



Gender Difference and Therapeutic Effectiveness of Platelets Rich Plasma Intra-Articular Injections Among Elderly with Knee Osteoarthritis

Thesis

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Abstract

Introduction: Osteoarthritis (OA) is the most common form of arthritis. It is among the most prevalent and disabling chronic conditions worldwide. It is predicted to be the single greatest cause of disability in the general population by 2030. The prevalence increases with age, and by the age of 65, approximately 80 percent of the population is affected. Nearly 60% of populations with arthritis are women.

Aim of the Work: This study was conducted in order to assess gender difference response to platelets rich plasma intra articular injections in patients with knee osteoarthritis.

Patients and Methods: One arm clinical trial was conducted to study the efficacy of PRP injections in elderly and to assess gender difference response to PRP intra articular injections in elderly patients with knee osteoarthritis.

In this study about 250 patients attended outpatient clinics and inpatient wards of Ain Shams University Hospital were examined and the diagnosis of bilateral knee osteoarthritis disease was established. Among those patients a sample of 44 patients (22 females and 22 males) fulfilling inclusion and exclusion criteria in our study was randomly selected by simple random sampling to participate in the study.

Results: The study sample comprised 44 elderly participants aged sixty years and above with mild to moderate knee osteoarthritis according to Kellgren-Lawrence Grading Scale: (Kellgren and Lawrence, 1957). The studied sample was divided into two equal matched age groups:

Group A: 22 male patients 60 years old and above with knee osteoarthritis.

Group B: 22 female patients 60 years old and above with knee osteoarthritis

Conclusion: Intra-articular injection of PRP in knee OA may be a valid alternative treatment for knee osteoarthritis.

Recommendations: PRP intraarticular therapy should be considered as an alternative therapy in management of knee OA among the elderly. Radiographic imaging assessment should be included to evaluate OA progression and provide objective data on clinical improvement of cartilage quality.

Keywords: Therapeutic Effectiveness, Platelets Rich Plasma, Intra-Articular Injection , Knee Osteoarthritis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسببائك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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List of Abbreviations

ACD	Anticoagulation citrate dextrose
ACR	American College of rheumatology
ADL	Activities of daily living
AGEs	Advanced glycation end products
AP	Anteroposterior
BA	Bronchial asthma
BMI	Body mass index
BMP	Bone morphogenic protein
Ca	Calcium
CBC	Complete blood count
CLD	Chronic liver disease
COPD	Chronic obstructive pulmonary disease
CTGA	Connective tissue growth factors
DALYs	Disability adjusted life years
DM	Diabetes mellitus
GDS	Geriatrics depression scale
GFs	Growth factors
GI	Gastrointestinal
HA	Hyaluronic acid
HGF	Hepatocyte growth factor
HRQoL	Health related quality of life

List of Abbreviations

HTN	Hypertension
IA-CS	Intraarticular corticosteroids
IGF	Insulin growth factor
IKDC	International knee documentation committee
IL	Interleukin
IL-1Ra	Interleukin-1 receptor antagonist
INR	International normalized ratio
ISHD	Ischemic heart disease
JSN	Joint space narrowing
KOOS	Knee Injury and Osteoarthritis Outcome Scores
MMPs	Matrix metalloproteinases
MMSE	Mini-mental state examination
MRI	Magnetic resonance imaging
MSC	Mesenchymal stem cells
NFkB	Nuclear factor pathway
NHANES	National health and nutrition examination survey
NRS	Numeric rating scale
NSAIDs	Non steroidal anti-inflammatory drugs
OA	Osteoarthritis
PDGFs	Platelets derived growth factors
PRP	Platelets rich plasma
PT	Prothrombin time

List of Abbreviations

PTT	Partial thromboplastin time
RBCs	Red blood cells
RCTs	Randomized clinical trials
REC-FMASU	Research ethics committee; Faculty of medicine Ain Shams University
rhFGF	Recombinant human fibroblast growth factor
ROS	Reactive oxygen species
RPM	Revolutions per minute
SASP	Senescence associated secretory phenotype
TGF	Transforming growth factor
TNF-α	Tumor necrosis factor alpha
TUG	Time up and go test
VAS	Visual analogue scale
VEGF	Vascular endothelial growth factor
WHO	World health organization
WOMAC	Western Ontario and McMaster Universities Arthritis Index
YLDs	Years lived with disabilities

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Introduction

Osteoarthritis (OA) is the most common form of arthritis. It is among the most prevalent and disabling chronic conditions worldwide. It is predicted to be the single greatest cause of disability in the general population by 2030. The prevalence increases with age, and by the age of 65, approximately 80 percent of the population is affected. Nearly 60% of populations with arthritis are women (*Arya and Jain, 2013*).

