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Research Article

Evaluation of Vitamin D and CRP levels with Periodontal Parameters in Dialysis Patients

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Abstract

Objectives: Therapy modalities of chronic renal failure (CRF) consist of hemodialysis (HD) and peritoneal dialysis (PD). Periodontal disease (PeD) is the most common bacterial infection in humans. C-reactive protein (CRP) is prototypic marker of inflammation can elevate in periodontal inflammation. Vitamin D, is an anti-inflammatory mediator, and may be related with PeD. We aimed to compare the periodontal parameters, CRP and 25 hydroxy vitamin D(25(OH)D) levels of HD and PD patients.

Materials and Methods: 131 patients (57 PD, 44 HD and 30 control) were included in our study. Plaque index (PI), gingival index (GI), probing pocket depth (PPD), clinical attachment levels (CAL), calculus index (CI) values and decayed, missing, filled teeth index (DMFT) of these patients were recorded. Additionally, possible relationship between CRP, 25(OH)D levels and periodontal parameters were evaluated.

Results: CAL, CI and DMFT values were not different in PD group than in HD group. PI, GI and PPD values were lower in PD group than in HD group ($p < 0.05$ for all). In PD and HD groups PI, GI, DMFT, CI, PPD and CAL values were higher than in control group ($p < 0.05$ for all). Also CRP levels of dialysis patients were higher than control group ($p < 0.05$ for all). There was a positive correlation between PI, GI and CRP levels in dialysis patients. There was a positive correlation between DMFT, PI, GI, PPD, CAL and CRP levels in control group ($p < 0.05$ for all).

Conclusions: Low oral hygiene habits that may explain the worse periodontal parameters and DMFT found in dialysis patients. Elevating CRP levels with periodontal parameters in dialysis patients and healthy controls can contribute at least in part to the increased risk for systemic inflammation.

Keywords: *Hemodialysis; Peritoneal dialysis; periodontal parameters; C-reactive protein; 25 hydroxyl vitamin D*

Introduction

End stage renal disease (ESRD) is the stage in which most of nephrons are lost and kidneys cannot provide needs of metabolic requirement of human body enough. At this stage, to supply the cessation of effective kidney function and to protect patients from uremia, which threat life, patients can be subjected to dialysis therapy. Dialysis can clean the blood from nitrogen waste and other toxic products of metabolism. In peritoneal dialysis (PD), it is purposing to use of the patients' healthy peritoneal membrane. In hemodialysis (HD), a semipermeable membrane is used, blood filtration is carried out by a machine (dialyzer).

On maintenance dialysis therapies exposure to dialyzer machine and membranes; possible exposure to endotoxins, foreign bodies and the presence of intravenous tunnel dialysis catheter may all be caused of chronic or recurrent infection. Also in these population, one of the potential infection focus is periodontal disease (PeD) which is chronic inflammatory disorder of the supporting tissues of the teeth

resulting from infection and interaction of the bacteria with the host's immune response. Several studies have been published, providing evidence for an increased prevelance of PeD, because of general debilitation and depression of the immunologic response in dialysis patients [1-3]. PeDs are a negligent source of chronic systemic inflammation in dialysis patients. Detection and treatment of PeD can decrease systemic inflammation and improve erythropoietin responsiveness. Thus enhance the life quality of CRF patients. For monitoring the progression of inflammation condition and cause of inflammation different parameters can be used such as, total leukocyte count, erythrocyte sedimentation rate, serum albumin, serum ferritin, C-reactive protein (CRP), Vitamin D deficiency, etc. [4,5]. CRP is an acute phase reactant plasma protein and the levels of CRP rise earlier than those of other reactants. CRP has been used as an early and sensitive marker of infection and inflammation.

Vitamin D, can be defined as an anti-inflammatory mediator, which has potential benefits for physical and periodntal inflammation. It was known that, vitamin D deficiency is commonly related with kidney function declines [6,7]. It was indicated that there is a reverse relationship between serum 25-hydroxyvitamin D_3 ($25(OH)D_3$) levels and periodontal helath [8]. There is information about the association of $25(OH)D_3$ deficiency and inflammation in the general population without CRF and in patients with CRF [9].

