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Evaluation of vitamin C as an adjunct to periodontal therapy - Systematic review

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Abstract---Background: Periodontitis is an inflammatory disease that affects the periodontium, which is the protective apparatus that surrounds a tooth and includes the gingiva, alveolar bone, cementum, and periodontal ligament and is initiated by bacterial infection, subsequently progresses because of altered host response, and causes periodontal tissue destruction. These bacteria have the capacity to destroy the collagen fibres and ground substance directly by releasing virulence factors like enzymes - collagenase and toxins - gingipains. Indirectly act on various receptors like toll receptors and activate host immune response. Some immune cells like neutrophils, start producing reactive oxygen species (ROS). Vitamin C acts as an antioxidant, by acting as an electron donor. Thereby preventing lipid peroxidation by ROS. Vit. C also controls collagen synthesis by directly activating collagen synthesis transcription and stabilizing procollagen mRNA. Along with other properties, Vitamin C is said to have anti-inflammatory and wound healing properties. Aim: This study aimed to systematically review to assess the effect of Vitamin C, as an adjunct to periodontal therapy. Materials and Method: The electronic databases PUBMED, GOOGLE SCHOLAR, and COCHRANE LIBRARY, from 1984 to 2021 along with complementary manual search of all available periodontics journals till the year of 2021 was done based on structured questions. Results: Out of 6 studies selected, 4 of them showed that vitamin C was effective as an adjunct for non surgical periodontal therapy. Conclusion: This review emphasizes the importance of vitamin C in preventing the onset and progression of periodontal disease. Out of 6 studies, 4 of them supported that vitamin C is effective in acting as adjunct for

periodontal therapy in terms of probing depth, clinical attachment level and other biochemical parameters. More research into the use of unified periodontal markers and the effects of other factors are needed to improve our understanding of the relationship between vitamin C and periodontal disease.

Keywords---vitamin C, clinical attachment, periodontal therapy.

Introduction

Periodontitis is an inflammatory disease that affects the periodontium, which is the protective apparatus that surrounds a tooth and includes the gingiva, alveolar bone, cementum, and periodontal ligament and is initiated by bacterial infection, subsequently progresses because of altered host response, and causes periodontal tissue destruction.(1,2) It starts as gingivitis, with up to 90% of the population suffering from it and it is caused by bacteria and dental plaque. When gingivitis has developed into a chronic and irreversible inflammatory disease condition, it is called periodontitis. The bacteria that cause gingivitis can now penetrate deeper into the tissues and periodontium surrounding it.(3) Periodontitis causes tooth to lose its attachment, which then leads to alveolar bone loss and the eventual loss of the affected tooth. This causes the host to react in order to protect itself against the invading bacteria. However, in the process of defending against the bacteria, the host's defenses often cause the periodontium to be destroyed.(4,5,6)

Periodontal disease is caused by periodontopathic bacteria. A shift in bacterial species in the gingival sulcus from gram-positive, facultative, fermentative microorganisms to predominately gram-negative, anaerobic, and proteolytic organisms has been linked to periodontal tissue breakdown. These bacteria have the capacity to destroy the collagen fibres and ground substance directly by releasing virulence factors like enzymes - collagenase and toxins - gingipains. Indirectly act on various receptors like toll receptors and activate host immune response. Some immune cells like neutrophils, start producing reactive oxygen species (ROS), to neutralize and eliminate the bacteria responsible for the host tissue destruction. At higher concentrations, ROS have a detrimental effect on periodontal host tissues.(7,8) Multiple treatment options have come up to prevent and treat periodontal disease.

Vitamin C or ascorbic acid, a unique vitamin which exerts a reducing and antioxidant effect, scavenger for free radicals, and most importantly acts as an enzyme cofactor in collagen synthesis.(9) It is said to have astounding wound healing properties. Vitamin C is considered an essential dietary oxidant for periodontal health since it scavenges excessive ROS.(10) Vit. C serves as a cofactor for the enzymes prolyl and lysyl hydroxylase, the enzymes that are responsible for stabilizing and cross-linking the collagen molecules. Vitamin C act as an antioxidant, by acting as an electron donor. Thereby preventing lipid peroxidation by ROS.(11) Vit. C also controls collagen synthesis by directly activating collagen synthesis transcription and stabilizing procollagen mRNA.(12)

Along with other properties, Vitamin C is said to have anti-inflammatory and wound healing properties.

