Moxifloxacin as an Adjunctive Antibiotic in The Treatment of Chronic Periodontitis.

Thesis

Submitted in partial fulfillment

For the Requirements of Master Degree in

Oral Medicine, Oral Diagnosis and Periodontology

By

Huda Hamed Basheer Mohamed

BDS (Garyounis university, Libya)

Oral Medicine and Periodontology Department

Faculty of Oral and Dental Medicine

Cairo University

(2012)

SUPERVISORS

Prof. Dr. Mohamed Sherien Hasan

Vise Dean of Environment Affairs
and
Professor of Periodontology
Faculty of Oral and Dental Medicine
Cairo University

Prof. Dr. Olfat Gamil Shaker

Professor of Medical Biochemistry and Molecular Biology
Faculty of Medicine
Cairo University

Dr. Eman Yossef El-Firt

Lecturer of Oral Medicene, Oral Diagnosis and periodontology
Faculty of Oral and Dental Medicine
Cairo Universit

Acknowledgement

My most grateful and deep sincere appreciation are due to ***Prof. Dr. Mohamed Sherien Hasan,*** Professor of Periodontology, Faculty of Oral and Dental Medicine, Cairo University, who gave me the opportunity to do this research & generously gave me of his expertise & time.

I would like to extend my greatest thanks and gratitude to my co-supervisor **Dr. Eman Yossef El Firt,** Lecturer of Oral Medicene, Oral Diagnosis and Periodontology, Cairo University, for her invaluable guidance, encouragement & support.

Also I would like to express my deepest appreciation to ***Prof Dr. Olfat Shaker***, Professor of Medical Biochemistry and Molecular Biology, Faculty of Medicine, Cairo University, which made the lab work easy but meticulous.

Also I would like to extend my thanks to ***Dr. Khaled Kira,*** for conducting the statistical analysis of this project.

Dedication

To whom I did not found the words to thank

My husband

&

My parents

To my children
Who I didn't fulfill their rights because of my work and my study

To my brothers and my sister
For their endless assistance, Guidance and support.

To my friends and all those who helped me and gave me the support to complete this thesis

Last but not least; thanks must also be extended to my special volunteer patients.

Table of Content

Pages

LIST OF ABBREVIATIONS

Aa	Aggregatibacter actinomycetemcomitans
AMX	Amoxicillin
BDE	Bacteremia following dental extraction
BOP	Bleeding on probing
CAL	Clinical attachment level
CFB	Cytophaga Flavobacteria-Bacteroides
CSF	Cerebral Spinal Fluid
DOX	Doxycyclin
ELISA	Enzyme-linked immunosorbent assay
FDA	Food drug administration
FimA	Fimbrillin
FQs	Fluoroquinolone
H_2O_2	Hydrogin peroxide
Ig	Immunoglobulin
IL	Interleukin
INR	International Normalized Ratio
Kgp	K-gingipain
LPS	Lipopolysaccharides
MAP	Mitogen-Activated Protein
MET	Metronidazol
MICs	Minimum inhibitory concentrations
MMP	Matrix metalloproteinases

MXF	Moxifloxacin
NDA	New drug application
NSAIDs	Non-steroidal anti-inflammatory drug
PASW	Predictive Analytics Soft Ware
PBS	Phosphate-buffered saline
PCR	Polymerase Chain Reaction
P.g	Porphyromonas gingivalis
PGE2	Prostaglandin - E2
P.i	Prevotella intermedia
PMNS	Polymorph nuclear leukocyte
PPD	Probing Pocket depth
PRP	Proline-rich protein
PVP-iodine	Povidone-iodine
RA	Rheumatoid Arthritis
Rgp	R-gingipaine
SD	Standard Deviation
SRP	Scaling root planing
T. denticola	Treponema denticola
T. forsythia	Tannerella forsythia
TNF	Tumor necrosis factor
U S	United States

LIST OF FIGURES

LIST OF TABLES

Introduction

Chronic periodontitis is a complex disease in which disease expression involves intricate interactions of the biofilm with the host immune-inflammatory response and subsequent alterations in bone and connective tissue homeostasis ***(Tatakis et al., 2005, Taubman et al., 2007).***

According to the 1999 international workshop classification of periodontal disease, the severity of chronic periodontitis can be characterized based on the amount of clinical attachment loss (CAL) into; slight destruction with 1-2mm CAL, moderate destruction with 3-4mm CAL, and sever destruction with more than 5mm CAL ***(Armitage, 1999).***

Bacterial plaque is considered the principle etiological factor in the onset and progression of periodontitis ***(Zambon et al., 1996, Offenbacher et al., 1999).*** *Actinobacillus actinomycetem comitans, Porphyromonas gingivalis, Tannerella forsythia, Prevotella intermedia and micromonas micros* are strong markers of periodontitis in adults and have been linked to disease progression ***(Zambon et al., 1996, Van winkelhoff et al., 2002).***

