International Journal Dental and Medical Sciences Research
Volume 6, Issue 5, Sep - Oct 2024 pp 346-355 www.ijdmsrjournal.com ISSN: 2582-6018

Comparative Evaluation of Oxygen Releasing Gel as an Adjunct to Scaling and Root Planing With Scaling and Root Planing Alone In Treatment of Chronic Periodontitis

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Submitted: 10-10-2024 Accepted: 20-10-2024

ABSTRACT:
Background: Periodontitis is a multifactorial disease that impairs the tooth's supporting structures. Periodontal disease is also caused by a local bacterial infection with pathogenic microflora in the periodontal pocket. Gram negative anaerobic bacteria make up the majority of the periodontal disease. Within the affected sulcus or periodontal pocket, the resident anaerobic bacteria interact with the host inflammatory reactions leading to a lower oxygen or hypoxic environment. Under a chronic inflammatory state, hypoxia induces protective cellular responses or a local defence. If the cause of inflammation cannot be eradicated, such hypoxic reactions can be the pathophysiology of inflammation leads to disease progression and pathogenesis of the disease. oxygen releasing gel (blue®m) is centred on the controlled release of topical oxygen. Application of topical oxygen quickly reverse tissue hypoxia in situ. Also, it can kill anaerobic bacteria and enhances immune cells function to address all other pathogens. The increase of local oxygen level in wounded tissues can promote better healing.
Aim: To assess the effect of oxygen releasing gel (blue®m) as local drug agent in the treatment of Chronic Periodontitis.
Materials And Methods: 40 Chronic Generalized Periodontitis Patients with pocket depth of 4 - 6mm. they are grouped in to two. Group I (20)received Full mouth Scaling root planing only, whileGroup II (20) had undergone Full mouth Scaling root planing along with intrapocket application of oxygen releasing gel and periodontal dressing.Periodontal dressing will be removed at the 7th day.Clinical periodontal parameters will be assessed at Baseline,6th week,12th week and 18th week. anti-inflammatory level was assessed by evaluating TNF-α level at base line and 6th week.
Results : The result showed significant reduction ($p<0.05$) in all the clinical parameters. i.e. (SBI), (PPD) (CAL) and TNF-α levels for both the Group I & II. On inter-group analysis, intrapocket application of oxygen releasing gel in combination with SRP showed significantly more reduction for SBI, PPD, CAL and TNF-α in comparison to SRP alone.
Conclusion: Intrapocket application of oxygen releasing gel along with SRP showed significant reduction in all the clinical parameters and TNF-α levels as compared to SRP alone. Hence, it confirmed the potential additive effect of oxygen releasing gel along with SRP.
Keywords: chronic periodontitis, hypoxia, oxygen, oxygen releasing gel

I. INTRODUCTION

Periodontitis is a chronic multifactorial inflammatory disease associated with dysbiotic plaque biofilms and characterized by progressive destruction of the tooth-supporting apparatus. Its primary features include the loss of periodontal tissue support, manifested through clinical attachment loss (CAL) and radiographically

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Volume 6, Issue 5, Sep - Oct 2024 pp 346-355 www.ijdmsrjournal.com ISSN: 2582-6018

assessed alveolar bone loss, presence of periodontal pocketing and gingival bleeding1.

The microbiome in the oral cavity is one of the most complex and diverse human microbiomes, with at least 700 bacterial species identified. Several of these bacteria have important roles in maintaining oral health and normal function. Shifts in the oral microbiota ecology can lead to oral diseases such as caries, gingivitis, and periodontal disease.(2)

Oxidative species, such as Haemophilus, Aggregatibacter, and Neisseriaceae, occupy the oxygen-rich periphery, while anoxic conditions at the biofilm centre allow the growth of pathogenic bacteria like Capnocytophaga, Leptotrichia, and Fusobacterium.(3)

In anoxic periodontal pockets, Gram-negative bacteria (e.g., Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola) dominate the subgingival biofilm, facilitated by protein–protein and lectin-carbohydrate interactions. Bacterial cell signalling and communication play a crucial role in biofilm formation.(3)

The activity of periodontal disease is determined by a complex interplay between the immune system and periodontal pathogens. Alterations in subgingival microbiota have long been associated with the development and progression of periodontitis. In susceptible individuals, perturbations in host homeostasis are induced by changes in the polymicrobial community, with several microorganisms frequently being associated with periodontal lesions.(4)

Gram negative anaerobic bacteria in the subgingival area interact with the host inflammatory reactions leading to a lower oxygen or hypoxic environment. Hence oxygen is an essential molecule for survival.Variations in tissue oxygen needs are attributed to a number of physiological or pathological states(5).

