UNIVERSITI PUTRA MALAYSIA

SURGICAL, CLINICAL AND PATHOLOGICAL COMPARISON ON THE USE OF OMENTAL PEDICLE AND BONE MARROW STROMA CELL THERAPY FOLLOWING SCIATIC NERVE NEUROTMESIS IN RABBIT MODEL

HAMEED ALI KADHIM

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By

HAMEED ALI KADHIM

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

October 2011

DEDICATION

This thesis is dedicated to my late parents. This thesis is also dedicated to my wife, who encouraged and inspired me to do my best and my children, Wael, Raya, Rawa and Sadan who have always been a source of inspiration.

DECLARATION

I declare that the thesis is my original work except for quotation and citation which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently, submitted for any other degree at Universiti Putra Malaysia or at any other institution.

HAMEED ALI KADHIM

Date:24th October 2011

Abstrak tesis yang dikemukaka kapeda senat auniversiti Putra Malaysia
senagai memenuhi keperluan Doctor Falsafah

PERBANDINGAN SURGERI, KLINIKAL DAN PATOLOGI PENGGUNAAN TERAPI PEDIKEL DAN SEL STROMA SUM-SUM TULANG EKORAN NEUROTMESIS SARAF SKIATIK PADA MODEL ARNAB

Oleh

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October 2011

Pengerusi: Profesor Madya Rashid Ibrahim

Fakulti : Perubatan Veterinar

Di benua Europa dan Amerika dianggarkan 300,000 kecederaan saraf pinggir (KSP) berlaku setiap tahun. Pada kebiasaannya kecederaan ini berlaku disebabkan oleh trauma mekanikal tepat (transeksi, kecederaan remuk, traksi atau avulsi), kemampatan, kecederaan terma dan neurotoksin. Pengurusan KSP memerlukan pengetahuan Anatomi, Patologi, Patofisiologi dan prinsip prinsip pembedahan. Masa kini kadar kejayaan pemulihan fungsi daripada lesi saraf pinggir adalah jauh daripada memuaskan meski pun terdapat mikropembedahan termaju. Kelemahan ini dikaitkan dengan fakta instrinsik pada sel motor atau sel deria dan elemen elemen pada tapakan kecederaan. Elemen elemen ini merangkumi jurang saraf, pembentukan tisu parut dan jangka masa yang tidak mencukupi untuk menampung faktor tumbesar menjadi berkesan dan bagi molekul matriks ekstrasel yang terbukti diperlukan untuk penjanaan semula saraf. Dalam kajian ini suatu penyelidikan yang komprehensif ditujukan kepada membangunkan prosedur

untuk memperbaiki penjanaan semula saraf dengan menumpukan perhatian kepada pendekataan biologikal untuk mempromosi penyembuhan saraf melalui : i) mengkaji peranan pedikal omentum dalam menjana semula dan pemulihan fungsi saraf, ii) pegasingan dan pengenalpastian sel stem mesenkim daripada sum sum tulang yang masa kini merupakan sasaran kajian keatas penjanaan semula tisu dan organ mengambilkira plastisiti sel sel tersebut.

Kajian ini telah dijalankan dengan hipotesis transposisi pedikal omentum (TPO) dan implan sel stem mesenkim mempromosi penjanaan semula dan pemulihan fungsi saraf siatik dalam model haiwan, arnab. Dengan ini objektif penyelidikan adalah untuk mengkaji kesan keatas transposisi pedikal omentum dan implan sel stem mesenkim sum sum tulang ekoran neurotmesis saraf siatik. Ke arah tujuan ini kajian membandingkan efikasi mentransposisi pedikal omentum dan implan sel stem mesenkim keatas saraf siatik yang telah di putuskan. Penjanaan semula saraf hasil setiap satu pendekatan di atas dinilai dari segi pameriksaan klinikal, neurohistologi, ultarstruktur, histomorfometri dan kenaikan relative berat otot gastronemius.

Enam puluh ekor arnab digunakan dalam kajian ini. Haiwan kajian telah dibahagikan dalam tiga kumpulan (n=20) dan disubjekkan kepada koaptasi saraf siatik menggunakan suture epineural yang membentuk kumpulan kawalan (SEN), transposisi pedikal omentum (TPOM) dan implan sel stem mesenkim sum sum tulang (SMST) yang membentuk kumpulan kumpulan rawatan. Penilaian keatas penjanaan semula dan pemuluhan fungsi saraf

siatik terputus berasaskan pendekatan pendekatan tersebut diatas dilakukan pada hari hari 14, 28, 56, 112 pasca bedah (PB).

