

Role of Mesenchymal Stem Cells in treatment of Knee Osteoarthritis in Elderly Females – Pilot Study

Thesis

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List of Abbreviations

Abbreviation:	Meaning:
ACL	Anterior cruciate ligament
ADL	Activity of the daily living
AMSCs	Adipose tissue -derived mesenchymal Stem cells
BM	Bone marrow
BMI	Body Mass Index
BMSCs	Bone marrow-derived mesenchymal Stem cells
CBC	Complete blood count
COX-2	Cyclooxygenase-2
CRP	C –reactive protein
DEXA	Dual-energy X-ray absorptiometry
ES	Embryonic stem
ESR	Erythrocyte sedimentation rate
GDS15	Geriatric depression scale15
GM-HSPC ..	Gene-modified hematopoietic stem and Progenitor cells
HA	Hyaluronic acid
Hb	Haemoglobin

HBVHepatitis B Virus
HCVHepatitis C Virus
HIVHuman Immunodeficiency Virus
HSCsHematopoietic stem cells
HUCPVCs ...Human umbilical cord perivascular cells
IL-1Interlukin 1
IL-6Interlukin 6
IL-8Interlukin 8
IL-10Interlukin 10
IL-18Interlukin 18
INRInternational normalized ratio
Kg/m2Kilogram / square meter
KOOSKnee Injury and Osteoarthritis Outcome Score
LAT FCLateral femoral condyle
LAT TPLateral tibial plateau
MED FCMedial femoral condyle
MED TPMedial tibial plateau
MMPsMatrix Metalloproteinase
MMP-1Matrix Metalloproteinase -1
MMP-2Matrix Metalloproteinase -2

MMP-8Matrix Metalloproteinase -8
MMP-9Matrix Metalloproteinase -9
MMP-13Matrix Metalloproteinase -13
MMSEMini-mental Status Examination
MRIMagnetic resonance imaging
MSCsMesenchymal stem cells
NSAIDsNon-steroidal anti-inflammatory drugs
OAOsteoarthritis
PBPCsPeripheral blood progenitor cells
PCLPosterior cruciate ligament
PGE-2Prostaglandin E-2
PLTPlatelets
RARheumatoid arthritis
RECFMASU Research Ethical Committee Faculty Of
Medicine Ain Shams University
SCOTSStem Cell Ophthalmology Treatment Study
TAUGTime up and go
TGF- β Tissue growth factor- β
TIMP-1Tissue inhibitors of metalloproteinase-1
TIMP-3Tissue inhibitors of metalloproteinase- 3
TJRTotal joint replacement

TKRTotal knee replacement
TLCTotal leucocytic count
TNF alphaTumor necrosis factor alpha
WHOWorld Health Organization
YLDYears lived with disability

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INTRODUCTION

Osteoarthritis (OA) is one of the most prevalent conditions resulting in disability particularly in elderly population (*Grazio et al., 2009*).

The economic costs of Osteoarthritis (OA) are high, including those related to treatment, individuals and their families who must adapt their lives and homes to the disease, and those due to lost work productivity (*Altman, 2010*).

Knee Osteoarthritis (OA) is considered the leading cause of musculoskeletal disability in the elderly population worldwide (*Zhang et al., 2010*). The incidence of knee Osteoarthritis (OA) increases by age and further increase with longer lifetime and higher average weight of the population (*Bliddal et al., 2009*).

Knee Osteoarthritis (OA) is not a localized disease of cartilage alone but is considered as a chronic disease of the whole joint, including articular cartilage, meniscus, ligament, and peri-articular muscle that may result from multiple patho- physiological mechanisms (*Hayami, 2008*).

The most recent estimates of the World Health Organization (WHO) Global Burden of Disease Study 2010 reported that Osteoarthritis (OA) of the knee is now ranked

as the 11th leading cause of years lived with disability (YLD [prevalence of a condition multiplied by the disability weight associated with that condition]), up from the 15th position in 1990. There was an estimated 64% increase in the global burden of OA-related YLD between the years 1990 and 2010. Globally approximately 250 million people have osteoarthritis (OA) of the knee (3.6% of the population) (**Vos et al., 2012**).

Knee Osteoarthritis (OA) has a particularly significant impact on affecting elderly individual's ability to perform activities of daily living, and combined with the high cost of its management, it poses a major social issue, especially in populations with a long life expectancy (**Buckwalter, 2002**).