It is thought there is a potential relationship between the CRP and deficiency of vitamin D and infectious-inflammatory disorders. Chronic systemic inflammation is an obvious risk factor of dialysis patients. Therefore, the aim of present study is to examine the association between the level of serum CRP and 25(OH)D with periodontal parameters in HD and PD patients.

Materials and Methods

Participants

Total of 101 patients (57 PD and 44 HD) were recruited from the Department of Nephrology, Faculty of Medicine. The control group (30 patients) of this study were chosen from the participants who referred to the Periodontology Department, Faculty of Dentistry and has no systemic diseases that may influence periodontal tissues and calculus formation, periodontal treatment in the last 6 months. Before enrollment, all patients were briefly informed about the treatment protocol and they gave an informed consent to cooperate on this project. All procedures followed the tenets of the Declaration of Helsinki and the study protocol was approved by the Local Ethics Committee of Atatürk University (24.07.014-8). No change in the medication of dialysis and control groups patients was made prior to the study for at least 3 months.

Clinical examination and indices

Before clinical examination, medical history of participants was recorded. Periodontal examinations were performed at 10:30-11:30 hours before a midweek HD session in the HD group and in the same time period in the PD and control groups. Dental examinations were performed using a mouth mirror and a Williams periodontal probe, to determine the periodontal indexes. All clinical examinations performed by one clinicians.

The presence and thickness of microbial dental plaque on dental surfaces was assessed with PI of Silness and Löe [10]. Priorly, the teeth were dried, then the microbial dental plaque was scraped by a periodontal probe and evaluated by unaided eye.

Gingival situation was evaluated using GI of Löe and Silness [11]. The amount of calculus accumulation was evaluated by the calculus index, 0 = No calculus present, 1 = Supragingival calculus covering less than third of the exposed tooth surface, 2 = Supragingival calculus covering more than one third but not more than two thirds of the exposed tooth surface or the presence of subgingival calculus around the cervical portion of the tooth or both, 3 = Supragingival calculus covering more than two third of the exposed tooth surface or a presence heavy band of subgingival calculus around the cervical portion of the tooth or both.

PPD and CAL were measured to determine the periodontal status. PPD was measured by the mean distance between the bottom of the pocket and the margin of the gingiva and CAL was measured by the mean distance between the bottom of the pocket and the cemento enamel junction. Both of them measured from six sites of each tooth (mesiobuccale, midbuccale, distobuccale, distolingual, midlingual, and mesiolingual).

DMFT index was used for the assessment of dental health status. DMFT index is occurred by the sum of the teeth as decayed (D), missing (M), and filled (F) according to the WHO crite¬ria for each patient.

Blood samples were collected for the determination of CRP and vitamin 25(OH)D levels between at the same session to obtain standardization. Then the serum was stored at -80°C. CRP was measured using the Cobas Integra 400 automatic analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Vitamin 25(OH)D levels were measured by chemiluminescent radioimmunoassay (Diasorin, Stillwater, MN).

Statistical analyses

Statistical analyses were performed using a software (SPSS for Windows Software Package, Version 11.5.0; SPSS Inc., Chicago, IL, USA). Pearson chi-squared test was used to determine the difference between the distribution of the gender of the PD, HD, and control groups. Evaluation of periodontal parameters (PI, GI, PPD, CAL, CI), DMFT, CRP and 25(OH)D levels between groups were made by the Kruskal-Wallis test and two-group comparisons were made by Mann-Whitney U test. To determine the relationship between biochemical test results of CRP and 25(OH)D levels and periodontal parameters the Spearman's rank correlation test was used. The level of significance was set at $p < 0.05$.

Results

Means of age for HD, PD and control were 49.7 ± 17.6, 50.4 ± 16.7, 48.2 ± 17.1 and female/male were 38/19, 22/22, 16/14 respectively. The causes of renal failure included hypertension (36.2%), chronic interstitial nephritis (22.6%), glom¬erulonephritis (18.9%), amyloidosis (8.3%), polycystic kidney disease (5.4%), and unknown (8.6%).