Pemeriksaan klinikal dan patologi kasar menunjukkan pemulihan lengkap insisi kulit pada kaki yang telah dibedah dengan bukti bukti perlekatan sederhana diantara saraf siatik koaptasi dengan tisu disekelilingnya dalam kumpulan implan SMST sementara dalam kumpulan TPOM tidak terdapat sebarang bukti keberlekatan saraf dengan kulit. Petanda motor klinikal pada kaki yang telah dibedah dan berjalan dalam kumpulan TPOM dan SMST menunjukkan pemulihan yang lebih awal berbanding dengan kumpulan kawalan pada hari 55 PB. Petanda klinikal disokong oleh cacatan kuasa kontraksi otot yang lebih awal dalam kedua-dua kumpulan sementara dapatan balik massa otot berlaku lebih awal dalam kumpulan TPOM. Isyarat klinikal deriaan menunjukkan kemajuan deria rasa pada hari 112 PB.dalam kedua-dua kumpulan.

Hasil kajian histopatologi segmen proksimal saraf siatik dalam kumpulan TPOM and SMST menunjukkan penjanaan semula saraf berlaku lebih awal dikesan daripada penyusunan selari gentian saraf, peningkatan angiogenesis, bertambah kepadatan sel Schwann dan pembentukan tisu parut yang minima pada hari 28 PB. Hirisan separa nipis segmen proksimal dan distal saraf terputus menunjukkan susunan dan taburan lazim gentian saraf dan pembentukan normal epineurium. Ganglion akar dorsal dan korda spina mengandungi neuron dengan badan Nissl yang menunjukkan pemulihan saraf

dalam kumpulan TPOM dan SMST. Cerapan histopatologi penjanaan semula tisu saraf ini menyokong petanda klinikal pada kaki yang dibedah.

Penjanaan semula gentian saraf diperkuat seterusnya oleh cerapan ultrastruktur saraf siatik yang menunjukkan pembentukan myelin yang sempurna, sel Schwann, membrane asas dan endoneurium saraf yang utuh. Analisis histomorphometri menunjukkan peningkatan bilangan dan ukuran garispusat gentian saraf bermielin di samping peningkatan ketebalan sarung myelin dan akson dalam kumpulan TPOM dan SMST menunjukkan kesempurnaan penjanaan semula saraf terputus. Namun demikian perubahan penjanaan semula dalam kumpulan TPOM belaku sedikit lebih awal berbanding dengan kumpulan SMST yang mungkin memberi petunjuk bahawa transposisi pedikal omentum mempunyai sedikit kelebihan berbanding dengan implan sel stroma dari segi terapi putus saraf. Dapatan balik berat massa otot gastroknemius kearas normal menunjukkan pensarafan semula otot berkenaan.

Penemuan daripada kajian ini memberi bukti yang mencukupi bahawa aplikasi transposisi pedikal omentum dan implan sel stem sum sum tulang dalam kecederaan saraf pinggir mempromosi penjanaan awal dan pemulihan fungsi saraf yang terputus. Dengan ini terdapat potensi yang tinggi dalam aplikasi transposisi pedikal omentum dan implant sel stem sum sum tulang sebagai terapi kepada kecederaan saraf pinggir.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Doctor of Philosophy

SURGICAL, CLINICAL AND PATHOLOGICAL COMPARISON ON THE USE OF OMENTAL PEDICLE AND BONE MARROW STROMA CELL THERAPY FOLLOWING SCIATIC NERVE NEUROTMESIS IN RABBIT MODEL

