



EFFECT OF ORAL MESOTHERAPY TECHNIQUE USING VITAMIN C AS AN ANTI-INFLAMMATORY AGENT IN PERSISTENT GINGIVAL INFLAMMATION: A CLINICAL STUDY

Dentistry

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ABSTRACT

Context: Mesotherapy is a minimally invasive procedure that involves local intramucosal therapy (LIT) with biologically active substances given in minor quantities to the area of pathology. Vitamin C is an important antioxidant agent that can modulate the attenuation of the inflammatory process and enhance tissue repair. **Aims:** This study aimed to determine whether local vitamin C injections are effective in treating persistent gingival inflammation. **Methods and Material:** Local Intramucosal injection with 1 mL vitamin C (150 mg concentration) using insulin syringes was administered into the keratinized gingival tissues. Thirty patients with persistent gingival inflammation even after phase I therapy were included in this study. The remission of gingival inflammation was assessed in each patient every week. **Statistical analysis used:** Paired t-test. **Results:** Improvement in inflammation was seen in all cases after two injections. All the treated patients responded effectively to the treatment and showed satisfaction with the results. Statistically significant reductions were seen in the sulcus bleeding index score. None of the patients reported adverse side effects or the need to use analgesics. **Conclusions:** Mesotherapy using vitamin C directly on to gingiva was safe and effective in reducing gingival inflammation. The present study may represent a clinically valuable treatment option for persistent gingival inflammation within its limits. It shows the synergistic effect of scaling and root planing.

KEYWORDS

Vitamin C, Mesotherapy, Periodontal therapy, Anti-inflammatory drugs, Inflammation

INTRODUCTION:

Plaque-induced gingival inflammation is most commonly seen within the population, which can destroy the periodontium if left untreated. Plaque control is an effective treatment. However, it may not completely eliminate the etiology i.e. dysbiotic microbiota and dysregulated inflammation. Host modulation therapy as an adjunct to conventional therapy reduce the destructive effect of host inflammatory response.

Vitamin C is a strong antioxidant & anti-inflammatory agent.^[1] The role of vitamin C in maintaining periodontal health has been cited in the literature.^[2] Hence, this study aimed to investigate the efficacy of mesotherapy using vitamin C for the treatment of persistent gingival inflammation.

Subjects and Methods:

Patients were chosen for recruitment following the inclusion and exclusion criteria after being referred to the Department of Periodontology and Implantology. The verbal and written informed consent were taken from all the participants. The institutional ethics committee granted ethical approval for the study with Project No. 03/01/2023(Ver. 2.0).

Inclusion criteria:

(1) Age group ≥ 18 years (2) Systemically healthy and (3) Diagnosed with plaque-induced gingivitis.

The subsequent patients were not included in the research: (1) Individuals with underlying medical illness, (2) Pregnant/lactating women, (3) Those who had undergone treatment with antibiotics within 1 month before the study, (4) Presence of other factors (smoking, mouth breathing, and local trauma), (5) Patients who are taking nutritional supplements.

The full mouth scaling and root planing (SRP) procedure was performed with the use of ultrasonic scalers. Oral hygiene instructions

were given. Patients were advised to use mouth rinse twice a day for two weeks with 0.2% chlorhexidine gluconate mouthwash. All patients were placed on 4-week maintenance recall appointments. Following the 4-week maintenance phase, the trial was limited to patients with persistent gingival inflammation and a plaque score of less than 15%.

The same examiner carried out each injection procedure. 1:200,000 lidocaine-adrenaline was used to anesthetize the affected area.

Insulin syringes were used to inject 0.1 mL (150 mg concentration) of vitamin C (Figure 1) into the keratinized gingival tissues at the epithelium-connective tissue junction (equivalent to epidermal-dermal junction) till the tissues blanch (Figure 2). If required, the patient was provided 200 mg of ibuprofen (as and when required) as an analgesic after each session.

After one week, the same dosage was given again until the inflammation had significantly decreased. The patient was then reassessed after an additional week. The final evaluation of the patient was performed one week following the second injection.

Measurements were taken before the injection process, as well as one and two weeks later, for the Plaque Index (PI) and the Sulcus Bleeding Index (SBI).^[3,4]



Figure-1 Armamentarium



Figure-2 Procedure

RESULTS:

A total of 30 patients with persistent gingival inflammation gave consent for the study. Out of 30 patients, 10 were males and 20 were females. The average age was 30.33 years. All the enrolled patients completed the entire follow-up period.

Improvement in inflammation was seen in all cases after two injections (Figure 2).

The intragroup comparison for baseline to 1 week ($P < 0.05$) (Figure-4) and baseline to 2 weeks ($P < 0.05$) (Figure-5) shows a significant reduction in plaque index score and sulcus bleeding score in all patients.