Knee Osteoarthritis (OA) is a painful and disabling disease that affects millions of patients (**Hayami, 2008**). Excess mortality is observed in patients with osteoarthritis (OA) and this is related to increasing functional impairment in those patients (**Zhang et al., 2010**).

Conservative treatment measures comprise non-pharmacological options, such as weight reduction, land-based and aquatic exercises, or physical therapy, and pharmacological approaches based on non-steroidal anti-inflammatory drugs, opioid analgesics, intra-articular

corticosteroid or hyaluronic acid injections (*Kon et al., 2012*).

Surgical options for knee osteoarthritis include osteotomies to transfer the weight load from the damaged compartment to undamaged areas and uni compartmental or total joint replacement (*Kurtz et al., 2011*).

Knee Osteoarthritis (OA) is the most common reason for total knee replacement (TKR), usually accounting for more than 90% of knee replacement procedures (TKR). The incidence of total knee replacement (TKR) for knee OA is rising steeply, and should continue to rise dramatically, with a more than 6-fold increase expected by 2030 in the US (*Kurtz et al., 2011*).

However, no conservative or operative treatment procedure for either focal or generalized articular cartilage deterioration promotes restitution. Hyaline cartilage is never obtained and the fibro cartilaginous repair tissues are incapable of withstanding mechanical stresses over time. This shortcoming in patient care urgently necessitates the quest for novel treatment options for articular cartilage defects (*Patrick et al., 2014*).

This consequence is the driving force behind numerous ongoing efforts to develop new tissue engineering-

based strategies for the treatment of OA (*Hardingham et al., 2002*).

Stem cells are the self-renewing progenitors of several body tissues and are classified according to their origin and their ability to differentiate. Current research focuses on the potential uses of stem cells in medicine and how they can provide effective treatment for a range of diseases (*Choumerianow et al., 2008*).

Mesenchymal stem cells (MSCs) have attracted attention for clinical use, because of their multilineage potential, immunosuppressive activities, limited immunogenicity, and relative ease of growth in culture. Furthermore, MSCs are an autologous source of cells, eliminating concerns regarding rejection and disease transmission, and they are less tumorigenic than their embryonic counterparts. Therefore, MSCs have been suggested for use in the cell-based treatment of cartilage lesions (*Raghunath et al., 2005*).

To date, there have been very few clinical studies on MSC transplantation for cartilage repair especially among elderly subjects. However, results from animal experiments on the use of MSCs for the prevention and treatment of experimental osteoarthritis (OA) are encouraging (*Lee et al., 2007*).

AIM OF THE WORK

To evaluate the efficacy of Adult Mesenchymal Stem Cells in treatment of Knee Osteoarthritis among Elderly Females.

Chapter (1):

KNEE OSTEOARTHRITIS AMONG ELDERLY FEMALES

Osteoarthritis (OA) is a type of joint disease that results from breakdown of joint cartilage and underlying bone. Osteoarthritis (OA) is one of the most prevalent conditions that result in disability especially among elderly population (*Grazio et al., 2009*).

OA is considered the most common articular disease of the developed world and a leading cause of chronic disability, particularly because of the knee OA and/or hip OA (*Grazio et al., 2009*).

The economic costs of OA are high, either those related to treatment, or those related to the burden on individuals and their families who must adjust their lives and homes to the disease, and those related to lost work and income (*Altman, 2010*).

Patients with OA are at a higher risk of death in comparison with the general population (*Bliddal et al., 2009*). In addition, Pain and other symptoms of OA may have an obvious effect on the quality of life affecting both physical function and psychological parameters of the population.

Knee OA is considered a chronic disease of the whole joint. It is not a localized disease of the cartilage alone. Knee OA is a painful and disabling disease that affects millions of people (*Hayami, 2008*).

Prevalence of knee osteoarthritis:

OA of the knee is one of the most common reasons for disability (*Kim et al., 2011*). Global statistics reveal over 100 million people worldwide suffer from knee OA, which is one of the most common causes of disability (*Hinman et al., 2010*).

About 13% of women and 10% of men aged 60 years and older have symptomatic knee OA. The proportions of people affected with symptomatic knee OA is likely to increase due to the aging of the population and the rate of obesity or overweight in the general population (*Zhang et al., 2010*).

About 80 % of elderly patients with knee osteoarthritis have some limitation of movement, and 25 % cannot perform major activities of daily living (ADL). Approximately 11% of elderly with knee osteoarthritis need help with personal care (*Ringdahl & Pandit, 2011*).

During a one-year period, 25% of people over 55 years may demonstrate persistent episode of knee pain, in which