The effect of infusion of bone marrow versus adipose tissue derived stem cells on cardiovascular complications in diabetic rats

Thesis
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Dedication

I dedicate this simple work to my Late father ***Dr. Barsoum Nashid Barsoum****, Professor of analytic chemistry, faculty of science, Cairo university God rests his soul and to my mother who supported me a lot, many thanks.*

Abstract

Mesenchymal stromal cells (MSCs) are present in adult tissues, including bone marrow and adipose, from which they can be easily isolated and cultured ex vivo. MSCs do possess plasticity of differentiation and under appropriate in vitro culture conditions can be modified to adopt pancreatic, cardiomyocyte and vascular cell phenotypic characteristics and facilitate both myocardial repair and neovascularization in models of cardiac injury.

We used male albino rats divided into 5 groups: Group (1): control (C) group, Group (2): diabetic (D) group, Group (3): diabetes and heart failure (D+HF) group, Group (4): bone marrow derived mesenchymal stem cells injected (BMMSCs) group and Group (5): adipose tissue derived mesenchymal stem cells injected (ATMSCs). Our study concluded that BMMSCs and ATMSCs showed improvement in pancreatic and cardiac functions after 4 weeks of treatment reflected on insulin levels and cardiac performance (both in-vivo and in vitro). On histopathological basis this was associated with preservation of vulnerable cardiomyocytes and regeneration of some pancreatic islets. Despite equivocal functional results, at the tissue level BMSCs were more effective in rescuing the myocardium and pancreas than adipose stem cells.

Key words:

Diabetes mellitus - cardiovascular complications of diabetes mellitus - stem cells- bone marrow derived mesenchymal stem cells - adipose tissue derived mesenchymal stem cells - plasticity of stem cells - transdifferentiation- mechanism of action of stem cells.

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Abbreviations

ADM: adipogenic differentiation medium.

ADR: adriamycine.

ADSCs: adipose derived stem cells.

AFSCs: Amniotic fluid-derived stem cells.

AGE: Advanced glycation end-products.

ASCs: Adipose stromal cells.

α-SMA: alpha smooth muscle actin.

AT-MSCs: adipose tissue mesenchymal stem cells.

BAT: Brown Adipose Tissue.

BH_4: tetrahydrobionitrate.

BMC: unfractionated bone marrow cells.

BM: Bone marrow.

BMAT: Bone Marrow Adipose Tissue.

BMSCs: bone marrow stem cells.

BM-MSCs: bone marrow derived mesenchymal stem cells.

BMMNCs: bone marrow mononuclear cells.

BMPCs: Bone marrow pluripotent cells.

BrdU: bromo deoxy uridine.

CAMs: cell adhesion molecules.

CAN: cardiac autonomic neuropathy.

CAT: catalase enzyme.

CCCP: carbonyl cyanide m-chloro phenyl hydrazone.

CD: cluster of differentiation.

CFU-F: colony forming unit fibroblast.

c-Kit: Mast/stem cell growth factor receptor (SCFR) also known as proto-oncogene c-Kit or tyrosine-protein kinase Kit or CD117 is a protein that in humans is encoded by the KIT gene.

$CTLA_4$: costimulatory receptors for T cell activation.

CVD: cardiovascular diseases.

DOX: doxorubicin.

DSCs: Dental stem cells.

ECs: endothelial cells.

EGF: epidermal growth factor.

eNOS: endothelial nitric oxide synthase.

ENSA: alpha endosulphine.

EPCs: endothelial progenitor cells.

ESCs: Embryonic stem cells.

ES/EG: embryonic stem cells and embryonic germ cells.

FACS: fluorescent activating cell sorting.

FAD: Flavin adenosine dinucleotide.

FADP: fas associated dead protein.

FBS: fetal bovine serum.

FDA: Food and Drug administration.

FMN: flavin nononucleotide.

GAD: glutamic acid decarboxylase

GAGS: glycosaminoglycans.

GFP: green fluorescent protein.

G- CSF: granulocyte colony stimulating factor.

GSH-Px: glutathione peroxidase.

h- ASCs: human adipose stem cells.

HGF: hepatocyte growth factor.

HIF-1α: hypoxia inducible factor-1α.

HLA: Human leucocytic antigen.

HNO_2: nitrous oxide.

HOCl: hydrochlorus acid.

H_2O_2: hydrogen peroxide.

HRO_2^-: hydroperoxyl.

HSC: hematopoietic stem cells.

HPC: hematopoietic progenerator cells.

IA-2: a transmembrane protein–tyrosine phosphatase.

IDO: indoleamine 2-3 dioxygenase.

IFN: interferon.

IGF-1: insulin-like growth factor-1.

IGRP:islet specific glucose 6 phosphatase protein.

IL-10: Interleukin 10.

iPSCs: induced pluripotential stem cells.

LEC: lectin domain of selectin.

MAPK: mitogen activated protein kinase.

MEF: myocyte enhancer factor.

MHC II: Major histocompatibility II.

MMP: matrix metalloproteinases.

MSCs: Mesenchymal stem cells.

NADH: nicotinamide adenine dinucleotide.

NADPH: nicotinamide adenine dinucleotide phosphate.

$NF_{\kappa}B$: nuclear factor kappa B.

NanOg: Land of youth in Irish language.

NO: nitric oxide.

NO_2^-: nitrogen dioxide.

NOD: non obese diabetic mice.

O_2^-: superoxide.

Oct4: octamer-binding transcription factor 4.

$ONOO^-$: peroxynitrites.

PARP: poly (ADP-ribose) polymerase.

PBS: phosphate buffer saline.

PCR: polymerase chain reaction.

PDGF: platelet derived growth factor.

Pdx1: pancreatic specific transcription factor 1.

PGE: prostaglandin E.

PKC: protein kinase C.

PPARγ: Peroxisome proliferator-activated receptor gamma.

RAAS: Renin- Angiotensin- Aldosterone System.

RAGE: receptors of advanced glycation end products.

RNS: reactive nitrogen species.

RO_2: peroxyl.