Critical Care Medicir
OFFICIAL JOURNAL OF THE SOCIETY OF CRITICAL CARE

Critical Care Medicine:Volume 36(3)March 2008pp 873-880

Autologous transplantation of bone marrow-derived endothelial progenitor cells attenuates monocrotaline-induced pulmonary arterial hypertension in rats [Laboratory Investigations]

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Abstract

Objectives: Bone marrow-derived endothelial progenitor cells have been shown to circulate to damaged vascular endothelium and differentiate into mature endothelial cells. This study investigated whether bone marrow-derived endothelial progenitor cell therapy ameliorates monocrotaline (MCT)-induced pulmonary arterial hypertension in a rat model.

Design: Male Sprague-Dawley rats were randomized to receive MCT (75 mg/kg) only (group 1), MCT plus autologous bone marrow-derived endothelial progenitor cell (1.2×10^6 cells) transplantation (group 2), and saline injection only (group 3). Mononuclear cells were obtained from femoral bone marrow of group 2 rats and isolated by Ficoll gradient centrifugation. The cells were cultured for 21 days in endothelial culture medium.

Setting: An animal research laboratory at Kaohsiung Chang Gung Memorial Hospital.

Measurements: Hemodynamics, ventricular weight, expressions of connexin43, endothelial nitric oxide synthase messenger RNA gene, Bcl-2, and number of alveolar sacs and small lung arterioles were measured.

Results: Hemodynamic measurements on day 28 after MCT treatment revealed the development of significantly increased pulmonary arterial hypertension in MCT-treated groups ($p < .0001$). The bone marrow-derived endothelial progenitor cells were intravenously transplanted in group 2 on day 28 after MCT-induced pulmonary arterial hypertension. By day 90 after MCT treatment, the right ventricular systolic blood pressure and right ventricular hypertrophy were significantly increased in group 1 compared with groups 2 and 3 (all p values <.01). In addition, connexin43 and endothelial nitric oxide synthase messenger RNA gene expressions of lung and right ventricle and Bcl-2 protein expression of right ventricle were significantly lower in group 1 than in groups 2 and 3 (all p values <.01). Furthermore, the number of alveolar sacs and small lung arterioles were significantly lower in group 1 than in groups 2 and 3 (all p values <.01).

Conclusions: Autologous bone marrow-derived endothelial progenitor cell transplantation effectively ameliorates MCT-induced pulmonary arterial hypertension.

Level and Value of Circulating Endothelial Progenitor Cells in Patients After Acute Ischemic Stroke

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Background and Purpose—Endothelial progenitor cells (EPCs) migrate from bone marrow to systemic circulation in response to tissue ischemia where they differentiate into mature endothelial cells for angiogenesis in situ. This study tested the hypothesis that the level of circulating EPCs is substantially increased and predictive of prognostic outcomes after acute ischemic stroke (IS).

Methods—The level of circulating EPCs (staining markers: CD31/CD34 [E_1], CD62E/CD34 [E_2], and KDR/CD34 [E_3]) were examined using flow cytometry at 48 hours after acute IS in 138 consecutive patients. The EPC level was also evaluated once in 20 healthy volunteers and in 40 at-risk control subjects.

Results—Level of circulating EPCs (E_{1-3}) was significantly higher in patients with IS than in at-risk control subjects ($P<0.05$). Additionally, EPC (E_{1-3}) level was significantly lower in patients with severe neurological impairment (defined as a score ≥12 on the National Institutes of Health Stroke Scale) than in patients with less severe impairment (National Institutes of Health Stroke Scale < score 12) at 48 hours after IS ($P<0.0001$). Moreover, the EPC (E_3) level was strongly correlated with improved National Institutes of Health Stroke Scale ≥4 on day 21 after IS ($P=0.0004$). Furthermore, low circulating EPC level was independently predictive of severe neurological impairment (National Institutes of Health Stroke Scale ≥12) at 48 hours (E_{1-3}) and combined major adverse clinical outcomes (defined as recurrent IS, any cause of death, or National Institutes of Health Stroke Scale of ≥12) on day 90 (E_1) after IS ($P<0.001$).

Conclusions—Level of circulating EPCs is independently predictive of prognosis after IS. (***Stroke*. 2008;39:69-74.**)

Key Words: circulating endothelial progenitor cells ■ ischemic ■ neurological impairment ■ stroke