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Should we be giving dietary advice to prevent periodontal disease? The effect of a low-carbohydrate diet in reducing periodontal inflammation

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By **Bev Littlemore**[1] and **Sarah Duerden**[2]

INTRODUCTION

Dietary advice in the dental setting predominantly focuses on the prevention of dental caries with very little thought given to periodontal disease. Indeed, the common risk factor approach proposed by Sheiham and Watt (2000) links diet to dental decay, obesity, cancers and cardiovascular disease – it does not associate diet with periodontal disease.[1] However, periodontal disease is the sixth most prevalent disease affecting approximately 20–50% of the global population.[2] At least one in ten adults worldwide suffer from periodontal disease, making it more prevalent than cardiovascular disease.[3,4,5] Severe periodontitis has a standardised prevalence of 11.2% worldwide[6] and is a significant public health concern.[7] Recent studies have questioned the role of dietary intake in the reduction of periodontal inflammation; it is plausible that future dietary advice may include specific advice to reduce such periodontal inflammation.

Periodontal disease and inflammation

Periodontal diseases are mediated as a result of an inflammatory response to microorganisms within the dental biofilm.[8] The bacteria within dental biofilm release biologically active components, such as lipopolysaccharides, chemotactic peptides, and organic acids.[9] Detection of microbial pathogen-associated molecular patterns (PAMPs) by the host immune pattern recognition receptors (PRRs) induces the immune response and the production of pro-inflammatory cytokines including tumour necrosis factor alpha (TNF-α), interleukin- (IL-) 6, IL-8, IL-12, interferon-γ (IFN-γ) and acute-phase proteins such as C-reactive protein (CRP).[10,11,12,13] Activation of the complement system produces complement peptides, anaphylatoxins C3a, C4a and C5a that attract host immune cells monocytes, lymphocytes and neutrophils.[14]

Not only is complement a central component of the innate immune system, it is an important mediator of the adaptive immune responses.[15] The complement cascade can be activated through three pathways: classical, lectin, and the alternative pathways. Periodontal diseases primarily activate the alternative pathway via bacterial polysaccharides, including aggregated IgA and lipopolysaccharide, through properdin (factor P) to cleave C3. Factors B and D, along with C3b convert C5 into C5a and C5b and the cascade continues until completion.[8,16]

This signals the transition from the innate to the acquired immune response. The presence of pro-inflammatory cytokines results in the recruitment of host immune cells and the infiltration of neutrophils, natural killer (NK) cells, and lymphocytes to recognise antigens on dendritic cells.[17] T-lymphocytes, B-lymphocytes, macrophages and plasma cells predominate, collagenolytic activity increases, blood flow decreases.[8] T-lymphocytes express CD8+ (cytotoxic) and CD4+ (helper T-cell) cells that generate pro-inflammatory cytokines IL-1, IL-4, IL-10, TNF-α, IFN-γ and transforming growth factor β (TGF-β).[11] Additionally, CD4+ lymphocytes produce the cytokine RANK-L, that signals the stimulation of reactive oxygen species (ROS) in osteoclasts.[18,19] The presence of ROS is increasingly implicated in the connective tissue degradation, particularly the alveolar bone.[18,20]

The presentation of antigens to the dendritic cells attracts polymorphonuclear leukocytes (PMNs) to the site; degranulation of PMNs releases proteases and other lytic enzymes, defensins and ROS that help in degrading the pathogens during phagocytosis.[21]