Scaling and root planing is one of the gold standard and first line of treatment for treating periodontal disease followed by surgical therapy. Adjunctive therapy like local drug delivery, oral suspension of different formulations, photodynamic therapy, herbal irrigations etc. In few trials, vitamin C was assessed using dietary intake or blood-vitamin C concentrations. Furthermore, gingivitis and periodontitis are two forms of periodontal disease with distinct pathologies and probably different interactions with vitamin C. This systematic review is to understand the current knowledge on the use of Vitamin C as adjunctive therapy in periodontal disease.

AIM

This study aimed to systematically review to assess the effect of Vitamin C, as an adjunct to non-surgical periodontal therapy. To assess its efficiency in avoiding surgical periodontal therapy.

Structured question?

Is Vitamin C effective as an adjunct in treating periodontal disease?

P- Patients undergoing non-surgical therapy for gingivitis and periodontitis.

I- Vitamin C

O- Clinical and biochemical parameters.

Materials and Method

Literature search protocol:

Publication of interest within the scope of the focused systematic review was searched using the following electronic databases.

1. The electronic database National Library of Medicine (Pubmed)
2. Google scholar
3. Cochrane

No limits and language restrictions were applied during the electronic search in order to include all the relevant articles pertaining to the topic of interest.

Keywords

P- Periodontitis, Chronic Periodontitis, Aggressive Periodontitis, Severe Periodontitis, Moderate Periodontitis, Mild Periodontitis, Juvenile Periodontitis, Early Onset Periodontitis, Necrotizing Ulcerative Periodontitis, Adult Periodontitis, Refractory Periodontitis, Non-smokers, Systemically healthy, Gingivitis, Necrotizing Ulcerative Gingivitis, Puberty Gingivitis, Pregnancy Gingivitis, Acute Gingivitis, Chronic Gingivitis, Leukemic Gingivitis, Periodontal disease, Non-surgical periodontal therapy.

I- Vitamin C, Ascorbic acid, Ascorbate, L- ascorbic acid, Sodium ascorbate, Magnesium ascorbate, Ferrous ascorbate.

O- Oral Hygiene Index, Periodontal Index, Dental Plaque Index, Bleeding Index, Gingival Bleeding Index, Antiplaque, Anti-Gingivitis, Probing Depth, Clinical Attachment Loss, Debris Index, Calculus Index, Patient Hygiene Performance Index, Modified Gingival Index, Sulcus Bleeding Index, Modified Sulcus Bleeding Index, Total antioxidant capacity.

Article eligibility criteria

Inclusion criteria:

1. Clinical trials;
2. Randomised controlled clinical trial;
3. Case-control studies;
4. Cohort studies;
5. Human studies;
6. Patients diagnosed with periodontal disease;
7. Studies where Vitamin C was used along with non-surgical periodontal therapy.

Exclusion criteria:

1. In-vitro studies;
2. Animal studies;
3. Literature reviews.

Article selection

Search results:

The title and abstract of the entries yielded from the initial electronic database searches were read. After this initial filter, the full-text versions of the studies that could be potentially included in this review were read and a final selection of articles was done after applying the eligibility criteria.

Results of literature selection process:

The initial search yielded 178 entries in the PubMed database, Google Scholar and Cochrane. Excluding all the duplicate articles, a total of 96 articles were there. Excluding all animal studies, case series, case reports, systematic reviews, 12 articles were there. Out of 12 articles, 5 articles were excluded for not maintaining homogeneity and 1 article was excluded after full-text review of the literature review. A final selection of 6 articles were made. (Figure 1)

