The effect of in vivo mobilization of bone marrow stem cells on the pancreas of diabetic albino rats (A histological & immunohistochemical study)

Thesis

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DEDICATED TO:

MY MOTHER Dr. FARIDA H. AHMED

AND MY FAMILY

ABSTRACT

The rapidly increasing number of diabetic patients across the world drew the attention to develop more effective therapeutic approaches. Recent investigations on newly differentiated insulin producing cells (IPCs) revealed that they could be derived from embryonic, adult mesenchymal and hematopoietic stem cells. This work was planned to evaluate the role of StemEnhance in mobilizing naturally occurring bone marrow stem cells in addition to the effect of this mobilization in improving streptozotocin-induced diabetes mellitus in rats.

Forty four adult male albino rats were included in this study. They were divided into four groups namely the control, the diabetic, the positive control-StemEnhance and the diabetic-StemEnhance groups. The mean number of CD34 immunopositive cells was measured by flowcytometry and random blood sugar was measured weekly. The pancreas was removed from the sacrificed rats and processed for staining with H&E and immunohistochemical staining for CD34 +ve and insulin +ve cells. Data obtained by morphometric study were discussed in relation to the findings detected by microscope.

CD34+ve cells increased in the blood after introduction of StemEnhance. CD34 +ve cells were observed in the pancreas throughout the four weeks of treatment and the insulin producing cells in the islets of Langerhans gradually increased from the first to the fourth week of treatment. Blood glucose level decreased but it was still higher than the control level after four weeks of treatment with StemEnhance.

KEY WORDS: Diabetes, Stem cells, CD34, StemEnhance, Streptozotocin, Pancreas.

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LIST OF ABBREVIATIONS

Abbreviations	Words
AFA	Aphanizomenon flos-aquae
AMD3100	Plerixafor or 1,1′-[1,4 Phenylenebis(methylene)]bis [1,4,8,11-tetraazacyclotetradecane]
ASCs	Adult stem cells
B.M	Bone marrow
BMC	Bone Marrow Cell
BSA	Bovine serum albumin
CD	cluster of differentiation
CFU	Colony forming unit
CFU-F	Fibroblast Colony forming unit
CK	Cytokeratin
CXCR4	Chemokine receptor 4
D.M	Diabetes Mellitus
EPCs	Endothelial precursor cells
ESCs	Embryonic stem cells
FACS	Fluorescence-Activated Cell Sorting
G-CSF	Granulocyte-colony stimulating factor
GIT	Gastrointestinal tract
GLUT	Glucose transporter
GM-CSF	Granulocyte-monocyte colony stimulating factor
HSCs	Hematopoietic stem cells
I.P	Intraperitoneal
ICM	inner cell mass
ihcworld	immunohistochemestry world
IL	Interleukin
IPCs	insulin-producing cells
LFA-1	Lymphocyte function-associated antigen 1
LSL	L-selectin ligand

Abbreviations	Words
MSCs	Mesenchymal stem cells
NAD	Nicotinamide dinucleotide
PARP	Poly (ADP-ribose) polymerase
PBS	Phosphate buffered saline
rhIL	Recombinant human interleukin
ROS	Reactive oxygen species
SCF	Stem cell factor
SDF-1α (CXCL12)	Stromal cell- derived factor-1α
SE	StemEnhance
STZ	Streptozotocin
TE	Trophectoderm
vWF	vonWillebrand factor
+ve	Positive

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Introduction

Introduction and Aim of the Work

Introduction:

Diabetes mellitus is a major health problem affecting more than 200 million of adult populations worldwide and is expected to affect at least 5 % of global population by the year 2025. The association of diabetes with micro and macrovascular complications as well as cardiomyopathy makes it a major cause of morbidity and mortality in the world **(Wild et al., 2004; Joshua et al., 2005).**

Diabetes mellitus has two forms: Type I (insulin-dependent) caused by an autoimmune destruction of the insulin-producing β-cells. Type II (noninsulin-dependent), results from a combination of reduced insulin sensitivity of tissues and impaired function of the insulin-secreting β-cells **(DeFronzo et al., 2004).**

Treatments of diabetes by different regimens of insulin injections failed to offer complete cure and could not prevent secondary complications associated with diabetes, such as diabetic retinopathy, nephropathy and neuropathy. Moreover, insulin therapy was frequently associated with severe hypoglycemic episodes **(Mandrup-Poulsen., 1998; Vija et al., 2009).**

Early treatment of patients by restoration of their β-cell function through pancreas or islet transplantation can relieve the patients from their dependency on insulin, achieve lifelong normoglycemia and prevent related complications **(Juang et al., 1996; Weir and Bonner-Weir., 1998; Shapiro et al., 2000; Robertson et al., 2004)**