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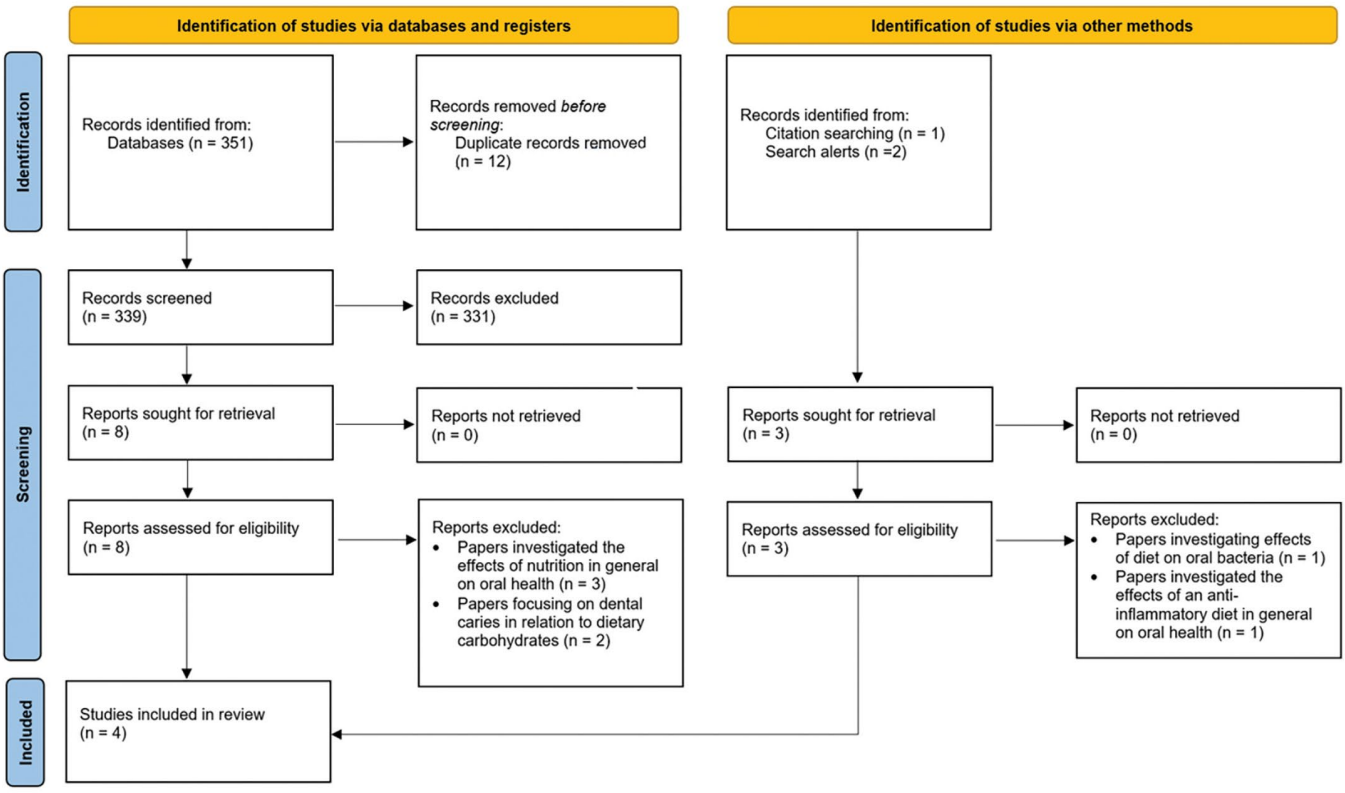

Fig. 1 PRISMA Flow Diagram. From: Page M J, McKenzie J E, Bossuyt P M *et al.* The PRISMA 2020 statement: an updated guideline for reporting systemic reviews. *BMJ* 2021; doi: 10.1136/bmj.n71. For more information visit http://www.prisma-statement.org/

However, whilst this aids in the elimination of the microbial burden, it also has the effect of connective tissue fibres destruction, resulting in an additional local damage.

The excessive inflammatory response (both innate and acquired) mediates the connective tissue damage and alveolar bone loss.[22] Furthermore, the tissue breakdown products provide a nutrient source for the pathogenic bacteria thus inducing an unfortunate self-sustainable feed-forward cycle of escalating dysbiosis and disease progression.[13,23,24] Consequently, although the initial inflammatory response in periodontal inflammation is of microbial origin, the subsequent tissue destruction is predominantly host mediated.[13]

Low-carbohydrate diets

A Western lifestyle, high in carbohydrates with a high ratio of Omega-6 to Omega-3 fatty acids, can promote inflammatory processes.[25] Diets containing glucose-rich refined carbohydrates cause exaggerated postprandial surges in glucose and triglycerides;[26] ROS is generated at a rate that exceeds that of antioxidant defences, resulting in oxidative stress.[27,28] This postprandial dysmetabolism is associated with the initiation of inflammation.[26,28]

The National Diet and Nutrition Survey[29] report a daily average intake of carbohydrates of 198 g for women and 252 g for men, representing approximately 47–48% of food energy intake. The parameters of a low-carbohydrate diet range between 100–150 g of carbohydrates daily and due to claims of weight loss success, have gained substantial popularity in recent years.[30,31] As carbohydrates work directly to raise the blood glucose concentration, a low-carbohydrate diet is often recommended in the management of type 2 diabetes.[32] Similarly, the palaeolithic or 'stone age' diet attempts to emulate the diet of our ancestors and restricts food intake to lean meats, fish, insects, eggs, fruit, berries, vegetables, and nuts while limiting grains and legumes. Notably, dairy products and refined carbohydrates are excluded from the diet.[33] It has been observed that adopting a palaeolithic diet can not only promote weight loss but is also associated with reduced systemic inflammation.[34,35]

