

**Evaluation of Pain Relief in Platelet Rich Plasma
(PRP) Intraarticular Injections Versus Occlusal
Splinting for the Treatment of Temporomandibular
Joint Osteoarthritis**

A Randomized Clinical Trial

Thesis submitted to the Oral and Maxillofacial Surgery
Department

In partial fulfillment of the requirements for master degree
Faculty of Oral and Dental Medicine,
Cairo University

By

Rania Ihab Younis

B.D.S

Faculty of Oral and Dental Medicine,

October University for Modern Sciences and Arts (MSA) (2010)

2017

**Evaluation of Pain Relief in Platelet Rich Plasma
(PRP) Intraarticular Injections Versus Occlusal
Splinting for the Treatment of Temporomandibular
Joint Osteoarthritis**

A Randomized Clinical Trial

Thesis submitted to the Oral and Maxillofacial Surgery
Department

In partial fulfillment of the requirements for master degree
Faculty of Oral and Dental Medicine,
Cairo University

By

Rania Ihab Younis

B.D.S

Faculty of Oral and Dental Medicine,

October University for Modern Sciences and Arts (MSA) (2010)

2016

Supervisors

Professor Dr. Mohamed Galal Beheiri

Professor Oral and Maxillofacial Surgery, Faculty
of Oral and Dental Medicine,

Cairo University

A. Professor Dr. Maggie Ahmed Khairy

Associate Professor Oral and Maxillofacial
Surgery, Faculty of Oral and Dental Medicine,

October 6 University

Acknowledgements

I would first like to thank my thesis supervisor **Professor Dr. Mohamed Galal Beheiri** Professor Oral and Maxillofacial Surgery, Faculty of Oral and Dental Medicine, Cairo University, for his continuous support, patience, motivation, enthusiasm, and immense knowledge. His guidance helped me in all the time of research and writing of this thesis.

My deepest gratitude will go to **Associate Professor Dr. Maggie Ahmed Khairy**, Associate Professor Oral and Maxillofacial Surgery, Faculty of Oral and Dental Medicine, October 6 University, for providing me with the tools that I needed to choose the right direction and successfully complete my thesis. Without her passionate participation and input, this thesis could not have been successfully conducted.

Many thanks go to Professor **Dr. Dina Sabry**, Professor Biochemistry, Faculty of Medicine, Cairo University, for her great efforts in the laboratory analysis of this thesis.

Finally, I must express my very profound gratitude to my parents for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Rania Ihab

Contents

I. Introduction.....	1
II. Review of Literature.....	3
III. Aim of the Study.....	28
IV. Patients and Methods.....	29
V. Results.....	42
VI. Discussion.....	58
VII. Summary.....	62
VIII. Conclusions.....	63
IX. Recommendations.....	64
X. References.....	65
XI. Appendix.....	75
XII. Arabic Summary.....	77

List of Abbreviations

Abbreviation	
TMJ	Temporomandibular Joint
TMD	Temporomandibular Disorder
OA	Osteoarthritis
PRP	Platelet Rich Plasma
PPP	Platelet Poor Plasma
RDC	Research Diagnostic Criteria
IL	Interleukin
TNF	Tumor Necrosis Factor
CT	Conventional Tomography
CBCT	Cone Beam Conventional Tomography
MRI	Magnetic Resonance Imaging
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
SS	Stabilization splint
RCT	Randomized Clinical Trial
GFs	Growth factors
TGF β	Transforming Growth Factor Beta
VAS	Visual Analogue Scale
HA	Hyaluronic acid
MIO	Maximal Interincisal Opening
SPSS	Statistical Package for Social Sciences
ELISA	Enzyme Linked Immunosorbent Assay
PCR	Polymerase Chain Reaction
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
$\Delta\Delta Ct$	Critical Threshold

