Relationship of root canal treatment to C-reactive protein as an inflammatory marker for cardiovascular disease

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ABSTRACT

INTRODUCTION: Periodontal disease and elevated C-reactive protein (CRP) tests both are positively correlated with cardiovascular disease (CVD) in many studies. Some health practitioners have concerns that root canal treatment may provide a source for inflammation and hence increase the risk for CVD.

AIM: To explore the relationship between CRP as a marker of inflammation and presence and number of root canal treatments in primary care patients.

METHODS: Cross-sectional questionnaire about dental care followed by a blood test for serum CRP in patients from two New Zealand urban family practices.

RESULTS: One hundred and 34 patients participated. The study showed no significant association between CRP and root canal treatment on multivariate analysis controlling for socioeconomic status, age, gender and smoking. The CRP level for those with ≥3 root-treated teeth was 1.68 while the level for those with <3 was 2.36, but the p-value was not statistically significant (p=0.198). Age, missing teeth and smoking were all significantly related to CRP levels so the sample has biological validity.

DISCUSSION: Root canal treatment was not associated with higher CRP levels. The CRP levels were non-significantly lower in those with higher numbers of root-treated teeth. While there are a number of potential biases in this paper, the dataset appears to be biologically valid and consistent with known facts. These findings do not support the hypothesis that root canal treatment is associated with higher levels of inflammation. At this point patients should not consider having their root canal teeth removed.

KEYWORDS: Periodontal diseases; C-reactive protein; inflammation; cardiovascular diseases; gingivitis; root canal treatment

Introduction

The pathogenesis of atherosclerosis is accepted widely to involve inflammation. C-reactive protein is a sensitive inflammatory marker which has been recognised as a moderate predictor of cardiovascular disease (CVD) risk,[1-4] however some studies argue otherwise.[5] The summary risk for CVD in one review ranged from 1.24 (95% CI (1.10–1.51) to 1.34 (95% CI 1.10–1.63).[6] Several studies suggest poor oral health contributes to higher levels of CRP in blood.[1,7,8] However, periodontal disease as a risk factor for cardiovascular disease is only weakly associated.[9–13] Both periodontal disease and cardiovascular disease are common in the population, hence a small improvement in dental hygiene has the potential to cause a large absolute decline in cardiovascular disease.[9,14] The local complementary and

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alternative medicine specialists advocate against root canal treatment, with the notion that such foreign bodies embedded in gums may induce a chronic inflammatory response which in turn may cause atherosclerosis. We wished to explore this hypothesis.

In this study, we looked at whether a dental care procedure such as root canal treatment increases the levels of C-reactive protein as an inflammatory marker associated with cardiovascular disease. We hypothesised that the greater the number of teeth with root canal treatment, the higher the level of C-reactive protein.

Methods

Literature review

We searched the literature using the Medline database under the terms C-reactive protein, Oral Hygiene/ or Dental Care and "Tooth Root"/ or Dentistry/ or Denture Retention/ or Dental Pulp Cavity/ or Patient Care Planning/ or Dental Abutments/ or Denture Design/ or Dental Bonding/ or Denture Repair/ or "Root Canal Filling Materials"/ or root canal treatment/ or endodontic/ or treatment of periapical infection/ or apical periodontitis/ or endodontic failure/ and Cardiovascular disease. We limited this search to articles from 1987 onwards. We also did a specific search for "root canal therapy" and CRP and this revealed no papers.

Study participants

To conduct our study we identified two general practice clinics: one from a high socioeconomic suburb and one from a lower socioeconomic suburb in Auckland, New Zealand. All individuals having visited the clinic(s) in the last year were considered eligible, from whom 495 were selected from clinic 1 and 250 randomly selected from clinic 2. The study was based on a postal self-report questionnaire and a free blood test form sent to all selected individuals. In the questionnaire, respondents were asked about their general health, oral health and health habits. We did not seek information about blood pressure or lipids as these are known risk factors for CVD. The blood test was used to obtain respondents' C-reactive

protein levels rather than others such as erythrocyte sedimentation rate as there is research relating C-reactive protein to CVD. All participants were informed about the process and informed consent was obtained in writing. The laboratory tests were all done by Diagnostic Medlab Limited which uses validated techniques for C-reactive protein.