Several studies have investigated the role of nutrition in the prevention and management of periodontal inflammation.[36,37] It is known that both micro and macronutrients modulate pro-inflammatory or anti-inflammatory cascades, influencing inflammatory status.[26] Much of this research is focused around micronutrients.[38,39,40,41] It is considered that such inflammatory processes can be resolved with the aid of Omega-3 fatty acids.[42] Additionally, dietary antioxidants are crucial for maintaining redox equilibrium to reduce oxidative stress;[43] several studies have demonstrated a positive impact of antioxidants Vitamin C and D on periodontal inflammation.[44] Few studies have assessed the effects of macronutrients,[44] even fewer investigating the effects of a low-carbohydrate diet on periodontal inflammation.[38]

This review critically evaluates the empirical evidence to establish whether reducing carbohydrate intake can reduce periodontal inflammation in patients with periodontal disease.

METHOD

A systematic review was conducted using PICO methods to align the inclusion and exclusion criteria with the research question to facilitate development of the research strategy. Concepts and synonyms were used to identify key words to be used when searching databases. After searching the Cochrane Register for existing systematics reviews on the research topic, bibliographic databases Medline, Dentistry and Oral Sciences Source, CINAHL Complete and ProQuest were

Table 1 Inclusion and exclusion criteria

PICO	Inclusion	Exclusion
Population	It is expected that papers in this review will include the following: Subjects with gingivitis/gingival inflammation – gingival erythema, oedema, ≥10% gingival bleeding **AND/OR** Periodontitis – pocket probing depths ≥4mm, evidence of clinical attachment loss, bleeding on probing ≥10%	It is expected that papers in this review will exclude the following: Subjects with systemic disease that may affect the periodontium eg diabetes Pregnancy/lactating mothers Subjects with a carbohydrate or insulin related disease eg diabetes Medications that may affect the periodontium (calcium channel blockers, cyclosporine, phenytoin) Medications that might influence bleeding and /or gingival inflammation including non-steroidal anti-inflammatories, anticoagulants and cortisone Subjects who have undergone treatment of periodontitis within the preceding 12 months Smokers or previously smoked within the last 10 years Intake of any other nutrient supplements Subjects regularly exceeding recommended daily limits for alcohol ingestion
Intervention/s	Diet conditions with a main criterion of a maximum processed carbohydrate intake of 25%/130g TDE OR Dietary intake consisting solely of the limited carbohydrate regimes akin to those consumed in the stone age or Palaeolithic time periods.	Papers evaluating the effect of micronutrients on periodontal health Evaluating the effects of nutrients on dental caries Evaluating the effects of low-carbohydrate diet/nutrition of plaque bacteria
Comparator/s	Normal or Western diet high in carbohydrates	Comparators of different population groups or interventions
Outcome/s	Improved periodontal clinical parameters: Reduced gingival inflammation (GI) Reduced bleeding on probing (BoP) Reduced pocket probing depth (PPD) Reduced plaque index (PI) Periodontal inflamed surface area (PISA)	Dental caries only (dmf-t/DMF-t) Serological parameters only Microbiota only

searched. Investigation of the grey literature and citation chaining completed the searches.

Inclusion and exclusion criteria

The inclusion and exclusion criteria were defined using the PICO model[45] to objectively identify those papers relevant to the research question.[46] The exclusion criteria include factors or characteristics that may be confounders for the outcome parameter (Table 1).

SEARCH RESULTS

An initial 354 papers were identified and following de-duplication, 342 abstracts

Table 2 Summary of quality assessment using EPHPP Tool

Reference	Selection Bias	Study Design	Confounders	Blinding	Data Collection Methods	Withdrawals/ Dropouts	Global Rating
Baumgartner *et al.*, 2009[49]	Moderate	Moderate	Moderate	Weak	Strong	Moderate	**Moderate**
Woelber *et al.*, 2016[50]	Moderate	Strong	Strong	Weak	Strong	Strong	**Moderate**
El Makaky *et al.*, 2019[51]	Moderate	Strong	Strong	Moderate	Strong	Moderate	**Strong**
Woelber *et al.*, 2019[52]	Moderate	Strong	Strong	Moderate	Strong	Moderate	**Strong**

were screened for relevance with 331 papers excluded based on inclusion and exclusion criteria. Full text papers were retrieved for 11 studies; a further seven papers were excluded at this stage. A final four papers were included in the review: three RCTs and one case series.

