Role of Platelet Rich Plasma Therapy on Rotator Cuff Disease

Thesis

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Contents

List of Abbreviations

AC ..... Acromioclavicular
ACD ..... Anticoagulant Citrate Dextrose
ADP ..... Adenosine Di-Phosphate
ARC ..... Angiogenesis-Related Cytokines
ATP ..... Adenosine Tri-Phosphate
C ..... Cervical
CBC ..... Complete Blood Picture
ECM ..... Extracellular Matrix
ELIZA ..... Enzyme-Linked Immunosorbent Assay
ESR ..... Erythrocyte Sedimentation Rate
ESWT ..... Extracorporeal shock wave therapy
FBS ..... Fasting Blood Sugar
FGF ..... Fibroblast Growth Factors
HGF ..... Hepatocyte Growth Factor
IGF-1 ..... Insulin-Like Growth Factor-1
IL ..... Interleukin
IL-1β ..... Interleukin one beta
L ..... Lumbar
L-PRF ..... Leukocyte-Rich Platelet-Rich Fibrin
L-PRP ..... Leukocyte-Rich Platelet Rich Plasma
MHz ..... Mega Hertiz
mm ..... millimeter
mmHg ..... millimeter Mercury
MMP ..... Matrix Metallo-Proteases
MRI ..... Magnetic Resonance Imaging
MSU ..... Diagnostic Musculoskeletal Ultrasound
ng/L ..... Nanogram per Liter
NSAIDs ..... Non-steroidal Anti-Inflammatory Drugs
OB ..... Optical Density
PDGF ..... Platelet Derived Growth Factor
pg/L ..... Picogram per Liter
P-PRF ..... Pure Platelet-Rich Fibrin
P-PRP ..... Pure Platelet Rich Plasma
PRP ..... Platelet Rich Plasma
RCD ..... Rotator Cuff Disease
RCT ..... Rotator Cuff Tendinopathy

List of Abbreviations Con.

RF ..... Rheumatoid Factor
ROM..... Range of Motion
SGOT ..... Serum Glutamic Oxaloacetic Transaminase
SGPT ..... Serum Glutamate Pyruvate Transaminase
SLAP ..... Superior Labrum Anterior–Posterior
T..... Thoracic
TBF- β ..... Transforming Growth Factor-beta
TIMP..... Tissue Inhibitor of Matrix Metalloproteinase
TNF- α..... Tumor Necrosis Factor-alpha
TNF..... Tumor Necrotic Factor
U/S ..... Ultrasound
VAS..... Visual Analogue Scale
VEGF..... Vascular Endothelial Growth Factor
WBC..... White Blood Cell
WORC ..... Western Ontario Rotator Cuff
α ..... Alpha
µm ..... micrometer

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INTRODUCTION

Rotator cuff tendinopathy (RCT) and rotator cuff diseases (RCDs) are leading cause of shoulder pain and a significant source of disability and loss of work ***(Kuijpers et al., 2006, Rha et al., 2013 and Whittle & Buchbinder, 2015)***.

It is a common disorder; approximately 16% of the general population is believed to have RCD at any given time ***(Erstad, 2008)***. Its prevalence increases substantial with age and with occupations involving overhead activities. They are affecting more than 50% of population above 60 years ***(Seitz et al., 2011)***.

In spite of the long standing history and many studies and reviews found in literature concerning RCDs and mechanism of development of tendon tear, the pathophysiology of rotator cuff tendon diseases is still a controversial topic and hasn't been fully understood ***(Rha et al., 2013)***. The biochemical and molecular events leading to RCD and tear have not yet been defined and still a matter of debate ***(Beasley et al., 2000; Dean et al., 2012 and Petterson et al., 2017)***.

Disease course pass through 3 stages begin with acute tendinitis then progress to fibrosis and partial tear, end finally in full thickness tear ***(Kesikburun et al., 2013)***.