By

HAMEED ALI AL-TIMMEMI

October 2011

Chairman: Assoc. Prof. Rashid Bin Ibrahim, Ph D

Faculty : Veterinary Medicine

In Europe and U.S.A. approximately 300,000 peripheral nerve injuries occur each year. Common causes of peripheral nerve injuries are direct mechanical trauma (transection, crush injury, traction, or avulsion), compression, thermal injury, and neurotoxins. Management of peripheral nerve injury (PNI) requires an understanding of the Anatomy, Pathology, Pathophysiology and surgical principles. However, the rate of success of functional recovery from PNI is far from satisfactory in spite of advances in microsurgery. The poor functional recovery has been attributed to factors intrinsic to the motor or sensory cell body and to elements at the site of injury including nerve gaps, scar tissue formation

and inadequate time frame required for both supportive growth factors and extracellular matrix molecules to be effective for nerve regeneration. Thus in this study a comprehensive investigation was directed toward developing procedures to improve nerve regeneration focusing on biological approaches to promote nerve healing through: i) the role of omental pedicle in nerve regeneration and functional recovery. ii) Isolation and identification of the mesenchymal stem cells from bone marrow, which currently is the target of studies on tissue and organ regeneration in view of their plasticity for nerve regeneration and functional recovery.

This study was conducted with the hypothesis that omental pedicle transposition (OMPT) and bone marrow stromal cells (BMSCs) implantation promote sciatic nerve regeneration and functional recovery. Hence the objective of the study was to investigate the effects of omental pedicle transposition and bone marrow mesenchymal stem cells implantation on the sciatic nerve following neurotmesis in a rabbit model. Towards this end, the investigation compares the efficacy of omental pedicle transpositioning and mesenchymal stem cells implantation on transected sciatic nerve. Evaluation of nerve regeneration brought about by each treatment was based on clinical, neurohistological, ultrastructural, histomorphometric examinations evaluation and relative gastrocnemius muscle weight gain.

Sixty healthy rabbits were used in the study. The animals were divided into three equal groups (n=20) and subjected to coaptation of transected sciatic nerve with epineural sutures (ENS) which served as control and omental pedicle transposition (OMPT) and bone marrow stromal cells (BMSCs) implantation comprising the treated groups. Evaluation on the regeneration and functional recovery of the transected sciatic nerve based on the above approaches were performed on days 14, 28, 56 and 112 post operations (PO).

Clinical and gross pathological examinations showed complete healing of the skin incision of the operated limb with evidences of mild adhesion between the coaptated sciatic nerve and the surrounding tissues in the BMSCs implanted group while there was no evidence of adhesion in the OMPT group. Clinical motor signs of the operated limb and walking in the OMPT and BMSCs implanted groups showed earlier recovery compared to the control group on day 55 PO. Clinical signs were supported by the earlier registration of muscle contractions force in both groups while regain of muscle mass ensued earlier in the OMPT group. Sensory clinical signs indicated the progress of sensation on day 112 PO in both the OMPT and BMSCs implanted groups.

Histopathological findings of the proximal segment of the sciatic nerve in the OMPT and BMSCs implanted groups indicated early regeneration demonstrated by parallel arrangement of nerve fibers, increased angiogenesis, increased concentration of Schwann cells and minimal scar tissue formation on day 28 PO.

Semi-thin sections of the proximal and distal segments of the transected nerve showed normal arrangement and distribution of nerve fibers and normal epineurium development. The dorsal root ganglia and spinal cord contained neurons with Nissl bodies indicating nerve recovery of the OMPT and BMSCs groups. Histopathological findings of the gastrocnemius muscle in the OMPT and BMSCs groups showed progressive regeneration. These histopathological finding of nerve tissue regeneration supported the clinical signs in the operated limb.

Regeneration of nerve fibers was further strengthen by ultrastrutural finding of the sciatic nerve which showed well-developed myelination, activated Schwann cells, well-developed basement membrane and endoneurium which confirmed the histological and pathophysiological regeneration of the transected sciatic nerve in the OMPT and BMSCs groups.

Histomorphometric analysis showed an increase in the number of myelinated nerve fibers, increased diameter of myelinated nerve fiber and increased thickness of myelin sheath and axon diameter in the OMPT and BMSCs groups, indicating sound reinnervation of the transected nerve. However, regenerative changes in the OMPT group occurred slightly earlier compared to the BMSCs group. This could indicate that omental pedicle transposition has a slight advantage over stromal cell implant in terms of transected nerve therapy. Gastrocnemius muscle

mass weight gain progressed to normal in the OMPT and BMSC groups indicated the reinnervation of the gastrocnemius muscle.

The findings of this study provided ample evidences that surgical application of omental pedicle transposition and bone marrow stem cells implantation on injured peripheral nerve could promote early regeneration and functional recovery of the transected nerve. Thus, there is tremendous potential in the application of OMPT and BMSCs implantation in the treatment of peripheral nerve injuries.

