ABSTRAK

POTENSIASI SEKRETOM YANG DISEKRESIKAN OLEH SEL PUNCA MESENKIMAL DARAH TALI PUSAT DENGAN ATORVASTATIN TERHADAP MIGRASI SEL PROGENITOR ENDOTEL DARAH TEPI PADA PASIEN PENYAKIT JANTUNG KORONER STABIL

Suryo Ardi Hutomo, Yudi Her Oktaviono, Djoko Soemantri

Latar Belakang: Modulasi fungsi *endothelial progenitor cells (EPCs)* dapat menjadi strategi baru dalam tata laksana penyakit jantung koroner. Sekretom yang disekresikan oleh sel punca mesenkimal darah tali pusat (*human umbilical cord blood-mesenchymal stem cells/hUCB-MSC*) memiliki kemampuan menginduksi proses neovaskularisasi dan angiogenesis, oleh karena itu diperkirakan dapat meningkatkan migrasi EPCs. Atorvastatin pada penelitian terdahulu terbukti juga terbukti meningkatkan migrasi EPCs.

Tujuan: Studi ini dilakukan untuk mengetahui pengaruh pemberian sekretom terhadap migrasi EPCs, serta mengetahui adanya potensiasi antara atorvastatin dan sekretom terhadap proses migrasi EPCs darah tepi pasien PJK stabil.

Metode: Penelitian eksperimental laboratoris (*in-vitro study*) dengan melakukan kultur EPC dari darah tepi penderita PJK, lalu diberi perlakuan berupa *hUCB-MSCs-derived secretome* (0.2%, 10%, 20%) atorvastatin (2.5 µM), kombinasi atorvastatin dan sekretom, dan kelompok kontrol, dengan desain *"posttest only control group design"*. Migrasi EPCs dinilai menggunakan *transwell migration assay*

Hasil: Terdapat perbedaan migrasi EPCs yang signifikan antara kelompok perlakuan *hUCB-MSCs-derived secretome* (0.2%, 10%, 20%) dibandingkan dengan kelompok kontrol (17.20±1.92 $x10^3$, 27.00±4.00 $x10^3$, 51.00±5.15 $x10^3$ vs 3.20±0.84 $x10^3$, $p<0.05$). Perbedaan migrasi EPCs yang signifikan juga terdapat antara kelompok kombinasi (atorvastatin 2.5 µM+ *hUCB-MSCs-derived secretome* 0.2%; 10%; 20%) dibandingkan dengan kontrol (38.20±3.49 $x10^3$, 50.20±5.31 $x10^3$, 76.40±7.50 $x10^3$ vs 3.20±0.84 $x10^3$, $p<0.05$), kelompok atorvastatin 2.5 µM saja (vs 34.4 ±3.05 $x10^3$, $p<0.05$) dan kelompok *hUCB-MSCs-derived secretome* saja ($p<0.05$).

Kesimpulan: Pemberian *hUCB-MSCs-derived secretome,* dan kombinasinya dengan atorvastatin meningkatkan migrasi EPCs darah tepi pasien PJK stabil. Efek peningkatan tersebut bersifat *dose-dependent.*

Kata kunci: *hUCB-MSCs-derived secretome, atorvastatin, endothelial progenitor cells, coronary artery disease, cardiovascular regenerative therapy*

ABSTRACT

POTENTIATION OF HUMAN UMBILICAL CORD BLOOD MESENCHYMAL STEM CELLS–DERIVED SECRETOME AND ATORVASTATIN IN THE MIGRATION OF ENDOTHELIAL PROGENITOR CELLS

Suryo Ardi Hutomo, Yudi Her Oktaviono, Djoko Soemantri

Background: *Endothelial progenitor cells (EPCs) modulation is a novel treatment strategy for coronary artery disease. Human umbilical cord blood mesenchymal stem cells (hUCB-MSCs)-derived secretome has a potential in cardiovascular regenerative therapy through inducing angiogenesis and neovascularization, therefore it is expected to have capabilities to enhanced (EPCs) migration. Atorvastatin was the cornerstone of coronary artery disease (CAD) therapy through its pleiotropic effects, and proven has capabilities in enhancing EPCs migration.*

Objective: *This study aims to figure out the effect of hUCB-MSC-derived secretome and its potentiation with atorvastatin in migration of EPCs derived from CAD patient's peripheral blood.*

Methods: *This is an in vitro true experimental post-test only control group design. EPCs were cultured from mononuclear cells (PB-MC) that was isolated from CAD patient' peripheral blood. EPCs will be treated with various doses of hUCB-MSCs-derived secretome (0.2%, 10%, 20%), atorvastatin (2.5 µM), combination of atorvastatin and hUCB-MSCs-derived secretome, and control group. EPCs migration was evaluated with Transwell migration assay kit*

Results: *There were significant differences between hUCB-MSCs-derived secretome group (0.2%, 10%, 20%) compared with control group (17.20±1.92 $x10^3$, 27.00±4.00 $x10^3$, 51.00±5.15 $x10^3$ vs 3.20±0.84 $x10^3$, $p<0.05$). There were also significant differences between combination groups (atorvastatin 2.5 µM + hUCB-MSCs-derived secretome 0.2%; 10%; 20%) compared with control group (38.20±3.49 $x10^3$, 50.20±5.31 $x10^3$, 76.40±7.50 $x10^3$ vs 3.20±0.84 $x10^3$, $p<0.05$), atorvastatin 2.5 µM only group (vs 34.4 ±3.05 $x10^3$, $p<0.05$) dan hUCB-MSCs-derived secretome group.*

Conclusion: *HUCB-MSC-derived secretome and its combination with atorvastatin treatment increase EPCs migration, with dose-dependent manner*

Keywords: *hUCB-MSCs-derived secretome, atorvastatin, endothelial progenitor cells, coronary artery disease, cardiovascular regenerative therapy*