List of Figures

Figure (1) Digital vernier caliper	32
Figure (2) Measurement of the MIO using a digital vernier caliper.....	32
Figure (3) Auricotemporal block using articane 4%.....	35
Figure (4) Blood sample was taken from the antecubital vein.....	35
Figure (5) Blood drawn into glass test tubes containing sodium citrate.....	36
Figure (6) Centrifuge.....	36
Figure (7) 3 layers: a red bottom layer containing red blood cells; a pink middle layer containing PRP and a yellow top layer containing PPP.....	36
Figure (8) Landmarks.....	37
Figure (8') Obtaining the synovial fluid sample.....	37
Figure (9) 14 gauge spinal to enter the superior joint space.....	37
Figure (10) Occlusal Splint with acrylic.....	39
Figure (11) Patient wearing the occlusal Splint,,.....	39
Figure (12) Bar chart representing comparison between mean VAS in the two groups	45
Figure (13) Bar chart representing comparison between mean VAS scores at different time periods in each group	48

Figure (14) Bar chart representing comparison between mean MIO in the two groups.....	49
Figure (15) Bar chart representing comparison between mean MIO at different time periods in each group.....	51
Figure (16) Bar chart representing prevalence of joint sounds in the two groups.....	52
Figure (17) Bar chart representing comparison between mean TGF-β1 gene expressions in the two groups.....	54
Figure (18) Bar chart representing comparison between mean TGF-β1 gene expression before and after treatment in each group.....	55
Figure (19): Bar chart representing comparison between mean TGF-β1 level (pg/ml)s in the two groups.....	56
Figure (20): Bar chart representing comparison between mean TGF-β1 level (pg/ml) before and after treatment in each group.....	57

List of Tables

Table (1)	43
Table (2)	44
Table (3)	47
Table (4)	48
Table (5)	49
Table (6)	50
Table (7)	52
Table (8)	53
Table (9)	53
Table (10)	54
Table (11)	55
Table (12)	56
Table (13)	57

Introduction

Temporomandibular disorder (TMD) is a multifactorial disease that embraces a number of clinical conditions, which involve: the temporomandibular joints (TMJs), masticatory muscles and associated structures (*Winocur et al., 2010*).

Internal derangement (ID) of the temporomandibular joint (TMJ) is one of the most common temporomandibular disorders. In *1983, Dolwick* defined it as an abnormal relation between the temporomandibular disc with respect to the mandibular condyle, the temporal fossa, and the temporal eminence of the TMJ (*Gil-di and Jose, 2011*).

Internal derangement is associated with Temporomandibular joint Osteoarthritis (TMJ OA) because temporomandibular joint Osteoarthritis is the end stage of internal derangement (*Stegenga, 1989 ; De Bont et al., 1995 ; Dimitroulis, 2005*).

Osteoarthritis is a chronic, progressive, and debilitating disease that is defined as the gradual deterioration (degeneration) of the cartilage in a joint. This disorder is associated with damage to the cartilage and surrounding tissues and is characterized by pain, stiffness, and loss of function (*Kiliç et al., 2015*).

A variety of noninvasive means of treatment have been proposed for pain resolution, improvement of symptoms such as joint clicking and limitation of mouth opening, and modification of the course of TMJ OA, with variable success rates (*Hayami, 2008*).

Occlusal appliances have been shown to be beneficial in the treatment of TMJ OA. Several studies were conducted and proved the efficacy of occlusal splint therapy in individuals with severe TMJ OA. Results showed reduction of clinical signs and symptoms by inducing favorable bone remodeling in the anterior division of the condylar head (*BjØrnland et al., 2007 ; Mejersjö and Wenneberg, 2008 ; Kim Yongi et al., 2014*).

Platelet-rich plasma (PRP) injections have been suggested for use in TMJ OA to increase the rate of bone deposition and quality of bone regeneration (*Ohkub et al., 2003*).

Platelet-rich plasma (PRP) is a simple, low cost, and minimally invasive method that allows one to obtain from the blood which is a natural concentrate of autologous Growth Factors (GFs) (*Anitua et al., 2004*).

The present study was designed to compare the effects of PRP injections versus occlusal splints in relieving of pain and dysfunction of TMJ OA in adult patients.

Aim of the study

The aim of this study was to evaluate the pain relief in PRP intraarticular injections versus occlusal splinting for the treatment of TMJ OA.