Knee OA is the most common presentation of OA, with an estimated prevalence between 12% and 35% in the general population and is considered the leading cause of musculoskeletal disability in the elderly population worldwide (*Quintana et al., 2008*).

Globally; approximately 250 million people have osteoarthritis of the knee (3.6% of the population), accounting for 25% of visits to primary care physicians, and half of all NSAID prescriptions. It is estimated that 80% of the population have radiographic evidence of OA by age 65, although only 60% of those will have symptoms (*Vos et al., 2012*).

In individuals older than 55 years, the prevalence of osteoarthritis is higher among women than among men

including osteoarthritis of the knee joints. Women not only are more likely to have OA than men, they also have more severe OA (*Srikanth et al. 2005*).

High prevalence of osteoarthritis entails significant costs to society. Direct costs include clinician visits, medications, and surgical intervention. Indirect costs include such items as time lost from work. Costs associated with osteoarthritis can be particularly significant for elderly persons, who face potential loss of independence and who may need help with daily living activities (*Leung et al., 2013*).

Physical manifestations of knee OA have direct impact on other aspects of patient's lives such as social interactions, mental functioning and sleep quality. Limitations in walking, stair climbing and squatting are common patient complaints that greatly interfere with activities of daily living and recreation (*Far et al., 2013*).

Pain is usually the predominant symptom in patients with symptomatic OA. Pain in OA affects different domains of one's quality of life (QoL): sleep interruption, psychological stress, reduced independence, poorer perceived health and increased healthcare utilization. The likelihood of mobility problems increases as pain increases. Patients experience significant pain may have QoL

compromise even before OA has progressed enough to produce radiographic abnormalities (*Wilkie et al., 2007*).

Osteoarthritis often gradually worsens by time; but staying active, maintaining a healthy weight and other treatments may slow progression of the disease and help to improve pain and joint function (*Miller et al., 2014*).

The goals of osteoarthritis treatment include alleviation of pain and improvement of functional status. Optimally, patients should receive a combination of nonpharmacologic and pharmacologic treatment. Nonpharmacologic interventions, which are the cornerstones of osteoarthritis therapy, include Patient education, Weight loss, Exercise, Physical therapy, Occupational therapy and Unloading in certain joints (eg, knee, hip) (*Zhang et al., 2008*).

There are different methods used for alleviating the symptoms of patients with knee osteoarthritis (OA), including various medications and supplements (NSAIDS, glucosamine, and chondroitin-sulfate), intra-articular injections (glucocorticoids, hyaluronic acid), physical agents (prescription of appropriate braces, shoes and insoles, exercise therapy, laser therapy, application of heat and cold modalities, etc.), and surgical interventions (*Filardo et al., 2011*).

Although some of these treatments have had short- and mid-term effects on improving patients' functions and decreasing the level of disability, there still remain controversial results about their effects on decreasing the amount of articular damage and slowing the rate of disease progression. It seems that existing treatments cannot change the pathophysiology of the disease (*Tate and Crane 2010*).

Modern therapeutical methods stimulating cartilage healing process and improving its damage, include application of matrix metalloproteinase inhibitors, gene therapy, cytokinase inhibitors, stem cells, and growth factors (*Wang-Saegusa et al., 2011*).

The platelet growth factors stimulate the healing process and lead to partial modification of the damaged tissue. Platelet-rich plasma (PRP), with higher platelet concentrations than the mean blood measures, is one of the sources for growth factors (*Smyth et al., 2013*).

The use of platelet-derived growth factors over the last decade has led to a broadening of the fields of use; in particular for new treatments in orthopedics. These include the use of growth factors contained in platelet-rich plasma (PRP), obtained from centrifugation of autologous blood and applied to the site of tissue lesions in order to activate