Under a chronic inflammatory state, hypoxia induces protective cellular responses or a local defence. If the cause of inflammation cannot be eradicated, such hypoxic reactions can be thepathophysiology of inflammation leads to disease progression and pathogenesis of the disease(6).

Oxygen is involved in multiple wound healing processes including oxidative killing of bacteria, reepithelialization, angiogenesis, and collagen synthesis(7).

Oxygen has been explored as a therapeutic modality to aid wound healing in either of topical or hyperbaric from to induce healing. Hence Topical oxygen therapy using active oxygen releasing gel mainly focuses to improve wound healing and prevention of dysbiosis(8)

Progression of periodontitis can be assessed by various biomarkers that in present in the saliva.Tumor necrosis factor (TNF) is one such pro-inflammatory cytokine that causes periodontal tissue destruction. TNF is active in 2 forms: TNF-α and TNF-β. TNF-α is produced by the activated macrophages, neutrophils, keratinocytes, monocytes, and mast cells in response to lipopolysaccharides (LPSs).The present study aims to assess the effect of oxygen releasing gel as a local drug agent in the treatment of Chronic Periodontitis. (9)

II. MATERIAL AND METHOD

40 subjects with chronic generalized periodontitis as per AAP international workshop for classification of periodontal diseases, in the age group of 20-50 years with 4-6mm probing pocket depth was selected for the study in the Department of Periodontics and Oral Implantology, Azeezia College of Dental Sciences and Research.An informed consent was taken from all the subjects before the start of the study. The ethical committee of the university was presented the synopsis and a clearance was obtained after their approval.

INCLUSION CRITERIA

1. Patients with chronic periodontitis
2. An age group of 20 – 50 years
3. Both sexes are included
4. Presence of two or more non-adjacent tooth with Probing pocket depth less than or equal to 4 – 6mm

EXCLUSION CRITERIA

1. Subjects who had priorly taken antibiotics or were on antibiotics
2. Medication taken by patients that would induce gingival enlargement
3. Pregnant women or lactating mothers
4. smokers
5. Patients with habit of tobacco chewing 6. Diabetic patients and immunocompromised patients.

CLINICAL PROCEDURE

After proper case recording, the eligible and selected patients who gave their consent were assigned into two groups randomly. All patients received oral hygiene instructions. Full-mouth oral prophylaxis was done. Intraoral and extraoral antisepsis was achieved using the povidone-iodine solution. After administering local anesthesia (2%

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lignocaine HCl in the ratio of 1:80,000) and achieving profound anesthesia, in Group I, scaling and root planing, whereas, in Group II, scaling and root planning intrapocket application of oxygen releasing gel (Blue-M) and periodontal dressing. All subjects were recalled, Periodontal dressing will be removed onthe 7th day. Clinical periodontal parameters assessed at Baseline,6th week,12th week, and 18th week. saliva samples were collected at baseline and 6th week for evaluation of TNF-α levels.

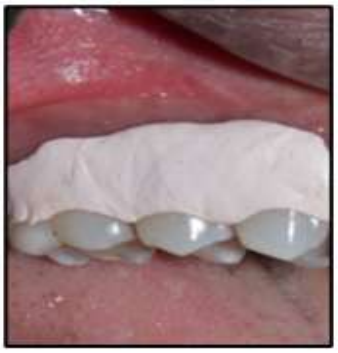
LAB INVESTIGATION

Saliva collection will be completed before clinical periodontal measurements and/or any dental/periodontal intervention in the morning between 09:30 and 10:30 h, and patients will be instructed not to brush their teeth or eat or drink anything except water for up to 1 hr before sampling. A total of 4–5 ml of unstimulated saliva will be collected using passive drool collection method (Oski's et al 2009). The samples will then be frozen and stored at ≤ 20°C until thawed in the laboratory immediately before assaying. Saliva will be centrifuged at 1000 g for 15 min at 2-8°C, and the supernatants will be collected. The total amounts of TNF-α in the samples will be analysed by sandwich enzyme-linked immunosorbent assay using commercially available kits. The standard detection limits of TNF-α assays, as reported by the manufacturer, ranged from a minimum of 15.63-1000 pg/ml.In this study, primary variables will be the changes in TNF-α levels following oxygen releasing gel application. Samples will be collected at baseline and 6th week of recall

OUTCOME MEASUREMENTS:

Periodontal Clinical Parameters:

1. Sulcus bleeding index, Muhleman and Son
2. Probing pocket depth (PPD): It is measured from the crest of gingival margin to the base of the pocket.
3. Clinical attachment level (CAL): It is the distance between a fixed point on the crown such as cemento-enamel junction (the level at which gingiva attached to the tooth) to the base of the pocket



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STUDY METHOD:

Subjects with chronic generalized periodontitis as per AAP international workshop for classification of periodontal diseases, in the age group of 20-50 years.

