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The Effect of 2% White Turmeric (*Curcuma zedoaria*) Gel as Adjunctive Therapy of Scaling and Root Planing Treatment towards the Interleukin 6 Level in Chronic Periodontitis

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Abstract : Chronic periodontitis is an infectious disease caused by plaque bacteria that leads to an increasing proinflammatory cytokines Interleukin-6 (IL-6). White turmeric is one of the herbal remedies with anti-inflammatory properties.The objective of this study was to determine the effect of white turmeric gel as adjunctive therapy towards the Interleukin-6 levels in the gingival sulcus fluid after scaling and root planing treatment in chronic periodontitis patients.

Methods : This research was performed with the randomised controlled trial technique and the split-mouth design by analysing the gingival sulcus fluid of 22 chronic periodontitis patients who have pocket with the depth of ≥ 5 mm. The 2% white turmeric gel was applied towards the treatment side on day 0 and day 7. The gingival sulcus fluid was taken on day 0 and day 14 for Interleukin-6 level analysis on both the treatment side and the control side. The Interleukin-6 level was then analysed with the ELISA method. The data obtained were then processed statistically using the Wilcoxon and Mann-Whitney test with the significance values of $p<0.05$.

Results: The results showed a decreasing level of Interleukin-6 both on the treatment side and the control side. The average difference of Interleukin-6 level before and after treatment on the treatment side was 8.807 pg/mL and as much as 1.675 pg/mL on the control side. There was a significant difference in the IL-6 level decrease between the treatment and control side ($p=0.011$).

Conclusion: The 2% white turmeric gel was proven to be effective in decreasing the Interleukin-6 level after scaling and root planing treatment in chronic periodontitis patients.

Keywords : Chronic periodontitis, Interleukin-6 level, White turmeric gel.

Introduction

Chronic periodontitis is a chronic inflammation of periodontal tissue affecting the gingival part and the supportive periodontal structure, preceded by an accumulation of plaque bacteria destroying the periodontal

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ligaments and alveolar bone, followed by the pocket formation, recession, or both.[1,2] Chronic periodontitis induces local and systemic proinflammatory cytokines, and these molecules play an important role in the periodontal tissue and alveolar bone destruction. Interleukin-6 is an interleukin that acts as the proinflammatory and anti-inflammatory cytokine. This type of cytokine is associated with bone destruction in advanced periodontal disease.[2]

Scaling and root planing as periodontal treatment was aimed to heal inflamed tissue, remove pockets, and reduce the number of pathogenic bacteria and its products through the means of mechanical instruments. Complete debridement cannot be done especially in the deep pockets and other areas that are difficult to achieve by mechanical instruments. Such conditions required the administration of additional chemotherapeutic agents in the form of local and systemic antibiotic to suppress or eliminate specific periodontal pathogenic microorganisms as part of periodontal therapy.[3,4]

Topical antiseptics and antibiotics may be used as an additional treatment, especially in the cases of recurrent periodontitis (refractory periodontitis). Tetracycline, metronidazole, amoxicillin and clindamycin are antibiotics recommended as additional treatment. Provision of additional treatment in the form of antibiotics administration both local and systemic, however, have many negative side effects such as toxicity reactions, hypersensitivity and an increasing risk of bacterial resistance.[4,5,6] This is the basis of consideration for using other chemotherapeutic agents as additional treatment in periodontal therapy. One of the herbal ingredients can be used as a natural chemotherapeutic agent with the safe and non-toxic properties is white turmeric (*Curcuma zedoaria*).[7,8]

Curcuma zedoaria, also known as white turmeric, is an ancient herbal remedy belongs to the *Zingiberaceae* family that generally grows in East Asian countries such as Vietnam, India, Bangladesh, Indonesia, Malaysia, and Japan. This plant was able to grow up to one and a half feet or more, and the length of its leaves ranges from eighty centimetres, with the purplish brown colour along the length of the two leaf surfaces.[9,10] Curcumin is a yellow extract with bioactive properties as antioxidant, antibacterial, antiviral, antifungal, analgesic, antiallergic, antiseptic, and anti-inflammatory properties, and thus able to act as a remedy for various diseases.[11,12,13] According to a previous study conducted by Hosadurga et al., 2% of curcumin gel extracted from *Curcuma longa* applied in mice was showed anti-inflammatory effects and showed a reduction in pocket depth and gum inflammation.[14] This study was aimed to analyse the effect of topical application of 2% white turmeric gel (*Curcuma zedoaria*) towards the IL-6 levels as an additional treatment after scaling and root planing in chronical periodontitis patients.