(I) Table -1 Intragroup comparison of PI and SBI from baseline to 1 week

	BASELINE		1 WEEK		P VALUE
	MEAN	SD	MEAN	SD	
PLAQUE SCORE(PI)	1.266	0.45	1.110	0.31	0.0960
SULCUS BLEEDING INDEX(SBI)	3.377	0.72	1.730	1.14	0.0001

(II) Table-2 Intragroup comparison of PI and SBI from baseline to 2-week

	BASELINE		2 WEEK		p VALUE
	MEAN	SD	MEAN	SD	
PLAQUE SCORE(PI)	1.266	0.45	1.000	0.00	0.0029
SULCUS BLEEDING INDEX(SBI)	3.377	0.72	1.100	0.84	0.0001

(III) Table-3 Intragroup comparison of PI and SBI from 1 week to 2 week

	1 WEEK		2 WEEK		P VALUE
	MEAN	SD	MEAN	SD	
PLAQUE SCORE(PI)	1.110	0.31	1.000	0.00	0.0831
SULCUS BLEEDING INDEX(SBI)	1.730	1.14	1.100	0.84	0.0001

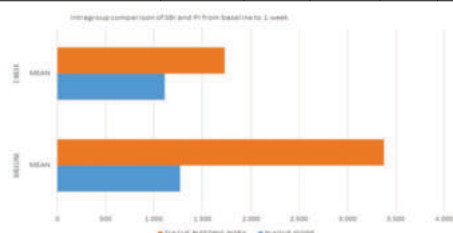


Figure-3 Intragroup comparison of SBI and PI from baseline to 1 week

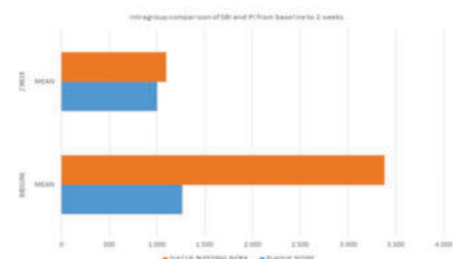


Figure-4 Intragroup Comparison of SBI and PI from baseline to 2 weeks

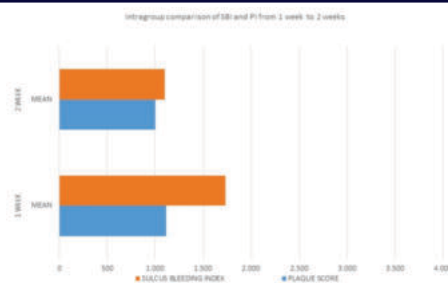


Figure-5 Intragroup Comparison of SBI and PI from 1 week to 2 weeks

All treatment sites exhibited uneventful healing without any complications. All the treated patients responded effectively to the treatment and showed satisfaction with the results. None of the patients reported adverse side effects or the need to use the rescue analgesic.

DISCUSSION:

This study was designed to determine the possible anti-inflammatory effect of vitamin C using mesotherapy, which is a minimally invasive approach for the treatment of persistent gingival inflammation as studied by Mammucari M et al. in 2011.^[5]

Persistent inflammation identified by persisting redness, bleeding on probing, and varying grades of tissue edema that can be diffuse or localized persists even with the elimination of the local etiologic factors and reinforcement of oral hygiene.

Results from this clinical study demonstrated a significant reduction of gingival inflammation in the locally injected area. Improvement was seen in color, contour, consistency, Sulcus bleeding index score, and plaque score.

Ascorbic acid (AA), often known as vitamin C, is a highly labile substance that is abundant in nature. It is a water-soluble vitamin that is significantly lost during the preparation of food. AA plays a significant role in crucial metabolic processes and is essential for the development and maintenance of healthy bones, teeth, gums, ligaments, and blood vessels. For healthy persons, the recommended daily intake of AA is 40–60 mg.^[6]

Vitamin C performs a variety of biochemical processes, including the stimulation of certain enzymes, collagen synthesis, hormonal activation, antioxidant activity, histamine detoxification, leukocyte phagocytosis, production of nitrosamine, and proline hydroxylation. Vitamin C performs a variety of biochemical processes, including the stimulation of certain enzymes, collagen synthesis, hormonal activation, antioxidant activity, histamine detoxification, leukocyte phagocytosis, production of nitrosamine, and proline hydroxylation.^[7] The gene for gulonolactone oxidase, the final enzyme in the AA production pathway, has undergone mutations that render it non-functional making it an essential vitamin for humans.⁷ Therefore, humans get this vitamin from their diet or from vitamin supplements. It is a necessary nutrient for the manufacture of collagen, L carnitine, and the transformation of dopamine into norepinephrine.^[8]

Vitamin C can improve tissue healing and influence the attenuation of the inflammatory process. In cells, this vitamin serves as an antioxidant, reducing agent, and scavenger of free radicals.^[9]