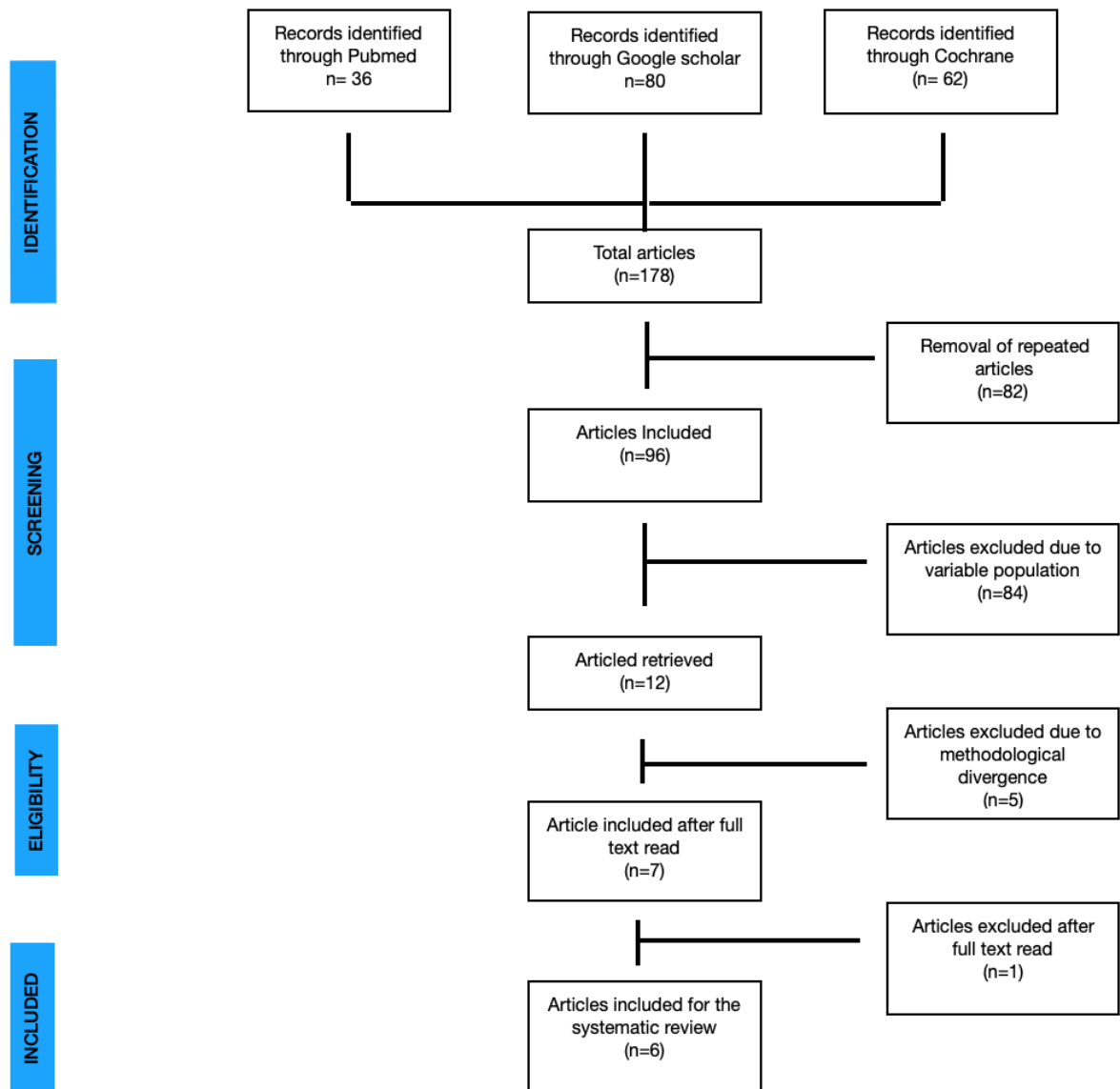
Prisma Flow Chart

Figure 1: Prisma flow chart explaining the search process and data collection

Excluded studies

Table 1: Summarized excluded studies during data collection.

S. NO	AUTHOR AND YEAR	TITLE	REASON
1	Xiao Li et al, 2018	Role of vitamin C in wound healing after dental implant surgery in patients treated with bone grafts and patients with chronic periodontitis	Irrelevance based on outcome measures
2	Woelber et al, 2019	The influence of an anti-inflammatory diet on gingivitis. A randomized controlled trial.	Irrelevance based on title
3	Shimada et al, 2009	Effects of ascorbic acid on gingival melanin pigmentation in vitro and in vivo.	Irrelevance based on title
4	Hong JY et al, 2019	A randomized, double-blind, placebo-controlled multicenter study for evaluating the effects of fixed-dose combinations of vitamin C, vitamin E, lysozyme, and carbazochrome on gingival inflammation in chronic periodontitis patients.	Irrelevance based on formulation of the intervention.
5	Lingstrom et al, 2005	The release of vitamin C from chewing gum and its effects on supragingival calculus formation	Irrelevance based on title
6	Vogel et al, 1986	The Effects of Megadoses of Ascorbic Acid on PMN Chemotaxis and Experimental Gingivitis	Irrelevance based on formulation of the intervention.

