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Effectiveness of 1% curcumin gel subgingival application on interleukin-6 levels in chronic periodontitis patients

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Abstract

Chronic periodontitis is inflammation caused by bacterial plaque that can cause periodontal tissue damage and ultimately cause tooth loss. In periodontitis patients, the production of proinflammatory cytokines such as IL-6 increases, these cytokines can influence the progression of periodontitis. The periodontitis treatment is mechanical therapy which is coupled with the administration of antimicrobial and anti-inflammatory drugs. Curcumin has antimicrobial and anti-inflammatory effects by increasing the production of IL-6 induced by lipopolysaccharides. This study aims to analyze the effectiveness of 1% curcumin gel subgingival application on IL-6 levels reduction before and after scaling and root planing. This study is experimental with pre and posttest control group design and is divided into 3 groups from 21 patients with chronic periodontitis. Each group before scaling and root planing was examined for IL-6 levels in the gingival crevicular fluid and then applied 1% curcumin gel, 0.2% chlorhexidine gel, without gel application and re-examined on the 7th day. IL-6 levels were analyzed by ELISA method. The data obtained were processed statistically using the Wilcoxon Test and T test with a significant value of $p < 0.05$. There was a statistically significant decrease in IL-6 levels. The difference of IL-6 levels in curcumin 1% gel group before scaling and root planing was 53.23 pg / mL and after scaling and root planing treatments were 40.00 pg / mL with the percentage reduction of IL-6 levels being 14, 96%. Subgingival application of curcumin 1% gel as an adjunct therapy of scaling and root planing treatments has proven to be effective in reducing levels of IL-6 in patients with chronic periodontitis.

Keywords: Curcumin, interleukin-6, chronic periodontitis

Introduction

Periodontal disease is one of the most common diseases affecting human race, with the primary etiology of pathogenic bacteria in the subgingival region [1-4]. Prevalence rates range from 25% to 54% in gingivitis and 43% in periodontitis. The American Academy of Periodontology defines periodontitis as inflammation of the gingiva characterized by loss of clinical attachment due to damage to the periodontal ligament and adjacent supporting bones. Periodontitis is caused by increased levels of proinflammatory cytokines which are considered to have an important role in the inflammatory process of chronic periodontitis [5]. Various compounds such as cytokines can be detected in gingival crevicular fluid (CKG). Cytokines function as inflammatory mediators and can be used as diagnostic markers in periodontitis. IL-6 is a very important parameter in periodontal research because of its effect on inflammation and bone resorption through osteoclast stimulation activity. IL-6 is produced by different cells such as monocytes, fibroblasts, osteoblasts and vascular endothelial cells in response to inflammation [5, 6]. IL-6 also has a role in B cell differentiation, T cell proliferation and differentiation of monocytes into osteoclasts that are plays a role in bone resorption [5, 6]. The level of IL-6 expression is associated with the severity of periodontal disease and age. Periodontitis treatment includes mechanical therapy coupled with the administration of antimicrobial and anti-inflammatory drugs. Mechanical therapy like scaling and root planing, aims to eliminate hard or soft deposits that are attached to the surface and roots of teeth as a place for bacterial growth [1, 3, 7, 8]. Mechanical debridement of teeth with deep periodontal pockets is difficult to achieve. Therefore, administration of systemic or local drugs needs to be given because the main etiology of periodontitis is bacterial plaque [1, 8].

Herbal medicines have been used for thousands of years by developing countries and more than 80% of the population depends on their use for health care needs. Turmeric, aloe vera, clove and cinnamon are among the herbal products that are commonly used in dentistry. The most active part of turmeric called curcumin, which is responsible for the color of turmeric, was first identified in 1910 by Lampe and Milobedzka [2, 9]. Curcumin consists of 80% complex curcuminoids and the rest consists of demethoxycurcumin (17%) and bisdemethoxycurcumin (3%) [9].

Curcumin has anti-inflammatory effects through several inflammatory pathways that inhibit the production of proinflammatory cytokines such as Tumor Necrosis Factor α (TNF- α), Interleukin (IL-1, 2, 6, 8 and 12), decreasing the regulation of cyclooxygenase 2 (COX 2) enzymes, lipoxygenase enzymes and inducible Nitric Oxide Synthase (iNOS). 10 This study aims to analyze the effectiveness of subgingival application of curcumin 1% gel as an adjunct therapy aside from scaling and root planing to decrease Interleukin-6 levels in patients with chronic periodontitis.

