Rekayasa Dinding Jantung Artifisial untuk Terapi Infark Miokardium: Perbandingan Rasio Densitas Penyemaian Sel 1:5 dan 1:6 pada Ko-kultur Kardiomiosit dan Human Amnion Epithelial Stem Cells pada Scaffold Patch Amnion secara In-Vitro = Artificial Cardiac Wall Engineering for Treatment of Myocardial Infarction: Comparison of 1:5 and 1:6 Cells Seeding Density Ratio of Cardiomyocytes and Human Amnionic Epithelial Stem Cells Co-Culture on Amnion Scaffold Patch In-Vitro

Chaidar Muttaqin, author

Abstrak

Latar belakang: Terapi sel punca dikembangkan sebagai alternatif terapi gagal jantung akibat infark miokardium. Bermacam tipe sel dengan berbagai metode implantasi telah banyak dikembangkan tetapi belum mendapatkan hasil optimal. Sel h-AECs (Human Amnion Epithelial Stem Cells) memiliki sifat yang sangat mendukung sebagai sumber sel bagi terapi sel punca pada jantung. Teknologi rekayasa jaringan dengan melakukan ko-kultur kardiomiosit dan h-AECs pada biomaterial scaffold diyakini dapat menjawab permasalahan pada pengembangan terapi sel punca pada gagal jantung.
Metode: Penelitian ini adalah studi eksperimental in-vitro dengan penyemaian ko-kultur sel kardiomiosit dan h-AECs ke dalam scaffold patch. Kardiomiosit berasal dari otot ventrikel kanan pasien penderita penyakit tetralogy of Fallots yang dilakukan operasi koreksi TOF. Sedangkan sel h-AECs didapat dari epitel amnion yang merupakan limbah operasi seksio sesarea. Setelah dilakukan karakterisasi pada kardiomiosit dan h-AECs, dilakukan ko-kultur pada scaffold amnion dengan perbandingan densitas penyemaian 1:5 dan 1:6. Evaluasi hasil ko-kultur dilakukan dengan penilaian viabilitas sel, ekspresi gen spesifik kardiomiosit dan uji toksisitas patch.
Hasil: Hasil ko-kultur kardiomiosit dan h-AECs tidak terdapat perbedaan bermakna pada rerata jumlah sel viabel pada hari kedua dan kelima (p>0,05). Sedangkan pada hari kedelapan terdapat perbedaan bermakna pada jumlah sel viabel, rasio 1:5 menghasilkan jumlah sel viabel lebih baik dibanding rasio 1:6 (p=0,011). Ekspresi gen spesifik kardiomiosit konsisten tampak pada kelompok rasio 1:6 dan mulai menunjukkan signifikan pada hari kedelapan, terdapat perbedaan bermakna pada ekspresi gen di hari kedelapan, kelompok rasio 1:6 mengekspresikan gen cTnT dan ACTN2 lebih baik dibanding kelompok 1:5 (p=0,000 dan p=0,001). Pada uji toksisitas, tidak terdapat perbedaan bermakna pada jumlah ATP dan kadar TNF antara kelompok 1:5 dan 1:6.
Simpulan: Teknik ko-kultur yang dikembangkan dapat menghasilkan sel kardiomiosit baru. Kelompok rasio 1:6 menghasilkan sel yang memiliki sifat spesifik kardiomiosit lebih baik dibanding kelompok rasio 1:5 tetapi menghasilkan jumlah sel viabel lebih sedikit. Patch hasil ko-kultur tidak bersifat toksik.
.....Background: Stem cell therapy was developed as an alternative therapy for heart failure due to myocardial infarction. Various types of cells with various methods of implantation have been developed but have not yet obtained optimal results. h-AECs (Human Amnion Epithelial Stem Cells) have very supportive properties as a source of cells for stem cell therapy in the heart. Tissue engineering technology by co-culturing cardiomyocytes and h-AECs on scaffold biomaterials is believed to be able to answer problems in

the development of stem cell therapy in heart failure.
Method: This study is an in-vitro experimental study by seeding co-cultures of cardiomyocytes and h-AECs into the scaffold patch. Cardiomyocytes were derived from the right ventricular muscle of patients with tetralogy of Fallot disease who underwent TOF correction surgery. Meanwhile, the h-AECs cells were obtained from the amniotic epithelium which is the waste from cesarean section. After characterization of cardiomyocytes and h-AECs, co-culture was performed on amnion scaffold with seeding density ratio 1:5 and 1:6. Evaluation of co-culture results was carried out by assessing cells viability, expression of specific cardiomyocytes gen and patch toxicity tests.
Result: The results of co-culture of cardiomyocytes and h-AECs showed no significant difference in the mean number of viable cells on the second and fifth days ($p>0.05$). While on the eighth day there was a significant difference in the number of viable cells, a ratio of 1:5 resulted in a better number of viable cells than a ratio of 1:6 ($p=0.011$). Cardiomyocyte-specific gene expression was consistently seen in the 1:6 ratio group and began to show significantly on the eighth day, there was a significant difference in gene expression on the eighth day, the 1:6 ratio group expressed cTnT and ACTN2 genes better than the 1:5 group ($p= 0.000$ and $p=0.001$). In the toxicity test, there was no significant difference in the amount of ATP and TNF levels between the 1:5 and 1:6 groups.
Conclusion: The developed co-culture technique can generate new cardiomyocytes. The 1:6 ratio group produced cells that had better cardiomyocyte-specific properties than the 1:5 ratio group but produced fewer cells. Co-culture of h-AECs and cardiomyocytes on patch was not toxic.