Porphyromonas gingivalis (P.g) belongs to the genera Porphyromonas from the family Bacteroidaceae. These bacteria are Gram-negative strict anaerobic coco-bacilli ***(Sanz et al., 2004)***. Several lines of evidence support its etiological role as a true periodontal pathogen, more likely associated with chronic periodontitis ***(Socransky et al., 1998)***. Its importance as a periodontal pathogen is also highlighted by

the research efforts aimed at developing a vaccine immunizing against this bacterial species and thus preventing periodontitis ***(Gibson & Genco, 2001, Nakagawa et al., 2001, Rajapakse et al., 2002, Yang et al., 2002)***.

Prevotella intermedia (P.i) a species of gram-negative anaerobic rod- shaped bacteria originally classified within the bacteroides genus, this bacterium is a common commensal in the gingival crevice and often isolated from cases of gingivitis, chronic periodontitis and other purulent lesions in the oral cavity. *P.intermedia* is considered as one of the organisms of the orange complex, it is black pigmented, and their virulence is determined by its capability of adhesion to hard surfaces and soft tissues of the oral cavity.

In a study by ***Dzink et al., (1988),*** in chronic periodontitis patients, *P.gingivalis* and *P.intermedia* were elevated at disease active sites and were associated with disease progression. Also, their elimination by therapy was associated with an improved clinical response according to ***Wennstrom et al., 1987, Slots et al., 1988, Christersson et al., 1991 and Haffajee et al., 1997.***

A combination of mechanical treatment with antibiotic therapy is required for the management of bacteria in recurrent or persistent periodontal disease sites even after the mechanical debridement. Note worthily that recent reports of the European Federation of Periodontology and the American Academy of Periodontology that evaluated the overall contribution of systemic antimicrobials to the treatment of periodontal diseases suggest that patients with chronic periodontitis appear to markedly benefit from the adjunctive use of the antibiotics ***(Herrera et al., 2002, Haffajee et al., 2003).***

A combination of metronidazole and amoxicillin has shown to be an effective antibiotic regimen to combat *P. intermedia* and *P.gingivalis* associated periodontal infection ***(Walker et al., 2002).*** This treatment protocol is still considered as effective as an adjunctive to full-mouth scaling and root planing in patients with moderate to severe chronic periodontitis ***(Cionca et al., 2009).***

Moxifloxacin (MXF) is an oral 8-methoxy-quinolone with broad-spectrum activity against Gram-negative and multi-resistant Gram-positive aerobic and anaerobic bacteria. It is approved for use in the treatment of acute exacerbations of chronic bronchitis, community-acquired pneumonia, acute bacterial sinusitis, and uncomplicated skin infections ***(Keating and Scott, 2004)***. *Moxifloxacin* also showed good in vitro activity against odontogenic pathogens according to ***Milazzo et al., 2002, Sobottka et al., 2002 and Limeres et al., 2005.***

Moxifloxacin appeared to be a promising candidate as an adjunctive systemic antibiotic therapy in periodontal infections with *A.actinomycetemcomitans* ***(Muller et al., 2002).*** More recently, ***Tomas et al., (2007)*** indicated that MXF could represent a possible alternative antimicrobial agent against obligate anaerobes of oral origin, particularly in those patients with allergy, intolerance or lack of response to amoxicillin-clavulinic acid or metronidazole.

REVIEW OF LITERATURE

The most common diseases of the periodontal tissues are inflammatory processes of the gingiva and the attachment apparatus of the tooth including gingivitis and periodontitis. Gingivitis is inflammation of the gingiva that does not result in attachment loss and it is readily reversible by removal of etiologic factors and effective oral hygiene. Periodontitis is inflammation of the gingiva and the adjacent attachment apparatus and is characterized by loss of periodontal attachment and alveolar bone ***(American Academy of Periodontology, 2001).*** Periodontitis is a complex disease in which disease expression involves intricate interactions of the biofilm with the host immunoinflammatory response and subsequent alterations in bone and connective tissue homeostasis ***(Tatakis et al., 2005, Taubman et al., 2007).***

The classification of periodontal diseases has evolved a great deal over the years. In the most recent report of ***the American Academy of Periodontology,*** published in ***(1999***), the various forms of periodontal disease were classified on the basis of cause, severity and site of disease ***(Armitage, 1999).*** Experts now distinguish among generalized and localized chronic periodontitis, generalized and localized aggressive periodontitis, periodontitis associated with systemic diseases, periodontitis associated with endodontic lesions and necrotizing ulcerative periodontitis. Of these, chronic periodontitis is the most frequently encountered in the adult population.