Materials and Methods

This study is experimental with pre and posttest control group design that is measuring and observing before and after treatment. Gingival crevicular fluid samples were taken from periodontitis patients in the Periodontia Installation of RSGM FKG USU who met the inclusion criteria. Selection of study sample is done by purposive sampling technique. The number of samples in this study were 21 people. The inclusion criteria in this study were periodontitis aged 25-65 years, pocket depths of 4-6 mm, the number of teeth in the oral cavity is at least 10 teeth, healthy condition (active and not suffering from systemic disease), willing to undergo examination and sign an informed consent. Exclusion criteria for patients with a history of systemic diseases that can affect periodontal status, pregnancy and lactation, taking vitamins, antibiotics, and anti-inflammatory drugs during the past 1 month, using mouthwash regularly, patients diagnosed with aggressive periodontitis, have a history of allergic to chlorhexidine. The study was approved by the Health Research Ethics Commission of Faculty of Medicine, University of North Sumatra / RSUP H Adam Malik Medan with number 306.

The material used in this study is curcumin. The basic components of making gels in this study were obtained from research conducted by Olivia AH, 1% curcumin gel was made 40gram so the basic ingredient composition of making gels was made. The treatment group was given scaling and root planing treatment, then applied with 1% curcumin gel and closed with a periodontal pack. The positive control group was given scaling and root planing treatment, then applied with 0.2% chlorhexidine gel and closed with a periodontal pack. The negative control group was only given scaling and root planing treatment. Measurement of IL-6 levels was done before scaling and root planing treatment and 7 days afterwards. Gingival crevicular fluid is taken using a 1 - 10 μ L sized microcapillary that has been placed on a micropipette. The microcapillary tip is inserted slowly into the pocket, then slowly withdrawn so that the gingival crevicular fluid is sucked into the microcapillary. Gingival crevicular fluid samples should not be contaminated with plaque and blood, then the fluid is transferred into the Eppendorf tube and labeled with a name and then an IL-6 examination was done at the USU FK Integrated Lab.

Results

This research was conducted to see the comparison of IL-6 levels in patients with applications of 1% curcumin gel, 0.2% chlorhexidine gel and no gel. Subjects were chronic periodontitis patients who came to Periodontia Installation FKG USU from April to June 2019. Subject groups were selected based on inclusion and exclusion criteria and is given treatment after basic scaling and root planing. The study subjects consisted of 7 people with 1% curcumin gel, 7 people with 0.2% chlorhexidine gel as a positive control group and 7 people without gel as a negative control group. Difference test results before and after treatment and percentage of IL-6 reduction in various treatment groups are shown in Table 1.

Table 1: Difference test results before and after treatment of IL-6 levels and percentage of IL-6 levels reduction in various treatment groups on day 1 and day 7.

Groups	Before	After	Percentage of IL-6 reduction	p value
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
Curcumin	53,23 \pm 0,23	40,00 \pm 0,04	14,96 \pm 3,81	0,018*
Control (+)	53,00 \pm 0,10	47,31 \pm 0,93	11,20 \pm 2,28	0,000*
Control (-)	56,21 \pm 0,78	53,20 \pm 0,79	6,34 \pm 1,20	0,000*

* $p < 0,05$

Figure 1 showed a graph of IL-6 level reduction before and after treatment in each group.

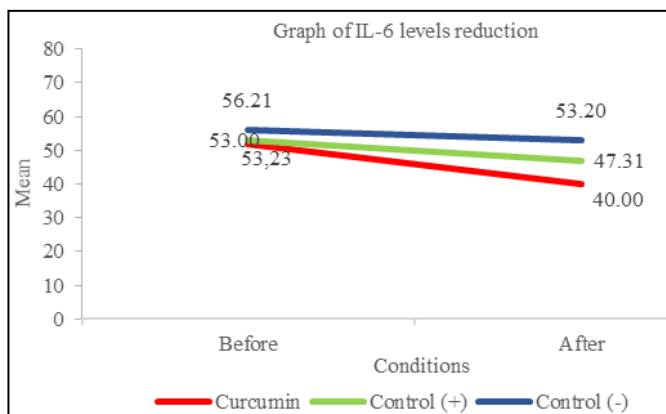


Fig 1: Graph of IL-6 levels reduction

The difference test results of IL-6 levels reduction effectiveness in various treatment groups are shown in Table 2.

Table 2: Difference test results on IL-6 levels reduction effectiveness in various treatment groups as an additional therapy for scaling and root planing in patients with chronic periodontitis.

