HAEMATOPOITIC STEM CELL TRANSPLANTATION IN PATIENTS WITH (CHILD-C) END STAGE LIVER CIRRHOSIS

Submitted by

Dr. Nagwa Ramadan Ahmed
Assistant Lecturer of Internal Medicine, Cairo University

Under Supervision of

Prof. Dr. Noaman Elgarm
Prof of internal medicine, Gastroenterology &Hepatology
Faculty of Medicine – Cairo University

Prof. Dr. Mona Amin
Assistant Prof of internal medicine,
Gastroenterology &Hepatology
Faculty of Medicine – Cairo University

Prof. Dr. Hala Gaber
Prof of clinical pathology
Faculty of Medicine – Cairo University

Faculty of Medicine
Cairo University
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ABSTRACT

As there is huge demand for liver transplantation but there are never enough organs and the procedure is not always successful, we can use bone marrow or umbilical cord blood stem cells to help treat liver disease and reduce the need for liver transplantation ***(Hunter D, 2003).***

The discovery of adult tissue specific stem cells such as haemopiotic stem cells, which have the ability to transdifferentiate into other tissues, has generated much excitement among cell biologists and transplant clinicians**.** It opens new avenaes for basic biological research by using stem cells from adults as an alternative to stem cells from embryos. It also carries important implications for the treatment of many liver, heart, and neurogenerative diseases ***(Kuehnle I and A Goodell M, 2002)***.

HSCs have been reported to produce not only all of the blood lineages, but also skeletal muscle ***(Gussoni E et al, 1999),*** neurons ***(Brazelton TR et al, 2000)***, cardiac muscle ***(Orlic D et al, 2001)***, pulmonary epithelium ***(Krause DS and Theise ND, 2001),*** and liver epithelium ***(Petersen BE et al, 1999).***

These reports on stem cell plasticity and the observations on the expression of hematopoietic markers in oval cells described earlier led to the hypothesis that bone marrow stem

cells may give also rise to epithelial cells, including hepatic oval cells. This was confirmed experimentally in 1999 by ***Petersen*** and coworkers ***(Petersen BE et al, 1999)***. A murine study showed that not only oval cells but also hepatocytes could be derived from donor bone marrow ***(Thomas ED et al, 1975).***

Although most published information on adult stem cells draws heavily from studies with animal models, there is increasing clinical evidence to support the concept of stem cells transdifferentiation ***(Theise et al, 2000).***

Recent findings indicate that adult BM also contains cells that can differentiate into additional mature, nonhematopoietic cells of multiple tissues including epithelial cells of the liver, kidney, lung, skin, gastrointestinal (GI) tract, and myocytes of heart and skeletal muscle ***(Erica L et al, 2003).***

The new discovery that stem cells can also turn into liver cells inside patients means that marrow stem cells could eventually be used to repair damaged livers as well ***(White D, 2000).***

Thus, presence of such hepatocyte progenitor cells in BM could explain that in vivo differentiation of bone marrow into hepatocytes noted in recent studies (***(Lagasse E et al, 2000).***

To ensure that the human stem cells developed into liver-like cells, the researchers tested for the presence of a human

protein, albumin that is only produced by the liver ***(Hunter D, 2003).***

In some reports the degree of hepatocyte replacement achieved after hematopoietic repopulation equaled or exceeded the results obtained by hepatocyte transplantation ***(Theise ND et al, 2000).***

The result of present work shows that stem cell transplantation have a beneficial effect on synthetic function of the liver and possibly improve survival and quality of life of patients with end stage liver disease. Hepatocyte transplantation may not be able to reverse portal hypertension, or the development of HCC, but improvement in liver physiology and patient survival could be possible and could play a significant role in the management of patients with liver failure.

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LC: Liver cirrhosis

PDGF: Platelet derived growth factor

EGF: Epithelial growth factor

NFKB: Nuclear factor kappa B

PrP: Prion protein

ET1: Endothelin 1

IGF: Insulin like growth factor

MCP-1: Monocyte chemotactic peptide 1

IL1B: Interleukin 1B

TNF: Tumor necrosis factor

MMPs: Matrix metalloproteinase

TIMMPs: Tissue inhibitors of matrix metalloproteinase

HCC: Hepatocellular carcinoma

VEGF: Vascular endothelial growth factor

HGF: Hepatocyte growth factor

HMG: High mobility group

TCF: Transcription factor 4

TGF-B1: Transforming growth factor B1

AST: Aspartat aminotransferase

ALT: Alanine aminotransferase

LDH: Lactate dehydrogenase

GGT: Gamma glutamyl transferase

SBP: Spontaneous bacterial peritonitis

PCR: Polymerase chain reaction

ANA: Anti-nuclear antibody

AMA: Anti-mitochondrial antibody

ASMA: Anti-smooth muscle antibody

HCC: Hepatocellular carcinoma

MELD: Model for end stage liver disease

TIPSS: Tansjugular intrahepatic portosytemic stent shunt

MEGX: Monoethylglycinexylidide

HAV: Hepatitis A virus

HBV: Hepatitis B virus

HCV: Hepatitis C virus

HDV: Hepatitis delta virus

PBC: Primary biliary cirrhosis

SBC: Secondary biliary cirrhosis

CREST syndrome: (Calcinosis, Raynauds phenomenon, esophageal involvement, sclerodactely and skin changes in the fingers, telangiectasia)

INR: International normalized ratio

NASH: Non alcoholic steatohepatitis

SAAG: Serum ascites albumin gradient

KGF: Keratinocyte growth factor

PMN: Polymorphonuclear

WBC: White blood cell

CT: Computed tomography

NSAIDs: Non steroidal anti-inflammatory drugs

PSE: Portosystemic encephalopathy

ALD: Alcohol induced liver disease

PUL: Poly unsaturated lecithin

SAM: S-adenosyl1-1 methionin

PSC: Primary sclerosing cholangitis

MMF: Micophenolate mofetile

UDCA: Ursodeoxy cholic acid

MU: million units

IFN: Interferon

BCAAs: Branched chain amino acids

OA: L-ornithin-L asparetate

CTP: Child-Turcotte-Pugh

ICP: Intra cranial pressure

UNOS: United Network for Organ Sharing

CMV: Cytomegalovirus

HMG-CoA: 3 hydroxy-3-methyl glutaryl co enzyme A

ESc: Embryonic stem cells

G-CSF: Granulocyte colony stimulating factor

HSC: Hematopiotic stem cell

BMSC: Bone marrow stem cell

SDF-1alpha: Stromal derived factor1 alpha

CD34: Cluster of differentiation

CK19: Cytokeratin 19

SVR: Sustained virologic response

CYP: Cytochrome P