The Possible Therapeutic Role of Platelet Rich Plasma on a Model of Osteoarthritis in Albino Rat: A Histological Study

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Histology and Cell Biology

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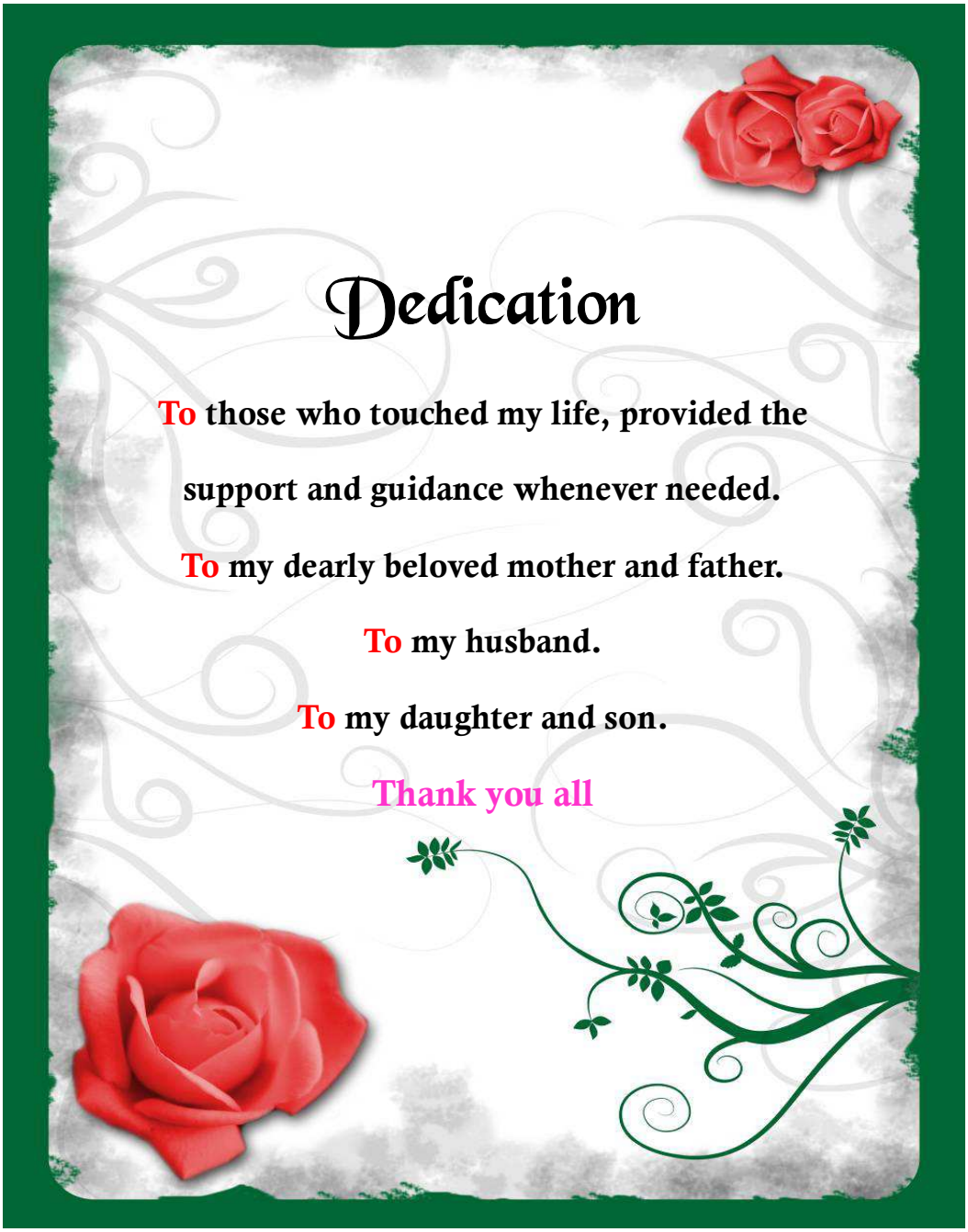

Dedication

To those who touched my life, provided the support and guidance whenever needed.

To my dearly beloved mother and father.

To my husband.

To my daughter and son.

Thank you all

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List of Abbreviations

ANOVA	Analysis of variance
COX	Cyclo-oxygenase
ECM	Extracellular matrix
EDTA	Ethylene diamin tetra-acetic acid
EM	Electron microscope
FGF	Fibroblast growth factor
GAGs	Glycosaminoglycans
H&E	Hematoxylin and Eosin
HA	Hyalorunic acid
IL-1	Interleukin-1
IL-1ra	Interleukin-1 receptor antagonist
Kg	Kilogram
LP-PRP	Leukocyte poor- platelet rich plasma
LR-PRP	Leukocyte rich- platelet rich plasma
LSD	Least significance difference
Ml	Milliliter
MMPs	Matrix metallo-protineases
MSCs	Mesenchymal stem cells
NF-κB	Nuclear factor kappa B
NO	Nitric oxide

NSAIDs	Non steroidal anti-inflammatory drugs
OA	Osteoarthritis
PAP	Platelet average plasma
PBS	Phosphate buffered saline
PDGF	Platelet derived growth factor
PPP	Platelet poor plasma
PRP	Platelet rich plasma
RBCs	Red blood cells
ROM	Reduced range of movement
rpm	Revolution per minute
SPSS	Statistical Package for the Social Sciences
sTNF-R	Soluble tumor necrotic factor receptor
TEM	Transmission electron microscope
TGF-β	Transforming growth factor-β
TNF-α	Tumor necrotic factor-α
VEGF	Vascular endothelial growth factor
WBCs	White blood cells
µm	Micrometer

Abstract

Introduction and aim of the study: Osteoarthritis (OA) is a degenerative joint disease characterized by joint pain and progressive loss of articular cartilage. This study was conducted to evaluate the therapeutic effect of platelet-rich plasma (PRP) of the knee joint in a rat model of OA.

