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ORIGINAL RESEARCH

Effect of Lycopene in the Treatment of Periodontal Disease: A Clinical Study

Sphoorthi Anup Belludi, Shiras Verma, Ruchi Banthia, Prashanth Bhusari, Simran Parwani, Sameer Kedia, SV Saiprasad

ABSTRACT

Purpose: Several epidemiologic studies have suggested a role of tomato products in decreasing the risk of the development of diseases related to oxidative stress (cancer and other chronic diseases). Oxidative stress may result in periodontal tissue damage either directly or indirectly. Lycopene, a powerful antioxidant and the main carotenoid in tomato products possesses the greatest quenching ability of singlet oxygen among the various carotenoids and is effective in protecting blood lymphocytes from NOO-radical damage. Hence, the aim of the present study is to compare the effect of systemically administered lycopene as an adjunct to scaling and root planing in patients with gingivitis and periodontitis.

Materials and methods: Twenty systemically healthy patients were involved in a randomized, double-blind, parallel study and based on their clinical signs were divided into two groups of mild to moderate periodontitis (A) and moderate gingivitis (B). The subjects under the groups A and B were randomly distributed between the two treatment groups: test group (n = 5), 4 mg lycopene/day for 2 weeks with oral prophylaxis (full mouth scaling and root planing (SRP) completed within 24 hours) and controls (n = 5), receiving only oral prophylaxis. Pre- and post-therapeutic periodontal parameters were evaluated.

Results: In group A, statistically significant improvement in CAL was reported in test group as compared to control group. In group B, the difference between pretreatment and post-treatment bleeding on probing scores was found to be statistically non-significant in both groups.

Conclusion: Results show that lycopene is a promising treatment modality as an adjunct to full mouth SRP of the oral cavity in patients with moderate periodontal disease.

Clinical significance: Modulation of the free radical production seems to be essential for the inhibition of tissue destruction, and treatment with antioxidants, like lycopene, which is the most potent among them will block the production of free ROS or its effects might prove to be therapeutically valuable.

Keywords: Antioxidants, Gingivitis, Periodontitis, Lycopene, Tomatoes.

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INTRODUCTION

Lycopene belongs to a class of compounds known as the carotenoids which are the yellow, orange and red pigments synthesized in plants. The five principle carotenoids found in human plasma, as the result of ingesting plants, including alpha and beta-carotene, beta-cryptoxanthin, lutein and lycopene. Over 600 carotenoids have been identified to date. The greatest known source of lycopene is tomatoes, which are widely employed in cooking.[1] There is a positive relationship between lycopene consumption and a reduction in the risk of development of degenerative diseases caused by free radicals, such as cancer, cardiovascular diseases, asthma, arthritis, stroke, cataractogenesis, hepatitis and also periodontitis.[2-4] Lycopene has the uncommon feature of becoming bound to chemical species that react to oxygen, thus being the most efficient biological antioxidizing agent.[3] Due to this property, studies have been enthusiastically conducted with lycopene, in order to find out whether or not it could be an alternative to protect patients against the damaging effects of free radicals.[3] Literature is deficient in the studies regarding the effect of lycopene on periodontal health, hence the present study aims to evaluate the effect of lycopene as an adjunct to mechanical therapy in the management of periodontal disease (gingivitis and periodontitis).

MATERIALS AND METHODS

Twenty systemically healthy patients (30 ± 41.6 years) were involved in a randomized, double-blind parallel study. The patients were divided into two groups of mild to moderate periodontal disease (group A) and moderate gingivitis (group B). The subjects under the groups A and B were randomly distributed between the two treatment groups: test group

(n = 5), 4 mg lycopene/day for 2 weeks with oral prophylaxis (full mouth scaling and root planing completed within 24 hours) and controls (n = 5) receiving only oral prophylaxis.

Inclusion and Exclusion Criteria

Patients who had not been treated for gingival or periodontal disease, who had not used any medications, such as antibiotics for past 6 months or over the counter antioxidants like Vit C, Vit B, β-carotene within past 3 months and did not report any side effects or drug allergies were included in this study. Patients with systemic disease, such as diabetes, cardiovascular diseases, pregnant and lactating women, current and former smokers and patients with mobile teeth and abscesses were excluded from the study.