Mean levels of PI, GI, PPD, CAL, CI and DMFT values of PD, HD and control groups are shown in Table 1. CAL, CI, DMFT values and CRP levels were not different in PD group than in HD group ($p > 0.05$). PI, GI and PPD values were lower in PD group than in HD group ($p = 0.040$, $p = 0.020$ and $p = 0.019$ respectively). Control group has, statistically significant lower PI ($p = 0.0001$), GI ($p = 0.0001$), DMFT ($p = 0.001$), CI ($p = 0.001$), PPD ($p = 0.017$), CAL ($p = 0.001$) values and CRP levels ($p = 0.004$) than PD group. Control group has, statistically significant lower PI ($p = 0.0001$), GI ($p = 0.0001$), DMFT ($p = 0.004$), CI ($p = 0.0001$), PPD ($p = 0.0001$), CAL ($p = 0.0001$) values and CRP levels (0.0001) than HD group.

There was a positive correlation between the CRP levels, PI ($r = 0.206$, $p = 0.039$) and GI ($r = 0.223$, $p = 0.025$) scores in dialysis patients. There was a positive correlation between the CRP levels, PI ($r = 0.448$, $p = 0.013$), GI ($r = 0.680$, $p = 0.0001$), DMFT ($r = 0.392$, $p = 0.032$), PPD ($r = 0.475$, $p = 0.008$) and CAL ($r = 0.455$, $p = 0.0012$) scores in control group.

		PD	HD	Control	p values		
					PD vs HD	PD vs Control	HD vs Control
PI	mean ± SD minimum maximum	1.9±0.6 0.5 3.0	2.1±0.7 0.5 3.0	1.0±0.5 0.0 0.5	0.040	0.000	0.0001
GI	mean ± SD minimum maximum	1.7±0.6 0.1 3.0	2.0±0.7 0.0 3.5	0.8±0.5 0.0 2.0	0.020	0.000	0.0001
PPD	mean ± SD minimum maximum	3.2±1.1 2.0 7.0	3.7±1.3 2.0 7.0	2.6±0.6 2.0 4.0	0.019	0.017	0.0001
CAL	mean ± SD minimum maximum	1.6±1.6 0.0 5.0	1.9±1.7 0.0 7.0	0.4±0.6 0.0 1.8	0.326	0.001	0.0001

CI	mean ± SD minimum maximum	1.5±1.0 0.0 3.0	1.5±0.8 0.0 3.55	0.8±0.6 0.0 2.0	0.891	0.001	0.0001
DMFT	mean ± SD minimum maximum	13.0±7.8 0.0 28.0	12.8±8.0 0.0 28.0	7.1±3.9 1.0 15.0	0.847	0.001	0.004
CRP (mg/L)	mean ± SD minimum maximum	4.9±6.3 0.3 35.0	7.7±9.2 0.3 41.0	1.9±2.2 0.5 10	0.102	0.004	0.0001
25(OH)D (ng/ml)	mean ± SD minimum maximum	9.0±8.4 0.0 47.0	9.8±8.0 4.0 38.0	10.6±8.6 4 47	0.463	0.150	0.534

Table 1: *Periodontal parameters, CRP and 25(OH)D levels in peritoneal dialysis, hemodialysis and control groups.*

CAL: Clinical attachment levels, calculus index. DMFT: Decayed, missing, filled teeth index, GI: Gingival index, PI: Plaque index, PPD: Probing pocket depth.

25(OH)D levels showed no statistically difference between the groups and also no correlations with other investigated parameters in dialysis patients and control group ($p > 0.05$).

Discussion

The findings of this study presented that dialysis patients, specially HD patients don't have attention to support their oral care as much as PD patients and control group. Control group have better periodontal parameters than dialysis patients. Higher CRP levels in dialysis patients is cause of higher level of inflammation than control group. CRP levels were increased with increased scores of periodontal parameters, thus, periodontal inflammation can cause of systemic inflammation in healthy controls and dialysis patients.

In the present study PI of dialysis patients were higher than control group. In addition, PI of HD patients were higher than PD group. This indicates that control group and PD patients morely aware of their oral hygiene care. Bayraktar., *et al*. [12] found that plaque accumulation of the PD group was not different than the HD group, not similar with our study. This difference can cause of worse oral hygiene scores in their studied population than in our groups. The higher plaque levels in the dialysis patients, especially in HD group indicated the neglected oral self-care.