40 Chronic Generalized Periodontitis Patients with pocket depth of 4 - 6mm.

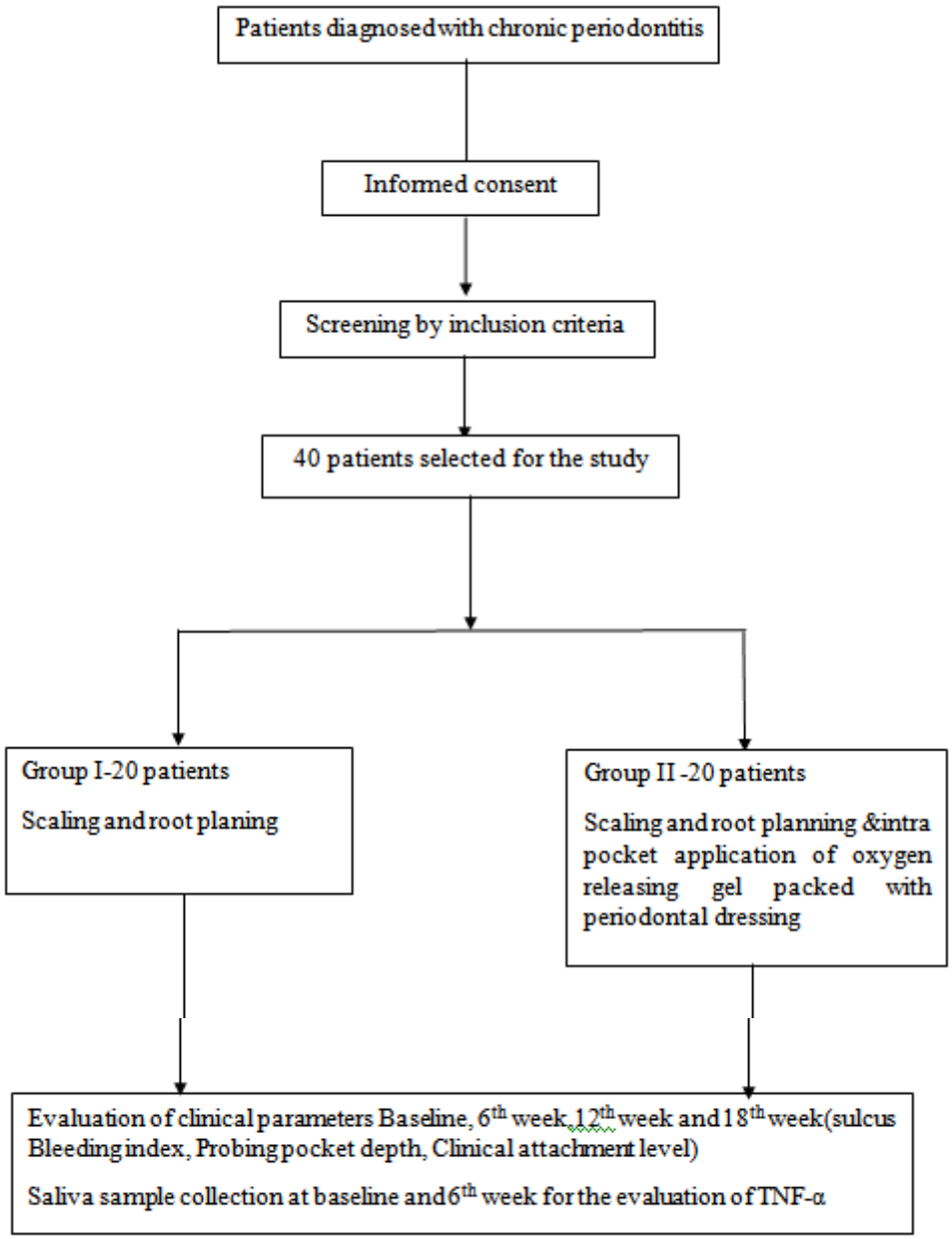
Grouped into two:

Group I (20): Full mouth Scaling root planing only

Group II (20): Full mouth Scaling root planing, intrapocket application of oxygen releasing gel and periodontal dressing. Periodontal dressing will be removed at the 7th day.