Two hypotheses including a combination of extrinsic and intrinsic mechanisms are generally thought to be responsible for the RCD ***(Dean et al., 2012)***, including biomechanical and anatomic dysfunctional causes. Subacromian impingement, tendon degeneration, alternation in tendon mechanical properties, increase tendon overload and overuse especially with overhead activities are contributing factors in disease progression and development of partial and full thickness tears ***(Tytherleigh-Strong et al., 2001, Lewis, 2009 and Seitz et al., 2011)***. Although the multiple factor which contribute to develop of RCDs pathophysiology, but the mechanical and biochemical events lead to cuff degeneration and tear need for further investigations and studies ***(Voloshin et al., 2005)***.

The potential role of inflammatory cytokines, proteases and Angiogenesis-related cytokines (ARC) remain unclear. Recent studies using immune-histochemistry techniques and synovial fluid samples revealed that the hallmark of RCD pathogenesis including proinflammatory, anti-inflammatory_process, an abnormal immune response, angiogenesis and altered variables of vascularity ***(Löhr & Uhthoff, 2007)***. Angiogenesis is a fundamental process and relationship between it and degenerative changes in RCDs is attracting increasing attention ***(Folkman, 1995)***. Vascular endothelial growth factor (VEGF) found to be highly expressed in degenerated tendon. This cytokine thought to play a pivotal role in

process of tendon degeneration and repair ***(Savitskaya et al., 2011)***.

As cytokines signal the normal process of inflammation and repair, they play important role in cell chemotaxis, proliferation, matrix synthesis and remolding. These molecules have the potential to improve RCT healing ***(Petersen, 2005 and Savitskaya et al., 2011)***. IL-1β, TNF, IL-6, IL-10, proinflammatory cytokines and matrix metallo-proteases (MPP) are expressed in subacromial bursa in patients with RCD ***(Voloshin et al., 2005)***.

Accurate and sensitive methods for measuring and detection of cytokines are important for understand cytokine biology and biochemistry for assessment of cytokine involvement in pathophysiology and molecular mechanisms of RCDs ***(Bauer, 2008)***. The combat between proinflammatory, anti-inflammatory and angiogenic factors that end eventually in a failed healing response, which is considered to play a principle part in pathogenesis of chronic tendon diseases ***(Fealy, 2006 and Savitskaya et al., 2011)***.

Management of RCD without full thickness tear is mainly conservative ***(Andrews, 2005)*** with use of physiotherapy, manipulation, NSAID and local steroid injection with high rate or recurrence and persistent pain ***(Mantone et al., 2000 and Chou et al., 2010)***. Lack of

healing response and limited ability of rotator cuff tendon to regenerate is the main cause of the unsatisfactory results of conservative treatment and considered to play a principal part in the pathogenesis of chronic tendon disease ***(Rees et al., 2006)***. Therefor growth factors have been suggestive to be used to influence the healing process and promote tendon regeneration during treatment ***(Rees et al., 2009 and and Wu et al., 2017)***.

Despite a growing body of research that has identified numerous cytokines that can positively affect tendon healing, there are significant limitations to single-factor therapy. Healing is a highly complex biological process with precise coordination. Application of a single exogenous factor does not mimic the highly coordinated spatial and temporal expressions of various factors that are required for cell proliferation, differentiation, matrix synthesis and eventual remolding. This limitation of single factor therapy forms the rationale for the use of Platelet rich plasma (PRP) and related substances to improve healing ***(Kaux & Crielaard, 2013)***. Because the alpha granules and dense granules in platelets contain several cytokines and other bioactive factors, PRP allows delivery of numerous cytokines in "physiological balance" ***(Rodeo et al. 2012)***.

PRP is obtained by blood centrifugation and contains a higher platelet concentration than whole blood ***(Paoloni et al., 2011)***. Also it contain cellular component of plasma that settle after centrifugation as well as growth factors.