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The Effect of Granulocyte Colony Stimulating Factor Administration on Mobilization, Proliferation and Differentiation of Mesenchymal Stem Cells

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Abstract: Objectives: Mesenchymal stem cells (MSCs) are routinely harvested from bone marrow. Bone marrow derived MSCs have several drawbacks including limited volume of aspiration and donor site morbidity, therefore an alternative donor site is needed. Isolation of MSCs from peripheral blood mitigates such issues. However, the MSCs isolated from peripheral blood are significantly lower in quantity. Granulocyte colony-stimulating factor (GCSF) administration in aphaeresis technique mobilizes mononuclear cells and increases the number of isolated haematopoietic stem cells. It is also recently known that administration of GCSF PB mobilizes MSCs from the bone marrow into the peripheral blood, thus increasing the number of MSCs isolated from peripheral blood. The objective of this study is to evaluate the effect of subcutaneous administration of GCSF to both bone marrow and peripheral blood MSCs. Isolated MSCs were evaluated in terms of its proliferation and differentiation capacity. Findings from this study will evaluate the potential use of GCSF to enhance bone marrow MSCs and GCSF-mobilized peripheral blood as an effective donor site for MSCs.
Method: Fourteen male New Zealand white rabbits were randomly divided into control and treatment groups. Each bone marrow and peripheral blood sample was collected consecutively from one rabbit. Therefore, there were 7 rabbits in control groups; group 1control for bone marrow (C-BM, n=7) and group 2 control for peripheral blood (C-PB, n=7). The other 7 rabbits were in treatment group; group 3 treatment for bone marrow (T-BM, n=7) and group 4 treatment for peripheral blood (T-PB, n=7). Treated animals received subcutaneous injection of GCSF, 10 mcg/kilogram body weight/ day for 7 days prior to sample collection. Isolated samples were purified, analysed for cell expansion, differentiation capacity and time.
Results: MSCs were obtained from all groups with varying degree of isolated cell quantity and quality. Mean initial isolated cell number for C-BM3.07 x 10^6, C-PB 2.11 x 10^6, T-BM 2.89 x 10^6 and T-PB 7.35 x 10^6.($p<0.001$). Mean confluency time for C-MB 25.8 days, C-PB 35.7 days, T-BM 26 days and T-PB 19,7 days ($p<0.001$). Mean confluent cell number for C-BM: 6.54 x 10^6, C-PB: 4.61 x 10^6, T-BM: 5.94 x 10^6, and T-PB: 11.14 x 10^6 ($p<0.001$). Mean differentiation time into osteoblast for C-BM: 15.5 days, C-PB: 25.4 days, T-BM: 15.4 day, andT-PB:11.2 days ($p<0.001$). Statistically significant differences were found for mean initial isolated cell number between C-BM and T-PB ($p<0.001$), C-PB and T-PB ($p<0.001$), and T-BM and T-PB ($p<0.001$). Posthoc analysis for confluency time, confluency cell number and

differentiation time was found significantly different for all groups except group C-BM and T-BM (p=1.0).
Conclusion: This study has successfully isolated MSCs from GCSF mobilized-peripheral blood. Isolated MSCs from GCSF-mobilized peripheral blood showed typical MSC histological characteristics with enhanced proliferative and differentiation capacity compared to non-mobilized samples. GCSF-mobilized peripheral blood is a promising alternative donor site for MSCs with clinical potential.
Keywords: Granulocyte colony stimulating factor, mesenchymal stem cells, mobilization, proliferation, differentiation.

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