THE ROLE OF STEM CELLS TRANSPLANTATION IN SPINAL CORD INJURY

An Essay
Submitted for partial fulfillment for the requirement of Master Degree in ***General Surgery***

By

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Acknowledgment

I would like to express my profound gratitude to **Professor Doctor/ Khaled M. Abd ElAziz Hosny,** *Professor of General Surgery, Faculty of Medicine, Ain Shams University for his most valuable advises and support all through the whole work and for dedicating much of his precious time to accomplish this work.*

I am also grateful to **Doctor/ Omar Youssef Hammad,** *assistant Professor of Neurosurgery, Faculty of Medicine, Ain Shams University and* **Doctor/ Mostafa Fouad Mohammad**, *Lecturer of General Surgery, Faculty of Medicine – Ain Shams University for their unique efforts, considerable help, assistance and knowledge he offered me through out the performance of this work.*

Last but not least, I would like to express my deepest thanks and gratitude to each one helped me to finish this work.

Ahmed Fathalla Zayed

LIST OF CONTENTS

LIST OF FIGURES (Cont…)

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBRAVATION

ADI	Atlantodens interval
ALL	Acute lymphocytic leukaemia
AML	Acute myeloid leukaemia
B١٠٤	Neuroblastoma cell line B١٠٤
BDNF	Brain derived neurotropic factor
bFGF	Basic fibroblast growth factor
Brdu	Bromodeoxy uridine
C	Cervical
CT	Computerized tomography
CNS	Central nervous system
CML	Chronic myeloid leukaemia
CD١٩	B cell antigen
CD٢٠	B cell antigen
CD٣٣	Myeloid antigen
CGRP	Calcitonin gene related peptide
CG٤ cell	An oligodendrocyte type ٢progeginator cell line
ChAT	Choline acetyl transferase
C١٧.٢	A prototypical neural stem cell line
DCSA	Dorsal column sensory axons
DMSO	Dimethyl sulfoxide (as preservative for stem cells)
ES cell	Embryonic stem cell
EC cell	Embryonic carcinoma cell
EG cell	Embryonic germ cell
EBs	Embryoid bodies
EGF	Embryonic growth factor
FGF	A known mitogen for stem cell
GFP	Green fluorescent protein
GRP	Glial restricted precursors
GDNF	Glial cell line neurotrophic factor
GFAP	Astroglial marker
GFAP	Glial fibrillary acidic protein
HSCs	Hematopoietic stem cells

LIST OF ABBRAVATION (Cont...)

hNTERA٢	Human pluripotent embryonal carcinoma cell
HGF	Hepatocyte growth factor
HNRP	Human neural restricted precursors
ITSF medium	Media supplemented with insulin, transferrin, selenium and fibronectin
LIF	Leukaemic inhibitory factor
LGE	Lateral ganglion eminence
MRI	Magnetic resonance imaging
MGE	Medial ganglion eminence
md	Myelin deficient
MAP	Microtubule associated protein
MSCs	Mesenchymal stem cells
NT٣	Neurotrophin٣
NGF	Nerve growth factor
NTERA٢	Pluripotent embryonal carcinoma cell
NRP	Neuronal restricted precursors
NCAM	Neural cell adhesion molecule
NSCs	Neural stem cells
NSE	Neuron specific enolase
O٢A	Oligodendrocyte precursors
OECs	Olfactory ensheathing cells
PNS	Peripheral nervous system
PGCs	Primordial germ cells
PERV	Porcine endogenous retrovirus
PSA-NCAM	Polysialysed form of neural cell adhesion molecules
QC	Quality control
RN٣٣B NSC	A type of restricted neuronal stem cell
SPIO	Superparamagnetic iron oxide
SCI	Spinal cord injury
SCID	Spinal cord injury model
SSEA٣	Specific embryonic antigen

LIST OF ABBRAVATION (Cont...)

SSEA١	Specific embryonic antigen
SSEA٤	Specific embryonic antigen
SCNT	Somatic cell nuclear transfer
SVZ	Subventricular zone
SEZ	Subependymal zone
Tra-١-١٦٠	Specific embryonic antigen
Tra-١-١٨٠	Specific embryonic antigen
TLSO	Thoracolumbar supporting orthosis
ts T-ag	Temperature sensitive T antigen
V-myc	Propagation gene
VEGF	Vascular endothelial growth factor
wk	Weak

INTRODUCTION

Human stem cells research holds enormous potential for contributing to our understanding of fundamental human biology. Although it is not possible to predict the outcomes from basic research, such studies will offer the possibility for treatments and ultimately for cures for many diseases for which adequate therapies do not exist ***(Audrey et al., ١٩٩٩).***

Key questions regarding adult stem cells are: (١) Their identity, (٢)Their tissue source of origin, (٣)Their ability to form other cell or tissue types, and (٤)The mechanisms behind such changes in differentiation and effects on tissues and organs ***(Ramer et al., ٢٠٠٠).***