The process by which the papers were identified can be seen in the PRISMA flow diagram (Fig. 1).

Assessment of methodological quality

Identified studies were reviewed, data extracted and critically appraised for their methodological quality using the Effective Public Health Practice Project (EPHPP) Tool.[47] This tool has the advantage of continuity and consistency as it is applicable across a variety of intervention study designs and not specific to any one study design.[48] The overall outcome of the quality assessment for each study is rated as either strong, moderate, or weak; the results are summarised in Table 2. Critical analysis of the methodological quality of the included papers enabled consideration of impact of the quality assessment on the review findings and recommendations.

After assessment of the individual quality components, two of the RCTs[51,52] had a strong global rating, characterised as having no weak ratings in any component. The paper by Baumgartner *et al.* (2009)[49] and the RCT by Woelber *et al.* (2016)[50] were appraised as being of moderate quality due to both being considered weak when assessing the blinding component of the quality assessment.[47] As no papers received a global rating of weak, no paper was excluded on this basis. However, the various limitations observed across the papers will need to be considered when interpreting the results.

Data extraction and study characteristics of included studies

The data extraction form was adapted from the Cochrane Effective Practice and Organisation of Care (EPOC) data extraction tool for randomised and non-randomised trials.[53] Two reviewers extracted and evaluated relevant data to enable a comparison of methodology and outcomes to facilitate the assessment of the effectiveness of the regimes.[54]

A summary of findings, including pertinent characteristics of participants, oral hygiene, and dietary regimes along with the outcomes have been summarised in Tables 3, 4, 5 and 6.

The considerable heterogeneity in terms of interventions, populations and study duration precluded statistical synthesis in the form of meta-analysis, consequently, data extracted from the studies was synthesised to form a narrative in which to determine the range of clinical outcomes reported.[55]

REVIEW FINDINGS

Clinical parameters

The included studies were appropriate to address the aims of this review. There were disparities in terms of participants and study design, particularly between the case series[49] and the three RCTs.[50,51,52] Despite this, in relation to the research question, there were comparable similarities observed in the primary and secondary outcomes measured.

All four papers observed reductions in periodontal inflammation, as measured by reduced gingival inflammation, bleeding on probing and reduced pocket probing depths. The three RCTs observed significant reductions in GI and BoP,[50,51,52] only the case series observed an increase in GI from baseline to the end of the study however, it was of no statistical significance.[49] Similar reductions were observed for bleeding on probing with Baumgartner *et al.* (2009)[49] and Woelber *et al.* (2016)[50] reporting significant reductions. BoP also reduced significantly in the intervention group in the RCT by Woelber *et al.* (2019),[52] however when compared to the control group, the difference was not significant. These results, in conjunction with the increases seen in the control groups are indicative of the effectiveness of the intervention as both gingival index and bleeding on probing are accurate indicators of gingival health.[7] Likewise, probing depth is an important clinical parameter in the assessment of the clinical status of periodontal tissues.[56] The three papers that evaluated the effect of the dietary regime on PPD all observed significant reductions within the intervention groups.[49,50,52]

A relatively new index, PISA is considered beneficial for quantifying periodontal inflammation[57] as it integrates multiple periodontal indices, such as BoP, PPD, and PI into a single numerical index. The two RCTs that carried out this index observed reduced inflammation in the intervention groups compared to the control groups.[50,52] Although the reduction observed in the more recent

Table 3 Study characteristics: general information, population characteristics, interventions and outcomes (Continued on pg 60)