Key Words: omental pedicle, mesenchymal stem cells, sciatic nerve regeneration, surgical application, rabbit.

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Foremost, praise to the All Mighty, Allah SWT who led the way and gave me the patience, strength and resilience to undertake and complete this thesis. This thesis is dedicated to my beloved country, Iraq and I am most grateful to Baghdad University for giving me the opportunity to pursue graduate studies in Malaysia where I spent four fruitful years which benefitted me both academically and socially.

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I certify that a Thesis Examination Committee has met on (24th October 2011) to conduct the final examination of (Hameed Ali Kadhim) on his thesis entitled "Surgical, Clinical And Pathological Comparison On The Use Of Omental Pedicle And Bone Marrow Stroma Cells Therapy Following Sciatic Nerve Neurotmesis In Rabbit Model" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P. U. (A) 106] 15 March 1998. The Committee recommends that the student be awarded the doctor of philosophy.

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AD	Anno Domini
ANS	Autonomic nervous system
α	Alpha
µ	Micrometer
ATPase	Adenosin triphosphetase
BDNF	Brain derived neurotrophic factor
bFGF B2	Basic fibroblastic growth factor B2
β	beta
BM	Bone marrow
BMSCs	Bone marrow stromal cells
CFU-F	Colony forming unit-fibroblast
CNS	Central nervous system
CNTF	Ciliary neurotrophic factor
CSF	Cerebral spinal fluid
CXCR4	C-X-C chemokine receptor type 4
δ	Delta
D	day
DRG	Dorsal root ganglia
DMEM	Dublecco modified eagl's medium
ECM	Extra cellular molecule
EC	Embryonic cells
EDTA	Ethylene diamine tetra acetic acid
ENS	Epineurial nerve sutures
ErK1/2	extracellular-signals-regulated kinase1/2
ESCs	Embryonic stem cells
et al.,	*abbr*.*Latin* et alii (and others)
FACS	Fluorescent activated cell sorting
FGF, 1 and 2	Fibroblast growth factor 1 and 2
FGF	Fibroblast growth factor
FXIIIa)	Coagulation factor XIIIa
γ	Gamma
GABA	γ-aminobutyric acid
GAGs	Glycosaminoglycan
GAPs	Growth associated proteins
GFP	Green fluorescent protein

GM-CSF	Granulocyte macrophage-colony stimulating factor
H&E	Hematoxylin and Eosin
HOME	Human omental microvascular endothelial
HSCs	Hematopoietic stem cells
5HT	5-hyroxy tryptamine
IFN-Y	interferon-y
IGF 1and 2	Insulin like growth factor 1 and 2
IL-1	Interleukin-1
IL-2	Interleukin-2
KD	Kilo dalton
LT-HSCs	long-term hematopoietic stem cells
MACS	Magnetic activated cell sorting
MAPCs	Multiple adult progenitor cells
MBP	Myelin basic protein
M	Mean
MESO	Mesothelial
MHC	histocompatibility complex
MPC	Mesenchymal progenitor cells
MSF	Marrow stromal fibroblast
MMTS	Meyer's modified trichrome stain
µm	Micrometer
MPC	Mesenchymal progenitor cells
MSCs	Mesenchymal stem cell
MSF	Marrow stromal fibroblast
MMP	Matrix metalloprotinase
N-CAM	Neural cell adhesion molecule
NGF	Nerve growth factor
NEFM	Neurofilaments medium
NEFL	Neurofilaments light
NEFH	Neurofilaments heavy
NMDA	N-methyl D-aspartate
NMDA	N-Methyl-D-aspartic acid
NT3	Neurotrophin 3
NT4/5	Neurotrophin 4/5
NSC 34	Neural Stem Cell-34
OAF	Omentalangiogenic lipid factor
OMPT	Omental pedicle transposition

