The Antidiabetic Effect of MSCs is not Impaired by Insulin Prophylaxis and is not Improved by a Second Dose of Cells

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Resumen

Type 1 diabetes mellitus (T1D) is due to autoimmune destruction of pancreatic beta-cells. Previously, we have shown that intravenously administered bone marrow-derived multipotent mesenchymal stromal cells (MSCs) allows pancreatic islet recovery, improves insulin secretion and reverts hyperglycemia in low doses streptozotocin (STZ)-induced diabetic mice. Here we evaluate whether insulin prophylaxis and the administration of a second dose of cells affect the antidiabetic therapeutic effect of MSC transplantation. Insulitis and subsequent elimination of pancreatic beta-cells was promoted in C57BL/6 mice by the injection of 40 mg/kg/day STZ for five days. Twenty-four days later, diabetic mice were distributed into experimental groups according to if they received or not insulin and/or one or two doses of healthy donor-derived MSCs. Three and half months later: glycemia, pancreatic islets number, insulinemia, glycated hemoglobin level and glucose tolerance were determined in animals that did not received exogenous insulin for the last 1.5 months. Also, we characterized MSCs isolated from mice healthy or diabetic. The therapeutic effect of MSC transplantation was observed in diabetic mice that received or not insulin prophylaxis. Improvements were similar irrespective if they received one or two doses of cells. Compared to MSCs from healthy mice, MSCs from diabetic mice had the same proliferation and adipogenic potentials, but were less abundant, with altered immunophenotype and no osteogenic potential. Our preclinical results should be taken into account when designing phase II clinical trials aimed to evaluate MSC transplantation in patients with T1D. Cells should be isolated form healthy donor, insulin prophylaxis could be maintained and a second dose, after an elapse of two months, appears unnecessary in the medium-term.

Palabras clave

KeyWords Plus: MESENCHYMAL STEM-CELLS; HEPATOCYTE GROWTH-FACTOR; VERSUS-HOST-DISEASE; BONE-MARROW-CELLS; STROMAL CELLS; ISLET TRANSPLANTATION; PROGENITOR CELLS; DIABETIC MICE; IN-VITRO; TISSUE-REPAIR