Author/s	Baumgartner S, Imfeld T, Schicht O, Rath C, Persson R E, Persson G R.	Woelber J P, Bremer K K, Vach K, König D, Hellwig E, Ratka-Krüger P, Al-Ahmad A, Tennert C.	El Makaky Y, Beltagy T, El Makakey A.	Woelber J P, Gärtner M, Breuninger L, Anderson A, König D, Hellwig E, Al-Ahmad A, Vach K, Dötsch A, Ratka-Krüger P, Tennert C.
Year of Publication	2009	2016	2019	2019
Study Duration	4 weeks	8 weeks	4 weeks	8 weeks
Country of Study	Switzerland	Germany	Egypt	Germany
Study Design	Longitudinal case series	Pilot Randomised Controlled Trial	Randomised Controlled Trial	Randomised Controlled Trial
Study Aims/Objectives	To assess the oral microbiota and clinical data in subjects without access to traditional oral hygiene methods and who ate a diet available to humans during the Stone Age.	To evaluate an oral health optimized diet low in carbohydrates, and rich in Omega 3-fatty acids, vitamins C and D, antioxidants and rich in fibre.	To assess the effects of an anti-inflammatory diet on gingival health and serological parameters in child participants.	To investigate the influence of an anti-inflammatory diet on clinical, serological and subgingival microbiome parameters.
Ethical approval obtained	Yes, ethical approval obtained from the University of Zurich.	Yes, ethical approval was obtained from the University of Freiburg Ethics committee and the study was registered with the German Clinical Trials Register.	Yes, ethical approval obtained from the Research Ethics Committee, Faculty of Dentistry; Kafrelsheikh University.	Yes, ethical approval was obtained by the University of Freiburg Ethics committee and the study was registered with the German Clinical Trials Register.
Study Quality (EPHPP)	**Moderate**	**Moderate**	**Strong**	**Strong**
No. of Participants Recruited	10	16	40 (Intervention Group n = 20 Control Group n = 20)	38
Withdrawal/Dropouts	None	1 intervention group participant	None	6 withdrawn due to unsuitable dietary regime 2 control group participants dropped out due to medical reasons
No. of participants after withdrawals/ dropouts	**10**	**15** (Intervention Group n = 10 Control Group n = 5)	**40** (Intervention Group n = 20 Control Group n = 20)	**30** (Intervention Group n = 15 Control Group n = 15)
Patient demographics: Gender Ratio Age	5 males: 5 females 7 adults (18-46yrs) 3 children (8-12yrs)	**Intervention Group:** 4 males: 6 females Mean age 34.4 ± 14.1 years, ranging from 23 to 70 years **Control Group:** 2 males: 3 females Mean age 34.0 ± 16.5 years, ranging from 24 to 63 years	**Intervention Group:** 9 boys: 11 girls Mean age 11.90 ± 1.410 years, ranging from 10 to 14 years **Control Group:** 8 boys: 12 girls Mean age 11.75±1.410 years, ranging from 10 to 14 years	**Intervention Group (n = 15):** 6 males: 9 females Mean age 27.2 ±4.7 years **Control Group (n = 15):** 7 males: 8 females Mean age 33.7 ±13.1 years
Follow-up Time	After 4 weeks	Weekly intervals at weeks 5, 6, 7, 8	After 4 weeks	Weekly intervals at weeks 5, 6, 7, 8
Oral Hygiene Regime Intervention Group	None allowed other than the use of twigs and other natural products foraged.	At the start of the first week all participants were instructed to stop all interdental hygiene procedures for the next eight weeks.	Normal toothbrushing but no interdental cleaning	Participants were instructed not to perform any interdental hygiene throughout the study period.
Oral Hygiene Regime Control Group	N/A	At the start of the first week all participants were instructed to stop all interdental hygiene procedures for the next eight weeks.	Normal toothbrushing but no interdental cleaning	Participants were instructed not to perform any interdental hygiene throughout the study period.

Table 3 Study characteristics: general information, population characteristics, interventions and outcomes (Continued from pg 59)