All the patients in the two groups were randomly assigned into control group (n = 5) received thorough full mouth scaling and root planing (SRP) completed within 24 hours and test group (n = 5) received thorough full mouth SRP completed within 24 hours along with lycopene (Lycotas, Pharma co). Lycopene was prescribed for 2 weeks, twice daily. Each capsule contained lycopene 6%—2000 mcg, Vit C—50 mg, Vit A—2500 IU, zinc sulfate monohydrate—20.6 mg, chromium picolinate—75 mcg. Clinical parameters namely PPD (probing pocket depth), CAL (clinical attachment loss) and BOP (bleeding on probing) were recorded from Ramfjord's six teeth (Ramfjord 1959) at baseline (0 day) and then again at 14 days post-treatment with William's periodontal probe in patients under group A. PPD and CAL were measured at four sites per tooth. Bleeding on probing were recorded from Ramfjord's six teeth (Ramfjord 1959) at baseline (0 day) and then again at 14 days post-treatment with William's periodontal probe in patients under group B. Participants were instructed against changing their oral hygiene habits or taking any other medication throughout the study period. All procedures were carried out with adequate understanding and written consent of all the patients and ethical clearance to conduct this study was obtained from the ethical committee of Modern Dental College and Research Centre.

Data thus collected was subjected to unpaired and paired t-tests. Null's hypothesis was that adjunctive use of lycopene along with mechanical therapy resulted in the same clinical outcome as compared to SRP alone.

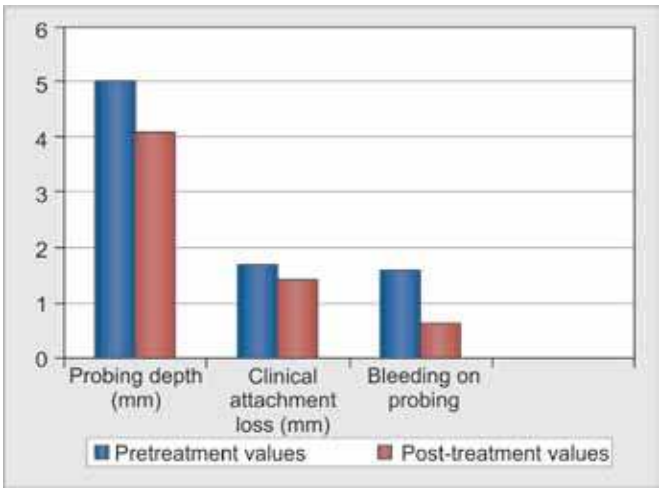
RESULTS

Group A

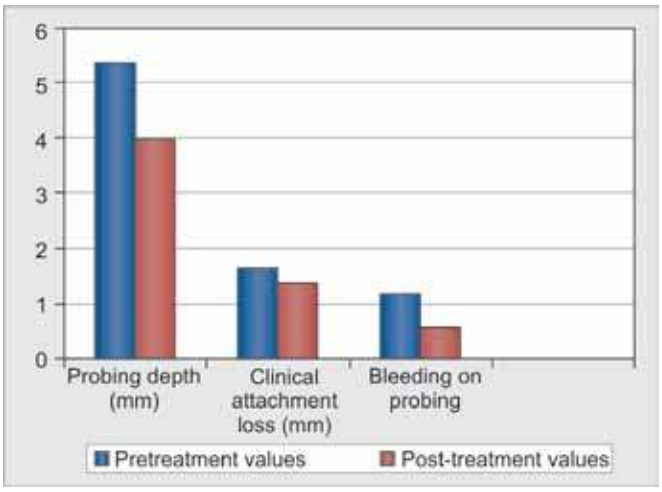
In group A, the pretreatment probing pocket depths of test and control groups were 5.37 ± 1.52 mm (mean ± standard deviation) and 5.03 ± 1.56 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 0.405 probability (unpaired t-test score was 0.83). Fourteen days post-treatment probing pocket depths of test and control groups were 4 ± 1.44 mm (mean ± standard deviation) and 4.10 ± 1.65 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 0.918 probability (unpaired t-test score was 0.10). The difference between pretreatment and post-treatment probing pocket depths was found to be statistically highly significant in both test group (paired t-test value is 5.76 at 0.00 probability) and control group (paired t-test value is 4.06 at 0.00 probability).

