

## **Effects of nonsurgical periodontal therapy on serum inflammatory factor levels in patients with chronic kidney disease and periodontitis.**

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### **Abstract**

**Objective:** To evaluate the effects of Nonsurgical Periodontal Therapy (NPT) on periodontal clinical parameters and Serum Inflammatory Factor (CRP, IL-6, TNF- $\alpha$ ) levels of patients with Chronic Kidney Disease (CKD) and periodontitis.

**Methods:** Fifty-three patients were randomly divided into Groups A and B, and another 30 patients with periodontitis but without systemic diseases were included as Group C. Groups A and C were given NPT including ultrasonic scaling, subgingival scaling and root planning, as well as oral hygiene instruction. CKD of Groups A and B were further treated by routine methods, but Group B was only given oral hygiene instruction without any periodontitis treatment. Periodontal examination was performed and serum levels of CRP, IL-6 and TNF- $\alpha$  were detected before and 6 weeks after treatment.

**Results:** The attachment loss, probing depth and positive percentage of Bleeding On Probing (BOP%) of Groups A and C significantly decreased after treatment compared with those before treatment ( $p < 0.05$ ), and BOP% of Group B also significantly reduced ( $p < 0.05$ ). The serum hsCRP, IL-6 and TNF- $\alpha$  levels of Group A significantly dropped after treatment compared with those before treatment ( $p < 0.05$ ). The serum hsCRP and TNF- $\alpha$  levels significantly reduced ( $p < 0.05$ ), but that of IL-6 barely changed ( $p > 0.05$ ). Group C had significantly decreased serum levels of hsCRP and IL-6 ( $p < 0.05$ ), but that of TNF- $\alpha$  did not change significantly ( $p > 0.05$ ).

**Conclusion:** After patients with CKD and periodontitis received combined routine CKD treatment and NPT for 6 weeks, the serum hsCRP, IL-6 and TNF- $\alpha$  level all dropped.

**Keywords:** Periodontal diseases, Inflammation, Kidney diseases, Periodontitis.

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### **Introduction**

As an infectious disease of periodontal tissues induced by dental plaque biofilm, periodontitis has been related with many systemic diseases such as diabetes, coronary heart disease and chronic kidney disease. In China, about 80-97% of adults suffer from different degrees of periodontal diseases, and the incidence rates of periodontitis range from 60% to 70%, mainly leading to tooth loss [1]. Microorganisms can directly damage periodontal tissues through toxic components, but the damages have mainly been attributed to the host immune response induced by microorganisms and their metabolites. The resulting inflammatory factors may be associated with some systemic diseases including CKD [2].

CKD is well-established as one of the main diseases endangering public health worldwide [3]. According to a cross-sectional survey in China, the morbidity rate of adult CKD was 10.8%, i.e. about 119.5 million people were affected [4].

As a group of progressive chronic diseases, CKD refers to chronic kidney structural and functional disorders caused by various factors (history of kidney damage:  $>3$  months). CKD is

defined by the National Kidney Foundation Practice Guidelines for Chronic Kidney Disease as [5]: 1) Kidney damage (kidney structural and functional disorders) for  $\geq 3$  months, with/without decrease in the Glomerular Filtration Rate (GFR) manifested as abnormal pathological examination results or kidney damage parameters (blood or urine samples, or imaging examination); 2)  $GFR < 60$  ml/(min:  $1.73$  m<sup>2</sup>) for  $\geq 3$  months, with/without kidney damage evidence.

Up to now, the therapeutic effects of Nonsurgical Periodontal Therapy (NPT) on patients with CKD and periodontitis remain largely unknown. Therefore, in this study, we selected such patients, and detected the changes of serum inflammatory factor (CRP, IL-6, TNF- $\alpha$ ) levels before and after NPT.