Table 2: Summarized characteristics of the selected studies

S. NO	AUTHOR AND YEAR	TITLE	STUDY DESIGN	INTERVENTION	TYPE OF STATISTICS USED	OUTCOME MEASURES
1	Ali E. Abou Sulaiman et al,2010	Assessment of total antioxidant capacity and the use of vitamin C in the treatment of non-smokers with chronic periodontitis.	Randomised controlled clinical trial	Non-surgical periodontal therapy and vitamin C administration	The chi-square test was used to analyze the age and sex differences between study groups. The Mann-Whitney <i>U</i> test was used to assess the differences of plasma Total antioxidant capacity (TAOC) levels between study groups. the relationship between the levels of plasma TAOC and the clinical indices was assessed by means of a Spearman rank correlation test.	Plaque index, bleeding on probing, probing depth, clinical attachment level, gingival index and total antioxidant capacity.
2	Neeraja et al,2013	A short-term evaluation of the relationship between plasma ascorbic acid levels and periodontal disease in systemically healthy and type 2 diabetes mellitus subjects.	Randomised controlled clinical trial	Non-surgical periodontal therapy (scaling and root planing; SRP) and vitamin C administration	Pair-wise comparison of plasma Ascorbic acid Levels between groups 1–4 were carried out using Tukey's multiple post hoc procedures. Comparison between subgroups A and B within were carried out using the paired <i>t</i> test.	Plaque index, bleeding gingival score and pocket probing depth.
3	Yoshio Shimabukuro et al,2015	Effects of an Ascorbic Acid–	Double masked,	Dentifrice containing	Baseline scores for each dentifrice were	Gingival index, gingival redness,

		Derivative Dentifrice in Patients With Gingivitis: A Double-Masked, Randomized, Controlled Clinical Trial	Randomised controlled clinical trial	L-ascorbic acid 2-phosphate magnesium salt	compared using a <i>t</i> test. The incidence of adverse events was compared between the groups using Fisher exact test.	total antioxidant capacity, Gingival severity score.
4	Chitsazi et al, 2017	Effects of adjective use of melatonin and vitamin C in the treatment of chronic periodontitis: a randomized clinical trial.	Randomised clinical trial	Non-surgical periodontal therapy and melatonin with and without vitamin C administration	Paired t-test, one-way ANOVA and repeated-measures ANOVA with Statistical significance was set at $P < 0.05$.	Gingival index, probing depth and clinical attachment level.
5	Amaliya et al, 2017	Effect of guava and vitamin C supplementation on experimental gingivitis: A randomized clinical trial.	Randomised controlled clinical trial	Non-surgical periodontal therapy (scaling and root planing: SRP) and vitamin C Administration and Guava supplementation	Changes over time within experiment groups were analysed with analysis of variance (ANOVA). Differences in changes between experimental groups over time were analysed with a linear mixed model analysis	Plaque index, gingival index, bleeding gingival score
6	Kunsongkeit et al, 2019	Effect of vitamin C as an adjunct in nonsurgical periodontal	Randomised controlled clinical trial	Non-surgical periodontal therapy	Within and between group comparisons were done using Wilcoxon signed rank test and	Plaque index, bleeding on probing, probing depth, clinical attachment level, gingival index

		therapy in uncontrolled type 2 diabetes mellitus patients.		and vitamin C administration	Mann–Whitney U test, respectively. Within and between group, comparisons of periodontal parameters were done using Friedman test and Mann–Whitney U test, respectively. For multiple intragroup comparison, Bonferroni post-hoc test was performed.	and bleeding gingival score
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Table 3- Summarized outcome measures of the selected studies

S. NO	Author and year	Study design	Popula- tion	Groups	Interven- tion	Duration	Plaque Index	Gingival index	Bleeding gingival score	Probing pocket depth	Clinical attachment level	Bleeding on probing	Gingival redness	Gingival severity score	Total antioxid ant capacity
1.	Ali E. Abou Sulaiman et al,2010	Rando mised controll ed clinical trial	Chronic periodontits (n-30) Healthy (n-30)	G1- Healthy G2- CHP1 G3- CHP2	SRP+Vit amin C SRP	3 months	0.37±0.22 0.55±0.44	1.53±0.52 1.87±0.46	NA	2.88 ±0.48 3.07±0.61	2.96±0.53 3.31±0.83	28.41±14.78 37.38±22	NA	NA	655.8±43.2 652.4±63.3
2.	Neeraja et al,2013	Rando mised controll ed clinical trial	Gingivit is and periodontitis (n-120)	G 1- Healthy G 2- Gingivit is G 3- Periodontitis G 4- periodontitis with T2DM Sub G 1- SRP+ ascorbic acid Sub G2 - SRP	SRP+ Ascorbi c acid (450mg) SRP	2 weeks	G2- 1.00±0.56 1.23±0.70 G3- 1.38±0.48 1.21±0.37 G4- 1.24±0.46 1.34±0.40	NA	G2- 2.29±0.04 2.34±0.34 G3- 1.28±0.35 1.37±0.37 G4- 1.66±0.52 1.70±0.36	NA G3- 6.34±1.50 6.87±1.10 G4- 6.26±1.34 6.61±1.62	NA	NA	NA	NA	

