STEM CELL TRANSPLANTATION IN PATIENTS WITH CEREBRAL PALSY

THESIS
Submitted for partial fulfillment of M.D. Degree in Neurology

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2010

بسم الله الرحمن الرحيم

"ويسئلونك عن الروح قل الروح من أمر ربي
وما أوتيتم من العلم إلا قليلا"

صدق الله العظيم
(الآية: ٨٥، سورة الإسراء)

ACKNOWLEDGEMENT

I would like to express my deepest gratitude and sincere thanks to Prof. Dr. **Mahassen Ali Hassan**, Professor of Neurology, Cairo University, the unique Neurologist, for her continuous guidance, supervision and suggestion of this work. I appreciate her hard support and powerful push and above all acceptance of my annoyance with endless patience, she was really the heart of this work.

I wish to express my deepest thanks and gratitude to Prof. Dr. **Hala Gabr**, Professor of Clinical Pathology, Cairo University, for her kind support, constructive criticism and valuable assistance specially In performing the lab work, without which, this work could not have been accomplished.

I am extremely grateful to Dr. **Shereen Fathi**, Ass. Professor of Neurology, Cairo University, for her great care, continuous guidance, excellent supervision and valuable suggestion, saving no effort or time during the whole work.

I would like to extend my appreciation and deep thanks to Dr. **Gehan Ramzy,** Ass. Professor of Neurology, Cairo University for her kind, calm and extremely helpful attitude.

I wish to express my deepest thanks to Dr. **Nermin Adel**, Ass. Professor of Neurology, Cairo University, for her kind support and valuable assistance.

I would like to extend my appreciation to Dr. **Heba Fathi,** Lecturer of Psychiatry,Cairo University for her kind help in choosing scales used in the study.

I would like to thank Dr. **Mariam Thabet**, a Clinical Pathologist, for her kind help in performing the lab work .

I wish to thank all members of Neurology Department, Cairo University, for their support and encouragement throughout the work.

Finally, I am really grateful to all patients who participated in this work.

Amr Hassan

2010

TO MY BELOVED
FATHER
(GOD BLESS HIM)

TO MY GREAT
MOTHER

TO MY FAMILY

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ABSTRACT

Background:Cerebralpalsy is an "umbrella term covering a group of non-progressivemotor impairment syndromes secondary tolesions or anomalies of the brain arising in the early stagesof its development". Stem cells are well known to be capable of differentiating into specialized cells performing different functions in the body. A stem cell transplantation (SCT) technology represents a new feasible approach to the treatment for a number of diseases including cerebral palsy.**Purpose of study**: was to study the impact ofSCTonpsychomotor functions in patients with cerebral palsy.**Subject and Methods**:This randomized control trial was conducted on 52 Egyptian patients presenting with cerebral palsy,they were divided into 2 groups; Group I: Patients who underwent stem cell transplantation and Group II (control group): Patients who did not undergo stem cell transplantation .All patients (Group I & II) were subjected to the following battery of assessment after parent/s consent; history taking, examinationand clinical measures of disabilities that includeGross Motor Function Classification System(GMFCS),Boyd's Progress Developmental Scale and the 100 Points Scale. SCTwas done group I through bone marrow aspiration then isolation and culturing of MSCS followed by reinjectioninto the subarachinoid space via lumbar puncture.All patients were reassessed 1 year after the initial assessment.**Results**:Assessment of the patients in study group (group I) using Boyd's developmental progress scale revealed that mean score for the motor skills was 8.19 ±8.75 prior to SCT &9.19±8.99 after SCT, score for the independence skills was 9.23±8.55 prior to SCT &10.19±8.99after SCT, mean score for the communication skills was 10.19± 8.99 prior to SCT &11.5±7.39after SCT, all these differences were statistically significant (P value < 0.05).Assessment of the patients in study group (group I) using 100 points scale revealed that mean score was 47.3 ±32.68 prior to SCT & 50.57±34.00 after SCT, this difference was statistically significant (P value < 0.05).As regard GMFCS , mean score was 4.23±1.37prior to SCT &4.15±1.46after SCT, this difference was statistically insignificant (P value > 0.05).***Conclusion***: Autologous stem cell transplantation could be a safe &helpful tool in the management of patients with cerebral palsy.

Keywords:

- Autologous stem cell transplantation
- Cerebral palsy.

LIST OF ABBREVIATIONS

AABB :American Association of Blood Banks
AAN :American Academy of Neurology
BDNF :Brain derived neurotrophic factor
BM :Bone marrow
BW :Body weight
CD :Cluster of differntiation
CNS :Central nervous system
CP :Cerebral palsy
CSF :Cerebrospinal fluid
CT :Computerized tomography
DMEM :Dulbecco's Modified Eagle Medium
DNA :Deoxy Nucleic Acid
EDSS :Expanded disability status scale
EEG :Electroencephalography
EG :Embryonic germ
EGF :Endothelial growth factor
ES :Embyronic stem cells
FACS :Fluorescence-activated cell sorting
FDA :Food and Drug Administration
FFT :Fast Fourier transformer
FITC :Fluorescene isothiocyanate
FGF-2 :Fibroblast growth factor-2
G-CSF :Granulocyte colony stimulating factor
GMFCS :Gross Motor Function Classification System
HLA :Human leukocyte antigen
hNSCs :Human neural stem cells
HSC :Human stem cells
hUCSC :Human umbilical cord stem cell
IMDM :Iscove's modified Dulbecco's medium
LRP :Lineage restricted precursors
MNC :Mononuclear cells
MRI :Magnetic resonance imaging
MS :Multiple sclerosis
MSCs :Mesenchymal stem cells
NGF :Nerve growth factor
NSCs :Neural stem cells
NSPs: :Neural stem/progenitor cells
NT3: :Neurotrophin-3

P	:Probability
PBS	:Phosphate buffer saline
PE	:Phycoerythrin
PET	:Positron emission tomography
PMT	:Photomultiplier tubes
RMS	:Rostral migratory stream
ROM	:Range-of-motion
rpm	:round per minute
SCs	:Stem cells
SCID	:Severe combined immunodeficiency
SCT	:Stem cell transplantation
SD	:Standard deviation
SP	:Side population
SPSS	:Statistical Package Social Science
SVZ	:Subventricular zone
TBI	:Traumatic brain injury
TNF	:Tumor necrosis factor
UCB	:Umbilical cord blood

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Introduction

INTRODUCTION

Cerebral palsy is "an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development." ***(Mutch et al., 1992).***

This condition has devastating consequences for the individual and for society. Multiple factors can cause injury to the developing brain leading to cerebral palsy. Many preconceptional, prenatal and perinatal factors (oxidative damage, perinatal hypoxia/ischemia and maternal infection among others) are known to be associated with brain injury ***(Stanley et al., 2000).***

There are no effective means to repair the brain once damage has occurred. Moreover, since many of these insults occur in utero, prevention may prove difficult, and regenerative strategies may be a better alternative to reduce the damage to the brain ***(Plane et al., 2004).***

Neural stem/progenitor cells (NSPs) have been recently identified in the mammalian central nervous system, including humans, at all stages of life. Defined as self-renewing, primordial cells with the capacity to give rise to all cell lineages in all regions of the nervous system, Neural stem/progenitor cells (NSPs) are found in the germinal zone in the brain of the embryo and fetus where they participate in central nervous system formation. Cells