%	Percentage
P0	Protein zero
PO	Post operative
PNI	Peripheral nerve injury
PNS	Peripheral nervous system
PMP22	Peripheral myelin protein-22
SC	Schwann cells
SCI	Spinal cord injury
SD	Standard deviation
SDF-1α	Stromal-cell-derived factor-1α
SFI	Sciatic function index
SM22X	Smooth-muscle-specific gene
sq mm^2	Square millimeter
SSCs	Stromal stem cells
ST-HSCs	Short-term hematopoietic stem cells
TIMP-1	Tissue inhibitor of matrix metalloproteinase
T&AO	Thionine and acridine orang stain
TNF-alpha	Transforming neurotropic factor-alpha
TNF-α	tumor necrosis factor- α
tPA	tissue plasminogen activator
Trk B	Tyrosin kinase receptor
UA&LC	Uranyl acetate and lead citrate
VEGF	Vascular endothelial growth factor
WD	Wallerian degeneration
WT-1	Wilms tumor protein

CHAPTER I

GENERAL INTRODUCTION

The nervous system is a giant and integrated communication network. It is commonly subdivided into three major categories: the central nervous system (CNS), the peripheral nervous system (PNS) and the autonomic nervous system (ANS). The CNS is that part of the nervous system consisting of the brain and spinal cord. The PNS is that part of the nervous system consisting of the nerve fibers outside the brain and spinal cord. The ANS, which is subdivided into the sympathetic and parasympathetic nervous system is that part of the nervous system which participate in the regulation of the activity of smooth muscle, cardiac muscle and glands (Kierszenbaum, 2002).

Injuries to the PNS occur frequently and are a major source of disabilities. PNS injuries are classified as being traumatic, non-traumatic or surgical in nature. Traumatic nerve injuries result from collisions, motor vehicle accidents, gunshot wounds, fractures, lacerations or other forms of penetrating trauma (Colohan *et al*., 1996). In 2002, more than 250,000 patients suffered traumatic peripheral nerve injuries in the U.S.A (Evans, 2000). Peripheral nervous system injuries impair the ability to move muscles, which results in painful neuropathies due to loss of normal sensation and cause autonomic dysfunctions in the involved segments of the body and also degeneration of distal segment of transected nerve known as the Wallerian degeneration (Waller, 1850).

Regeneration of peripheral nervous system involved the non-neuronal cells which include Schwann cells, macrophages, fibroblasts, and lymphatic cells. Schwann cells are supporting cells that wrap around the axons. Schwann cells forms a multilamellar sheath of myelin, a phospholipids-containing substance, around an axon that serves as an insulator and increases nerve conduction velocity (Wolman, 1992; Suter *et al*., 1993). An individual Schwann cell may ensheathe several unmyelinated axons, but only one myelinated axon, within its cytoplasm (Dodla, 2007).

Schwann cells of uninjured nerves are quiescent. Following nerve injury, the Schwann cells become active and proliferate. Schwann cells migrate into the injury site and then form cell strand called Schwann cell column or band of Bungner within the basal lamina tubes that provide guidance cues for regenerating nerve fiber (Stoll and Muller, 1999).

Reactive Schwann cells have been shown to offer a highly preferred substrate for axon migration and release of bioactive factors that further enhance nerve regeneration (Ahmed *et al.*, 1999). For instance, Schwann cells produce extra cellular molecule (ECM) such as laminin and collagen, and express many cell adhesion molecules and receptors including L1, N-cadherin, γ1 integrins, and neural cell adhesion molecule (N-CAM). Schwann cells also synthesize and secrete a cocktail of neurotrophic molecules such as nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), and ciliary neurotrophic factor (CNTF) (Nakahara *et al*., 1996). These ECM and neurotrophic factors

are essential for survival of neurons and axonal migration (Krewson *et al.*, 1995, Chen *et al.*, 2000; Dertinger *et al.*, 2002; Geuna *et al.*, 2004).

Nerve regeneration is a complex biological phenomenon and functional recovery following nerve transection still remains unsatisfactory and suboptimal (Hoke, 2006). This phenomenon not only involves axons and tissue or structures surrounded them at the site of injury but extend to involve the neurons which may lead to permanent disability. Primary injury of the peripheral nerve is followed by Wallerian degeneration of the distal stump of the nerve. Retrograde neuronal cell death in the corresponding neurons of the spinal cord (Shi *et al*., 2001; Anders *et al*., 2004), and in the dorsal root ganglia (Hart, 2003) also occurred. Immune mediators (cytokines) secreted at the site of injury as a response to inflammatory reaction played an essential role in degeneration and regeneration of the peripheral nerve (Stoll *et al*., 2002). Despite more than a century of intensive research in microsurgery the outcome of peripheral nerve repair is often poor. Peripheral nerve injury (PNI) thus remains a significant clinical challenge and current gold standard in clinical practice in the field of injured nerve reconstructive and microsurgical suture repair remains the (Lundborg, 2000). The environment of sensory and motor axons supports axonal regeneration, however it is often compromised by intraneural scarring which occurred after microsurgical repair and serves as a mechanical barrier to regenerating axons. Inflammatory cells from the surrounding tissues are likely to contribute to scar formation (Henry *et al*., 2008) while non specific reinnervations of target organs caused by misdirected axonal growth at the repair site and end-organ