Author/s	Baumgartner S, Imfeld T, Schicht O, Rath C, Persson R E, Persson G R.	Woelber J P, Bremer K K, Vach K, König D, Hellwig E, Ratka-Krüger P, Al-Ahmad A, Tennert C.	El Makaky Y, Beltagy T, El Makakey A.	Woelber J P, Gärtner M, Breuninger L, Anderson A, König D, Hellwig E, Al-Ahmad A, Vach K, Dötsch A, Ratka-Krüger P, Tennert C.
Dietary Regime Control Group	N/A	Continue with usual diet mainly based on carbohydrates	No change in usual dietary habits	The control group was instructed not to profoundly change their diet for the next 6 weeks
Dietary Regime Intervention Group	Restricted Stone Age diet consisting of: basic supply of whole grains of barley, wheat, spelt salt, herbs, honey, milk, meat from domestic animals (goats and hens), berries, edible plants fish	Reduction of the intake of carbohydrates <130 g/d: **See Table 5: Dietary Regime** Dietary recommendations were delivered verbally in an information brochure. This was done after the 2nd baseline measurements were taken. 2 further weeks were given to allow participants to adjust to the new dietary regime. Participants were required to encouraged to follow the new diet for the remaining 4 weeks, completing a daily food diary.	Low-carbohydrates diet <130 g/ day: **See Table 5: Dietary Regime** Plus: almonds and walnuts gluten-free whole grains olive oil and soy-based foods herbs and spices Detailed verbal data about dietary protocol was given to each patient and participant's parents/ caregivers.	At baseline, both groups had to continue their Western diet for 2 weeks. After this, the test group had to change to an anti-inflammatory diet (AID) protocol for 4 weeks after two transitional weeks. Reduction of the intake of starches <130 g/day: **See Table 5: Dietary Regime** Participants received detailed verbal introduction into the AID protocol for 30 min. All participants were instructed to fill out a 24 hr-dietary diary for 1 week at the second, fifth and eighth week
Statistical analysis	Paired t-test to assess changes in the clinical indices PD, BOP, GI, and PI over time. Significance declared at the P <0.001 level.	Mixed linear regression analysis used to test for differences between groups. Multiple testing was corrected using the Scheffe method	Paired t-test to detect general changes within groups. Mean and standard deviation for simple descriptive analysis (age and sex). Student t-test used to assess changes between groups. P-value 0.05 was considered as a level of significance.	Linear regression model used to analyse changes between groups. Linear mixed model used to compare changes between groups over time, Bonferroni used to correct for multiple testing. All analyses regarding the clinical (and serological) data were calculated with STATA 14.2.
Conclusions	Diet restriction, coupled with abstinence from oral hygiene, did not result in increased gingival inflammation; decreases in BOP and PDs were observed.	A low-carbohydrate diet that is rich in Omega-3 fatty acids, vitamins C and D, antioxidants and fibre can significantly reduce periodontal inflammation.	A low-carbohydrate, anti-inflammatory diet was able to significantly gingival inflammation.	The evaluated anti-inflammatory diet was able to significantly reduce gingival inflammation in a clinically relevant range.
Comments	Daily television reports were broadcast about participants experiences.	As a reward for participating in the study, the patients were given an electric toothbrush with a value of about 70 Euro.	N/A	Participants received 100 Euros for participation.

Table 4 Dietary regime restricted carbohydrate diets <130 g

Dietary Regime: Restricted Carbohydrates <130 g	
El Makaky *et al.*, 2019 **Woelber *et al.*, 2016** **Woelber *et al.*, 2019**	**Macronutrients:** Reduction in the amount of processed (fibre free) carbohydrates (disaccharides) such as sweetened beverages and meals, flour containing foods, rice and potatoes Reduction in the amount of omega-6 fatty acids (such as margarine, safflower oil, corn oil, sunflower oil, sesame oil Decrease the amount of industrial animal proteins (such as processed meat products and industrial dairy) as far as possible Reduction in the quantity of trans-fatty acids Daily intake of supplements of omega-3 fatty acids (such as two spoons of flaxseed oil, a portion of the sea fish, etc) Daily intake of vegetables such as tomatoes, broccoli, carrots, spinach, sweet potatoes, beets, cabbage, and beans Daily intake of fruits such as orange, cherries, blueberries, strawberries, cantaloupe, watermelon, avocados, and kiwifruit
	Micronutrients: Daily intake of vitamin C (from fruit/vegetables such as oranges, kiwi, bell peppers) Daily intake of vitamin D Daily intake of nitrates such as beet/spinach Daily intake of fibre (such as legumes, fruit, vegetables, bran) Daily intake of antioxidants (such as green tea, one pinch of Curcuma, coffee without milk, berries, and ginger)

RCT[52] was not deemed statistically significant, the results align with the findings of the other periodontal indices.

Age differences

The participants in one RCT[51] were children between the ages of 10-14-years; there are inherent challenges in assessing periodontal indices in children with a mixed dentition due to the presence of false pocketing as the permanent teeth are only partially erupted,[57] additionally, possibly due to hormonal changes, the prevalence of gingivitis peaks during puberty.[58] It is acknowledged in the case series[49] that such challenges may impact the results however, they observed no trends of differences to suggest any such impact that would differentiate the children from the adult participants within their study.

Oral hygiene regimes and plaque

Interproximal cleaning is important in maintaining interproximal gingival health[7] and the consequence of having no access to oral hygiene aids and being prohibited from carrying out interdental cleaning is reflected by the increase in supragingival plaque scores observed in two of the studies.[49,51] Interestingly, the increases in plaque levels observed were not accompanied by a corresponding increase in the severity of gingival inflammation which would normally be expected.[7] Indeed, it was concluded that even in the presence of persistent plaque levels, an anti-inflammatory diet significantly decreased gingival inflammation.[50]

Dietary regimes

When assessing compliance with dietary regimes, two studies[50,52] assessed dietary habits using self-reported diaries. Using diaries is not without challenges; they rely on subjects to accurately recall and record the relevant data and have questionable validity and reliability.[59]

Determining compliance was not necessary in the simulated Stone-Age case series,[49] although the authors acknowledge that it was difficult to assess precise dietary intake because analysis of carbohydrate consumption and other macro/micronutrients was not possible. However, this simulated palaeolithic environment likely precludes subjects exceeding carbohydrate limits imposed in the other studies included in this review.