It stimulates the production of Type I collagen that would have been reduced due to inflammation and alters the rate of growth of fibroblasts, diminishes scarring by preventing fibrosis and crosslinking between collagen fibers.^[10] It functions as a cofactor in the synthesis of hydroxyproline which forms collagen and enhances the vitality and function of endothelial cells. It is necessary for post-translational hydroxylation of proline and lysine residues. Hydroxyproline and hydroxylysine are essential for the formation of cross-links in the collagen fibers.^[11]

An optimal level of ascorbic acid is apparently required to maintain the integrity of the periodontal microvasculature as well as the vascular response to bacterial plaque and wound healing.^[1]

Although vitamin C is safe, it remains a weak acidic product which

may result in tissue necrosis if given an extra dose. The mucogingival junction, areas of thin gingival biotype, and gingival tissues without underlying bone loss are the most critical regions. So, care should be taken while administering vitamin C in these areas.^[11]

The reason behind the reduction of gingival inflammation can be due to the strong antioxidant effects of vitamin C. There is strong evidence linking reactive oxygen species to the pathological destruction of the connective tissue during periodontal disease. Studies done by Tada A et al. in 2019 have shown that this effect can be inhibited by exogenously added antioxidants.^[11]

Similar results were observed in a study conducted by Yussif et al. in 2016 where vitamin C was locally injected into the keratinized gingiva to treat gingival inflammation.^[12]

Another study done by Brahmavar B in 2021 showed that local injections of vitamin C can resolve resistant gingival inflammation by a hundred percent.^[13]

Daniels A, Jefferies S, and Shimabukuro Y. in 2015 Studied the effects of an ascorbic acid-derived dentifrice in patients with gingivitis and concluded that regular application of an APM (Ascorbic acid -2-Phosphate magnesium salt) containing dentifrice could reduce gingival inflammation.^[14,15]

Vitamin C has various biological and pharmaceutical functions. It inhibits melanin synthesis by inhibiting the catalytic activity of tyrosinase, the rate-limiting enzyme required for melanin biosynthesis. It is widely used in dermatology as a treatment modality for depigmentation of hyperpigmented spots on the skin. It has also been used for the treatment of gingival melanin hyperpigmentation.^[16] A systematic review carried out by Akio Tada et al. in 2019 concluded that improved gingival parameters were observed after vitamin C supplementation.^[11]

Some studies have investigated the effect of vitamin C supplementation on gingivitis previously but found minimal effect.^[2] However, administration of high systemic doses is required for adequate doses to be reached at the region of localized inflammation, which can be detrimental to patients. The required doses can be provided effectively by local intramucosal injections.

According to past research by Daniels et al. and Shimabukuro et al., the local injection of vitamin C is more advantageous than topically applied vitamin C dentifrice or gel.^[14,15] This is because the injection of vitamin C is water soluble and has a superficial penetrating effect.

The disadvantages associated with topical Vitamin C were prolonged time for noticeable improvement, lack of substantivity on the oral soft tissues, reduced absorption, and localized erosions of enamel.^[14,15]

Vitamin C is available in the market in a variety of creams, serums, and transdermal patches. It is unstable and in a nearly colorless state. Vitamin C, when exposed to heat, light, or air, gets oxidized to dihydro-Ascorbic acid, which is a reversible reaction, and subsequently to 2,3-diketo-L-gulonic acid. The latter reaction is irreversible and imparts a yellow color thereby resulting in loss of its physiological properties.^[16]

Several anti-inflammatory agents have been considered for use as host modulation therapy including corticosteroids, disease-modifying antirheumatic drugs, antibiotics, and non-steroidal anti-inflammatory drugs. Some of these drugs when used for prolonged periods tend to reduce gingival inflammation. However, a high rate of side effects was associated with prolonged use and hence their use is not recommended.^[17]

Therefore, safer nonsurgical remedies to treat such conditions or, at least, enhance tissue healing and decrease the signs and symptoms of inflammation before surgical procedures are required.^[18]

In this study, significantly reduced gingival inflammation was observed with no adverse events related to any of the doses of Vitamin C. Greater antioxidant doses, such as Vitamin C, are necessary because inflammation causes a rapid decline in tissue antioxidant levels, which increases the production of free radicals at the site. Antioxidants that share electrons with free radicals help to stabilize them.^[18]

These observations and other studies led researchers to realize that host response to bacterial challenge is the most important determinant of disease severity, progression, and response to therapy. Therefore, there is a need for other safer host-modulating agents to control or improve tissue healing and reduce inflammatory manifestations.

Histological assessment of resolution of inflammation was not done, short-term follow-up, and small sample size are some limitations of the study.

CONCLUSION:

Vitamin C has a synergistic interaction with scaling and root planing in the treatment of persistent inflammation of the gingiva. To confirm these findings, more research with longer follow-up periods is advised.

Acknowledgment: NIL

Key Messages:

Local application of vitamin C can be used as an adjunct to scaling and root planing for the treatment of gingival inflammation as it has antioxidant and anti-inflammatory properties.

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