In our study GI values of PD patients were lower than HD patients. Like our results, Bayraktar., *et al*. [12] found GI values of the PD group was significantly lower than that of the HD group and suggested that higher plaque levels in the HD group as well as the increased bleeding index might be the result of the anticoagulant medication they have to take. Also in our study control group had lower GI values, than the patients of HD and PD groups, this may be due to the effect of lower PI scores and well oral hygiene care than dialysis patients. PD and HD patients had more calculus accumulation than control group. Bayraktar., *et al*. [12] reported that, PD and HD groups had more calculus accumulation than healthy control group. Epstein., *et al*. [13] found higher calculus levels in HD patients than healthy controls. The alterations in serum phosphorus–calcium levels in CRF patients and higher salivary urea levels creates an appropriate environment for calculus formation. Additionally, worse oral hygiene care in dialysis patients was responsible from these results. Thus it can be suggested to dialysis groups to should pay more attention to support their oral hygiene and should more often brush their teeth to prevent calculus formation. Better results of control group may be the result of this attention.

PPD and CAL values of control group were significantly lower than in dialysis groups. Similar with the results of our study, Bayraktar., *et al*. [12] were found comparable PPD findings in the PD and HD groups than the healthy control group. Another study on CRF patients, reported higher CAL values when compared with healthy controls [2]. PPD values of PD patients were lower than HD patients. This can

be the result of higher GI values in HD group than in PD and control groups. Thorman., *et al*. [14] found, HD group had significantly more CAL than non-ureamic controls. The results of our study parallel with the previous studies and may be associated with the effect of gingival inflammation, on higher PPD and CAL values. Also as mentioned above, CRF resulting in the uremic syndrome, and uremia has been related with immune dysfunction including defects in lymphocyte and monocyte function [15]. Thus resulted with worse periodontal parameters observed in dialysis population.

		Dialysis Patients n=101	Control Group n=30
PI	r values p values	0.206 0.039	0.448 0.013
GI	r values p values	0.223 0.025	0.680 0.0001
PPD	values p values	0.123 0.220	0.475 0.008
CAL	r values p values	0.095 0.345	0.455 0.012
CI	r values p values	0.142 0.157	-0.083 0.663
DMFT	values p values	0.059 0.558	0.392 0.032
D vit	values p values	0.156 0.120	-0.081 0.671

Table 2: *Spearman's Correlations between periodontal parameters and CRP levels in dialysis patients and control groups.*

DMFT were significantly lower in control group than in the HD and PD groups. In PD group DMFT were not different than in the HD group. Naugle., *et al*. [16] found that HD patients have a high prevalence of caries than controls. Uremia, elevated pH, decreasing of salivary flow rate and bad oral hygiene care among these patients can cause of higher DMFT values for PD and HD patients.

CRP levels of dialysis patients were higher than control group. It was known, the prevalence of chronic inflammation is high in dialysis patients, and varies from 35% to 65% and elevated serum CRP levels in dialysis patients reconfirmed that. In addition, the level of CRP can be changed with PeD [17-19]. In the present study we found a positive correlation between the CRP levels, PI and GI scores in dialysis patients. Bayraktar., *et al.* [20] also reported a positive correlation between PI and CRP in PD patients. CRP is an inflammation related marker and GI is indicator of inflammation of gingival tissues. CRP levels in dialysis patients was found correlated with gingival inflammation according to our study. Certain pathogenesis of chronic inflammation is not known, but some factors such as uremic toxins, oxidative stress, infections and immune mechanisms may cause of inflammation in dialysis patients. In addition, periodontal inflammation in dialysis patients can be related with systemic inflammation and can effect the circulating CRP levels [21,22]. According to our results there were a positive correlation between the CRP levels, PI, GI, DMFT, CI, PPD and CAL scores in control group. Lata Goyal., *et al*. [17] found a significant correlation between CAL, PPD and CRP, which is consistent with our results. But findings of some studies did not find a correlation with severity of disease [23,24]. Moreover, it may be said the studied population is effective and there lies genetic susceptibility towards inflammatory hyperactivity. Thus, as the severity and extent of PeD increase, the systemic component of inflammation also increases and so increased production of CRP may be seen.

