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ANTIOXIDANTS IN THE HEALING OF POST PERIODONTAL FLAP SURGERY- A POST-SURGICAL CLINICAL TRIAL

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ABSTRACT

Introduction: Periodontitis is an inflammatory condition that results due to the loss of the critical balance between the virulence factors produced by microorganisms and the inflammatory host response. Antioxidants scavenge free radicals and prevent the damage caused by them. Ubiquinol (reduced form coenzyme Q10) serves as an endogenous antioxidant which increases the concentration of CoQ10 in the diseased gingiva and effectively suppresses advanced periodontal inflammation. **Objective:** This study aims to assess and compare clinically the wound healing after periodontal surgery in patients undergoing antioxidant therapy. **Methodology:** A total of 40 patients with chronic periodontitis who were required to undergo periodontal flap surgery between the age group of 25-45 years were enrolled for the study and grouped as follows: (i) Group I: (20 patients) antioxidant capsules were administered to the patients post periodontal flap surgery (twice daily for a week) and (ii) Group II: (20 patients) placebo capsules were administered to the patients post periodontal flap surgery. Wound healing was assessed on the 7th day using: Early wound index (Wachtel et al.), Wound evaluation scale, Wound Healing Index (Landry, Turnbull and Howley) and Visual analogue scale (VAS). **Result and Conclusion:** The scores of the indices showed significant reduction of gingival inflammation and pain along with better wound healing post periodontal flap surgery with the

use of Coenzyme Q10 oral supplements. Antioxidants may have beneficial effects on functional mechanisms regulating fibroblast migration and proliferation during gingival healing and periodontal repair.

KEYWORDS: Antioxidants, Coenzyme Q10, Periodontal flap surgery, Wound healing.

INTRODUCTION

Periodontitis is an inflammatory condition that results from the complex interactions and loss of critical balance between the virulence factors produced by microorganisms and the inflammatory host response.[1] There is suggestive evidence indicating that periodontal inflammation might be associated with systemic oxidative stress.[2]

The discovery of the role of free radicals in cancer, diabetes, cardiovascular diseases, autoimmune diseases, neurodegenerative disorders, aging, and other chronic diseases has led to a medical revolution comprising of various antioxidants that is promising a new paradigm of healthcare.[3] Antioxidants are defined as those substances which when present at low concentrations, compared to those of an oxidizable substrate, will significantly delay or inhibit oxidation of that substrate. Basically, antioxidants scavenge free radicals and prevent the damage caused by them.

The various mechanisms of tissue destruction by reactive oxygen species (ROS) include lipid peroxidation, DNA damage, protein damage, oxidation of important enzymes, and the release of pro-inflammatory cytokines by monocytes and macrophages.[4]

Ubiquinol (reduced form coenzyme Q10) serves as an endogenous antioxidant which increases the concentration of CoQ10 in the diseased gingiva and effectively suppresses advanced periodontal inflammation. Littaru and Henson have demonstrated the deficiency of CoQ10 in the gingival tissues of periodontitis subjects.[5] For the maintenance of optimal conditions and for the improvement of oral health, the introduction of adjunctive nutritional therapy is necessary. Coenzyme Q10 (CoQ10) had a favourable effect on the endothelium of the blood vessels when it was administered at a dose of 30mg daily.[1]

Wound healing monitoring is an important concern in all surgical procedures since it allows to identify signs or/and symptoms possibly related to surgical complications. However, no indications have been comprehensively reported on how wound healing monitoring should be performed after flap surgeries.[6]

Currently there are very few interventional studies in human periodontitis to substantiate clinical therapeutic benefit of CoQ10.

Hence, the present study was designed to evaluate the wound healing effect of antioxidant supplementation, and their effects in the wound healing process after periodontal flap surgery and to elucidate any associated changes in periodontal health.

MATERIALS AND METHODS

The study subjects comprised 40 periodontitis patients (23 males and 17 females, aged 25-45 years) who visited the Department of Periodontology, Rajarajeswari dental college and hospital. The criteria for inclusion in the study were patients diagnosed with chronic generalized periodontitis with 5-7mm probing pocket depth with at least 18 remaining teeth, that require periodontal flap surgery and systemically healthy patients. The exclusion criteria were patients allergic to antioxidants, pregnant and lactating women, smokers, presence of diabetes mellitus, chronic kidney diseases or disorders affecting wound healing, use of aspirin or other non-steroidal anti-inflammatory drugs or antibiotics within the previous 6 months of the study.

This study was approved by the ethical committee of Rajarajeswari dental college and hospital (RRDCHET/03/PERIO/2018). All patients provided written informed consent to participate in the study. The study was an interventional trial in which the 40 patients were randomly assigned by using a random number table method with no restriction. The dentist allocated the patients right after the surgery either to an intervention group, each member was provided with antioxidant capsules*(CoQ10) to consume twice daily over 7 days period after periodontal flap surgery (n=20), or to a control group, to which placebo capsules were provided (n=20).