Review of Literature

The field of TMDs has been receiving growing attention over the past years, with several studies discussing many concerns regarding their diagnosis and treatment (*Ying et al., 2013*).

Temporomandibular joint disorders are characterized by intra-articular positional and/or structural abnormalities which are presented clinically as: decreased mandibular range of motion, distinguished pain in muscles of mastication, generalized myofascial pain, TMJ pain, associated joint clicking with function, and a functional limitation and deviation of the jaw during opening (*Wadhwa, 2008 ; Rando and Waldron, 2012*).

In general, TMDs can be divided into articular (associated with intracapsular conditions) and non-articular disorders (associated with extracapsular conditions) (*Liu and Steinkeler, 2013*). Articular disorders are best classified according to the *Wilkes'* Staging Classification for ID of the TMJ (stages I–V). *Wilkes'* classification was based on clinical, radiologic, and anatomic findings.

Wilkes (1989) classified the 5 stages of TMJ ID as follows:

I. Early stage, clinical presentation featured no pain or decreased range of motion, possible clicking, and when imaged, the disc was anteriorly positioned with normal bony contours.

II. Early/intermediate stage, there are episodes of pain, headache, opening clicks and intermittent locking. Radiographic presentation showed anterior

disc displacement, thickened posterior disc, and normal bony contours. The Anatomic correlation viewed were early disc deformity, anterior displacement, normal bony contours.

III. Intermediate stage, there are many painful episodes, intermittent locking, multiple functional symptoms, decreased range of motion. When imaged, anterior disc displacement is seen with disc deformity. This disc reduces early in stage III, but progresses to non-reducing (locking) on opening in the later stage. The anatomic correlation showed marked disc displacement and deformity with normal bony contours. The disc is subjected to deformity because of the forward and downward push of the condyle.

IV. Intermediate/late stage, the pain is increasing relatively to earlier stages, headache and restricted mandibular range of motion. When imaged, bony changes are markedly noticed such as flattened eminence, condylar deformity and osteosclerotic changes. Anatomically, adhesions of disc, bony changes, evidence of osteoarthritis, osteophytes, and no disc perforations are present.

V. Late stage, episodic or continuous pain, crepitus, limited range of motion at all times, constant functional difficulties are present. Radiograph showed disc perforations, gross deformities of bony structures and cartilage and progressive arthritic changes. Anatomical correlations are gross hard and soft tissue changes, perforations, adhesions and subcortical cysts.

Obviously TMJ OA is the last stage of TMJ ID as stated by *Wilkes*. This is certified by many studies as *De Souza et al. (2012)* who concluded that TMJ OA doesn't occur alone and is a co-morbid disease process associated with other TMD. Therefore, OA is the end result of intra-capsular derangements.

The word Osteoarthritis is derived from the Greek 'osteo', standing for 'the bone', while 'arthro', means 'joint', and 'itis', meaning 'inflammation', which is the classical name of the disease (*Mejersjö and Wenneberg, 2008*).

TMJ OA is a chronic joint disorder that affects the bony articular surfaces of the mandibular condyle and fossa such as flattening of the head of the condyle, and presence of osteophytes (*Tanaka and Koolstra, 2008 ; Jeffrey Oksen, 2013*). This agrees with the findings of *Alexiou et al. (2009) and Cortes et al. (2011)* which proved that this disorder has a complex pathophysiology, with a multitude of risk factors interacting at an individual level.

OA is usually associated with synovitis. It affects all of the tissues of the joint, including low leukocyte counts in the synovium, subchondral bone eburnation, fibrous adhesions of capsule, ligaments inflammation and contraction of periarticular muscles. (*Brandt and Division, 2002 ; Mercuri, 2008*). Obviously, TMJ OA is a dysfunction that affects all articular structure of the joint (*Cevdanes et al., 2014*).

Etiology of TMJ OA was the subject of many studies which proved that the most common causes were: overloading, bruxism, unilateral chewing, genetic susceptibility, and internal derangement. Also, it was proved that deformity of the