok LDB + SPM IH dan mortalitas 28,6 pada kelompok LDB + SPM IS sebelum penelitian selesai. Tidak didapatkan perbedaan yang bermakna untuk fungsi hati seperti AST, ALT, bilirubin total, dan direk antarkelompok, namun terkesan median fungsi hati pada kelompok LDB lebih tinggi dibanding sham surgery, serta median kelompok LDB + SPM IH dan IS lebih menyerupai normal. Fungsi hati tampak lebih baik pada kelompok LDB + SPM IS dibanding LDB + SPM IH, meskipun secara statistik tidak bermakna. Pemeriksaan histopatologi kelinci yang dilakukan ligasi duktus bilier menunjukkan derajat fibrosis Laennec 4B, yang tidak berbeda antar ketiga kelompok. Area fraction fibrosis, jumlah hepatosit yang viabel dan nekrosis, serta jumlah sel progenitor dianalisis, tidak terdapat perbedaan yang ditemukan antara kelompok LDB + SPM IH dan LDB + SPM IS, namun kelompok yang diberikan SPM memiliki jumlah hepatosit viabel yang lebih banyak dibandingkan kelompok LDB.
Kesimpulan: Pemberian SPM intrahepatika dan intrasplenika tidak berpengaruh pada fungsi hati dan derajat fibrosis hati Oryctolagus cuniculus pascaligasi duktus bilier. Pemberian SPM akan meningkatkan jumlah hepatosit yang viabel pada model cuniculus pascaligasi duktus bilier.
.....Background: Mesenchymal stem cell (MSC) becomes an alternative to attenuate liver fibrosis and to improve liver function. A couple of administration route had been studied, but few compared one to another. This study aims to compare intrahepatic and intrasplenic route of administration of MSC in regards of liver function and degree of liver fibrosis in Oryctolagus cuniculus bile duct ligation model.

Method: This is an experimental study using rabbit (Oryctolagus cuniculus) bile duct ligation model. The subjects were randomized into 4 groups: sham surgery, bile duct ligation (BDL), intrahepatic route of MSC (BDL + MSC IH), and intrasplenic route of MSC (BDL + MSC IS). Umbilical cord MSC was administered in the fifth day of bile duct ligation, and the subject was observed until terminated on 14th day post BDL. The liver function, such as AST, ALT, total and direct bilirubin were evaluated, and the degree of fibrosis was evaluated with Laennec score.
Result: The subjects were grouped into 4 group: 2 sham surgery, and each had 7 in BDL, BDL + MSC IH and BDL + MSC IH groups. Mortality rate in control group was 57,1%, mortality in BDL + MSC IH group was 14,3% and in BDL + MSC IS group was 28,6%. No significant difference was found regarding liver function in each group such as AST, ALT, total and direct bilirubin, but the median of liver function in BDL group seemed worse than in sham sugery group, and the median of liver function in BDL + MSC IH and BDL + MSC IS groups were closed to sham operated (normal). Liver function seemed to be better in BDL + MSC IS group compared to BDL + MSC IH group, but showed no statistical difference. Histopathology examination in subjects undergone bile duct ligation (regardless of MSC) show the degree of fibrosis of Laennec 4B. Fibrosis area fraction, the number of viable and necrosis hepatocyte, and progenitor cell are analysed; no significant difference was found between BDL + MSC IH and BDL + MSC IS group, but the group administered with MSC shows larger number of viable hepatocyte compared to BDL group.
Conclusion: Administration of intrahepatic or intrasplenic MSC did not show significant improvement the liver function and liver fibrosis in Oryctolagus cuniculus bile duct ligation model. Administration of MSC would increase the number of viabel hepatocyte in Oryctolagus cuniculus bile duct ligation model.