Materials and Methods:

Forty adult male albino rats, weighing 200-250 gms, were used in this study, ten rats used as donors to obtain PRP. The other thirty rats were divided into two main groups. Group I: The control group (15 rats) in which the rats were subdivided into three subgroups. Subgroups IA and IB were sacrificed 4 and 6 weeks after the beginning of the experiment. Subgroup IC was left for 4 weeks then received intra-articular injection of PRP (0.2 ml) in the right knee joint which was repeated three times per week for 2 weeks then the animals were sacrificed. Group II: The experimental group (15 rats) in which OA was induced by surgical induction of cartilaginous defect in the right knee joints. The rats of group II were subdivided into three subgroups. Subgroups IIA and IIB were sacrificed 4 and 6 weeks after induction of OA respectively. Subgroup IIC received intra-articular injection of PRP (0.2 ml) in the right knee joints 4 weeks after surgery. The injections were repeated three times per week for 2 weeks then the animals were sacrificed. The right joints from all groups were collected, decalcified and processed for histological studies. Specimens were also processed for transmission electron microscopic study. The morphometric and statistical measurements were done.

Results: Histological examination of the right knee joints of OA group (subgroups IIA and IIB) resulted in thickening of the intimal lining of the synovial membrane, cellular infiltration, increased collagen content of the subintima and moderate expression of platelet derived growth factor (PDGF) and vascular endothelial growth factor (VEGF). The articular cartilage showed surface erosions, thinning of cartilage, chondrocytes and ground substance loss. Injection of PRP resulted in improvement of the structure of the articular cartilage and the synovial membrane with strong expression of PDGF and VEGF.

Conclusion: Intra-articular injection of PRP resulted in a significant improvement in the histological structure of the knee joint in a rat model of OA.

Keywords: Osteoarthritis, Synovial membrane, Knee joint, Platelet rich plasma

INTRODUCTION

Osteoarthritis is a degenerative joint disease characterized by joint pain and progressive loss of articular cartilage ***(Rosenberg, 2002).*** About 80% to 90% of individuals have evidence of osteoarthritis by the time they reach age 65 ***(Hinton et al., 2002).***

Osteoarthritis mostly affects the weight-bearing joints, like the knee, hips, cervical, lumbar and sacral spines ***(Lozada and Steigelfest, 2010).***

Platelet-rich plasma (PRP) has recently attracted interest in many medical specialties. PRP is defined as a plasma fraction that contain a higher concentration of platelets than the peripheral blood ***(Mc Carrel et al., 2014).*** PRP is composed of three to eight folds greater concentration of platelets, as compared to whole blood, and contains a hyper-physiological content of growth factors ***(Sun et al., 2010).***

The regenerative capacity of PRP is attributed to at least fifteen different factors that are known to be contained within platelets ***(Eppely et al., 2004)***, including platelet-derived growth factor (PDGF), transforming growth factor -β (TGF-β), vascular endothelial growth factor (VEGF), epidermal growth factor, and insulin growth factor (IGF).

Most of these factors have been demonstrated to have an effect on bone and tissue regeneration ***(Mishra et al., 2009)***.

Platelet rich plasma is also used for treatment of alopecia, diabetic foot ulcer, rupture of tendoachillis, atrophic acne scars and dermal degeneration ***(Almasry et al., 2014).***

Also, platelet rich plasma has antimicrobial activity, so used in treating infected wounds to promote healing. PRP has been proved to be safe and effective as hyaluronic acid in improvement of osteoarthritis ***(Labusca and Cionca, 2016).***

There is no risk of cross reactivity, immune reaction or disease transmission in use of PRP because it is autologus ***(Weibrich et al., 2001)***. As compared to the use of single recombinant human growth factor injection, PRP injection releases multiple growth factors and differentiation factors upon platelet activation ***(Sanchez et al., 2003).***

Platelet rich plasma is a safe, easy to prepare and relatively low cost procedure to deliver growth factors for cartilage healing and regeneration ***(Milano et al., 2012)***.

Platelet rich plasma injection for patients with knee osteoarthritis presented beneficial effects in alleviating joint inflammation, cartilage destruction, bone damage and repairing joint tissue. These results suggest that PRP may be

a potential therapeutic agent for knee osteoarthritis by suppressing inflammatory factors ***(Huang et al., 2018).***

Till now there is no known treatment that enables full regeneration of the injured articular cartilage of the patients suffering from osteoarthritis. Hence there is an urgent need for trials to develop more effective strategies for treating the disabling disorders of osteoarthritis.

AIM OF THE WORK

This thesis was conducted to study the possible therapeutic role of platelet rich plasma on a model of osteoarthritis in albino rat knee joint.