Once thought impossible, repairing the damaged spinal cord is now entering the realm of feasibility. Tow important concepts are shortening the path to successful restoration: ١) It is not necessary to cure a spinal cord injury, and ٢) A disproportional return of function can result from a small degree of regeneration. Substantial loss of spinal cord tissue, particularly gray matter, does not preclude near normal long tract function ***(McDonald et al., ٢٠٠٤).***

Several neural and non neural cell types, including olfactory ensheathing glia and Schwann cells ***(BUNGE and PEARSE, ٢٠٠٣),*** genetically modified fibroblasts ***(MURRAY, ٢٠٠٤)*** and marrow stromal stem cells ***(CHOPP and LI, ٢٠٠٢)*** have been shown to improve functional outcomes following transplantation into injured spinal cord.

AIM OF THE WORK

The aim of this study is to assess and evaluate the role of stem cells transplantation as a treatment for spinal cord injury.

ANATOMY OF THE SPINAL CORD

The spinal cord begins above the foramen magnum at the base of the skull as a continuation of the medulla oblongata. In young children it ends at the upper border of the third lumbar spine, while in adults it terminates at the lower border of the first lumbar spine or the upper border of the second one. (fig.١) ***(Kane, ١٩٨٨).***

Like the brain, the spinal cord is intimately enveloped by the pia mater, which contains numerous nerves and blood vessels; the pia mater merges with the endoneurium of the spinal nerve rootlets and also continues below the spinal cord as the filum terminale internum. The web like spinal arachnoids membrane contains only a few capillaries and no nerves. The denticulate ligament runs between the pia mater and the dura mater and anchors the spinal cord to the dura mater. In lumbar puncture, cerebrospinal fluid is withdrawn from the space between the arachnoids membrane and pia mater (spinal subarachnoid space), which communicates with the subarachnoid space of the brain. ***(Reinhard Rohkamm, ٢٠٠٤).***

The spinal dura mater originates at the edge of the foramen magnum and descends from it to form a tubular covering around the spinal cord. Its lumen ends at the S١–S٢ level, where it continues as the filum terminale externum, which attaches to the sacrum, thus anchoring the dura mater inferiorly. The dura mater forms sleeves around the anterior and posterior spinal nerve roots which continue distally, together with the arachnoids membrane, to form the epineurium and perineurium of the spinal nerves. Unlike the cranial dura mater, the spinal dura mater is not directly apposed to the periosteum of the surrounding bone (i.e., the vertebral canal) but is separated from it by the epidural space, which contains fat, loose connective tissue, and valveless venous plexuses ***(Reinhard Rohkamm, ٢٠٠٤).***

As the cord terminates at the lower border of the first lumbar vertebra, the lumbar and sacral roots descends down forming vertical leash of nerves around the filum terminale constituting the Cauda equina ***(Kane, ١٩٨٨).***

The cord tapers off inferiorly into what is called the conus medullaris, which lies opposite the first lumbar vertebra. A prolongation of the pia matter named the filum terminal arises from the apex of the conus medullaris and reaches down to the back of the coccyx (fig.٢) ***(Kane, ١٩٨٨).***

٣١ Pairs of spinal nerves Arise from the spinal cord at its whole length. Each nerve is formed from two roots, anterior (motor) root and posterior (sensory) root. The sensory root shows a slight enlargement called the posterior root ganglion which gives rise to peripheral and central nerve fibres. The spinal nerve roots passes from the spinal cord down to the intervertebral foramen where they join each other forming the spinal nerve (mixed sensory and motor). Once the spinal nerve emerges the intervertebral foramen it divides into anterior and posterior rami ***(Kane, ١٩٨٨).***

The lumbar segment of the cord lies opposite the lower three thoracic vertebrae, while the sacral and coccygeal segments lie opposite the first lumbar, and their roots descends down (Cauda equina). So an injury between the ١٢th thoracic and the first lumbar vertebrae could damage the conus as well as the roots of the Cauda equina ***(Kane, ١٩٨٨).***

***Arterial blood supply of the cord*: (fig. ١)**

The blood supply of the cord depends mainly on ٣ systems forming ٣ networks that surrounded the cord, one lies in direct contact with the cord, the second (interspinal) lies in the connective tissue, while the third (extra spinal) lies in the tissue planes around the vertebral column ***(Kane, ١٩٨٨).***

١- The anterior spinal artery which arises from the vertebral arteries, and run downwards within the anterior median fissure ***(Kane, ١٩٨٨).***

٢- Two posterior spinal arteries arise directly from the vertebral artery or from one of its branches. Each one is divided into two descending branches that run vertically downward, one of them runs anteriorly and the other posteriorly ***(Kane, ١٩٨٨).***

٣- Radicular arteries (medullary feeders). These are variable in number, and arise from the vertebral arteries in the neck, the aorta in the thoracic and upper