Exclusion and inclusion criteria

The exclusion criteria were long-term systemic inflammatory disease (e.g. rheumatoid arthritis), total tooth loss and infection either currently or in the last week, including periodontal disease (we used the term 'gum disease' for the patients to explain their condition). We attempted to engage dentists in the project but were unsuccessful and hence decided to do the project through general practitioners (GPs) and their patients.

The inclusion criteria were those with one or more teeth and over the age of 16.

Outcome variables

C-reactive protein levels as measured through a blood test and the number of teeth with root canal treatment as indicated on a self-report questionnaire were used as outcome variables. Those who have had root canal treatment were determined by the question *'Have you had any root canal treatment?'* Secondary to this, participants were asked *'If yes, please state how many of your teeth'*. A series of questions was asked to highlight particular aspects of health. These can be found in full in the appendix in the web version of this paper.

Health conscious behaviour was measured by the number of visits to dentists and to dental hygienists. Body mass index, dose of smoking and drinking were recorded. Conclusions were made on their oral health habits according to the number of fillings, number of permanent missing teeth, and frequency of brushing and flossing. Frequency of gums bleeding, number of teeth with aches/pain, history of gum infection and history of ulcers determined the oral health state.

A blood test was requested, within one week of completing the questionnaire, and one week after

remission from any acute infection. High-Sensitivity C-reactive protein, HS-CRP test was used to measure CRP. The socioeconomic status of the respondents was measured by their quintile score, as retrieved by the data stored on their family practice database. This quintile score is determined by the New Zealand deprivation 2001 census data, which synthesises data across income, employment, communication, transport, qualifications, living space and home ownership (a score of one represents the highest socioeconomic group and five the lowest).

The outcome variable of CRP as obtained from patients' blood tests has a high sensitivity. Commercial high sensitivity CRP tests are equally as efficacious as standard ELISA tests.[15] Based on population studies, low, moderate and high risk of CVD corresponds to CRP levels of <1.0, 1.0–3.0 and >3.0 mg/L.[4] There is more than doubling of risk between the lowest quartile and highest in both women and men.[16–18]

Statistical methods

We used the programme SPSS 14.0 to calculate with binary logistic regression. A 5% level of significance was used for statistical analysis.

This study was approved by the Northern Y Regional Ethics Committee (NTY/06/11/116).

Results

Of the 745 participants who were invited to participate, 644 were eligible. The number of replies totalled 134, providing a response rate of 20.8% (i.e. those who completed both a questionnaire and a blood test). There was no significant

Table 1. CRP levels controlled for using address quintile (socioeconomic measure), age, gender, smoking status and root canal (analysis by logistic regression)

Variables	Significance
Quintile	0.891
Age	0.077
Gender	0.715
Smokes per day	0.006
Root canals	0.747

WHAT GAP THIS FILLS

What we already know: C-reactive protein and periodontal disease are related to cardiovascular disease.

What this study adds: While there is a relationship between missing teeth and age with C-reactive protein there is no relationship with root canal treatment. This suggests that root canal treatment is not of concern in terms of C-reactive protein. This is the only published study on C-reactive protein and root canal treatment.

Table 2. Univariate analysis of the means of CRP for a range of variables

Variable		N	Mean	P-value
Root canals	<3	106	2.358	0.198
	≥3	25	1.684	
Age (years)	≥60	59	2.871	0.015
	<60	74	1.723	
Education	> secondary level	74	1.957	0.244
	≤ secondary level	57	2.635	
Missing teeth	≥1	81	2.651	0.034
	<1	52	1.581	
Flossing per day	≥1	18	1.561	0.185
	<1	115	2.337	
Smoking	No	97	1.941	0.048
	Yes	22	2.595	

association between root canal treatment and C-reactive protein levels when adjusted for age, sex, socioeconomic status and smoking as confounders (Table 1) (*p*=0.747). Table 2 shows the univariate analyses that then were used to adjust for confounders in the logistic regression analysis. Age, missing teeth and smoking were all statistically significant in this analysis. However, the mean CRP level suggests that if you have fewer than three root canal–treated teeth, you are (non-significantly) more likely to have a higher CRP (2.358) (*p*>0.05) than people who have greater than three root-treated teeth (1.684).

