



Department of Medical Studies for Children

Evaluation of Stem Cell Transplantation In Cerebral palsy

Thesis

Submitted for Partial Fulfillment of Ph.D. degree

In childhood studies Faculty of Postgraduate Childhood Studies

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2020

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبَّحْتَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

ACKNOWLEDGMENT

All praise to “**ALLAH**”, the most gracious and the most merciful, who guides us to the right way

I would like to thank heartily and to express my sincere gratitude to *Prof. Maisa Nasr Farid*, **Professor of Pediatrics, faculty of Postgraduate Childhood Studies, Ain Shams University** for her guidance, descent discussions, and continuous encouragement.

I am extremely indebted to *Prof. George S. Kobinia*, **Head of the Stem Cell Therapy Group Vienna Medical University of Vienna–Austria** for his endless flow of advices, valuable ideas, and helpful instructions.

I am also, deeply grateful to *Dr. Reham Sabry Tarkhan*, **Lecturer of Pediatrics, faculty of Postgraduate Childhood Studies, Ain Shams University** for her illuminating discussion, kind cooperation and endless support throughout this work.

To the spirit of the *Prof. Khaled Hussien Taman*, **Professor of Pediatrics, faculty of Postgraduate Childhood Studies, Ain Shams University** for his fatherhood guidance, descent discussions, and continuous encouragement

Mohamed Sedky Attia Abd El Kader

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 to evaluate 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 Scale between the two groups as regard injection score, there is significant improvement in Gross Motor Function Classification Scale from 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.

LIST OF CONTENTS

Title	Page
Abstract	I
List of Tables	III
List of Figures	IV
List of Abbreviations	VI
Introduction	1
Aim of the Work	5
Review of Literature	7
• Chapter (1): Cerebral Palsy	7
• Chapter (2): Stems Cell Transplantation	42
• Chapter (3): Stem Cell Transplantation In Cerebral Palsy	56
• Chapter (4):Gross Motor Skills	72
Subjects and Methods	82
Results	90
Discussion	121
Summary	132
Conclusion	135
Recommendations	137
References	139
الملخص العربي	١

LIST OF TABLES

No	Table	Page
1	Neurological Diseases in Which SCT Has Been Tried	50
2	Demographic characteristics of the studied cases	90
3	Demographic characteristics of the study Groups	93
4	Distribution of Birth risk factors among the studied Cases	96
5	Distribution of Birth risk factors among the studied Cases	98
6	Distribution of Different risk factors among the studied Groups	102
7	Comparison between changes in GMFCS between both groups	105
8	Pre-injection and over one year injection changes in GMFCS Group A	106
9	Pre-injection and final injection changes in GMFCS Group A	107
10	Pre-injection and over one year injection changes in GMFCS Group B	108
11	Pre-injection and final injection changes in GMFCS Group B	109
12	Association between Gender and final injection changes in GMFCS Group A	110
13	Association between Gender and final injection changes in GMFCS Group B	111
14	Association between Cause and final injection changes in GMFCS Group A	112
15	Association between Cause and final injection changes in GMFCS Group B	113
16	Other aspects of improvement after injection	114
17	Other aspects of improvement after injection in Group A & B	116

LIST OF FIGURES

No	Figure	Page
1	Magnetic resonance image (MRI) of a 16-month-old boy who was born at term but had an anoxic event at delivery	7
2	Magnetic resonance image (MRI) of a 1-year-old boy who was born at gestational week 27	38
3	Magnetic resonance image (MRI) of a 16-month-old boy who was born at term but had an anoxic event at delivery	39
4	Magnetic resonance image (MRI) of a 9-day-old girl who was born at full term and had a perinatal hypoxic-ischemic event. Examination of the patient at 1 year revealed findings consistent with a mixed quadriparetic cerebral palsy notable for dystonia and spasticity	40
5	Gender distribution of the studied cases	91
6	Mean age of the studied cases and maternal age	92
7	Mean Blood Pressure of the studied cases	92
8	Mean Weight of the studied cases	92
9	Mean age of the studied groups	94
10	Mean weight of the studied groups	94
11	Gender distribution of the studied Groups (A) represent % of Group A and (B) % of Group B	95
12	Mean Blood Pressure of the studied groups	96
13	Maternal Age Distribution of the studied cases	97
14	Mode of Birth Distribution of the studied cases	97
15	Causes Distribution of the studied cases	98
16	Maternal Age Distribution of the studied Groups (A) represented Group A while (B) represented Group B	99
17	Causes Distribution of the studied Groups (A) represented Group A while (B) represented Group B	100
18	Mode of Birth Distribution of the studied Groups (A) represented Group A while (B) represented Group B	101

No	Figure	Page
19	Frequency for all previous data for Group A	103
20	Frequency for all previous data for Group B	103
21	Distribution of different risk factors among the studied cases	104
22	Comparison between median changes in GMFCS between Groups A and Group B	106
23	Changes in GMFCS over time in group A	107
24	Preinjection and final injection changes in GMFCS Group A	108
25	Changes in GMFCS over time in Group B	109
26	Pre-injection and final injection changes in GMFCS group B	110
27	Significant between Gender and final injection change in GMS at Group A	111
28	Significant between Mode of birth and final injection change in GMS at Group A	112
29	Significant between Causes and final injection change in GMFCS at Group A	113
30	Significant between Causes and final injection change in GMFCS at Group B	114
31	Bladder & Bowel control Distribution of the studied cases	115
32	Cognitive Change Distribution of the studied cases	115
33	Convulsion Change Distribution of the studied cases	115
34	Bladder & Bowel Control Distribution of the studied Groups (A) represented Group A while (B) represented Group B	117
35	Cognitive Changes Distribution of the studied Groups (A) represented Group A while (B) represented Group B	118
36	Convulsion Changes Distribution of the studied Groups (A) represented Group A while (B) represented Group B	119

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	Positron 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 of associated medical conditions. While many of these treatments are helpful, none facilitate in reparative recovery of damaged brain. Recent advances in stem cell therapy 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**).

Woodbury et al claimed 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 models as well as in patients with other degenerative 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 towards developing a number of potential treatments for what are still considered untreatable diseases. However, controversy regarding the means and methods of study has slowed further progress within the field. **(Singhet al2020).**

Researchers are using several different types of stem cells to study brain injury to 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 some have 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 such research 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 of cell arise by differentiation **(Li et al,2000)**

Autologous stem cells transplantation:

That is transplantation in which stem cell(undifferentiated cell from 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 of the CP deficits e.g. motor functions.

Aim of The Work

The study aimsto:

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