3.	Yoshio Shimabukuro et al,2015	Double masked , Rando mised controll ed clinical trial	Gingivitis (n-300)	G 1- APM G 2- Control	0.3% APM (dentrifi ce)	3 months	NA	0.73±0.03 0.84±0.03	NA	NA	NA	NA	0.69±0.03 0.78±0.03	0.21±0.02 0.15±0.02	0.452±0.015 0.405±0.015
4.	Chitsazi et al ,2017	Rando mised clinical trial	Periodo ntitis (n-60)	G1- SRP G2- Melaton in + SRP G3- Melaton in+ Vitamin C+ SRP	Melaton in= 2mg – 4 weeks Vitamin C= 60mg- female 75mg- male- 4 weeks	6 months	NA	0.33±0.22 0.62±0.14 0.75±0.13	NA	4.92±1.53 3.54±1.45 3.08±1.12	4.56±1.16 3.22±1.52 3.00±1.53	NA	NA	NA	NA
5.	Amaliya et al,2017	Rando mised controll ed clinical trial	Gingivit is (n-48)	G 1- guava G 2- vitamin c G 3- Only water	200gms of guava fruit 200gms of vitamin c tablet (oral)	14 days	1.30±0.63 1.61±0.51 1.79±0.35	0.10±0.30 0.23±0.28 0.87±0.29	4.78±8.89 3.87±8.10 28.36±21.40	NA	NA	NA	NA	NA	NA
6.	Kunsong keit et al, 2019	Rando mised controll ed clinical trial	T2DM with periodo ntitis (n-31)	G1- Vitamin c G2- Control	500mg of vitamin C	2 months	0.15±0.07 0.16±0.08	0.42±0.09 0.45±0.10	0.57±0.24 0.59±0.24	3.25±0.96 3.6±0.90	3.78±1.17 3.93±1.41	NA	NA	NA	NA

APM- L-ascorbic acid 2-phosphate magnesium salt, T2DM-Type II diabetes mellitus, SRP- Scaling and root planing, NA- Not applicable

Table 4: Summarised results of the selected studies

S.no	Author and year	Intervention	Outcome measures	Groups	Result summary
1	Ali E. Abou Sulaiman et al, 2010	Non-surgical periodontal therapy and vitamin C administration	Plaque index, bleeding on probing, probing depth, clinical attachment level, gingival index and total antioxidant capacity.	G1- Healthy G2- SRP+ Vitamin C G3-SRP	Plasma TAOC levels were significantly lower in Chronic periodontitis patients than controls ($P < 0.001$). The periodontal therapy resulted in increasing plasma TAOC and improvements in clinical measures among both group 2 and 3 ($P < 0.001$). However, the adjunctive dose of vitamin C did not offer additional effect ($P > 0.05$).
2	Neeraja et al, 2013	Non-surgical periodontal therapy (scaling and root planing: SRP) and vitamin C administration	Plaque index, bleeding gingival score and pocket probing depth.	G 1- Healthy G 2- Gingivitis G 3- Periodontitis G 4- periodontitis with T2DM Sub G 1- SRP+ ascorbic acid Sub G2 - SRP	AAL plasma levels were significantly greater in group 1 than in group 2 ($p = .0007$) and in group 4 ($p = .0003$). A significant reduction in the bleeding gingival score was seen in the subgroups that received dietary supplementation of vitamin C within group 2 ($p = .0012$) and group 4 ($p = .036$).

3	Yoshio Shimabukuro et al,2015	Dentifrice containing L-ascorbic acid 2-phosphate magnesium sal	Gingival index, gingival redness, total antioxidant capacity, Gingival severity score.	G 1-APM G 2- Control	GI was significantly lower in the APM group ($P = 0.01$) than in the control group. In the APM group, gingival redness was significantly lower, and the difference from the baseline gingivitis severity index was significantly greater ($P = 0.04$ and $P = 0.02$, respectively). The total antioxidant activity of the saliva was significantly higher in the APM group ($P = 0.03$). The incidence of adverse events did not significantly differ between the groups ($P > 0.15$).
4	Chitsazi et al ,2017	Non-surgical periodontal therapy and melatonin with and without vitamin C administration	Gingival index, probing depth and clinical attachment level.	G1- SRP G2- Melatonin + SRP G3- Melatonin+ Vitamin C+ SRP	When compared to baseline, nonsurgical periodontal therapy increased PD and CAL 3 and 6 months after treatment ($P < 0.001$). The melatonin+ vitamin C group showed a substantial increase in PD and CAL scores at 6-month intervals relative to 3-month intervals ($P < 0.05$), but there were no significant differences in PD and CAL scores between the control and melatonin groups ($P > 0.05$). Therefore, an adjunctive dose of vitamin C offered an additional effect at this interval.
5	Amaliya et al,2017	Non-surgical periodontal therapy (scaling and root planing: SRP) and	Plaque index, gingival index, bleeding gingival score	G 1- guava G 2- vitamin c G 3- Only water	PI increased in guava, vitamin C and control group. However, the guava group developed significantly less plaque compared to the control group. The GI increase in both guava and vitamin C group was significantly less than the increase in the control group Adults consuming 5 mg vitamin C per day during 4 weeks, consumption of either 200 g guava/day