Clinical periodontal parameters will be assessed at Baseline,6th week,12th week and 18th week. Saliva sample collection will be done at baseline and 6th week.

FLOWCHART SHOWING STUDY DESIGN



III. RESULTS

A total of 30 patients were included in the study.

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Volume 6, Issue 5, Sep - Oct 2024 pp 346-355 www.ijdmsrjournal.com ISSN: 2582-6018

Table 1 shows comparison of mean SBI between the test and control group at baseline ,6th week,12th week and 18th week with significant results in test group compared to the control groups.

Table 2 shows comparison of mean pocket probing depth between test and control groups at baseline, 6th week ,12thweek, and 18thweek. in control group the baseline value was 2.74 that was reduced to 1.43.in test group baseline value was 2.76, that reduced to 1.22. significant results in test group compared to the control groups

Table 3 shows comparison of mean clinical attachment loss between test and control group at baseline ,6th week,12th week and 18th week .in control group the base line value was 6.22 which reduced to 4.92 at 18 th week follow up.in the test group the value was reduced from 6.08 to 4.05. significant results in test group compared to the control groups

Table 4 shows comparison of TNF-α between the test and control groups at baseline and 6 th week.in control group value was reduced from 44.94 to 29.06.in test group the level TNF-α was reduced from 46.82 to 29.06.

TABLE 1 comparison of mean SBI between the test and control group

Time period-	Groups	N	Mean	Std. Deviation	t value	p value
Baseline	Group I (SRP)	20	2.74	0.57	-0.098	0.92
	Group II (SRP+bluem)	20	2.76	0.48		
6th week	Group I (SRP)	20	1.67	0.43	1.71	0.092
	Group II (SRP+bluem)	20	1.46	0.31		
12th week	Group I (SRP)	20	1.43	0.43	4.89	**0.001***
	Group II (SRP+bluem)	20	0.73	0.44		
18th week	Group I (SRP)	20	1.22	0.41	5.21	**0.001***
	Group II (SRP+bluem)	20	0.66	0.23		

#independent t test; * statistically significant p<0.05

TABLE 2comparison of mean pocket probing depth between test and control

Time period-	Groups	N	Mean	Std. Deviation	t value	p value
Baseline	Group I (SRP)	20	5.58	0.54	2.21	**0.03***
	Group II (SRP+bluem)	20	5.27	0.33		
6th week	Group I (SRP)	20	5.03	0.33	11.04	**0.001***
	Group II (SRP+bluem)	20	3.99	0.24		
12th week	Group I (SRP)	20	4.76	0.22	11.85	**0.001***
	Group II (SRP+bluem)	20	3.89	0.27		
18th week	Group I (SRP)	20	4.24	0.30	9.90	**0.001***
	Group II (SRP+bluem)	20	3.49	0.15		

Table3: Comparison of Clinical Attachment Level between the groups

Time period-	Groups	N	Mean	Std. Deviation	t value	p value
	Group I (SRP)	20	6.22	0.47	0.66	0.51

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Baseline	Group II (SRP+bluem)	20	6.08	0.77		
6th week	Group I (SRP)	20	5.73	0.37	5.81	**0.001***
	Group II (SRP+bluem)	20	5.06	0.34		
12th week	Group I (SRP)	20	5.37	0.16	10.64	**0.001***
	Group II (SRP+bluem)	20	4.68	0.23		
18th week	Group I (SRP)	20	4.92	0.23	14.11	**0.001***
	Group II (SRP+bluem)	20	4.05	0.14		

#independent t test; * statistically significant p<0.05

Table4-Comparison of TNF-α Level between the groups

Time period-	Groups	N	Mean	Std. Deviation	t value	p value
Baseline	Group I (SRP)	20	44.94	2.54	-2.35	**0.02***
	Group II (SRP+bluem)	20	46.82	2.53		
6th week	Group I (SRP)	20	29.06	1.40	3.42	**0.001***
	Group II (SRP+bluem)	20	26.65	2.82		

#independent t test; * statistically significant p<0.05

IV. DISCUSSION

Periodontitis is a multifactorial disease that impairs the tooth's supporting structures. Periodontal disease is also caused by a local bacterial infection with pathogenic microflora in the periodontal pocket(10).