Pretreatment clinical attachment loss in test and control groups were 1.67 ± 1.24 and 1.70 ± 1.42 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 0.803 probability (unpaired t-test score was 0.25). Post-treatment clinical attachment loss in test and control groups were 1.40 ± 1.16 mm and 1.43 ± 1.33 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 0.803 probability (unpaired t-test score was 0.25). The difference between pretreatment and post-treatment clinical attachment loss was found to be statistically significant in test group (paired t-test value is 1.86 at 0.027 probability). The difference between pretreatment and post-treatment clinical attachment loss was found to be statistically significant in control group (paired t-test value is 2.11 at 0.043 probability). The difference between post-treatment values was significant in test group in comparison to the control group (paired t-test value is 2.31 at 0.024 probability). The results are depicted in Tables 1 and 2 and Graphs 1 to 3.

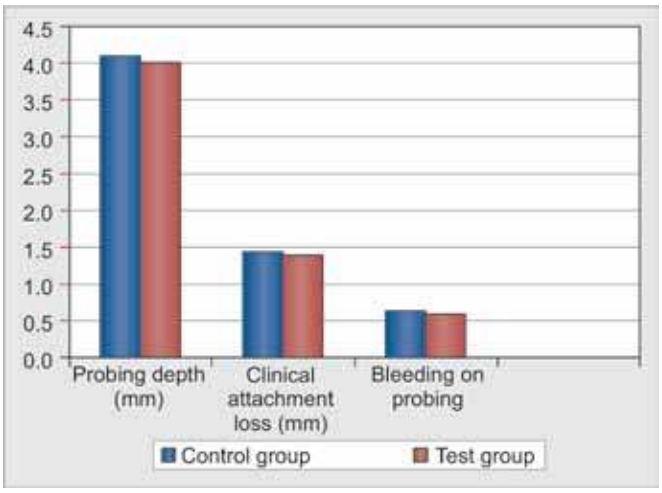
Pretreatment bleeding on probing scores of test and control groups were 1.2 ± 0.61 mm and 0.60 ± 0.56 mm respectively. Difference between test and control groups was found to be statistically nonsignificant at 0.923 probability (unpaired t-test score was 0.10). Post-treatment bleeding on



Graph 1: Pre- and post-treatment mean values of different parameters in control group



Graph 2: Pre- and post-treatment mean values of different parameters in test group

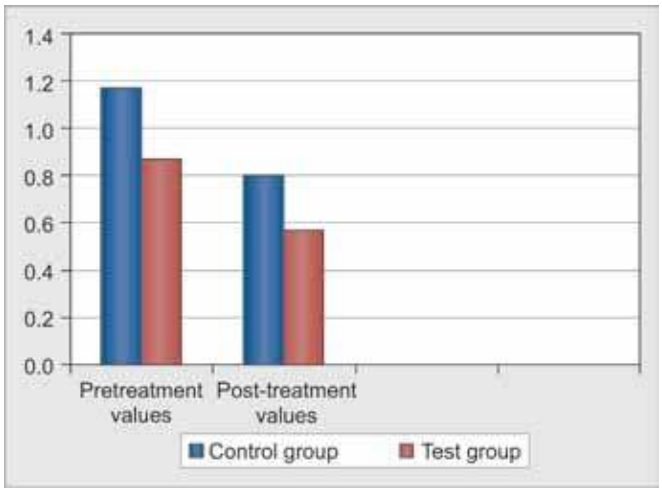


Graph 3: Comparison of post-treatment mean values of different parameters between control and test groups

probing scores of test and control groups were 0.60 ± 0.56 and 0.63 ± 0.67 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 1.000 probability (unpaired t-test score was 0.00). The difference between pretreatment and post-treatment bleeding on probing was found to be statistically highly significant in test group (paired t-test value is 5.28 at 0.000 probability). The difference between pretreatment and post-treatment bleeding in probing was found to be statistically highly significant in control group (paired t-test value is 6.92 at 0.000 probability).