		vitamin C Administratio n and Guava supplementati on			or 200 mg synthetic vitamin C/day prior to and during the oral hygiene abstention period has a preventive effect on the development of gingivitis as compared to the control group.
6	Kunson gkeit et al, 2019	Non-surgical periodontal therapy and vitamin C administration	Plaque index, bleeding on probing, probing depth, clinical attachment level, gingival index and bleeding gingival score	G1- Vitamin c G2- Control	All periodontal parameters were significantly improved from baseline in both groups. However, no significant difference was found between groups. In periodontitis patients with uncontrolled type 2 diabetes, supplementing with 500 mg of vitamin C a day had no additional benefit in terms of improving periodontal status.

SRP- Scaling and root planing, TAOC- Total antioxidant capacity, APM- L-ascorbic acid 2-phosphate magnesium salt,
AAL- ascorbic acid levels, PI- plaque index, GI- Gingival index

Level of Evidence

Table 5: According to Oxford Centre for Evidence- Based Medicine 2016 Levels of Evidence

S.NO	Author and year	Study design	Level of evidence
1.	Ali E. Abou Sulaiman et al,2010	Randomised controlled clinical trial	II
2.	Neeraja et al,2013	Randomised controlled clinical trial	II
3.	Yoshio Shimabukuro et al,2015	Double masked, Randomised controlled clinical trial	II
4.	Chitsazi et al ,2017	Randomised clinical trial	II
5.	Amaliya et al,2017	Randomised controlled clinical trial	II
6.	Kunsongkeit et al, 2019	Randomised controlled clinical trial	II

Risk of Bias- Major Criteria

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
All E. Abou Sulalman et al,2010	+	+	+	?	+	?	?
Amalya et al,2017	+	+	+	+	+	+	?
Chitsazi et al ,2017	+	+	?	+	?	+	?
Kunsongkelt et al, 2019	+	+	+	?	?	+	?
Neeraja et al,2013	-	-	-				
Yoshio Shimabukuro et al,2015	+	+	+	+	+	+	?

Figure 2: Risk of bias summary: review authors' judgements about each risk of bias item for each included study

Risk of bias graph

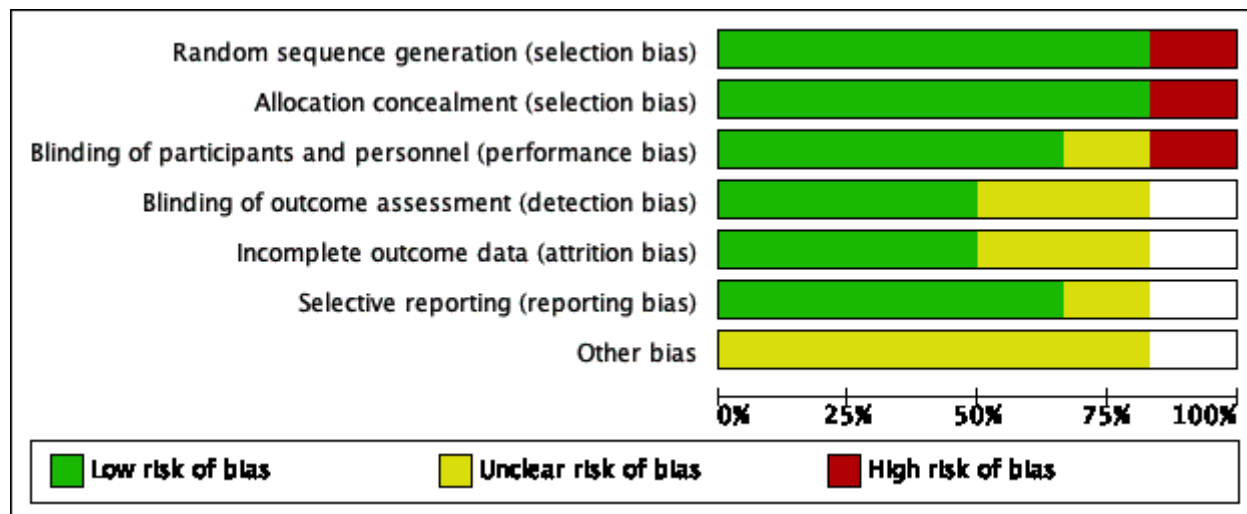


Figure 3: Risk of bias: review authors' judgements about overall risk of bias item for each included study