Gram negative anaerobic bacteria make up the majority of the periodontal disease(11). Due to the colonization by subgingival biofilm, oxygen is persistently consumed to various extents by the facultative anaerobic microbes within the periodontal sulcus (2.33–8.40 kPa). In the gingivitis-affected sulcus or periodontal pocket, the inflammation induced by the residential anaerobic bacteria with or without microulcerations or wounding leads to an even lower oxygen tension(12). Local hypoxia in periodontitis in turn enhances the anaerobic gram-negative pathogens' survival and further lowers the oxygen tension at the vicinity(13). The tissue hypoxia in periodontal disease has been characterized by increased HIF-1α protein(14). Hypoxia further encourages lip polysaccharide (LPS)-induced TNF-α, interleukin-1β, and interleukin 6 (IL-6) expressions (15).

Nonsurgical therapy is the first line of defence against periodontal infection. However, mechanical therapy itself may not always reduce or eliminate the anaerobic infection at the base of the pocket, within the gingival tissues, and in structures inaccessible to periodontal instruments(16). Although mechanical removal or disruption of subgingival biofilms by srp is usually an effective therapeutic approach, it does not sterilize the subgingival environment. Almost immediately after srp, bacteria left behind begin to recolonize the subgingival environment to form a new biofilm(17)

The utilization of oxygen therapy in medicine has been common place for nearly a century. Its application as a treatment for hypoxemia was discovered by Joseph Priestley in 1774. Oxygen therapy has been in use for almost a century and can be administered either systemically

or topically. Topical oxygen oral therapy (TOOTh) aims to improve wound healing in the oral cavity and control microbial dysbiosis.(3)

Recently, Dr Peter Blijdorp and his research group developed a novel topical oxygenating formula. Clinically, the blue®m formula (blue®m, Wapenveld, Netherlands) is administered intra-orally to prevent the growth of biofilms causing oral infections.(3)

The aim of the present study was to assess the effect of oxygen releasing gel as a local drug agent in the treatment of Chronic Periodontitis. The study population consists of forty patients grouped into two. Group I scaling and root planning alone, Group II scaling and root planning adjunct to oxygen releasing gel. The clinical parameters such as bleeding index, probing pocket depth, and clinical attachment level were recorded in the baseline,6th week, 12th week, 18th week and salivary TNF-α level were recorded in the baseline and 6th week

To evaluate gingival inflammation sulcus bleeding was recorded. The sulcus bleeding index (Muhlemann HR & Son S 1971) revealed scores of (2.74 ± 0.57) and (2.76±0.48) in group I and in group II respectively. On intergroup comparison, this difference was statistically non-significant (p value-0.92). At the 18 th follow up week sulcus bleeding index score were reduced to (1.22±0.41) in group I and (0.66±0.23) in group II. This difference was statistically significant (p-value = 0.001).

The intragroup comparison revealed a statistically significant difference at the 6th week, 12th week, 18th week follow up respectively from baseline in both groups. (p value <0.001). However, the results were highly significant in group II compared to group I. This reduction in bleeding from gingiva especially for group II could be attributed to the additional use of oxygen releasing gel. The following explanation may be attributed for the reduction ofgingival inflammation.

Use of oxygen releasing gel increase in oxygen tension in the tissue, accelerating the reduction in microorganisms, makes local defense mechanisms more effective and encourages regenerative processes. As a consequence, the acute inflammation can be brought under control more quickly(18). Elevating local oxygen levels in wounded tissues can promote more effective healing (3).it has been reported that persistence of anaerobic organisms in periodontal pocket is reported to have a highly significant relationship with bleeding on probing(19).Oxygenreleasing gel releases oxygen, as its small molecular size enables the active oxygenmolecule to penetrate the plaque biofilm and prevents adhesion of primary colonizer bacteria,thereby inhibiting colonies causing gingivitis and periodontitis(20). It has been demonstrated that asignificant shift in microbial composition toward a homeostasis state of biofilm after applyingoxygentherapy(3).Topically applied oxygen releasing gel has antibacterial and anti-inflammatory property as well as it induces VEGF and promote angiogenesis(21)

Study conducted by Tatiana Miranda Deliberador et al(2020) compared the effects of the oxygen gel blue®m in vitro on Porphyromonas gingivalis, blue®m at higher concentrations provided inhibitory effecton Porphyromonas gingivalis(22).