Group B

In group B, the pretreatment bleeding on probing scores of test and control groups were 0.87 ± 0.68 mm (mean ± standard deviation) and 1.17 ± 0.79 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 0.121 probability (unpaired t-test score was 0.10). Post-treatment bleeding on probing scores of test and control groups were 0.57 ± 0.63 mm and 0.80 ± 0.71 mm respectively. Difference between test and control group was found to be statistically nonsignificant at 1.000 probability (unpaired t-test score was 0.00). The difference between pretreatment and post-treatment bleeding on probing scores was found to be statistically nonsignificant in test group (paired t-test value is 0.77 at 0.081 probability). The difference between pretreatment and post-treatment



Graph 4: Comparison of pre and post-treatment mean values of bleeding index between test and control groups

Table 1: Pre- and post-treatment values of different parameters for test and control groups

Character	*Pretreatment Mean ± SD*	*Post-treatment Mean ± SD*	*'t' value*	*Probability*	*Significance*
Control group					
Probing depth (mm)	5.03 ± 1.56	4.10 ± 1.65	4.06	0.000	HS
Clinical attachment loss (mm)	1.70 ± 1.42	1.43 ± 1.33	2.11	0.043	S
Bleeding on probing	1.60 ± 0.72	0.63 ± 0.67	6.92	0.000	HS
Test group					
Probing depth (mm)	5.37 ± 1.52	4.00 ± 1.44	5.76	0.000	HS
Clinical attachment loss (mm)	1.67 ± 1.24	1.40 ± 1.16	1.86	0.027	S
Bleeding on probing	1.20 ± 0.61	0.60 ± 0.56	5.28	0.000	HS

NS: Nonsignificant; S: Significant; HS: Highly significant

Table 2: Comparison of different parameters in test and control groups

Character	*Control group*	*Test group*	*'t' value*	*Probability*	*Significance*
Before the experiment					
Probing depth (mm)	5.03 ± 1.56	5.37 ± 1.52	0.83	0.405	NS
Clinical attachment loss (mm)	1.70 ± 1.42	1.67 ± 1.24	0.25	0.803	NS
Bleeding on probing	1.60 ± 0.72	1.20 ± 0.61	0.10	0.923	NS
21 days after treatment					
Probing depth (mm)	4.10 ± 1.65	4.00 ± 1.44	0.10	0.918	NS
Clinical attachment loss (mm)	1.43 ± 1.33	1.40 ± 1.16	2.31	0.024	S
Bleeding on probing	0.63 ± 0.67	0.60 ± 0.56	0.20	0.835	NS

*Significant; **Highly significant; NS: Nonsignificant; S: Significant

Table 3: Pre- and post-treatment values of bleeding index for test and control groups

Character	*Pretreatment Mean ± SD*	*Post-treatment Mean ± SD*	*'t' value*	*Probability*	*Significance*
Control group	1.17 ± 0.79	0.80 ± 0.71	1.88	0.064	NS
Test group	0.87 ± 0.68	0.57 ± 0.63	0.77	0.081	NS

NS: Nonsignificant; S: Significant; HS: Highly significant

Table 4: Comparison of bleeding index values between test and control groups

Character	*Control group*	*Test group*	*'t' value*	*Probability*	*Significance*
Before the experiment	1.17 ± 0.79	0.87 ± 0.68	1.57	0.121	NS
21 days after treatment	0.80 ± 0.71	0.57 ± 0.63	1.34	0.184	NS

NS: Nonsignificant

bleeding on probing scores was found to be statistically nonsignificant in control group (paired t-test value is 1.88 at 0.064 probability).

The results are depicted in Tables 3, 4 and Graph 4.