Blinding was also ensured as one investigator administered the capsules while evaluation of results was done by a separate investigator who was unaware of the intervention given to the test groups.

**Recharje plus CoQ10 capsules*

Assessments

All the patients underwent scaling and root planing before the periodontal flap surgery and were instructed on the causes and consequences of periodontal disease and were shown how

to perform oral hygiene practices. Upon completion of the flap surgery under strict aseptic condition, the intervention and control group consumed the antioxidant and placebo capsules respectively, twice daily for 7 days. Visual analog score (VAS) for pain was recorded using patient self assessed reports (Scored 0-10) and the wound healing indices was recorded on the 7th post-operative day.

Early wound healing index (Wachtel et al. 2003) was recorded and scored from 1-5 as follows 1: complete flap closure – no fibrin line in the interproximal area 2: complete flap closure – fine fibrin line in the interproximal area 3: complete flap closure – fibrin clot in the interproximal area 4: incomplete flap closure – partial necrosis of the interproximal tissue 5: incomplete flap closure – complete necrosis of the interproximal tissue.[7]

Wound Healing index (by Landry, Turnbull and Howley)- healing was estimated with a 5 level score index evaluated with the following 4 parameters: tissue color, response to palpation, granulation tissue, and incision margin (table 1).[8]

Table 1: Wound Healing index (by Landry, Turnbull and Howley).

Healing index	Tissue colour	Bleeding on palpation	Granulation tissue	Incision margin	Suppuration
1- Very Poor: 2 or more signs are present	≥ 50% of red gingiva	yes	yes	not epithelialized, with loss of epithelium beyond incision margin	yes
2- Poor	≥ 50% of red gingiva	yes	yes	not epithelialized, with exposed connective tissue	no
3-Good	25 - 50% of red gingiva	no	no	no exposed connective tissue	no
4-Very Good	< 25% of red gingiva	no	no	no exposed connective tissue	no
5-Excellent	all pink tissues	no	no	no exposed connective tissue	no

Wound evaluation scale (Hollander)

The wound evaluation scale (WES) addresses 6 clinical variables, each one with a 1/0 (not present/present) score for a maximum total score of 6: step-off borders, contour irregularities (puckering), wound margin separation greater than 2 mm, edge inversion (sinking, curling), inflammation (redness, discharge), and overall cosmetic appearance (well/not well). A

scoring of 6/6 indicates optimal wound healing whereas a score of ≤5 indicates sub-optimal healing.[9,10]

Statistical analysis

Statistical analyses were performed using the Statistical Package for Social Science-SPSS for window version 18.5 (SPSS Inc. Chicago, IL, USA) software. Univariate analyses of the dichotomous variables encoded was performed by means of the Chi square test. The student 't' test was used to determine whether there was a statistical difference between pre-term and term groups in the parameters measured. P value of less than 0.05 was accepted as statistical significant.

RESULTS

Demographic parameters were similar across both the study groups. The average age of the test group was 35.8 years and of the control group was 37.9 years. The age difference between the two groups was statistically not significant.

Table 2 and Fig. 1 shows the scores for Early wound healing index (Wachtel et al.) This table signifies the frequency distribution of early healing index, with a lesser score of 1 was more at the test site (90%), and more percentage of the control site showed a higher score of 2 (80%). No sites showed scores 3-5.

Table 2, Fig. 1: Results of early wound healing index (Wachtel et al.)

	Early Wound Index		Total	χ^2 value	P value
	1	2			
Group 1	18	2	20	19.798	<0.001
	90.0%	10.0%	100.0%		
Group 2	4	16	20		
	20.0%	80.0%	100.0%		
Total	22	18	40		
	55.0%	45.0%	100.0%		

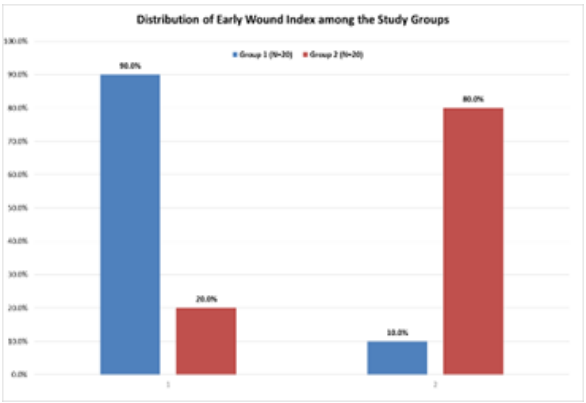


Table 3 and Fig. 2 shows the scores of wound healing index (Landry, Turnbull and Howley) 40% of antioxidants group showed excellent wound healing and 50% showed very good and 10% showed good healing.

