Cell therapy for the cardiovascular repair after an induced acute myocardial infarct in a swine animal model

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Abstract

The Aim of this study was to evaluate the results obtained after one year follow up, with the use of Bone Marrow derived Stromal Cells (BMSCs) and of Human Omentum derived Fat Stromal Cells (HOFSCs) in the repairing of myocardial infarct in pigs.

The BMSCs were harvested from bone marrow collected from ileal crest of pigs while the HOFSCs were obtained from human patients undergoing abdominal surgery. After the isolation the cells were cultured and characterized, were also detected their production of growth factors and cytokines and their angiogenic potential in vitro. After the approval of the Italian Ministery of Health, 30 pigs were enrolled in the study. The myocardial infarct was obtained by a permanent ligation of the inter ventricular artery (IVA). The pigs were divided in three groups: group 1 - treated with BMSCs, group 2 - treated with HOFSCs and group 3 - control group treated with placebo (Saline). In the group 1 and in group 2 after two hours from the ligation of IVA, the cells were injected into the proximal ischemic border zone. After surgery the animals were monitoring periodically by echocardiography, myocardial scintigraphy and cardiac MRI. The animals were euthanized at 3, 6 and 12 months and the hearts were harvested for histological and immunoistochemistry evaluations. In the infarcted area the microvessel density was evaluated using sections labelled for the endothelial markers.

In vitro conditions the cells showed the capacity to differentiate into osteogenic, adipogenic and cardiomyogenic cell lineages and were homogeneous for many markers and produce growth factors, cytokines and an high level of angiogenic factors.

The instrumental evaluations of the heart functionality (echocardiography, myocardial scintigraphy and cardiac MRI) showed an improvement of myocardial function at 3 months post infarct and a significant decrease of distress symptoms in all pigs treated respect to the control group, but at 6 and at 12 months post infarct they do not give indications of amelioration of the hearts condition and these aspects seemed to be the same to the ones of the control group.

The histological examinations at 3 months evidenced, in the treated groups, a reduction of a fibrotic and necrotic tissue and an increment of myogenic, cardyomyogenic and vascular markers that had suggested a better vascularitation and cardiomyogenesis respect to the control group. At 6 and 12 months after the surgery whereas it was possible to observe a major presence of necrotic tissue and an high reduction of cardiomyogenesis with a tickness of the infarcted area and with heart lesions similar to those observed in the control group.

The results obtained demonstrated that after a seeming amelioration at the initial stage (3 months) of the anatomical and clinical aspects, the cell therapy at the other interval of time (6 and 12 months) did not induce the expected improvement.