Results

Literature search from the electronic databases led to a collection of total 12 articles, from which one article was excluded after full text read and five were excluded during data extraction. So a total of 6 articles were included in this systematic review after only electronic search, no articles were included based on hand search. So the data to be extracted and the characteristics of included studies along with their summary of its contents have been tabulated. Then these articles were assessed, segregated and data was extracted based on different aspects of the structured question on "Is Vitamin C effective as an adjunct in treating periodontal disease?" According to the above articles Vitamin C is effective in acting as an adjunct for non surgical therapy.

Discussion

The following findings were observed after analysis of the above mentioned articles: (Table 1-5)

The study population consisted of 60 subjects: 30 diagnosed with ChP and 30 matched controls. Furthermore, patients from the ChP group were randomly allocated into ChP1 (15 patients received non-surgical treatment with adjunctive dose of vitamin C) and ChP2 (15 patients received non-surgical periodontal treatment alone). Plasma TAOC levels were measured by an ABTS assay at baseline and 1 month post-therapy. Plasma TAOC levels were significantly lower in ChP patients than controls ($P < 0.001$). The periodontal therapy resulted in increasing plasma TAOC and improvements in clinical measures among both ChP1 and ChP2 groups ($P < 0.001$). However, the adjunctive dose of vitamin C did not offer additional effect ($P > 0.05$). Lower levels of plasma TAOC are substantially correlated with ChP. Periodontal nonsurgical treatment appears to alleviate oxidative stress during periodontal inflammation. (13)

One twenty randomized subjects were subgrouped within groups, received either scaling and root planing (SRP) with dietary supplementation (450 mg) of ascorbic acid (AA) for two weeks or only SRP. After two weeks, the clinical parameters were reassessed. Plaque index, bleeding gingival score, probing pocket depth and plasma ascorbic acid levels (AAL) was analysed. AAL plasma levels were significantly higher in group 1 ($p = .0007$) and group 4 ($p = .0003$) than in the other groups. The bleeding gingival score was significantly lower in the subgroups of group 2 ($p = .0012$) and group 4 ($p = .036$) that obtained dietary vitamin C supplementation. Plasma AAL is below the normal range in systemically healthy subjects with gingivitis and diabetes with periodontitis. Dietary AA supplementation with SRP improves the bleeding gingival score in subjects with gingivitis and diabetes with periodontitis.(14)

In a multicenter, randomized, parallel group, controlled clinical trial involving 300 people with gingivitis, the clinical effects of APM were investigated. The APM-containing dentifrice was given to half of the participants, while the control dentifrice was given to the other half. The gingival index (GI) at three months was the primary outcome. Gingival redness as a measure of local gingival inflammation, gingival bleeding as a measure of gingivitis severity index, and overall antioxidant activity of the saliva were all secondary outcomes. GI did not vary significantly between the groups in the intent-to-treat study ($P = 0.12$). However, in a per-protocol study, the APM group had significantly lower GI ($P = 0.01$) than the control group. Gingival redness was significantly lower in the APM category, and the disparity between the baseline gingivitis severity index was significantly higher ($P = 0.04$ and $P = 0.02$, respectively). The total antioxidant activity of the saliva was significantly higher in the APM group ($P = 0.03$). The incidence of adverse events did not significantly differ between the groups ($P > 0.15$). These findings indicate that the regular application of an APM-containing dentifrice could reduce gingival inflammation.(15)

In this study, sixty people with chronic periodontitis were randomly assigned to one of three groups: 20 patients were assigned to one of three groups: group 1) received non-surgical periodontal treatment; group 2) received non-surgical periodontal treatment with the addition of melatonin; and group 3) received non-surgical periodontal treatment with the addition of melatonin and vitamin C. As compared to baseline, nonsurgical periodontal therapy increased PD and CAL 3 and 6 months after treatment ($P < 0.001$). The melatonin+ vitamin C group showed a substantial increase in PD and CAL scores at 6-month intervals relative to 3-month intervals ($P < 0.05$), but there were no significant differences in PD and CAL scores between the control and melatonin groups ($P > 0.05$). Combination therapy with melatonin and vitamin C can improve the results of non-surgical periodontal therapy.(16)