Carbohydrates and inflammation

Diets high in refined carbohydrates can cause an exaggerated postprandial surge in glucose and triglycerides.[26] This postprandial hyperglycaemia results in increased production of ROS and release of inflammatory cytokines.[60] It has already been established that dietary antioxidants maintain redox equilibrium, reducing oxidative stress[43] and not only do the dietary requirements in the three RCTs restrict carbohydrates to less than 130 g daily, they also incorporate elements that are anti-inflammatory; as such, the reduced clinical inflammation observed may be related to these components. Both studies by Woelber *et al.* (2016; 2019)[50,52] acknowledge it may be difficult to attribute the improved clinical parameters observed in the intervention group to any one specific component of the diet, although regression analysis did show significant association

Table 5 Results: Primary Outcomes

	Gingival Index					
	Group A Baseline	**Group A End of Study**	**Level of Significance**	**Group B Baseline**	**Group B End of Study**	**Level of Significance**
Baumgartner *et al.*, 2009	N/A	N/A	N/A	0.38	0.43	Not stat. significant
Woelber *et al.*, 2016	1.01 ± 0.14	1.22±0.17	p < 0.001	1.10 ±0.51	0.54±0.30	p < 0.001
El Makaky *et al.*, 2019	1.445 ± 0.4084	1.660 ± 0.3775	p=0.000	1.450 ± 0.4335	1.145 ± 0.4443	p=0.000
Woelber *et al.*, 2019	0.92 ±0.25	0.74 ± 0.18	p < 0.05	1.03 ± 0.21	0.61 ± 0.29	p < 0.05
	Bleeding on Probing (%)					
	Group A Baseline	**Group A End of Study**	**Level of Significance**	**Group B Baseline**	**Group B End of Study**	**Level of Significance**
Baumgartner *et al.*, 2009	N/A	N/A	N/A	34.8%	12.6%	p < 0.001
Woelber *et al.*, 2016	46.46% ±15.61	64.06% ± 11.27	p=0.012	53.57% ±18.65	24.17% ±11.57	p=0.012
El Makaky *et al.*, 2019	N/A	N/A	N/A	N/A	N/A	N/A
Woelber *et al.*, 2019	28.39% ± 13.32	27.09% ± 10.03	p=0.864	30.35% ± 11.07	23.55% ± 13.61	p=0.864

Key: Group A: Control Group; Group B: Intervention Group

between reduced clinical parameters and carbohydrate-reduction in the 2016 trial.[50]

Whilst the case series[49] did not specifically refer to this within their study, the dietary regime the participants were subjected to included berries high in antioxidants.[61] Although honey isn't a refined carbohydrate, it is a pure sugar and as such one might have expected this to be reflected in the results observed, however the reduced periodontal inflammation observed by the authors is possibly due to the anti-inflammatory and anti-bacterial properties of honey.[62] Indeed, the authors concluded it was likely the combination of a restriction of refined carbohydrates and the supplemental intake of antioxidants that reduced the observed periodontal inflammation and that consequently, dietary advice for patients with gingivitis and periodontitis may be very important.

Additional outcomes

One RCT[52] observed significant weight loss in the intervention group likely due to the reduced total energy intake associated with the low-carbohydrate regime. As evidence suggests low calorie intake is associated with improved periodontal health,[63] it is possible this had an adjunctive effect on the reduced inflammation observed in this study. Additionally, they found no significant differences between or within groups in relation to the subgingival microbiome. The significance of this is that the clinical results observed were likely a result of an altered immunological response due the dietary regime and not resulting from an altered microbial composition of the subgingival biofilm. This supports the findings observed in the case series,[49] which despite reporting an increase in subgingival bacterial counts found no pathogenic bacteria associated with periodontitis.

CONCLUSION AND RECOMMENDATIONS

Despite the heterogeneity and variable methodological quality of the studies, all four studies reported similar outcomes in that despite reduced oral hygiene measures, the restricted carbohydrate intake reduced periodontal inflammation.

