THE EFFECT OF OBESITY- INDUCED CHANGES IN THE SERUM LEVEL OF TUMOR NECROSIS FACTOR –ALPHA AND ADIPONECTIN ON THE CLINICAL OUTCOME OF PERIODONTAL TREATMENT

Presented By
AHMED EL SAYED HAMED AMR
B.D.S -Ain Shams University -2003

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SUPERVISORS

Prof. Dr. HALA KAMAL ABD EL GABER
PROFESSOR OF ORAL MEDICINE,
PERIODONTOLOGY AND ORAL DIAGNOSIS
FACULTY OF DENTISTRY, AIN SHAMS UNIVERSITY

Dr. MOHAMED SHERIF EL MOFTY
LECTURER OF ORAL MEDICINE,
PERIODONTOLOGY AND ORAL DIAGNOSIS
FACULTY OF DENTISTRY, AIN SHAMS UNIVERSITY

Dr. MADIHA AHMED OMAR
FELLOW OF CLINICAL PATHOLOGY
AIN SHAMS UNIVERSITY

FACULTY OF DENTISTRY
AIN SHAMS UNIVERSITY
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أحمد السيد حامد عمرو

بكالوريوس طب وجراحة الفم والاسنان٢٠٠٣

كلية طب الاسنان- جامعة عين شمس

معيد بقسم طب الفم وعلاج اللثة

توطئة للحصول علي درجة الماجيستير

تحت اشراف

أ.د / هـــــالة كـــــمال عبـــد الجـابـــــر

أستاذ طب الفم وعلاج اللثة والتشخيص

كلية طب الاسنان – جامعة عين شمس

د/محمـــد شـــريف المفـــتي

مدرس طب الفم وعلاج اللثة والتشخيص

كلية طب الاسنان – جامعة عين شمس

د/مديحة أحـــمد عمـــر

زميل الباثـــولوجيا الاكلينيكية

جامعة عين شمس

كلية طب الاسنان

جامعة عين شمس

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List of Abbreviations

ADIPOR1:	adiponectin receptor 1
ADIPOR2:	adiponectin receptor 2
BIA:	bioelectrical impedance analysis
BMI:	Body Mass Index
CAL:	Clinical Attachment Level
CRP:	C-reactive protein
CT:	Computerized Tomography
ELISA:	Enzyme-Linked Immunosorbent Assay
FGF:	Fibroblast Growth Factor
GCF:	gingival crevicular fluid
HDL:	high-density lipoprotein cholesterol
IGF:	Insulin Growth Factor
IL- 8:	Interleukin -8
IL-1:	Interleukin -1
IL-6:	Interleukin - 6
IL-7:	Interleukin-7
KDa:	Kilo Dalton
Kg:	Kilogram
LPS:	Lipopolysaccharides
LDL:	low-density lipoprotein-cholesterol
m :	meters
MMP:	Matrixmetalloproteinase

MCSF: macrophage colony-stimulating factor

NK cells: Natural Killer Cells

NHANES: National Health and Nutrition Examination Survey

PI: Plaque Index

PD: Probing Depth

PAI-1: plasminogen activator inhibitor-1

PDGF: platelet derived growth factor

RANKL: Receptor Activator for Nuclear Factor K B Ligand

ROS: reactive oxygen species

SBI: Sulcus Bleeding Index

TNF-α: Tumor necrosis factor-α

T-Cad: T-cadherin

TGF-β: Transforming Growth Factor-β

TNF-R1 : TNF receptor type 1

TNF-R2 : TNF receptor type 2

VEGF: Vascular Endothelial Growth factor

WAT: White adipose tissue

WC: Waist Circumference

WHO: World Health Organization

WHR: waist–hip ratio

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INTRODUCTION

Obesity, a common metabolic and nutritional disorder, is a complex multifactorial chronic disease that develops from an interaction of genotype and the environment ***(Dennison et al. 2007).***

Obesity can now be considered the fastest growing health related problem in the world ***(Haenle et al. 2006).*** Although the fundamental mechanisms underlying the increase in obesity is not well understood, it has become clear that genetic and environmental factors and socioeconomic and behavioral influence leading to excess caloric intake, decreased physical activity and metabolic and endocrine abnormalities are likely important factors ***(Robert J Genco et al. 2005).***

Periodontitis is among the most common chronic disorders affecting the world population. It is initiated by gingival colonization by pathogenic bacteria followed by the activation of defense mechanisms ***(Sculley and Langley-Evans 2003).*** It is generally accepted that much of the periodontal tissue destruction observed in periodontitis is host mediated through the release of proinflammatory cytokines by local tissues and immune cells in response to the bacteria and its products, especially lipopolysaccharides LPS ***(Page 1991, Socransky and***