Discussion

We found that root canal treatment was not associated with higher levels of C-reactive protein after adjustment for potential confounders such as socioeconomic status, age, sex and smoking. The greater the number of teeth having

undergone root canal treatment, the lower the C-reactive protein levels, although this result was not significant.

We analysed other aspects of our data to confirm biological consistency and found patients older than 60 years of age had a higher mean level of CRP of 2.87 compared to those under 60 years of age at 1.72 ($p<0.015$) The fact that CRP is significantly associated with age, missing teeth and smoking suggests that our data set has biological validity in spite of the low response rate and negates the notion of this contributing to internal bias. Our null results may have been due to type two statistical error, but that means we would be missing an effect less than smoking or age and hence possibly of little impact on cardiovascular disease.

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It is worth noting that although CRP related to root canal treatment was insignificant, this may not be a true reflection of the benefit/harms of root canal treatment. The only way to conclusively prove this would be to conduct a randomised controlled trial (RCT) of root canal treatment versus no root canal treatment with CRP and cardiovascular disease as an outcome. Such a trial would be difficult or impossible to conduct as pain dictates immediate treatment in most cases. The treatment is either root canal or extraction.

Limitations of the study

A major drawback is that a large part of the study design was based on a self-report questionnaire. We had hoped to engage a number of dental practices in this study but this did not eventuate. This would have helped us with the description of the number of roots in each tooth which had been filled. The advantage of using GP records is that we had access to the geo-coding for socioeconomic status of all of our patients. The results

may be biased in terms of quantity of response towards health conscious, higher socioeconomic status participants. However this type of bias will underestimate the relationship between CRP and root canal treatment, hence any significant result found is more likely to be of true significance.

According to Unell, the correlation between subjective findings and clinical evidence is strong.[19] This means, those variables that can be easily detected such as the number of missing teeth, had a strong positive correlation with CRP. An easily detectable symptom such as gingival bleeding, however, had a poor correlation with clinical gingivitis according to Buhlin.[20]

There were also several issues with the study design. Because this was a cross-sectional study, it is difficult to ascertain the causal relationship between root canal treatment and the level of CRP. A prospective trial—either an RCT or a cohort study—would be needed, but such a design would require significant resources.

The low response rate requires some comment. The largest impediment to a high response rate was the obligation for participants to take a blood test for CRP level measurements. The extra time required in doing this together with phobia of needles or blood created a large barrier for participation. In addition to this, the study took place over the end-of-year holiday period, when more participants were likely to be mobile and busy.

As far as we know, there have been no other studies looking into this subject; however one study comparing CRP levels post-dental implants on active end-stage periodontal disease patients found a reduction in CRP post-procedure.[21]

In summary, there is no significant association between root canal treatment and associated CRP levels when adjusted for socioeconomic status and other potential confounders. Flossing did not seem to be associated with lower CRP levels. Using mean CRP levels, those with more root-treated teeth had lower levels of CRP, but this was non-significant. According to our study, there is no basis for removing root-treated teeth in order to reduce chronic inflammatory response and cardiovascular disease risk.

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APPENDIX

ORAL HEALTH Questionnaire

Please complete this questionnaire and return it to Department of General Practice & Primary Health Care, UniversityofAuckland, Private Bag 92019, AMC, Auckland1142. *(Freepost envelope provided). The information in this survey will be used to determine if there is an association between oral health and levels of inflammatory markers in blood and the risk of cardiovascular disease.*

1. Your Name: *(We need your name in order to match it with your blood test)*

3. Date of Birth: *(day/month/year)*

4. Sex: ☐ Male   ☐ Female

5. Weight: (Please give in kg or pounds, *if not sure please guess*)

6. Height: (Please give in metres or feet/inches, *if not sure please guess*)

7. Ethnicity: ☐ NZ European   ☐ NZ Maori   ☐ Cook Island Maori   ☐ Samoan   ☐ Tongan
(Please tick one or more)   ☐ Niuean   ☐ Chinese   ☐ Indian   ☐ Other, Please State

8. Occupation:

9. Highest level of Education: *(eg. Level left highschool at, tertiary education)*

10. Do you see a dentist?
☐ No   ☐ Yes   If yes, please state how many times a year   If less than once a year, please state how often

11. Do you see a dental hygienist?
☐ No   ☐ Yes   If yes, please state how many times a year   If less than once a year, please state how often

12. Has a doctor ever told you that you have Diabetes? (Insulin or non-insulin dependent)
☐ No   ☐ Yes

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13. Has your doctor/dentist ever told you that you have longterm inflammatory disease?

