The Effect of Non-Surgical Periodontal Therapy on Salivary Visfatin Concentration in Chronic Periodontitis Patients

Thesis

Submitted to department of Oral Medicine, Periodontology, and Oral Diagnosis
Faculty of Dentistry - Ain Shams University
In partial Fulfillment of the Requirements of Master Degree in Oral Medicine, Periodontology, and Oral Diagnosis

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B.D.S Misr International University, 2009

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2017

Dedication

This thesis is dedicated to my family and fiancée for their endless love, support, and encouragement. They have always been backing me up in my hard times. I am really thankful for having them in my life. Your help is so much appreciated and I hope fulfilling my masters degree, bring you joy and confirm your trust in me.

Acknowledgments

Firstly, I would like to express my sincere gratitude to my advisor ***Prof. Dr Khalid Abd ElGhaffar*** Professor of Oral Medicine, Periodontology and Oral Diagnosis Ain Shams University And Minister of Higher Education & Scientific Researches, for the continuous support of my masters study and related research, for his patience, motivation, and immense knowledge. His guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my master's study.

My sincere thanks also goes to Dr. Ahmed Abd ElAziz lecturer in Oral Medicine and Periodontology department Ain Shams University who provided me with continuous support, motivation, effort, and time. He was always patient with me, and provided me with a lot of knowledge. Without his precious support it would not be possible to conduct this research.

Besides, I would like to thank Prof. Dr. Olfat Shaker head of Biochemistry department Cairo University for her insightful comments and encouragement, and also for helping me assess the results of my thesis biochemically.

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List of Abbreviations

Abb	Meaning
GCF	Gingival Crevicular Fluid
TNF-á	tumor necrosis factor alpha
IL	interleukins
RANKL	Receptor activator of nuclear factor kappa B-Ligand
NMN	nicotinamide mononucleotide
PRPP	phosphoribosylpyrophosphate
UTR	untranslated region
NAmPRTase	Nicotinamide phosphoribosyltransferase
FK-866	Hydrochloride hydrate
THP-1	Tamm Horsfall protein-1
oxLDLs	oxidized low-density lipoproteins
FITC	flourescein iso thio cyanate
IGT	impaired glucose tolerance
NGT	normal glucose tolerance
RA	Rheumatoid arthritis
CRP	C-reactive protein
PBEF1	pre B cell colony enhancing factor
RASFs	rheumatoid arthritis synovial fluid
MR	magnetic resonance
PGE2	prostaglandin E2
MMP- 9	matrix metalloproteinase 9

BMI	body mass index
LTB4	leukotriene B4
ICAM-1	Intracellular adhesion molecule1
VCAM-1	Vascular cell adhesion molecule
MCP-1	monocyte chemotactic protein-1
CA125	Cancer antigen 125
ROS/RNS	Reactive Oxygen Species/Reactive Nitrogen Species
HRP	Horseradish Peroxidase
OD	Optical density
ELISA	Enzyme linked immunosorbent assay
TN	Troponin

Introduction

Chronic periodontitis is a long-term inflammatory disease of the supporting structures of teeth characterized by remission and exacerbation. The expression of the disease results from the interaction of host defense mechanisms, microbial agents, environmental, and genetic factors. The most important periodontal pathogens associated with periodontal disease are Tannerella forsythia, Porphyromonas gingivalis, Treponema denticola, Prevotella intermedia, Fusobacterium nucleatum and Aggregatibacter actinomycetemcomitans ***Miller, et al., 2010***.

Imbalance in host inflammatory defense mechanism results in damage of periodontal structures appearing clinically as loss of connective tissue attachment with underlying connective tissue destruction and disorganization of its constituents, alveolar bone resorption and periodontal ligament demolition resulting in increased probing depth, gingival recession, furcation involvement and tooth mobility in advanced stages. Periodontal pathogens produce harmful by-products and enzymes such as hyaluronidases, collagenases, protease, that break down extracellular matrices, such as collagen in order to produce nutrients for their growth and subsequent tissue invasion. ***Kirkwood, et al., 2007***.

Microorganisms causing periodontal disease are predominantly gram-negative anaerobic or micro-aerophilic bacteria combined together forming a biofilm named dental plaque and are associated with disease initiation and progression. Periodontal disease starts as a microbial challenge between antigens and virulence factors either intrinsic or extrinsic factors inducting a host

response. Host response starts by releasing inflammatory mediators from neutrophils, T cells, macrophages and mast cells. These inflammatory mediators include: tumor necrosis factor, interleukins, matrix metllaoproteinases, and prostaglandins that induce extracellular matrix destruction ***(Kirkwood, etal. 2007).*** Although these mediators are essential for host defense mechanisms against bacterial inflammation, they initiate periodontal tissue destruction and stimulate bone resorption when present in excessive amounts. ***Buduneli, etal., 2011.***

Analysis of cytokine production levels in gingival crevicular fluid has been used as a tool for studying the local host response to a bacterial challenge by which they are used as diagnostic and prognostic markers for periodontal disease ***(Bae, etal. 2011).*** Multiple pro-inflammatory cytokines such as interleukins (IL-1, IL-6, IL-8), tumor necrosis factor alpha (TNF-α); as well as anti-inflammatory cytokines like IL-4 and IL-10, were most commonly studied in the GCF, gingival tissue and serum of the periodontally healthy, gingivitis and chronic periodontitis patients. Increased levels of cytokines may also exaggerate some systemic conditions as atherosclerosis, preterm birth, rheumatoid arthritis, and respiratory disease. ***Buduneli, et al., 2011***.

Clinical and radiographic examinations are the main standard methods for diagnosing periodontal disease, while saliva contains immunoglobulins and biomarkers providing additional information for diagnosing periodontal disease and help in developing new methods for treatment and modification of the disease activity. Saliva contains local and systemic biomarkers that can be collected in a non-invasive way ***Miller, et al., 2010***.

Visfatin is one of the main biomarkers present in saliva. It is a considered a pre-B cell colony-enhancing factor that is secreted from multiple types of cells, such as lymphocytes, trophoblasts, skeletal muscle cells, bone marrow cells, and fetal membranes. It is a biomarker that is present in saliva having several functions ranging from pro-inflammatory functions to pleiotropic facilitation of cytokines, growth factors, and enzymes. It has been proven that serum and plasma Visfatin concentrations increase with multiple inflammatory disorders including periodontal disease, where both Gingival Crevicular Fluid (GCF) and serum Visfatin levels increase remarkably. ***Pradeep, et al., 2012.***