Haffajee 1992). It is possible that many factors are associated with the development of periodontal disease and its progression and aggressiveness. Augmented secretion of proinflammatory cytokines increase the probability of the appearance of lesions in the periodontal tissue ***(Waddington 2000, Genco et al. 2005).***

Obesity has been suggested to associate with periodontal infection in several studies.(***Saito et al. 2001, Genco et al. 2005***). Through its impact on metabolic and immune parameters, obesity may increase the host's susceptibility to periodontal disease. ***(Nishimura and Murayama 2001, Genco et al. 2005).*** Many studies have shown that cytokines produced by adipose tissue could be one mechanism mediating the association between body weight and periodontal infection ***(Saito and Shimazaki 2007).***

Adipose tissue is inflamed in obesity with decreased expression of the anti-inflammatory adipokines (adiponectin) and increased secretion of a variety of proinflammatory cytokines as Tumor Necrosis Factor Alpha (TNF-α) ***(Lehrke and Lazar 2004).***
TNF-α is a major signal for cellular apoptosis; bone resorption, Matrixmetalloproteinases (MMP) secretion and Interleukin-6 (IL-6) production. IL- 6 once produced, stimulate formation of osteoclasts, and promote osteoclastic bone resorption ***(Yamamoto et al. 1997)***

Adiponectin is associated with the modulation of inflammatory responses. It attenuates the inflammatory response mediated by TNF-α and inhibits macrophage phagocytic activity and TNF-α production. Also, it inhibits osteoclasts formation stimulated by LPS from periodontal pathogenic bacteria ***(Yokota et al. 2000, Yamaguchi et al. 2007).***

AIM OF THE STUDY

To investigate the effect of the changes in the serum level of TNF-α and Adiponectin due to obesity on the clinical outcome of periodontal treatment, and finding whether the obese patient respond to periodontal treatment in a similar way to the normal weight patient or not.

REVIEW OF LITERATURE

Periodontitis is a complex infection of bacterial origin in which multiple factors are implicated. It is characterized by an inflammatory host response against microorganisms of the bacterial plaque and their products ***(Genco 1992).*** Periodontitis is among the most common chronic disorders affecting the world population ***(Sculley and Langley-Evans 2003).***

Chronic periodontitis represents a primarily anaerobic gram negative oral infection that leads to gingival inflammation, destruction of periodontal tissues, loss of alveolar bone and exfoliation of teeth in severe cases ***(Socransky and Haffajee 1992, Liljenberg et al. 1994).***

It is generally accepted that certain organisms within the microbial flora of the dental plaque are the major etiologic agents of periodontitis ***(Liljenberg et al. 1994).*** Most of these microorganisms can produce tissue destruction in two ways:

(a) directly, through invasion of the tissues and the production of harmful substances that induce cell death and tissue necrosis; and (b) indirectly, through activation of inflammatory cells that can produce and release mediators that act on effectors, with potent proinflammatory and catabolic activity. This action plays a crucial role in the destruction of periodontal tissue, some bacteria also interfere with the normal host defence mechanism

by deactivating specific antibodies or inhibiting the action of phagocytic cells ***(Williams 1990, Genco1992, Bascones and Gonzalez 2003).***

It is generally accepted that much of the periodontal tissue destruction observed in periodontitis is host mediated ***(Socransky and Haffajee 1992)*** and that endotoxins produced by the microorganisms are instrumental in generating a host mediated tissue destructive immune response ***(Offenbacher 1996).*** The local host response to periodontopathogens and their products includes the proliferation and release of macrophages and cytokines. These immune components are thought to play a crucial role in periodontitis ***(Graves 1999, Furugen et al. 2008).***

Osteoclasts, which differentiate from hematopoietic stem cells, have a crucial role not only in physiological bone remodeling, but they also function in the local bone destruction that occurs in association with chronic inflammatory diseases ***(Scheven et al. 1986, Kahn & Partridge 1991, Mills 1991).*** Most factors known to stimulate osteoclast formation (such as TNF-α, IL-1, IL-6, parathyroid hormone, and prostaglandins) bind to receptors on stromal cells/osteoblastic cells rather than binding to receptors on osteoclast progenitors to induce the release of osteoclast-stimulating factors ***(Boyce et al. 1999).***
Studies demonstrated that two essential factors supplied by stromal cells/osteoblastic cells for the differentiation and