Periodontal probing depth was evaluated, and there was an improvement seen in terms of reduction in probing depth from 5.27 to 3.49 for group II as compared to group I where the reduction was from 5.58 to 4.24. Statistically significant reduction is seen in group II when compared to group 1 in each time point.The intragroup comparison revealed a statistically significant difference at the 6th week ,12th week, 18th week follow up respectively from baseline in both groups. (p value <0.001). However, the results were significant in group II compared to group I

Studies have demonstrated that there is an inverse relationship between probing pocket depth and pocket oxygen tension (23).The adjunctive use of oxygen releasing gel is centred on the controlled release of topical oxygen. The low, stable, and safe concentration of hydrogen peroxide gradually release active oxygen without generating hydroxyl radicals with in the ulcered pocket epithelium. The release of both oxygen and lactoferrin from the oxygen releasing gel increases cellular metabolism, enhances collagen and epithelium synthesis, facilitates the release of growth factors, stimulates angiogenesis, and impedes the growth of pathogenic bacteria, exerts bactericidal action and promote the healing process(3)

The results obtained in this study are in conjunction with other studies by Niveda et al, Claudio et al,Basudan et al.

Niveda et al(2020) conducted a study where significant reduction in probing pocket depth in patients with chronic periodontitis treated with blue®m oxygen therapy, confirming its clinical advantage on periodontitis (8)

In a randomized controlled clinical trial by Claudio et al (2023)it was shown that the adjunctive application of blue®m gel directly within the periodontal pocketsled to a statistically

significant decrease in bleeding on probing and pocket depth. (24)

The study by Basudan et al (2024) have highlighted that adjunctive topical oxygen-based therapy in treatment of patients with gingivitis and periodontitis showed significant reduction in pocket probing depth and bleeding on probing.The results obtained in this study may also be attributed to the adjunctive use of oxygen releasing gel.(20)

The intergroup comparison of mean change in Clinical attachment level showed significantly improvement in group II (4.05±0.14) followed by group I (4.92±0.23). The intragroup comparison revealed a statistically significant difference at the 6^{th} week ,12^{th} week, 18^{th} week follow up respectively from baseline in both groups. (p value <0.001). However, the results were significant in group II compared to group I.

Following explanations may be attributed to the results obtained in this study. Topically applied oxygen releasing gel increases the partial pressure of oxygen of the superficial wound tissue and associated with higher VEGF expression. (25).oxygen releasing gel alsoenhances the synthesis of extracellular matrix components, such as collagen and hyaluronan, and stimulates the proliferation and migration of fibroblasts and keratinocytes, resulting in enhanced re-epithelialization.(3)

The intergroup comparison of mean change in TNF α level showed significantly improvement ingroup II (26.65 ±2.82) followed bygroup I (29.06±1.40). The intragroup comparison revealed a statistically significant difference between baseline and 6^{th} week in both groups. (p value <0.001). However, the results were significant in group II compared to group I

Studies have demonstrated that there is an inverse relationship between probing pocket depth and pocket oxygen tension .At the base of untreated periodontal pockets, low level of oxygen is a potent immunomodulatory signal and many inflammatory sites have such low-oxygen tensions generate a proinflammatory response characterized by activation of NF-kB and upregulation of pro-inflammatory genes such as TNF-α. Anaerobic bacteria, commonly found in deep pockets with lowered oxygen tensions, which might modulate the pro-inflammatory response of epithelium to these periodontal pathogens.(26).

The following explanation may be attributed for the reduction ofTNF-α. Theuse of oxygen releasing gel which may rapidly reverse tissue hypoxia in situ. Additionally, it may eradicate anaerobic bacteria and enhance the functionality of immune cells to combat various pathogens(24). Another significant component of oxygen releasing gel is Lactoferrin, a multifunctional glycoprotein which exhibits anti-inflammatory activity that neutralizes overabundant immune response(3).

Results obtained in the present study are in conjunction with other studies, Cl´audio et al (2023), conducted a randomized clinical trial in which the efficacy of blue®m gel as an adjunct therapy, with and without antimicrobial photodynamic therapy, showed a significant reduction in tumour necrosis factor α(TNF-α) levels at the 90-day mark.(27)

Study conducted by Michal Machnicki (1993),in which theeffects of bovine lactoferrin on the serum cytokine levels, significantly lowered the serum concentration of TNF-α. This provides a satisfactory explanation with regard to preventive activity of LF in infection(28).

The present study suggested that intrapocket application of oxygen releasing gel along with SRP can be considered as an effective adjunctive agent in non-surgical periodontal therapy. During the study, ten patients gave highly positive statements in the aspect of subjective feeling of improvement of periodontium condition, which additionally confirmed the effectiveness of applied supporting therapy. No adverse reactions were reported in the present study

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