Omentum-derived stromal cells improve myocardial regeneration in pig post-infarcted heart through a potent paracrine mechanism

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Introduction: Myocardial Infarction (MI) represents one of principal causes of human death. Cell-based therapy could be a valid new approach for MI. Different kind of cells, including embryonic stem cells as well as adult/progenitor stem cells, have been proposed as candidates for therapeutic purposes. However, many aspects, ranging from ethical questions to functional efficacy, still remain to be clarified. Among adult/progenitor stem cells, Adipose-derived stromal cells (ADSC) seem to have some advantages, mainly because of their easy tissue accessibility and iv tro an adequate rate of growth.

Aim of the study: To investigate the capacity of transplanted ADSCs, through functional, haemodynamic and histopathological assessment, to improve myocardial infarction and regeneration of experimental heart ischemia induced by permanent IVA-ligation in pigs.

Methods: ADSCs isolated from human adipose tissue (omentum fat) were cultured, expanded, and phenotypically characterized. Furthermore, in vitro pro-angiogenic, anti-inflammatory and anti-apoptotic properties were analyzed. 50x10⁶ cells/pig were transplanted by intramyocardial injection in acute infarcted hearts (treated-group, n=12 cell-injected pigs). Two months after MI induction echocardiographic and haemodynamic follow-up was performed. In addition, histopathological examination was conducted.

Results: As shown in Figure 1, in vitro ADSCs secreted high levels of pro-angiogenic, anti-inflammatory and immunomodulatory cytokines (VEGF, HGF and IL-6). Furthermore, they prevented monocytes activation as well as cardiomyocytes apoptosis (Figure 2). Finally, in vitro but not in vivo, ADSCs were able to trans-differentiate into cardiomyocyte-like cells (Figure 3). In vivo, ADSCs injection along the border of the ischemic area (Figure 4), reduced post-infarct pigs mortality, produced a significant ameliorative effect on heart haemodynamic parameters and slightly improved echocardiographic profile. Histological and immunohistochemical examination demonstrated some cardiac-regenerative capacities of ADSCs, showing an increase of vascular and cardiomyocyte markers only in animals treated with ADSCs (Figures 5 and 6).

Conclusions: Implanted ADSCs derived from omentum could improve myocardial function and regeneration through the concomitant capacity to release molecules, restore angiogenesis, reduce inflammation and prevent cardiomyocytes apoptosis. Since adipose tissue is one of the body’s richest known sources of regenerate cells, ADSCs could play a critical role in limiting or reversing heart damage caused by a heart attack.