However, all papers included anti-inflammatory components to the dietary regimes, consequently how much of this decrease in periodontal inflammation can be attributed to the reduction in carbohydrates alone and how much was as a result of additional anti-inflammatory components in the diets is difficult to ascertain.

Nevertheless, the results provided by these studies highlight the potential of combining dietary advice relating to anti-inflammatory low-carbohydrate diets with appropriate oral health regimes.

The implications of the findings of this review may have a wider impact on patients' general health and on healthcare; if periodontal inflammation can be reduced through the adoption of a low-carbohydrate diet, then systemic inflammation and the risk for other inflammatory conditions may also be reduced. This supports previous research reporting improved systemic inflammation as a result of low-carbohydrate dietary regimes.[34,35] Although the most recent RCT[52] observed no significant difference in serological markers between

Table 6 Results: Secondary Outcomes

	Plaque Index					
	Group A Baseline	Group A End of Study	Level of Signif.	Group B Baseline	Group B End of Study	Level of Signif.
Baumgartner *et al.*, 2009	N/A	N/A	N/A	0.68	1.47	p<0.001
Woelber *et al.*, 2016	0.75 ± 0.63	0.97 ± 0.70	p = 0.084	1.10 ± 0.51	0.84 ± 0.47	p = 0.084
El Makaky *et al.*, 2019	1.540 ± 0.7051	1.655 ± 0.6589	p= 0.001	1.550 ± 0.7585	1.560 ± 0.7618	p=0.733
Woelber *et al.*, 2019	0.58 ± 0.14	0.48 ± 0.12	p=1.0	0.58 ± 0.12	0.48 ± 0.13	p=1.00
	Pocket Probing Depth (mm)					
	Group A Baseline	Group A End of Study	Level of Signif.	Group B Baseline	Group B End of Study	Level of Signif.
Baumgartner *et al.*, 2009	N/A	N/A	N/A	2.23 ± 0.6	2.09 ± 0.63	P <0.001
Woelber *et al.*, 2016	2.31 ± 0.43	2.52 ± 0.40	Not given	2.19 ± 0.34	2.11 ± 0.35	Not given
El Makaky *et al.*, 2019	N/A	N/A	N/A	N/A	N/A	N/A
Woelber *et al.*, 2019	1.82 ± 0.24	2.00 ± 0.14	p=0.018	1.85 ± 0.27	1.84 ± 0.17	p= 0.018
	PISA (mm)²					
	Group A Baseline	Group A End of Study	Level of Signif.	Group B Baseline	Group B End of Study	Level of Signif.
Baumgartner *et al.*, 2009	N/A	N/A	N/A	N/A	N/A	N/A
Woelber *et al.*, 2016	662.24 ± 420.05	963.24 ± 373.78	p<0.01	638.88± 305.41	284.83 ± 174.14	p<0.001
El Makaky *et al.*, 2019	N/A	N/A	N/A	N/A	N/A	N/A
Woelber *et al.*, 2019	270.50± 140.97	286.00± 114.02	p=0.6	315.27± 148.68	252.37± 151.78	p=0.6

Key: Group A: Control Group; Group B: Intervention Group

control and intervention groups, another[51] reported significant reductions in serological inflammatory parameters TNF-α and IL-6.

As periodontal disease has been linked to several non-communicable diseases, reducing the incidence and prevalence of periodontal disease may subsequently decrease the incidence and prevalence of such conditions as cardiovascular disease. Not only will this reduce the overall burden of disease and the associated financial impact of such, but more importantly, improve the quality of life of patients.

> *'It seems that the next logical step would be a well-structured, sufficiently powered RCT investigating the effects of a low-carbohydrate diet…'*

Unfortunately, the paucity of high-quality research currently available suggests despite the positive results of this review, it is far from enough to inform policy change; it may however generate enough interest to influence further research in this arena. On considering a change in recommended treatment modalities in the management and prevention of periodontal disease, it seems that the next logical step would be a well-structured, sufficiently powered RCT investigating the effects of a low-carbohydrate diet, possibly as an adjunctive treatment to non-surgical periodontal therapy (NSPT) with a comparator group receiving NSPT alone.

From the limited evidence currently available, it is plausible that in addition to periodontal therapy, in the management of periodontal diseases dental professionals should consider assessing dietary habits with particular reference to intake of refined carbohydrates and an anti-inflammatory diet, providing dietary advice to reduce periodontal inflammation. However, further high quality longitudinal RCTs are needed in this topic area to strengthen the evidence base.

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