Materials and Methods

The type of this research was randomised controlled trial with the split-mouth design. The subjects of this research were patients who came to the Periodontics Clinic of Dental Hospital of Faculty of Dentistry Universitas Padjadjaran, with inclusion criteria as follows: Patients diagnosed with chronic periodontitis with periodontal pocket depth > 5mm bilaterally; aged over 30 years; and willing to follow the study by signing an informed consent. The exclusion criteria were: Patients with systemic disease; having periodontal treatment six months earlier; and smoking habits. The research design has been approved by the Medical Research Ethics Committee of Faculty of Medicine Universitas Padjadjaran with registration number 0416060542.

The materials used in this research were 2% white turmeric gel made in the Tropical BRC of Bogor Agricultural University. Control and treatment group selection was performed randomly. The treatment group was administered with the scaling and root planning treatment, then applied with 2% white turmeric and periodontal pack. The gel application was repeated on day 7 in the treatment group. The control group was only administered with the scaling and root planing treatment. Measurements of the Interleukin 6 (IL-6) levels were performed before the scaling and root planing treatment and 14 days after. The gingival sulcus fluid was taken using a Sterile Paper Points No. 30, inserted into the deepest pocket for 30 seconds, then put into an Eppendorf tube filled with a 500 µl phosphate buffer solution. The gingival sulcus fluid was taken three times and detected by the ELISA kit (USCN Cloude-Cloune®, USA) with pg/ml as the measurement unit.

White Turmeric Gel Preparation

The white turmeric gel preparation was performed through two stages. The first stage was the manufacture of a viscous extract from the small slices of cleaned white turmeric rhizome. As much as 1 kg of white turmeric rhizome that has been cleaned before was immersed in 1.5 litres of ethanol solution for one week then the ethanol extract and white turmeric was filtered. Afterwards, the evaporation process of the white turmeric and 1.5 litres of ethanol extract was performed to obtained as much as 30 grams of viscous white turmeric extract. The second stage was the preparation of 2% white turmeric gel from the viscous extract. The Carbopol® 934 was immersed in the water for 2 hours then neutralised by with the triethanolamine (TEA). The 2% white turmeric extract was added to the container containing the Carbopol® then stirred for 20 minutes. The mixed solution was then hydrated and expanded for 60 minutes. The final process was adjusting the pH with the 98% TEA until reached the desired pH value of about 6.8 - 7. The mixture then stirred slowly with a spatula during the pH adjustment process to form a homogeneous gel, then the gel was inserted into a syringe.

Statistical analysis

All obtained data were presented in the form of mean ± SD. Differences in the IL-6 levels before and after the scaling and root planing treatment was analysed by the Wilcoxon test and the Mann-Whitney test, with the significant difference (p-value), was $p<0.05$.

Results

The study was conducted towards as much as 22 chronic periodontitis patients consisted of 14 males and 8 females, with the age range was 30-69 years old, and the majority of age was 50-59 years old (41% of all samples), as presented in Table 1.

Table 1.Patients Characteristics

Characteristics	Number (n)	Percentage (%)
Gender		
Male	14	64%
Female	8	36%
Age (yo)	4	18%
30-39	7	32%
40-49	9	41%
50-59	2	9%
60-69		
Tooth amount	22	
Treatment	22	
Control		

Table2.The Average Interleukin-6 Levels on both treatment and control side before and after scaling and root planning treatment

Side	Condition	Mean	$Z_{countable}$	P-value
Treatment	Before	12.493	-4.074	0.000*
	After	3.686		
Control	Before	4.738	-3.880	0.000*
	After	3.063		

Notes: *Significant(p-value <0.05);Wilcoxon test

The average comparison of the Interleukin-6 levels before and after treatment on both treatment and control side was described in Table 2. The IL-6 level on the treatment side before scaling and root planing was 12.493 pg / mL and afterwards was 3.686 pg / mL. The statistical analysis showed that the $Z_{countable}$ value was -4.074, with the p-value = 0.000. The p-value was less than 0.05 meant there was a significant difference in the IL-6 level on the treatment side, before and after scaling and root planing treatment. The IL-6 level on the control side before scaling and root planing was 4.738 pg / mL and afterwards was 3.063 pg / mL. The result of the statistical analysis showed that the $Z_{countable}$ value was -3.880, with the p-value = 0.000. The p-value was less than 0.05 meant there was also a significant difference in the IL-6 level on the control side before and after scaling and root planing treatment.