### **Materials and Methods**

#### **Subjects**

Fifty-three patients with CKD and periodontitis, who were treated in our hospital from March 2015 to March 2016, were selected and randomly divided into Group A (n=26) and Group

B (n=27), and another 30 patients with periodontitis but without systemic diseases were included as Group C. This study has been approved by the ethics committee of Fujian Provincial People's Hospital, and written consent has been obtained from all patients. Group A consisted of 11 males and 15 females aged 42-73 years old, ( $58.1 \pm 8.4$ ) on average. Group B comprised 13 males and 14 females aged 40-75 years old, ( $56.9 \pm 8.5$ ) on average. Group C was composed of 21 males and 9 females aged 39-68 years old, ( $54.4 \pm 7.5$ ) on average. The three groups had similar baseline clinical data ( $p > 0.05$ , data not shown).

### **Inclusion criteria for CKD**

GFR < 60 ml/(min: 1.73 m<sup>2</sup>) for  $\geq 3$  months. eGFR was calculated according to the modification of diet in renal disease equation corrected for the Chinese [6].

### **Inclusion criteria for periodontitis**

1) Number of remaining teeth  $\geq 12$ ; 2) for at least 6 sites, Attachment Loss (AL)  $\geq 4$  mm and probing depth (PD)  $\geq 5$  mm; 3) without periodontal treatment within 6 months or using antibiotics or non-steroidal anti-inflammatory drugs within at least 3 months; 4) without other severe systemic diseases; 5) non-smokers (self-reported).

### **Periodontal examination**

Periodontal examination for all patients was completed by the same doctor. AL, PD and positive percentage of Bleeding on Probing (BOP%) for tooth positions 16, 11, 24, 36, 41 and 44 were detected before and 6 weeks after treatment. In case of tooth losses, the closest teeth were selected instead. Six sites were examined for each tooth, and the average was used.

**Table 1.** Periodontal clinical parameters before and after treatment.

Group	PD (mm)		AL (mm)		BOP%	
	Before	After	Before	After	Before	After
A	5.61 $\pm$ 0.57	3.93 $\pm$ 0.71	5.29 $\pm$ 0.95	4.27 $\pm$ 0.92	64.10 $\pm$ 11.34%	32.48 $\pm$ 7.96%
B	4.74 $\pm$ 0.77	4.56 $\pm$ 0.82	4.86 $\pm$ 0.64	4.37 $\pm$ 0.79	63.48 $\pm$ 9.64%	57.72 $\pm$ 12.06%
C	4.91 $\pm$ 0.72	3.45 $\pm$ 0.79	4.81 $\pm$ 0.71	3.86 $\pm$ 0.75	67.78 $\pm$ 10.87%	36.39 $\pm$ 9.28%

**Table 2.** Serum hsCRP, IL-6 and TNF- $\alpha$  level before and after treatment.

Group	hsCRP (mg/L)		IL-6 (pg/ml)		TNF- $\alpha$ (pg/ml)	
	Before	After	Before	After	Before	After
A	4.71 $\pm$ 1.55	3.70 $\pm$ 1.28	160.6 $\pm$ 36.8	145.92 $\pm$ 40.3	18.42 $\pm$ 5.62	14.57 $\pm$ 6.19
B	3.79 $\pm$ 2.21	3.37 $\pm$ 1.51	180.79 $\pm$ 39.1	162.48 $\pm$ 31.3	15.23 $\pm$ 4.29	14.36 $\pm$ 5.28
C	1.86 $\pm$ 0.52	1.47 $\pm$ 0.38	98.4 $\pm$ 30.8	96.8 $\pm$ 35.7	12.27 $\pm$ 3.93	10.94 $\pm$ 4.86

### **Treatment methods**

Group A was given routine CKD treatment in combination with NPT including ultrasonic scaling, subgingival scaling and root planing, accompanied by oral hygiene instruction. Group B was treated similarly, only without NPT. Group C was subjected to NPT and oral hygiene instruction.

### **Detection of serological parameters**

Fasting peripheral venous blood (3 ml) was collected in the early morning in the baseline period and 6 weeks after treatment, centrifuged at 3000 r/min and stored at -70°C in dark. Serum hsCRP, IL-6 and TNF- $\alpha$  levels were detected by ELISA kits (MyBioSource, USA) according to instructions.

### **Statistical analysis**

All data were analysed by SPSS17.0 and expressed as mean  $\pm$  SD. Comparisons before and after treatment were conducted by paired t-test, and inter-group comparisons were carried out by independent samples t-test.  $P < 0.05$  was considered statistically significant.