atrophy are regarded as reasons for a poor functional recovery (Barbara *et al*., 2001).

Significant advances in neurosurgical techniques of the PNS have been achieved involving end-to-end suturing over small gaps. However, end-to-end suturing is only effective if the nerve ends are directly adjacent to each other and could be connected without considerable tension. Special attentions should be given to the alignment of the fascicles (Lee and Wolfe, 2000), and also to biological factors rather than surgical techniques alone which limit improvements in nerve regeneration. Further advances may come from better understanding of the molecular mechanisms of nerve regeneration, advances in nerve cell culture, development of new biomaterials and grafting techniques (Millesi *et al*., 1972).

The slow and incomplete recovery process of the peripheral nerve injury made investigators resort to new techniques or agents to enhance the speed or completeness of nerve regeneration. All these treatment protocols were directed toward the prevention or minimizing secondary injury of the neurons in the spinal cord or dorsal root ganglia to promote regeneration at the site of injury (Rochkind *et al*., 1987; Wang *et al*., 1997; Hart *et al.*, 2002; Lundborg, 2003).

Transposition of omental pedicle to injured organ has been used to promote healing (Vineberg *et al*., 1966). The omentum have been used in different kinds of therapeutic treatment such as osteomyelitis (Mikami, 1981), skin

graft (Mclean, and Buncke, 1972), tracheal transplantation (Zonuzi *et al.*, 1999) bone repair (Mikami, 1981) and improvement of different kinds of ischemic anastomosis (Topor *et al*., 2001). The omentum has been extensively investigated in the management of spinal cord injury (SCI) in an animal model of spinal cord ischemia with the transposition of the omentum immediately after the ischemic insult (Zhan *et al*., 1989).

Bone marrow stromal cells (BMSCs) are known to play important supportive roles in spinal cord injury therapies. These cells could create a more favorable environment for limiting damage and promoting regeneration via immunoregulation (Aggarwal and Pittenger, 2005; Noel *et al.*, 2007), expression of growth factors and cytokines (Song *et al*., 2004), improved vascularization, providing a permissive growth substrate, and/or suppressing cavity formation (Hofstetter *et al*., 2002).

BMSCs have the ability to synthesize extracellular matrix proteins, e.g., fibronectin and collagen-type-1 (Azizi *et al.*, 1998; Zhao *et al*., 2002). These are molecules which stimulate nerve fiber growth *in vitro* (Carbonetto *et al.*, 1983*)* and exert neuroprotective effects after tissue ischemia *in vivo* (Sakai *et al*., 2001). BMSCs have the ability to promote regeneration and remyelination of damaged nerve axons. Thus, they are promising candidates for clinical applications since bone marrow is more easily accessible than neural or embryonic stem cells and has the advantage of having inherent host compatibility (Mimura *et al.*, 2004).

To date there are no reports on the study of omental pedicle and bone marrow stromal cells in the treatment of transected sciatic nerve. Therefore, the objectives of this study were:

1. To investigate the effects of omental pedicle transposition on neurorraphy of injured sciatic nerve recovery in rabbits.
2. To investigate the effects of bone marrow stromal cells on the recovery of sciatic nerve neurotmesis in rabbits.
3. To compare the efficacies on the use omental pedicle transposition and bone marrow stromal cells on regeneration of transected sciatic nerve in rabbits.

   Regeneration of the transected sciatic nerve is evaluated through:

   a. Clinical and surgical observations.
   b. Neurohistological examination.
   c. Histomorphometric evaluation and relative gastrocnemius muscle weight.

Hypothesis

Omental pedicle transposition and bone marrow stromal cells transplantation at the site of transected peripheral nerves could promote nerve structural regeneration and functional activity.

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