Periodontal conditions in relation to low-dose aspirin therapy in ex- and non-smokers

by

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Dedication

This thesis is dedicated to my loving wife Helen, and my children Vicky, Lambros and Margaret whose support, enthusiasm and tolerance enabled me to complete the work.

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Signed Statement

This research report is submitted in partial fulfillment of the requirements of the Degree of Master of Dental Surgery (Periodontics) in the University of Adelaide.

The thesis contains no material which has been accepted for the award of any other degree or diploma in any University and that, to the best of my knowledge and belief, the thesis contains no other material previously published or written by another person, except where due reference is made in the text of the thesis.

I give consent to this copy of my thesis, when deposited in the University Library, being made available for photocopying and loan if accepted for the award of the degree.

Arthur Drouganis.

November 1999

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These people have inspired and encouraged me to ask questions, to learn to reason and think independently. I truly believe I have been educated.

Thank you.

" *Do not be rash to make friends; but, when once they are made, do not drop them*"

DIOGENES (412-332 B.C.)

A Greek philosopher

I can quite honestly say that I have made life time friends.

Glossary of terms

ANS	Aspirin Never Smoked group
AXS	Aspirin eX-Smoker group
COX	Cyclo-oxygenase, an enzyme that produces the prostanoid and thromboxane mediators of inflammation
Cytokines	Polypeptide mediators released by cells involved in inflammation healing and homeostasis
EWS-PAL	The extreme worst site of PAL per subject, then averaged across each group
Extent	The proportion of tooth sites of an individual with PAL exceeding 1mm and often measured at various threshold values
GCF	Gingival Crevicular Fluid
IgG	Immunoglobulin-G
IL-1	Interleukin-1 an inflammatory cytokine involved in inflammation, immunity, tissue breakdown and homeostasis
IL-6	Interleukin-6 an inflammatory cytokine involved in inflammation, immunity, tissue breakdown and homeostasis
Low-dose aspirin	≤300mg per day
LPS	Lipopolysaccharide
Mean PAL	The average PAL of all sites per subject, then averaged across each group
MSS-PAL	The most severe site of PAL per tooth per person then averaged across each group
NANS	No Aspirin Never smoked group
NAXS	No Aspirin eX-Smoker group
NSAIDs	Non-steroidal anti-inflammatory drugs
PAL	Periodontal attachment loss
PGE_2	Prostaglandin-E2. A primary cyclo-oxygenase mediator of inflammation
Prevalence	The proportion of group who have PAL (ie cases)
Severity	The degree of PAL averaged per affected tooth sites
TNF-α	A proinflammatory cytokine with synergistic effects with other cytokines

Summary

In the 1970's, Vane proposed that the anti-inflammatory effects of aspirin and aspirin-like drugs (non-steroidal anti-inflammatory drugs, NSAIDs) were due to inhibition of the enzyme cyclo-oxygenase, which stops the production of prostanoids (prostaglandins and thromboxanes). By the early 1980's, high doses of aspirin and other NSAIDs were shown to significantly reduce gingivitis, periodontal attachment loss and alveolar bone loss in humans. However, long-term use of these agents in periodontal therapy was not advocated, due to their side effects and the inconsistent findings between studies. Often test and control groups were not from the same sample population, results were based on concurrent use of other NSAIDs, dosages and duration varied between groups, and there was no control for smoking effects. Research in the 1990's showed that periodontitis is a multifactorial disease, being dependent on genetic and environmental influences, which modify the host response to the microbial challenge. One of the primary environmental risk factors for periodontitis is cigarette smoking. Ex-smokers lie between non-smokers and current smokers with regard to the severity and extent of periodontal attachment loss and alveolar bone loss; people who quit smoking respond to periodontal therapy similarly to non-smokers.

There is no information in the literature about the periodontal effects of low-dose aspirin on the periodontium in either non-smokers or ex-smokers. The aim of this study was to assess the periodontal status of a self-selected sample of men (aged 50 and above), residing in metropolitan Adelaide, South Australia, with respect to aspirin intake and smoking history. Subjects were targeted by advertisements placed in the local press.