A 14-day pre-experimental duration with oral hygiene instructions, scaling, prophylaxis, and supplementation was included in the study. Following that, the experiment gingivitis was started while supplementation was continued. Plaque Index (PI) and Gingival Index (GI) were measured at baseline, Day 7 and Day 14 of experimental gingivitis. Dietary fruit and vegetable consumption was limited during the study. The PI of the guava, vitamin C, and control groups all increased (PI: 1.30, 1.61, and 1.79, respectively). However, as opposed to the control group,

the guava group formed substantially less plaque. Both the guava and vitamin C groups experienced substantially smaller GI changes than the control group (GI: 0.10, 0.24, and 0.87, respectively). When compared to a control group that established the normal amount of experimental gingivitis, intake of either 200 g guava/day or 200 mg synthetic vitamin C/day prior to and during the oral hygiene abstinence time has a protective impact on the production of experimental gingivitis in a population of young nonsmoking adults.(17)

Subjects received initial periodontal therapy plus 500 mg/day vitamin C for 2 months (n = 15) or placebo (n = 16). Plaque Index, Sulcus Bleeding Index, Gingival Index, pocket depth, and clinical attachment level were measured at baseline, 1 month, and 2 months post-treatment. Almost all subjects had low levels of plasma vitamin C at baseline. In the test group, plasma vitamin C was significantly increased to an adequate level at the end of 2 months. All periodontal parameters were significantly improved from baseline in both groups. However, no significant difference was found between groups. Supplementation of 500 mg/day vitamin C did not give an additional benefit in promoting periodontal status in periodontitis patients with uncontrolled type 2 diabetes mellitus.(18)

Out of 6 studies, 4 of them showed low risk of bias and 1 unclear bias and 1 of them showed high risk of bias overall.(Figure 2-3) Sulaman et al, 2010 showed low risk of bias when selection, performance, attrition bias and allocation concealment was assessed, whereas detection and reporting bias was unclear. Neeraja et al, 2013 showed high risk of bias among all the criteria. Shimabukuro et al, 2015 showed low risk of bias on complete assessment of the study. Amaliya et al, 2017 showed low risk of bias when selection, performance, detection, reporting, attrition bias and allocation concealment was assessed. Chitsazi et al, 2017 after assessment concluded that selection, performance, attrition bias was at low risk whereas others were at unclear risk. Kunsongkeit et al., 2019 attrition and detection bias was unclear whereas other bias were considered as low risk. Out of 6 studies selected, 4 of them showed that vitamin C was effective as an adjunct for non surgical periodontal therapy.

Vitamin C is readily derived from a wide range of foods. Grapefruit intake, which is high in vitamin C, was found to increase the sulcus bleed index in patients with chronic periodontitis. When it comes to promoting oral health in community dwellings, collaboration between oral health practitioners and dieticians in the public health sector is expected to be more effective. Vitamin C (VitC) prevents the auto inactivation of lysyl and prolyl hydroxylase, two primary enzymes in collagen biosynthesis, and thus helps to maintain a normal mature collagen network in humans. In a noncytotoxic range of concentrations, VitC induced a dose dependent increase in collagen type I deposits by normal human fibroblasts (NHF) cultured in monolayer, as well as enhanced extracellular matrix contraction by NHF in a lattice model. Exogenous VitC could thus help to maintain optimum collagenic density in the dermis and reinforce the collagen on a local level.(19)

Future scope of this present literature review to bring about use of Vitamin C for increasing the collagen synthesis activity, which may in turn help in treating periodontal disease with any surgical treatment options.

Conclusion

The aim of this review was to provide an overview and assessment of studies that analysed the relationship between vitamin C and periodontal disease. It emphasizes the importance of vitamin C in preventing the onset and progression of periodontal disease. Out of 6 studies, 4 of them supported that vitamin C is effective in acting as an adjunct for periodontal therapy. This systematic review throws light on the various ways in which vitamin C can be used as an adjunct in periodontal therapy. However, the use of vitamin C as local drug delivery, is yet to be tested. So, it paves the way for future studies. Further research into different modes of delivery of Vitamin C in periodontal therapy can be tested.

Limitations

1. First, the periodontal disease markers used in the reviewed studies were varied, which prevented us from comparing the findings of the studies. The assessment of periodontal disease sufferers based on the measure used, showing a positive association between periodontal disease and vitamin C.
2. Second, the number of articles for the review is small.
3. Thirdly, smoking and diabetes are factors that aggravate periodontal disease and reduce vitamin C's anti-inflammatory role. Vitamin C and tobacco-derived molecules, as well as those highly expressed in diabetes, can interact in some ways. However, the information available in the papers included in this analysis regarding this issue is perplexing, and the current research offers insufficient evidence addressing this concern.
4. There is no recurrent time frame in which these results were established which was one of the aims of the above study.

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