Table 3.Average Comparison of IL-6 Level Decrease Before and After Treatment on Both Treatment and Control Side

Group	Average	$Z_{countable}$	P-value	Conclusion
Treatment	8.807	-2.535	0.011*	Significant
Control	1.675			

***The Mann-Whitney test result showed significant difference of IL-6 level**

Comparison of the Interleukin-6 levels before and after treatment on both the treatment side and the control side was shown in Table 3. The difference of the IL-6 levels on the treatment side before and after treatment was 8.807 pg / mL and on the control side was 1.675 pg / mL. The results of the statistical analysis towards the IL-6 levels comparison of the treatment and control side before and after treatment was showed that the $Z_{countable}$ value was -2.535, with the p-value = 0.011. The result of the statistical analysis showed that the p-value was less than 0.05. Therefore, it can be concluded that there was a significant difference in the IL-6 level before and after treatment both on the treatment and control side. The mean of the IL-6 decreasing value on the treatment side was higher than the control side.

Discussion

This study was aimed to observe the effect of the topical application of white turmeric gel as adjunctive therapy of scaling and root planing in chronic periodontitis patients, by measuring the Interleukin-6 levels of the gingival sulcus fluid in the deepest pocket (pocket depth of $\geq$ 5 mm). The results obtained were then compared before and after application of white turmeric gel on both on the treatment and control side. After scaling root planing was performed, the topical application of white turmeric gel was only administered to the treatment side.

This research was using 2% white turmeric gel manufactured in the Tropical BRC of Bogor Agricultural University. The gel preparation was performed in two stages; the white turmeric extract preparation and the gel preparation taken from the extract. The results of the research showed that white turmeric contained bisdemethoxycurcumin, demethoxycurcumin, and curcumin. The phytochemical tests also showed that the white turmeric gel has the following content such as flavonoids, alkaloids, saponins, quinones, and triterpenoids, which are known for having the anti-inflammatory properties. White turmeric gel was inserted into a syringe to ease the application into the gingival sulcus. During the study, there were no allergic complaints were found thus the white turmeric gel was biologically acceptable by all of the patients. The patients felt only the bitter taste of the white turmeric.

Chronic periodontitis is an inflammatory disease caused by plaque bacteria that can cause damage to periodontal tissue that can eventually lead to tooth loss. The pathogenesis of periodontitis begins with the body's response to bacteria in the biofilm and the presence of an active proinflammatory mediator when plaque bacteria accumulate on the gingiva. In vivo studies, stated in periodontitis production of proinflammatory cytokines IL-1, IL-6, IL-8, TNF α increased. These cytokines can influence the progression of periodontitis disease as well as become targets in the treatment of chronic periodontitis.[15,16]

The results showed a significant decrease in the Interleukin-6 levels between before and after the initial scaling and root planing treatment both on the treatment and control side. This result was consistent with the study conducted by Atilla and Kutukcuker suggested that the IL-6 levels on the gingival sulcus were higher in gingivitis individuals than in the individual with healthy gingiva.[17]

Scaling and root planing are the initial chronic periodontitis treatment to eliminate the bacteria as the aetiological factors and help the tissue regeneration process. The treatment side applied with the white turmeric gel was shown a more significant decrease in the Interleukin-6 levels than the control side. The results of this study were consistent with an in-vitro study conducted previously by Yanti et al. which stated that curcumin was able to inhibit the IL-6. Yamamoto et al. also stated that flavonoid was able to suppress the NF-kβ expression. Curcumin suppressed the levels of Interleukin-6, TNF-α, and prostaglandin. Curcumin also able to improve the wound healing process by increasing the collagen deposition, angiogenesis, and fibroblasts.[18,19]

Overall, the results of this study showed that on the treatment side with a topical application of the white turmeric gel as adjunctive therapy of the scaling and root planing treatment had a more significant decreasing level of IL-6 compared to the control side. This result proved that white turmeric gel has an anti-inflammatory effect. Curcumin and flavonoids contained in white turmeric also had the antimicrobial, anti-inflammatory, antiallergic, analgesic, anti-hepatotoxic, and cytotoxic effects against cancer cells, and were able to inhibit bacterial growth and cytokines in inflammatory processes.[8,9]

Conclusion

Topical application of white turmeric gel as adjunctive therapy of scaling and root planing was proven to be effective in decreasing the Interleukin-6 levels in chronic periodontitis.

