LONG CHAIN OMEGA-3 FATTY ACIDS AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL THERAPY: A RANDOMISED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL

A thesis submitted to the University of Adelaide in partial fulfilment of the requirements of the Degree of Doctor of Clinical Dentistry (Periodontology)

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List of Abbreviations

AA	arachidonic acid
ATLs	aspirin-triggered lipoxins
COX-1	cyclo-oxygenase-1
COX-2	cyclo-oxyygenase-2
DFDBA	demineralised freeze-dried bone allograft
DHA	docosahexaenoic acid
DPA	docosapentaenoic acid
ECM	extracellular matrix
EPA	eicosapentaenoic acid
GLA	gamma-linolenic acid
FAMEs	fatty acid methyl esters
ICAM-1	intercellular adhesion molecule-1
IL-1R	human IL-1 receptor type 1
IκB	inhibitory subunit of NFκB
IP-10	interferon-gamma inducible protein-10
JAK-STAT	janus tyrosine kinase-signal transducer and activator of transcription
MAPK	mitogen activated protein kinase
MaR1	maresin 1
MCP-1/CCL2	monocyte chemotactic protein-1
MIP-1α/CCL3	macrophage inflammatory protein-1 alpha
miRNAs	microRNAs
MMPs	matrix metalloproteinases
mPGES-1	microsomal prostaglandin E synthase-1
NF-κB	nuclear factor kappa B
NSAIDS	non-steroidal anti-inflammatory drugs
LAP	localised aggressive periodontitis
LCn3PUFAs	long-chain n-3 polyunsaturated fatty acids
LOX	lipoxygenase
LPS	lipopolysaccaride
LTB_4	leukotriene B_4
OPG	osteoprotegerin
PAMPS	pathogen-associated molecular patterns

PAHs	polycyclic aromatic hydrocarbons
PCBs	polychlorinated biphenyls
PDL	periodontal ligament
PD1	protectin D1
PGG_2	hydroperoxy endoperoxide
$PGF_{2\alpha}$	prostaglandin $F_{2\alpha}$
PGH_2	endoperoxide
PMNLs	polymorphonuclear leukocytes
PPARγ	peroxisome proliferator-activated receptor gamma
RCTs	randomised controlled trials
RvE1	resolvin E1
TGF-β	transforming growth factor-β
Th-2	T-helper 2
TIMPS	tissue inhibitors of metalloproteinases
TLRs	toll-like receptors

Abstract

Background and Aim

Animal studies and early clinical trials suggest a role for long chain omega-3 fatty acids (LCn3PUFAs) in the treatment of periodontal disease due to their anti-inflammatory and pro-resolution actions. The aim of this study was to evaluate the clinical efficacy of fish oil supplementation as an adjunct to non-surgical periodontal therapy in the treatment of advanced chronic periodontitis. Specific objectives were to establish the relative benefit of docosahexaenoic acid (DHA) versus eicosapentaenoic acid (EPA) compared with a placebo.

Materials and Methods

Thirty-four subjects (10 male, 24 female; mean age 50.1) with advanced chronic periodontitis were recruited for this parallel group double-blind placebo-controlled randomised trial. All participants received non-surgical periodontal therapy and were randomly allocated to receive either adjunctive dietary fish oil supplements (equivalent of 2g LCn3PUFA per day) or placebo. Clinical parameters were recorded at baseline, 4, 7, 10 and 13 months. Additionally, erythrocytes were isolated from fasting blood samples to allow assessment of fatty acid biomarkers including EPA, DHA, Omega-3 Index and total LCn3PUFAs. Data for the 4 month follow-up is presented in this initial report.

Results

One participant was lost to follow-up (placebo group), reporting poor compliance with their allocated capsules. Both treatment groups were effective at improving clinical outcomes, demonstrating significant reduction of full-mouth bleeding scores, probing pocket depth reduction and clinical attachment gain. At the 4 month follow-up, no significant difference was seen between groups for the percentage of sites that had ≥2 mm gain of clinical attachment ($P = 0.229$) or reduction in probing pocket depth ($P = 0.264$). The mean number of sites with residual pocket depth ≥5 mm at follow-up were not significantly different for the test group (6.6%) or placebo group (5.3%) ($P = 0.264$). Additionally, there were no statistically significant differences in clinical parameters for subjects that received supplements containing EPA, DHA or placebo.

Conclusion

Within its limitations, the findings of this study do not support an additional benefit of adjunctive LCn3PUFA supplementation for the treatment of advanced chronic periodontitis. Additionally, no correlation was found between clinical periodontal parameters and fatty acid profiles, and there was no significant difference between EPA and DHA subgroups. There is a need for further research to establish the clinical efficacy of LCn3PUFA as a host modulatory therapy for the treatment of periodontitis, particularly larger multi-centre randomised controlled trials.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Acknowledgements

This study was supported by a grant from the Australian Dental Research Foundation. Materials for the study were generously provided by Novasel Australia.

I would like to express my sincere gratitude to Professor Mark Bartold for his invaluable assistance and guidance while conducting this study and throughout the Doctor of Clinical Dentistry candidature. I must also acknowledge Dr Bryon Kardachi for his encouragement and mentorship throughout my period of study.

I would also like to thank Kostas Kapellas and Suzanne Edwards for their expert advice and support with statistical analyses.