Department of Medical Studies for Children

Evaluation of Stem Cell Transplantation In Cerebral palsy

Thesis

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ABSTRACT

Background:Perinatal complications may result in life-long morbidities, among which cerebral palsy is the most severe motor disability. Once developed, cerebral palsy is a non-progressive disease with a prevalence of 2-3 per 1000 live births in developed countries. It demands an extensive and multidisciplinary care. Therefore, it is a challenge for our health system and a burden for patients and their families. Recently, stem cell therapy emerged as a promising treatment option and raised hope in patients and their families, Aim and objectives:the aim of the study is toevaluate the role of stem cells transplantation in cerebral palsy Patients, subjects and methods: this is a follow up study , that was carried out at Waady Elneel hospital , Cairo, the study was conducted on 20 diagnosed Cerebral Palsy patients classified according to age into two Groups : Group 1: one year to five years, and Group 2: five years to fifteen years, the study was carried out from January 2018 to January 2020,Follow up the patient with Gross Motor Function Classification Scale was done before injection of stem cell and 3 months, 6 months, 9 months, 12 months after injection of stem cell, Results: the results of the study revealed that there is no significant difference at Gross Motor Function Classification Scalebetween the two groups as regard injection score,there is significant improvment in Gross Motor Function Classification Scalefrom pre-injection to final injection score Conclusion:gross motor function and in children with cerebral palsy were remarkably improved at 6 months and 12 months after stem cell transplantation,
Keywords:Transplantation, **Gross Motor Function Classification System, Stem Cells, Cerebral Palsy**.

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LIST OF ABBREVIATIONS

AAN	American Academy of Neurology
AD-MSCs	Adipose derived mesenchymal stem cells
AKI	Acute kidney injury
ALS	amyotrophic lateral sclerosis
aMSCs	adipose-derived MSCs
BBB	Blood brain barrier
BDNF	brainderived neurotrophic factor
BDNF	Brain-derived Neurotrophic Factor
bmMSCs	bone marrow–derived MSCs
BMPC	bone marrow progenitor cells
BMSCs	bone marrow stromal cells
CCI	controlled cortical impact injury
CKD	Chronic kidney disease
CNS	tumor necrosis factor
CP	Cerebral Palsy
CT	computed tomography
DHA	Docosahexaenoic acid
DNA	Deoxyribonucleic acid
ECMs	Extracellular matrices
EEG	Electroencephalogram
EMG	Electromyography
ESC	embryonic stem cells
Flk1	fetal liver kinase 1
G-CSF	granulocyte colony stimulating factor
GDNF	glial-derived neurotrophic factor
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
hADSCs	human adipose-derived stem cells

HD	Huntington's disease
HLA	human leukocyte antigen
hNSCs	human NSCs
HSCs	hematopoietic stem cells
hUCBCs	human umbilical cord blood cells
hUC-MSCs	human umbilical cord derived mesenchymal stem cells
ICF	International Classification of Functioning
ICP	intracranial pressure
IGF-I	insulin-like growth factor-I
iPS cells	Induced pluripotent stem cells
MAPC	Multipotent adult progenitor cells
MMPs	Metalloproteinases
MRI	magnetic resonance image
MS	multiple sclerosis
MSA	multiple system atrophy
MSCs	MESENCHYMAL STEM CELLS
MuSCs	muscle stem cells
NGF	nerve growth factor
NSCs	Neural stem cells
OPC	Oligodendrocyte progenitor cells
PD	Parkinson's disease
PELOD	Pediatric Logistic Organ Dysfunction
PET	Positerron emission tomography
PILOT	Pediatric Intensity Level of Therapy
rNSCs	rat neuralstem cells
ROS	reactive oxygen species
SCT	stem cell therapy
SDF-1	stromal cell-derived factor 1

SGZ	subgranular zone
SVF	stromal vascular fraction
SVZ	subventricular zone
TBI	traumatic brain injury
TNF	tumor necrosis factor
UCB	Umbilical cord blood
VEGF	vascular endothelial growth factor
WJ-MSCs	Wharton's jelly mesenchymal stem cells

Introduction

Cerebral Palsy is the commonest cause of severe neurological disability in children. The general prevalence is 2-3 per 1000 live births and has slightly increased in recent years. This is due to the decreased mortality of low-birth-weight infants together with an increased rate of cerebral palsy in the survivors(**Hollunget al, 2018).**CP describes a group of permanent disorders of the development of movement and posture, causing activity limitations. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior,(**Takanoet al,2020)**.

Treatment programs for CP encompass physical and behavioral therapy, pharmacologic and surgical treatments, mechanical aids, and management ofassociated medical conditions. While many of these treatments are helpful, none facilitatein reparative recovery of damaged brain. Recent advances in stem celltherapy provide the hope of developing more effective interventions in treating CP. Research has shown that bone-marrow-derived cells could develop into neural tissue**(Weimann et al,2003).**

Woodburyetalclaimed that adult rat and human bone marrow stromal cell differentiate into neurons(Woodbury et al 2000). Stem cell transplantation has been reported to be effective in animal modelsas well asin patients with otherdegenerative neurological disorders such as stroke and demyelination**(Park et al 2008).**

Stem cell research originated in the 1980s within the field of biotechnology. Since then, progress has been made towardsdeveloping a number of potential treatments for what are still considered untreatable diseases. However, controversy regarding the means and methods of studyhasslowedfurtherprogress within thefield**.(Singhet al2020).**

Researchers are using several different types ofstem cellstostudy brain injuryto explore the possibilities for developing new treatments. In some of these studies, researchers do appear to have been able to reduce damage to the brain as somehave shown some improvements in their symptoms. However, these effects in patients are not yet fully understood, much more work is needed and it will be many years until suchresearch can be applied to treating cerebral palsy**(Korzeniewski et al2008).**

Concept of the study

Cerebral Palsy:

Cerebral palsy is considered a neurological disorder caused by a non-progressive brain injury or malformation that occurs while the child's brain is under development. Cerebral palsy primarily affects body movement and muscle coordination.(**Lepore et al,2005)**

Stem Cell:

An undifferentiated cell of a multicellular organism which is capable of giving rise to indefinitely more cells of the same type, and from which certain other kinds ofcell arise by differentiation(Li et al,2000)

Autologous stem cells transplantation:

That is transplantation in which stem cell(undifferentiated cellfrom other cell types develop), are removed and later are given back to the same person.

Hypothesis

- Autologous intrathecal stem cells transplantation leads to the improvement ofthe CP deficits e.g. motorfunctions.

Aim of The Work

The study aimsto:

- Evaluate the role of stem cells transplantation in CPPatients.
- As regards Motor Fuctions.