(e.g Crohns, Ulcerative Collitis, Rheumatoid Arthritis, Ankylosing Spondylitis, Gum disease)

☐ No   ☐ Yes   If yes, please state what disease you have

14. Do you currently have any infection in the mouth or elsewhere - or have you had one in the last week?

☐ No   ☐ Yes   If yes, please state what infection you have

(If yes, please wait for 1 week after recovery before getting the blood test. This is because markers of inflammation remain high in the blood for a week after an infection)

15. Has a doctor ever told you that you have a heart or a blood circulation condition?

(eg. Heart attack, Angina Pectoris, Stroke, narrowing of arteries)

☐ No   ☐ Yes   If yes, please state what condition you have

16. Has a doctor ever told you that you have any other serious medical conditions?

☐ No   ☐ Yes   If yes, please state what condition you have

17. Do you drink alcohol?   *Standard drink (roughly) = 1 can of beer, 1 glass of wine, 1 shot of spirits.*

☐ No   ☐ Yes   If yes, please state how many standard drinks in the last 30 days   If less than once in every 30 days, please state how often

18. Do you smoke cigarettes?   *(please tick the most relevant box)*

No	**Quit**	**Yes**
☐ (less than 100 cigarettes in a lifetime)	☐ (Do not smoke now and have not for atleast the last month)	☐ (smoke now and have smoked greater than 100 in a lifetime)
	If yes, how many cigarettes do you have per day	If less than once a day, please state how often

19. Do you have any fillings?

☐ No   ☐ Yes   If yes, please state how many you think you have

20. Are any of your permanent teeth missing?

☐ No   ☐ Yes   If yes, please state how many of your teeth

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21. Have you had any root canal treatment?

☐ No ☐ Yes   If yes, please state how many of your teeth   [＿＿＿]
0   1

22. Do you brush your teeth?

☐ No ☐ Yes   If yes, please state how many times per day [＿＿＿]   If less than once a day,   [＿＿＿]
0   1   please state how often

23. Do you floss your teeth or use any aids to clean between your teeth?
(eg. special toothpicks or brushes)

☐ No ☐ Yes   If yes, please state how many times per day [＿＿＿]   If less than once a day,   [＿＿＿]
0   1   please state how often

24. Do you use mouthwash?

☐ No ☐ Yes   If yes, please state how many times per day [＿＿＿]   If less than once a day,   [＿＿＿]
0   1   please state how often

25. Do your gums bleed with brushing, flossing or cleaning between your teeth?

☐ No ☐ Yes   If yes, please state how many times in the   [＿＿＿]   If less than once in   [＿＿＿]
0   1   last 30 days   every 30 days, please
                                                                         state how often

26. Do your gums bleed without anything touching them?

☐ No ☐ Yes   If yes, please state how many times in the   [＿＿＿]   If less than once in   [＿＿＿]
0   1   last 30 days   every 30 days, please
                                                                         state how often

27. Do you have a history of gum infection?

☐ No ☐ Yes   If yes, please state for how long you have   [＿＿＿]   *(Please give number in days, weeks or*
0   1   had gum infection   *years)*

28. Do you have tooth ache/pain?

☐ No ☐ Yes   If yes, please state how many of your teeth   [＿＿＿]
0   1   cause you pain

29. Do you get ulcers in your mouth?

☐ No ☐ Yes   If yes, please state for how many days of   [＿＿＿]
0   1   the year do you have ulcers

Thank you for taking the time to complete this survey. Please take a blood test at a diagnostic med lab ideally within 1 week of completing this form. This will help us relate the results of this survey with markers of inflammation in blood. We appreciate your participation. Thank you once again.

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