We also studied the effect of 25(OH)D levels on periodontal parameters and found no correlations between 25(OH)D levels and periodontal parameters. In populations without CRF and non-smokers, each 30 nmol/L increase in serum vitamin D level showed a 10% decrease in the odds of bleeding upon probing [25]. In some studies, better PPD and CAL scores were reported due to anti-inflammatory

effects of vitamin D [8, 25, 26]. Dietrich., *et al*. [25] found that individuals in the highest quintile of serum vitamin D presented significantly less gingival bleeding as well as lower mean PPD and CAL and number of missing teeth. It has also been suggested that vitamin D supplementation may have a positive effect on periodontal health, particularly on bleeding, GI and PPD [26,27]. The results of the present study are not parallel with the results of mentioned studies, which are objected on patients without ESRD. It can be said, the proposed anti-inflammatory role of vitamin D may be suppressed by the unfavorable systemic conditions of these ESRD patients. Additionally, the presence and strength of the relationship between 25(OH)D and various health conditions, including PeD is multifactorial. This can be dependent on population characteristics, such as the overall serum vitamin D level, environmental factors and genetic profile of the population. Therefore, additional studies are needed to examine to how vitamin D may play a role in protecting periodontal tissues from inflammatory breakdown in ESRD patients. In addition, 25(OH)D levels showed no difference between the groups. It was known that vitamin D deficiency is common in ESRD patients due to lack of 1α-hydroxylase activity. No difference between dialysis patients and healthy controls in our study can be the cause of low 25(OH)D levels in control group. Our residential region is a cold city and individuals could not go out due to such effect may not take benefit from the sunlight for a long time.

		Dialysis Patients	Control Group
PI	r values p values	0.056 0.579	-0.093 0.627
GI	r values p values	0.082 0.416	-0.066 0.728
PPD	values p values	0.034 0.738	-0.111 0.561
CAL	r values p values	-0.55 0.586	-0.157 0.408
CI	r values p values	-0.015 0.885	0.419 0.061
DMFT	values p values	-0.096 0.338	-0.275 0.141
CRP	values p values	0.156 0.120	-0.081 0.671

Table 3: *Spearman's Correlations between periodontal parameters and 25(OH)D levels in dialysis patients and control groups.*

According to our study serum 25(OH)D was not correlated with the inflammation markers of CRP in dialysis patients and healthy controls. In vitro studies showed that active vitamin D agonists decrease cytokine production by human blood mononuclear cells after various inflammatory stimuli [28,29], and in the clinic, administration of an active vitamin D agonists decreased CRP in patients with CRF [30]. However, the available data about the association of serum 25(OH)D with inflammation in dialysis patients are not clear. Our results can be due to effect of several systemic factors, genetic characteristics of population and low 25(OH)D levels in control groups.

In conclusion, the studied population presented low oral hygiene habits that may explain the high PI, GI, PPD, CAL, calculus values and DMFT found in dialysis patients. Also it can be said, HD and PD patients are subjected to a machine and dependent to medical centers. These patients would be depressed due to their unfavorable systemic situations, thus would neglect their oral health care. Higher serum CRP levels in dialysis patients can be related with the prevalence of chronic inflammation. In addidtion it can be suggested that elevated CRP levels with periodontal parameters in dialysis patients and healthy controls can contribute at least in part to the increased risk for systemic inflammation.

The major limitation of this study was the influence of some drugs, which have to use by dialysis patients, on their periodontal health status. However, this study aimed to evaluate and compare the clinical findings according to the current periodontal health status of these patients' together with the clinical outcomes of the medications that the dialysis patients have to take.

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The authors declare No competing financial interests exist.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Compliance with Ethical Standards

The approval of the Local Ethics Committee of Ataturk University Faculty of Medicine Local Ethics Committee (24.07.014-8). All patients were briefly informed and written informed consent was obtained before participation. All procedures followed the tenets of the Declaration of Helsinki.

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