## **Results**

### **PD, AL and BOP% before and after treatment**

Groups A-C had similar PD, AL and BOP% before treatment (Table 1). Six weeks after treatment, PD, AL and BOP% of Groups A and C all significantly decreased after treatment compared with those before treatment ( $p < 0.05$ ). In contrast, only BOP% of Group B reduced.

### **Serum hsCRP, IL-6 and TNF- $\alpha$ levels before and after treatment**

The serum hsCRP, IL-6 and TNF- $\alpha$  levels before and after treatment are summarized in Table 2. After treatment, the hsCRP levels of all groups, especially that of Group A, significantly decreased ( $p < 0.05$ ). The serum IL-6 and TNF- $\alpha$  levels of Groups A and C significantly dropped ( $p < 0.05$ ), but those of Group B did not change evidently.

### **Discussion**

Periodontitis has been correlated with CKD. By investigating 4053 adults aged over 40 years old, Fisher et al. [7] found that the degree of periodontal infection was positively correlated with chronic nephritis, with mutual effects. Epidemiological studies have proven that after diabetes mellitus and other potential synergistic factors were regulated, patients with CKD were more prone to periodontitis than those without CKD, with a more severe degree also [8,9]. Therefore, we herein aimed to assess the effects of NPT on periodontal clinical parameters and serum inflammatory factor levels of patients with CKD and periodontitis.

Six to twelve hours after inflammation begins, hsCRP can be detected by highly sensitive methods such as ELISA and latex-enhanced immunonephelometry or immunoturbidimetry [10]. Serum CRP level is raised in patients with periodontitis, being positively correlated with the severity of this disease [11]. Researchers have endeavoured to explore whether periodontitis can induce the changes of serum CRP level. Aiuto et al. [12] reported that serum CRP level reduced in 94 patients with chronic periodontitis who were subjected to NPT for 6 months. Similarly, in this study, serum hsCRP levels of Groups A and C dropped 6 weeks after NPT. Similar to the clinical periodontal examination result, serum hsCRP level was correlated with the degree of periodontal lesions.

With wide origins, IL-6 has been extensively studied and exhibits diverse biological activities, playing a crucial role in immune response and inflammatory response [13-16]. It has previously been reported that patients with CKD had significantly higher serum IL-6 level than that of normal subjects [17], so such level may decline after CKD was effectively treated. IL-6 level in the gingival sulcus fluid has been reported to drop after periodontal treatment [18]. Likewise, in this study, the serum IL-6 levels of Groups A and B both decreased after treatment. Nevertheless, the serum IL-6 level of Group C did not change obviously, probably because NPT only induced local IL-6 changes but not that in the serum.

TNF- $\alpha$  is generated by activated macrophages, monocytes and T cells, exhibiting high antitumor activity. Under normal conditions, the TNF- $\alpha$  level *in vivo* is low. Rossomando et al. [19] found TNF- $\alpha$  in the gingival sulcus fluid of patients with periodontitis before clinical attack, indicating that TNF- $\alpha$  may be able to predict periodontal disease. Upon periodontitis, considerable TNF- $\alpha$  is produced at local teeth [20], which stimulate fibroblasts in the gingiva to generate collagenase [21], thereby destructing periodontal tissues and stimulating

bone resorption in cooperation with IL-1 [22]. In this study, the serum TNF- $\alpha$  level of Group B hardly changed 6 weeks after treatment, being consistent with the results of Liu et al. [23] who found that patients with CKD had different TNF- $\alpha$  level from those of normal people after 6 months of treatment. As to Groups A and C, serum TNF- $\alpha$  levels both dropped 6 weeks after treatment compared with those before treatment, probably because effective NPT decreased pathogenic bacteria and toxins in the periodontal pocket. As a result, local inflammation was mitigated, and the numbers of monocytes/macrophages and lymphocytes decreased, which reduced TNF- $\alpha$  secretion and its serum level.

### **Conclusion**

In conclusion, in patients with CKD and chronic periodontitis, NPT decreased both the clinical parameters of disease as well as the serum markers of systemic inflammation. However, further studies with larger sample sizes are still in need.

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