Groups	Percentage of IL-6 reduction	p value
	Mean \pm SD	
Curcumin	14,96 \pm 3,81	0,018*
Control (+)	11,20 \pm 2,28	
Curcumin	14,96 \pm 3,81	0,000*
Control (-)	6,34 \pm 1,20	
Control (+)	11,20 \pm 2,28	0,000*
Control (-)	6,34 \pm 1,20	

* $p < 0,05$

Figure 2 showed graph of IL-6 level reduction percentage for each groups.

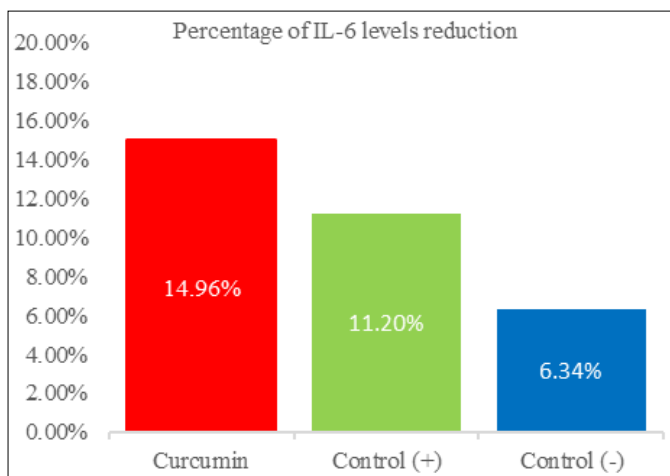


Fig 2: Percentage of IL-6 level reduction diagram

Discussions

This study is evaluating the effectiveness of 1% curcumin gel subgingival application as an additional therapy for scaling and root planing for IL-6 levels in patients with chronic periodontitis.

In this study, a decrease in IL-6 levels in the gingival crevicular fluid after being treated in the curcumin 1% gel group was statistically significantly higher than the positive control group and the negative control group. The percentage reduction in IL-6 levels in the curcumin gel group was also statistically significantly higher compared to the positive control group and the negative control group. The results of this study are consistent with previous *in vitro* studies by Yanti *et al.*, which stated that curcumin was able to inhibit IL-6 [11]. Yamamoto *et al.* also stated that flavonoids were able to suppress NF- κ B. Curcumin can suppress IL-6, TNF- α , and prostaglandin levels [12]. Study by Susanto *et al.*, who examined the effect of 2% white turmeric gel (*Curcuma zedoaria*) on levels of IL-6 expression in patients with conical periodontitis, was carried out for 14 days on 22 patients with chronic periodontitis consisting of 14 men and 8 women, with an age range of 30-69 years and the majority age was 50-59 years (41% of all samples). The result was significant difference in the levels of IL-6 expression in the treatment and control groups before and after the treatment of scaling and root planing [13].

Periodontitis is an infectious disease caused by periodontogenic bacteria-specific microorganisms that cause inflammation and progressive damage to periodontal tissue. Inflammation arises from untreated gingivitis, and if this process continues, it can invade tissue under the tooth structure and will form periodontal pockets, damage to periodontal ligaments which leads to loss of clinical attachment and resorption of alveolar bone and ultimately lead to tooth loss [14]. *In vivo* studies, stated that in patients with periodontitis, proinflammatory cytokine production such as IL-1, IL-6, IL-8, TNF α increases and these cytokines can influence the progression of periodontitis disease [13].

IL-6 is a multifactorial cytokine that acts both as a proinflammatory and anti-inflammatory. IL-6 also plays a role in various physiological and pathological responses. IL-6 has two different signal paths, namely classic signaling and trans signaling. Different pathways cause different IL-6 functions. In the classic signaling pathway (acute inflammation), the role of IL-6 is anti-inflammatory where IL-6 functions to recruit hepatocytes and lymphocytes to fight bacterial attacks and play a role in regenerative and antibacterial effects. In the

trans signaling pathway (chronic inflammation) the role of IL-6 changes to proinflammation and plays a role in tissue destruction. High levels of IL-6 are also caused by the role of IL-6 in chronic inflammatory activity in periodontitis

The results of this study indicate that the treatment group with subgingival application of 1% curcumin gel as an adjunct therapy aside from scaling and root planing treatment had a statistically more significant reduction in IL-6 levels compared to the positive control group and the negative control group. These results prove that curcumin gel has an anti-inflammatory effect. The use of curcumin as a local drug delivery system, is based on the bioadhesive properties of curcumin and various other properties such as anti-inflammatory, antibacterial, antimutagenic, anticarcinogenic, hepatoprotective and good healing properties without any side effects reported from study subjects [16].

Conclusions

Subgingival application of 1% curcumin gel as an adjunct therapy aside from scaling and root planing treatment proved to be effective on reducing interleukin-6 levels in chronic periodontitis patients.

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