Table 3 and Fig. 2: Results of wound healing index (Landry, Turnbull and Howley).

	Wound Healing Index			Total	χ^2 value*	P value
	Good	Very Good	Excellent			
Group 1	2	10	8	20	18.000	<0.001
	10.0%	50.0%	40.0%	100.0%		
Group 2	14	6	0	20		
	70.0%	30.0%	.0%	100.0%		

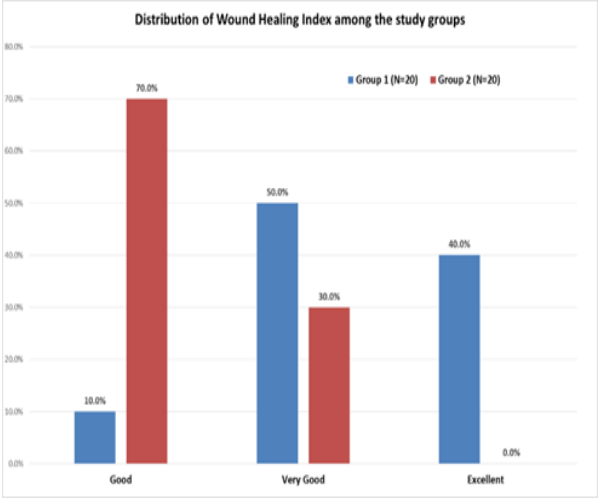
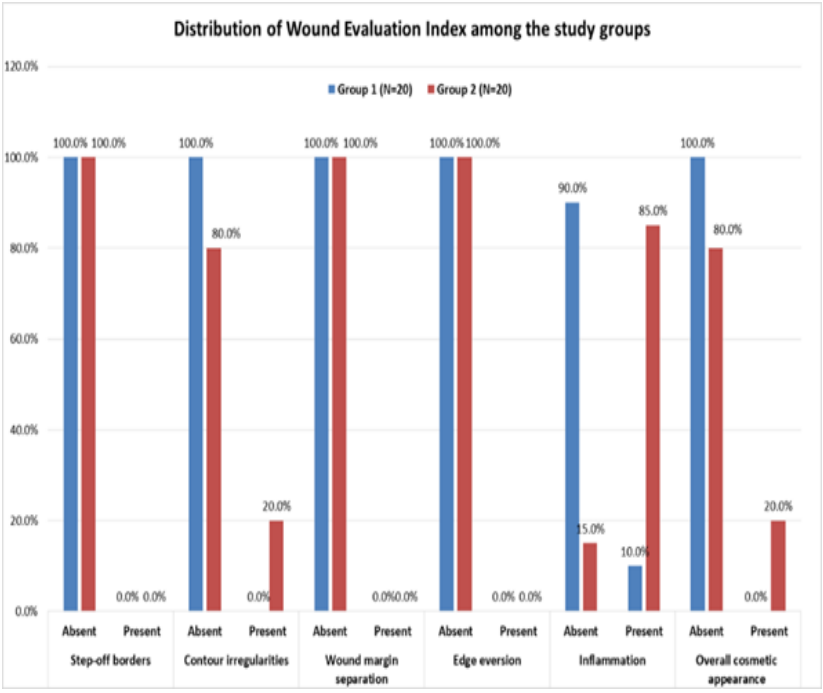


Table 4 and Fig. 3 shows the intergroup comparisons of wound evaluation scale at 1 week follow-up. The step off borders, wound margin separation and edge eversion were absent in both the groups. Only 15% of antioxidant group presented with inflammation whereas 85% inflammation was seen in control group And 20% of the control group showed contour irregularities. The overall cosmetic appearance was better in the antioxidant group and the total score of 90% in the antioxidant group indicates good healing. Most of the group 2 patients showed sub-optimal healing.

Table 4 and Fig. 3: Results of wound evaluation index (Hollander).

		Group 1 (N=20)		Group 2 (N=20)		χ^2 value*	P value
		n	%	n	%		
Step-off borders	Absent	20	100.0%	20	100.0%	-	-
	Present	0	0.0%	0	0.0%		
Contour irregularities	Absent	20	100.0%	16	80.0%	4.444	0.035
	Present	0	0.0%	4	20.0%		
Wound margin separation	Absent	20	100.0%	20	100.0%	-	-
	Present	0	0.0%	0	0.0%		
Edge eversion	Absent	20	100.0%	20	100.0%	-	-
	Present	0	0.0%	0	0.0%		
Inflammation	Absent	18	90.0%	3	15.0%	22.556	<0.001
	Present	2	10.0%	17	85.0%		
Overall cosmetic appearance	Absent	20	100.0%	16	80.0%	4.444	0.035
	Present	0	0.0%	4	20.0%		



The visual analog scale (VAS) pain scores (Table 5) during the postoperative 1 week follow-up period. The scores on the 1st day didn't show any statistical significance between the 2 groups. Since the 2nd day, the control group experienced greater pain throughtout day 7. Pain perception gradually decreased in the antioxidant group.