DISCUSSION

Periodontitis is an inflammatory condition representing the response of the periodontal tissues to lipopolysaccharide derived from Gram-negative anaerobic bacteria. Inflammation is known to be a protective response that focuses on the removal of the stimuli responsible for damage to the tissues, thereby leading to the restoration of health.[5,6] There is an increasing body of evidence available to implicate reactive oxygen species (ROS) in the pathogenesis of variety of inflammatory disorders, of which periodontal disease is no exception. A variety of ROS (e.g. superoxide and hydroxyl radicals, hydrogen peroxide, hypochlorous acid and singlet oxygen) which whilst not radicals in nature, can cause substantial tissue damage by initiating free radical chain reaction.[7-9] Modulation of the free radical production seems to be essential for the inhibition of tissue destruction, and treatment with drugs that block the production of free ROS or block its effects might be therapeutically valuable.[10-12] Recent investigations on animal models suggest that antioxidant therapies, which interfere with ROS, may be of benefit in the treatment of periodontitis.[12]

Many chemotherapeutic agents used in periodontics, in addition to their antiseptic and antimicrobial effects, are known to have an antioxidative activity against spontaneous oxidation.[13]

Among the common carotenoids, lycopene stands as the most potent antioxidant.[12] Lycopene exhibits the highest physical quenching rate with singlet oxygen[11,14] and is atleast three-fold more effective than β-carotene in preventing cell death by quenching NOO-radicals.[15]

Lycopene minimizes cell damage by:

1. Limiting free-radical formation
2. Destroying the free radicals or their precursors
3. Stimulating antioxidant enzyme activity
4. Repairing oxidative damage
5. Stimulating repair enzyme activity
6. Reversing DNA damage induced by H_2O_2.[16]

This study compared the effectiveness of lycopene (Lycotas, Pharma Co.) as an adjunct to mechanical therapy with that of mechanical therapy alone in patients with mild to moderate periodontitis (group A) and moderate gingivitis (group B).[17] All the patients enrolled in this study were compliant to the regimen. No adverse effects in the

form of any rashes or allergic reactions were reported by any of the patients. In group A, improvement in clinical parameters (PPD and BOP) was found to be statistically highly significant in both test and control groups. There was a significant improvement in CAL in both test as well as control groups. When both test and control groups were compared, PPD and BOP showed no significant difference, and only CAL showed statistically significant improvement. However, in group B, the difference between pretreatment and post-treatment bleeding on probing scores was found to be statistically nonsignificant in both test and control groups and between the two groups.

Similar results were also reported by Chandra et al[11] who concluded that there was a positive correlation between salivary uric acid levels and gingival parameters in gingivitis patients treated with lycopene as an adjunct to mechanical therapy. In this study, it was observed that although the mean reduction in GI (gingival index) was higher in the lycopene and SRP group than in the lycopene group, there were no statistically singnificant differences between these two groups.

A recent study investigated the relationship between monthly tomato consumption and serum lycopene levels, and self-reported history of congestive heart failure (CHF) in individuals with periodontitis. It was concluded that a relationship exists between periodontitis and CHF risk, and high monthly tomato consumption appears to affect this relationship in a positive direction in periodontitis subjects.[18]

Recent research suggests that mixtures of antioxidants are more effective than the single compounds and the synergistic effect is more pronounced when lycopene lutein is present.[19]

CONCLUSION

Results show that lycopene is a promising treatment modality as an adjunct to full mouth SRP of the oral cavity in patients with moderate periodontal disease. However, there is a paucity of studies that utilise potent antioxidants in the treatment of periodontal diseases and hence deserves long-term studies for the same.

CLINICAL SIGNIFICANCE

Modulation of the free radical production seems to be essential for the inhibition of tissue destruction, and treatment with drugs that block the production of free ROS or block its effects might be therapeutically valuable. Recent investigations on animal models suggest that, antioxidant therapies, which interfere with ROS, may be of benefit in the treatment of periodontal disease. As among the common carotenoids, lycopene stands as the most potent antioxidant, it may serve as a valuable therapy in the treatment of periodontal diseases.

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