References

1. Nagy RJ, Novak MJ. Chronic Periodontitis. In: Newman MG, Takei HH, Carranza FA. Carranza's Clinical Periodontology. 10th ed. Philadelphia: Saunders-Elsevier; 2006.p.494–9.
2. Silva N, Abusleme L, Bravo D, Dutzan N, Garcia-Sesnich J, Vernal R, et al. Host Response Mechanisms in Periodontal Diseases. J Appl Oral Sci. 2015 May-Jun;23(3):329-55. DOI: 10.1590/1678-775720140259
3. Cobb CM. Non-Surgical Pocket Therapy: Mechanical. Ann Periodontol. 1996 Nov;1(1):443-90. DOI: 10.1902/annals.1996.1.1.443
4. Greenstein G. Local Drug Delivery in The Treatment of Periodontal Disease: Assesing The Clinical Significance of The Results. J Periodontol. 2006 Apr;77(4):565-78. DOI: 10.1902/jop.2006.050140
5. Nandini N, Vidya D, Komal A. Comparative Evaluation of 1% Curcumin Solution and 0,2% Chlorhexidine Irrigation as An Adjunct to Scaling and Root Planing in Management of Chronic Periodontitis: A Clinico- Microbiological Study. J Pharm Biomed Sci. 2012;14(14):1-7.
6. Serrano C, Torres N, Bejarano A, Cavie M, Castellanos Me. Clinical and Microbiological Comparison of Three Non-Surgical Protocols for The Initial Treatment of Chronic Periodontitis. J Int Acad Periodontol. 2011 Jan;13(1):17-26.
7. Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of Local Drug-Delivery System Containing 2% Whole Turmeric Gel Used as An Adjunct to Scaling and Root Planing in Chronic Periodontitis: A Clinical and Microbiological Study. J Indian Soc Periodontol. 2011 Jan;15(1):35-8. DOI: 10.4103/0972-124X.82264
8. Kaushik ML, Jalalpure SS. Anti-Inflammatory Efficacy of Curcuma Zedoaria Rosc Root Extracts. Asian J Pharm Clin Res. 2011;4(3):90-2.
9. Tholkappiyavathi K, Selvan KM, Neyanila SK, Yoganandam GP, Gopal V. A Concise Review on Curcuma Zedoaria. Int J Phytotherapy. 2013;3(1):1-4.
10. Rastogi P, Anand V, Gulati M, Lal N, Dixit J, Singhal R. A Review of Curcumin in Reference to Its Use in Oral Diseases. Ann Ayurvedic Med. 2012;1(4):140-3.
11. Shehzad A, Rehman G, Lee YS. Curcumin in Inflammatory Diseases. Biofactors. 2013 Jan-Feb;39(1):69-77. DOI: 10.1002/biof.1066
12. Guimaraes MR, Coimbra LS, de Aquino SG, Spolidorio LC, Kirkwood KL, Rossa C Jr. Potent Anti-Inflamatory Effect of Systemically Administered Curcumin Modulate Periodontal Disease In Vivo. J Periodontal Res. 2011 Apr;46(2):269-79. DOI: 10.1111/j.1600-0765.2010.01342.x
13. Zhou T, Chen D, Li Q, Sun X, Song Y, Wang C. Curcumin Inhibit Inflammatory Response and Bone Loss During Eksperimental Periodontitis in Rats. Acta Odontol Scand. 2013 Mar;71(2):349-56. DOI: 10.3109/00016357.2012.682092

14. Hosadurga RR, Rao SN, Jose J, Rompicharla NC, Shakil M, Shashidhara R. Evaluation of The Efficacy of 2% Curcumin Gel in The Treatment of Experimental Periodontitis. Pharmacognosy Res. 2014 Oct;6(4).326-33. DOI: 10.4103/0974-8490.138287
15. Arief EM, Mubin MB, Zainuddin SLA, Abdullah NA, Ahmad B. Serum Interleukin-17 (IL-17) in Chronic Periodontitis Patients. Padjadjaran J Dent. 2017 Nov;29(3):138-42. DOI: 10.24198/pjd.vol29no3.14663
16. Alwan AH. Determination of Interleukin-1β and Interleukin-6(IL-6) in Gingival Crevicular Fluid in Patients with Chronic Periodontitis. IOSR J Dent Med Sci. 2015 Nov;14(11):81-90. DOI: 10.9790/0853-141148190
17. Nibali L, Fedele S, D'Aiuto F, Donos N. Interleukin-6 in Oral Diseases: A Review. Oral Dis. 2012 Apr;18(3):236-43. DOI: 10.1111/j.1601-0825.2011.01867.x
18. Yamamoto Y, Gaynor RB. Theurapeutic Potential of Inhibition of the NF-kappaβ Pathway in The Treatment of Inflammation and Cancer. J Clin Invest. 2001 Jan;107(2):135-42.
19. Yanti, Stephanie, Yuliani, Winarno FG, Suhartono MT. Inhibition of Interleukin-6 Expression by Curcumin in Rat Vascular Smooth Muscle Explants In Vitro. American J Biochem Biotech. 2014;10(4):260-6. DOI: 10.3844/ajbbsp.2014.260.266

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