Demographic data were collected from information obtained from a self-administered questionnaire and periodontal health was assessed by a periodontal examination carried out by one operator, blind to each subject's aspirin and smoking history. Measurements of pocket depths and gingival recession were made at six sites of all teeth present and were used to

compute periodontal attachment loss (PAL) for all subjects. Other parameters recorded were plaque and calculus accumulation, gingival and bleeding indices and tooth mobility.

Periodontal assessments were carried out in 392 men, aged 50-85 years. Significant age effects were found on PAL but these were of small magnitude in comparison to the significant influences that aspirin and ex-smoking had on PAL. The subjects were divided amongst four sub-groups:

- aspirin never smoked (ANS),
- aspirin ex-smokers (AXS).
- no aspirin never smoked (NANS)
- no aspirin ex-smokers (NAXS).

The extent and severity of PAL was evaluated against a background of age, ethnicity, socio-economic and dentition status. The study population comprised low, middle and higher educational levels and there were no significant distribution differences between the groups. The study population comprised a much higher group of educated subjects when compared to the general population of Adelaide. Higher educated subjects with good English skills brushed more frequently and had a more recent scale and clean than the lower educated groups. A measure of subjects' economic level was their pension status; pensioners representing low income. Approximately 58.9% of subjects were pensioners; there were no significant differences in mean PAL between pensioners and non-pensioners.

In order to correlate the effects of aspirin and smoking habits on advanced PAL, three measures of PAL were used; mean PAL, the most severe site of PAL (MSS-PAL) and the extreme worst site of PAL (EWS-PAL). Mean PAL was the overall mean PAL of all sites per tooth/per subject/per group. MSS-PAL was the most severe site of PAL of the six sites per tooth/subject. This method associated the effects of aspirin and ex smoking on advanced

PAL by reducing the overwhelming effects of sites with low PAL. EWS-PAL was the extreme worst site of PAL/mouth. The results were as follows:

	Mean PAL mm ± se	MSS-PAL mm ± se	EWS-PAL mm ± se
ANS	2.5 ± 0.01	3.7 ± 0.13	6.2 ± 0.22
AXS	2.8 ± 0.09	4.1 ± 0.11	7.0 ± 0.18
NANS	2.7 ± 0.08	4.0 ± 0.10	6.8 ± 0.17
NAXS	3.1 ± 0.08	4.4 ± 0.10	7.5 ± 0.17

Prevalence was measured using different threshold levels of PAL. Significant positive effects of aspirin for the extent of PAL were found for all threshold levels. At thresholds of ≥2mm PAL, the prevalence of PAL was approximately 94%. At a moderate threshold of 4mm PAL, 28.7% of subjects exhibited PAL ≥4mm with a mean severity score of 4.6 ± 0.03mm (se), indicating that the percentage of subjects with advanced PAL was low particularly at higher thresholds. Controlling for age, ANOVA analysis showed that the prevalence rate of PAL was significantly lower in aspirin takers when compared to non-aspirin takers and these effects were independent of smoking history. In addition, ex-smokers had significantly more PAL compared to non-smokers and this effect was independent of aspirin history. The prevalence of advanced PAL in subjects (using 7mm PAL as a threshold) was found to be 2.6% with a mean PAL of 7.7 ± 0.05mm (se).

Epidemiological studies (including this one) attribute all PAL to the effects of destructive periodontal diseases. No account is given to other causes of PAL such as continuous tooth eruption, alveolar dehiscence, cervical enamel projections, cracked or split roots and retrograde periodontitis. Taking these factors into account, the true prevalence of advanced PAL due to periodontitis within the community must be lower than the estimated rate of 10-15%.

My findings suggest that men aged 50 and above may benefit from taking low-doses of aspirin daily in order to reduce their risk of PAL. With the reduced severity and extent of PAL in ex-smokers taking aspirin, it is tempting to speculate that subjects with periodontitis may benefit significantly by taking low-dose aspirin to reduce their periodontal and cardiovascular risks, irrespective of their smoking history. Further research should aim to establish whether patients with periodontitis would benefit from taking low-dose aspirin as an adjunct to periodontal therapy and whether low-dose aspirin modulates the effects of periodontitis in females and current smokers.