

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

Thesis

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To whom I did not find the words to thank

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To my children

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Table of Content

	Pages
List of Abbreviations.....	5
List of Figures.....	55I
List of Tables.....	V
Introduction	1
Review of literature.....	4
Aim of the study.....	45
Subjects and Methods.....	46
Results.....	58
Discussion.....	85
Conclusion.....	95
Summary.....	96
References.....	99
Arabic summary.....	

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 ₂ O 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

FIGURE		PAGE
(1)	Diagrammatic representation of the chemical composition of the moxifloxacin	38
(2)	Clinical features of patient with severe chronic periodontitis showing plaque and calculus accumulation, associated with redness, swelling, edema of the gingival margin. Increased PPD and gingival recession, is evident. Spontaneous bleeding is present in some areas.	50
(3)	Periapical radiographs for patient with severe chronic periodontitis showing marked bone resorption.	50
(4)	Microbial sampling of the subgingival microflora, sterile endodontic paper point is placed subgingivally to the base of the pocket related to upper left 1 st premolar, after the tooth is dried and supragingival plaque is removed.	52
(5)	Apparatus used for Centrifuge.	57
(6)	Apparatus used for PCR.	57
(7)	Apparatus used for Electrophoresis	57
(8)	Clinical photographs of the chronic periodontitis patient in the moxifloxacin treated group showing periodontal pocket related to the mesial surface of upper right second premolar A , 5mm PPD at the base line. B , reduction of PPD to 4mm after 3 months. C , 6 months after therapy with remaining PPD 3mm.	59
(9)	Clinical photographs of the chronic periodontitis patient in the augmentin/ metronidazole treated group showing periodontal pocket related to the mesial surface of upper right first molar. A , 4mm PPD at the base line. B , reduction of PPD to 3mm after 3 months. C , 6 months after therapy with remaining PPD 2mm.	60
	Clinical photographs of the chronic periodontitis patient in the SRP treated group showing	

(10)	periodontal pocket related to the mesial surface of upper right first molar A , 4mm PPD at the base line. B , reduction of PPD to 3mm after 3 months. C , 6 months after therapy with remaining PPD of 3mm (white arrow pointing to edematous, glazed marginal gingiva with bleeding).	61
(11)	Agarose gel electrophoresis 2% stained with ethidium bromide showing PCR product amplification of P.g at 404 bp.	62
(12)	Agarose gel electrophoresis stained with ethidium bromide showing PCR product amplification of P.i at 575 bp.	63
(13)	Gender distributions in the three groups	65
(14)	Mean age values in the three groups	66
(15)	Mean PPD in the three groups	67
(16)	Changes by time in mean PPD of the three groups	68
(17)	Mean % reduction in PPD of the three groups	69
(18)	Mean CAL in the three groups	70
(19)	Changes by time in mean CAL of the three groups	71
(20)	Mean % reduction in CAL of the three groups	72
(21)	Mean PI in the three groups	73
(22)	Changes by time in mean PI of the three groups	74
(23)	Mean % reduction in PI of the three groups	75
(24)	Mean GI in the three groups	76
(25)	Changes by time in mean GI of the three groups	77
(26)	Mean % reduction in GI of the three groups	78
(27)	Mean log ₁₀ values of P. gingivalis in the three groups	79
(28)	Changes by time in mean log ₁₀ values of P. gingivalis in the three groups	80
(29)	Mean % change in log ₁₀ values of P. gingivalis in the three groups	81
(30)	Mean log ₁₀ values of P. intermedia in the three groups	82
(31)	Changes by time in mean log ₁₀ values of P. intermedia in the three groups	83
(32)	Mean % change in log ₁₀ values of P. intermedia in the three groups	84

LIST OF TABLES

TABLE		PAGE
1	The frequencies, percentages and results of Chi-square test for the comparison between gender distributions in the three groups.	65
2	The mean, standard deviation (SD) values and results of ANOVA test for the comparison between ages in the three groups.	66
3	The mean, standard deviation (SD) values and results of comparison between PPD in the three groups	67
4	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean PPD of each group	68
5	The mean %, standard deviation (SD) values and results of comparison between % reduction in PPD in the three groups	69
6	The mean, standard deviation (SD) values and results of comparison between CAL in the three groups	70
7	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean CAL of each group	71
8	The mean %, standard deviation (SD) values and results of comparison between % reduction in CAL in the three groups.	72
9	The means, standard deviation (SD) values and results of comparison between PI in the three groups	73
10	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean PI of each group	74
11	The mean %, standard deviation (SD) values and	75

	results of comparison between % changes in PI in the three groups	
12	The mean, standard deviation (SD) values and results of comparison between GI in the three groups	76
13	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean GI of each group	77
14	The mean %, standard deviation (SD) values and results of comparison between % reduction in GI in the three groups	78
15	The mean, standard deviation (SD) values and results of comparison between $\log_{10}$ values of P. gingivalis in the three groups	79
16	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean $\log_{10}$ values of P. gingivalis in each group	80
17	The mean %, standard deviation (SD) values and results of comparison between % reduction in $\log_{10}$ values of P. gingivalis in the three groups	81
18	The mean, standard deviation (SD) values and results of comparison between $\log_{10}$ values of P. intermedia in the three groups	82
19	The mean differences, standard deviation (SD) values and results of paired t-test for the changes by time in mean $\log_{10}$ values of P. intermedia in each group	83
20	The mean %, standard deviation (SD) values and results of comparison between % reduction in $\log_{10}$ values of P. intermedia in the three groups	84

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.