

Efek pemberian Granulocyte Colony Stimulating Factor pada mobilisasi, proliferasi, dan diferensiasi sel Punca Mesenkimal = The effect of Granulocyte Stimulating Factor administration on mobilization, proliferation, and differentiation of Mesenchymal Stem cell

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Abstrak

Pendahuluan. Sel punca mesenkimal yang dilaporkan mengaugmentasi penyembuhan fraktur umumnya diperoleh dari sumsum tulang. Donor sel punca dari sumsum tulang terbatas pada volume aspirat dan menimbulkan morbiditas donor sehingga diperlukan sumber alternatif. Darah perifer menutupi kekurangan tersebut walaupun memiliki kandungan sel punca yang lebih sedikit. Pemberian Granulocyte Colony Stimulating Factor (GCSF) dapat meningkatkan mobilisasi sel mononuklear pada teknik afaresis untuk sel punca hematopoetik. Bila pemberian GCSF diikuti dengan teknik kultur kearah sel punca mesenkimal maka dapat meningkatkan jumlah sel punca darah perifer sehingga memungkinkan penggunaan darah perifer sebagai donor alternatif sel punca. Oleh karena itu, diperlukan penelitian untuk mengevaluasi penggunaan darah perifer sebagai donor sel punca pasca pemberian GCSF dengan menilai kemampuan mobilisasi, proliferasi dan diferensiasi.

Metode Penelitian. Penelitian ini adalah penelitian eksperimental yang memakai hewan coba 14 ekor kelinci New Zealand White jantan, berat badan 2 kg di Pusat Studi Satwa Primata, Institut Pertanian Bogor. Sampel dibagi secara acak menjadi 4 kelompok yaitu kontrol dan perlakuan (injeksi GCSF dosis 10mcg/kg berat badan, subkutan, selama 7 hari) dimana pada masing-masing kelompok diambil aspirat darah perifer dan sumsum tulang (kelompok 1: kontrol sumsum tulang, kelompok 2: kontrol darah perifer, kelompok 3: perlakuan sumsum tulang, kelompok 4: perlakuan darah perifer). Pada tiap kelompok dilakukan isolasi, ekspansi dan diferensiasi menjadi osteoblas. Analisis statistik menggunakan uji one way Anova dan dilanjutkan uji posthoc untuk jumlah sel inisial, waktu konfluensi, jumlah sel konfluensi dan waktu diferensiasi.

Temuan dan Diskusi Penelitian. Sel punca mesenkimal pada seluruh kelompok penelitian mampu diisolasi, berproliferasi dan berdiferensiasi menjadi osteoblas. Rerata jumlah sel inisial kelompok 1: $3.07 \times 10^6/\text{mL}$, kelompok 2: $2.11 \times 10^6/\text{mL}$, kelompok 3: $2.89 \times 10^6/\text{mL}$ dan kelompok 4: $7.35 \times 10^6/\text{mL}$ ($p < 0.001$). Rerata waktu konfluensi kelompok 1: 25.8 hari, kelompok 2: 35.7 hari, kelompok 3: 26 hari, kelompok 4: 19.7 hari ($p < 0.001$). Rerata jumlah sel konfluensi kelompok 1: $6.54 \times 10^6/\text{mL}$, kelompok 2: $4.61 \times 10^6/\text{mL}$, kelompok 3: $5.94 \times 10^6/\text{mL}$, kelompok 4: $11.14 \times 10^6/\text{mL}$ ($p < 0.001$). Rerata waktu diferensiasi kelompok 1: 15.5 hari, kelompok 2: 25.4 hari, kelompok 3: 15.4 hari, kelompok 4: 11.2 hari ($p < 0.001$). Uji posthoc jumlah sel inisial ditemukan perbedaan pada kelompok 1 dan 4 ($p = 0.000$), 2 dan 4 ($p < 0.001$), serta 3 dan 4 ($p < 0.001$). Uji posthoc waktu konfluensi, jumlah sel konfluensi dan waktu diferensiasi didapatkan perbedaan diantara semua kelompok kecuali kelompok 1 dan 3 ($p = 1.000, 0.670, 1.000$).

Simpulan. Sel punca mesenkimal darah perifer pasca induksi GCSF mampu diisolasi, berproliferasi dan berdiferensiasi. Pemberian GCSF meningkatkan jumlah sel punca mesenkimal dan mempersingkat durasi kultur. Darah perifer memberikan harapan baru sebagai donor alternatif sel punca mesenkimal.

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Introduction. Mesenchymal stem cells, which had been reported to augment fracture healing, were routinely harvested from bone marrow. Bone marrow had several drawbacks regarding its limited aspiration volume and donor site morbidity, therefore alternative donor is needed. Peripheral blood may cover those disadvantages despite the fewer stem cells number. Granulocyte colony stimulating factor (GCSF) administration in aphaeresis technique could mobilized mononuclear cells to hematopoietic stem cells. If it is followed by culture for mesenchymal stem cells expansion, thus will increase peripheral mesenchymal stem cells number therefore might facilitate peripheral blood as an alternative donor. For that reason, further research is needed to evaluate the effect of GCSF induction to peripheral blood as stem cells alternative donor by assessing its capability on mobilization, proliferation and differentiation.

Methods. This is an experimental study using 14 male New Zealand White rabbit, weighted 2-3 kg in Primate Research Centre, Bogor Agricultural Institute. Sample was randomized into 4 groups as follow, control and treatment group (GCSF administration, 10mcg/kg body weight, subcutaneous, 7 days) in which peripheral blood and bone marrow aspiration was collected (group 1: control bone marrow, group 2: control peripheral blood, group 3: treatment bone marrow, group 4: treatment peripheral blood). Isolation, expansion and osteoblast differentiation were followed subsequently. Statistical analysis used one-way Anova and posthoc for initial cell number, confluency time, confluency cell number, and differentiation time.

Result and Discussion. Mesenchymal stem cells in all groups were able to be isolated, proliferate and differentiate to osteoblast. Initial cell number (mean) group 1: $3.07 \times 10^6/\text{mL}$, group 2: $2.11 \times 10^6/\text{mL}$, group 3: $2.89 \times 10^6/\text{mL}$ and group 4: $7.35 \times 10^6/\text{mL}$ ($p < 0.001$). Confluency time (mean) group 1: 25.8 days, group 2: 35.7 days, group 3: 26 days, group 4: 19.7 days ($p < 0.001$). Confluency cell number (mean) group 1: $6.54 \times 10^6/\text{mL}$, group 2: $4.61 \times 10^6/\text{mL}$, group 3: $5.94 \times 10^6/\text{mL}$, group 4: $11.14 \times 10^6/\text{mL}$ ($p < 0.001$). Differentiation time group 1: 15.5 days, group 2: 25.4 days, group 3: 15.4 days, group 4: 11.2 days ($p < 0.001$). Posthoc analysis for initial cell number was found significantly different for group 1 and 4 ($p = 0.000$), group 2 and 4 ($p < 0.001$) and group 3 and 4 ($p < 0.001$). Posthoc analysis for confluency time, confluency cell number and differentiation time was found significantly different for all groups except group 1 and 3 ($p = 1.000, 0.670, 1.000$).

Conclusion. Peripheral blood mesenchymal stem cells after GCSF induction are able to be isolated, proliferate and differentiate. GCSF administration increase mesenchymal stem cells number and shorten culture duration. Peripheral blood is a promising alternative donor for mesenchymal stem cells.