AUTOLOGUS TRANSPLANTATION OF BONE MARROW STEM CELLS IN PATIENTS WITH RENAL FAILURE

Thesis
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بسم الله الرحمن الرحيم

"قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم"

صدق الله العظيم

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ABSTRACT

Stem cells are non-specialized cells that have the capacity to self-renew and to differentiate into many different cell types when subjected to the right biochemical signals. MSC were separated from bone marrow aspirate of the chronic renal failure patients using their property of plastic adhesion and then injected into both renal arteries of the same patients. Follow-up of the patients showed improvement in renal functions including urea and creatinine and there are significant improvement in GFR. Stem cells are a promising new therapeutic approach to treat chronic renal failure.

Keywords:

(Chronic renal failure, autologous stem cell transplantation)

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List Of Abbreviation

ABCG2	**ATP-binding cassette class G2**
ACEIs	**Angiotensin converting enzyme inhibitors**
AKI	**Acute kidney injury**
ALDH	**Aldehyde dehydrogenase**
ATP	**Adenosin tri-phosphate**
BCRP1	**Breast cancer resistance protien**
BFGF	**Basic fibroblast growth factor**
BIO	**6-bromoindirubin- 3'-oxime**
BMCs	**Bone marrow cell**
BM	**Bone marrow**
CAM	**Cellular adhesion molecule**
CD	**Cluster of differentiation**
CFCs	**Colony forming cell**
CFU-F	**fibroblastoid colony forming unit**
DMEM	**Dulbeco's modified eagles'medium**
DNA	**Deoxyribo-nucleic acid**
ECM	**Extra cellular matrix**
EGF	**Epidermal growth factor**
EPCR	**Endothelial Protein C Receptor**
ES	**Embryonic stem cell**
FITC	**Fluorescin isothiocyanate conjugated**
G-CSF	**Granulocyte-colony stimulating factor**
GFP	**Green fluorescence protein**

GM-CSF	**Granulocyte-macrophage colony-stimulating factor**
GVHD	**Graft-versus-host-disease**
H-CAMs	**Homing-cellular adhesion molecules**
4-HC	**4-hydroxyperoxycyclophosphamide**
HA	**Hyaluronic acid**
HDT	**High-dose treatment**
HGF	**Hepatocyte growth factor**
HIV	**Human immunodeficiency virus**
HSCs	**Heamatopoietic stem cells**
ICM	**Inner cell mass**
ICAM	**Intercellular adhesion molecule**
IFN-γ	**Interferon-γ**
IL	**Interlukin**
IM	**Intermediate mesoderm**
LFA	**Lymphocyte function-associated antigen**
LIF	**Leucocyte inhibitory factor**
LIF	**Leukemia inhibitory factor**
LT-HSC	**Long-term self-renewing hemtopoietic stem cells**
LTC-IC	**Long term culture initiating cells**
MAPCs	**Multipotent adult progenitor cells**
MHC	**Main histocompatibility complex**
MM	**Multiple myeloma**
MSCs	**Mesenchymal stem cells**
NOD/SCID	**Nonobese diabetic severe combined immune-**

	dificient
OI	Osteogenesis imperfecta
PBS	Phosphate buffer saline
PDGF	Platelets-derived growth factor
PE	Phycoerythrin
RRT	Renal replacement therapy
SCF	Stem cell factor
SCT	Stem cell transplantation
SDF	Stromal derived factor
SH2	Dihydro-sulfur
SP	Side Population
TGF-β	Transforming growth factor- β
UCB	Umbilical cord blood
US	United States
VCAM	Vascular cell adhesion molecule
Wnt-pathway	Wingless Int gene

Introduction

INTRODUCTION

Stem cells have the unique ability to differentiate and self-regenerate **(Chamberlain et al, 2007).**

The bone marrow (BM) contains at least two populations of stem cells, haematopoietic stem cells (HSCs) and mesenchymal stromal cells (MSCs), which provide stromal support for HSCs **(Wagers and Weissman, 2004).**

The hematopoietic SC (HSC), which reside within the stromal compartment of the BM are undifferentiated cells capable of self-renewal and stepwise differentiation into fully specialized cells of the blood, e.g. erythrocytes, thrombocytes and leukocytes **(Benedetta et al, 2008).**

The MSC are undifferentiated adult SC of mesodermal origin that have the capacity to differentiate into cells of connective tissue lineages, including bone, fat, cartilage and muscle. They can be isolated and expanded with high efficiency in culture as plastic adherent cells **(Benedetta et al, 2008).**

Chronic kidney disease (CKD) is increasing at the rate of 6-8% per annum in the US alone. At present, dialysis and transplantation remain the only treatment options. However, there is hope that stem cells and regenerative medicine may provide additional regenerative options for kidney disease. Such new treatments might involve induction of repair using endogenous or exogenous stem cells or the reprogramming of the organ to reinitiate development **(Hopkins et al, 2008).**

Aim of the Work