Table 5: The visual analog scale (VAS) pain scores.

Visit		N	Mean	SD	Min.	Max.	't' value	'p' value
Day 1	Group 1	20	7.4	0.883	6	9	0.758	0.390
	Group 2	20	7.7	0.933	6	9		
Day 2	Group 1	20	5.2	0.834	3	6	26.725	<0.001
	Group 2	20	6.8	1.105	5	9		
Day 3	Group 1	20	3.2	1.196	2	6	66.471	<0.001
	Group 2	20	6.2	1.089	4	8		
Day 4	Group 1	20	1.7	1.418	0	5	94.410	<0.001
	Group 2	20	5.7	1.174	3	7		
Day 5	Group 1	20	1.0	1.191	0	4	125.819	<0.001
	Group 2	20	5.3	1.261	3	7		
Day 6	Group 1	20	0.8	1.196	0	4	91.999	<0.001
	Group 2	20	4.9	1.461	2	7		
Day 7	Group 1	20	0.8	1.070	0	3	57.289	<0.001
	Group 2	20	4.2	1.735	0	6		

DISCUSSION

Owing to the high prevalence of periodontal diseases, investigators have been attracted to research aimed to treat periodontal diseases; however, the treatments are always challenging.

Conventional treatment is focused on reducing the pathogens by standard scaling and root planing, improving oral hygiene, and if needed, periodontal surgery. In addition, host modulatory therapy (HMT) has emerged as a treatment concept that aims to reduce tissue destruction and stabilize or even regenerate the periodontium by modifying or down regulating the host immune response. HMT is systemically or locally delivered pharmaceuticals that are prescribed as a part of periodontal therapy and used as an adjunct to conventional periodontal treatment. The host modulatory agent used in this study is the CoQ10, has shown clinical benefits in the treatment of periodontal diseases.[1]

Even though a lot of indices have been proposed, a ready-to-use assessment system for early wound healing after flap surgery seems to be still missing.[6] There are several specific limitations of the previously described methods like, not all relevant parameters are considered, some of them are excessively comprehensive, some parameters might be difficult to assess objectively, hence multiple wound healing indices were used in this study.

Quinn et al. found that WES and VAS should be used together since it is reliable and sensitive in detecting clinically important outcome measures for wound healing.[11]

Pain perception, a third cardinal sign of inflammation, was not taken into consideration for the evaluation. Although pain is of high clinical importance, this symptom was considered too subjective for a clinical score and could negatively interfere with the objective assessment.[6]

Findings from the studies of Littaru, Henson and Nakamura support that periodontal disease is frequently associated with CoQ10 deficiency.[5] An adequate supply of CoQ10 to cells ensures efficient energy production, tissue oxygenation, and repair of periodontal tissues.[1] Manthena et al. in his study reported significant reduction in gingival inflammation was seen in patients who were put on oral supplements of CoQ 10 after scaling and root planning compared to patients who received only scaling and root planning. Wilkinson et al. reported that patients who recieved oral treatment with a form of CoQ10 showed significant reduction in pocket depth.[5]

Hanioka et al., suggested that the oxygen supply for inflamed gingiva may be increased. Evaluation of the effect of CoQ10 on the oxidative metabolism in gingiva of periodontitis patients using reflectance spectrophotometry suggested that the administration of CoQ10

improves oxygen utilization in the gingival tissue.[5] Denny et al., assessed the antioxidant and anti-inflammatory effects of coenzyme Q10 in 10 non-smoking periodontally healthy volunteers. They found decrease in gingival inflammation and this was hypothesized to have resulted from correction of deficiency of CoQ10 and restoration of the metabolic energy required for the diseased tissue.[12]

Studies have suggested that CoQ10 also exerts anti-inflammatory properties via NFκB1-dependent gene expression. Since it is a common pathway for periodontal inflammation, even this could be the possible mechanism for reduction in gingival inflammation due to CoQ10 supplementation. In patients with chronic periodontitis, therapy with CoQ10 can be included with the oral hygiene for an improved treatment of periodontal diseases.[13]

CONCLUSION

This study showed significant reduction of gingival inflammation and pain along with excellent wound healing post periodontal flap surgery with the use of Coenzyme Q10 oral supplements. Therefore, within the limitations of this study, we can come to a conclusion that CoQ10 supplementation after flap surgery can improve wound healing by reducing gingival inflammation. Further long term clinical trials with histological evidence for the outcomes of topical and systemic administration of CoQ10 are needed to affirm or refute the usefulness of CoQ10 as a therapeutic agent for periodontitis.

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