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COMPARISON OF WIDELY USED BIOCHEMICAL ANALYTES IN THE SERUM AND SALIVA SAMPLES OF DIALYSIS PATIENTS

POREĐENJE ČESTO UPOTREBLJAVANIH BIOHEMIJSKIH ANALITA U UZROCIMA SERUMA I SALIVE PACIJENATA NA DIJALIZI

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Summary

Background: The aim of this study is to determine whether the saliva analysis is an alternative to routine biochemical and immunoassay analyses in patients undergoing peritoneal dialysis (PD) or hemodialysis (HD).
Methods: Study group consisted of 40 healthy control, 44 PD and 44 HD patients. Routine biochemical analytes, thyroid stimulating hormone (TSH), free T3, free T4, vitamin B12, ferritin and folic acid were measured.
Results: Compared to pre-HD, urea, creatinine, uric acid, potassium levels were lower in post-HD, and calcium, magnesium, vitamin B12 levels were higher in post-HD both in saliva and serum. Positive correlations between saliva and serum were found for TSH and ferritin in control; urea, LDH, K in PD; urea, creatinine, alkaline phosphatase in pre-HD, and gamma-glutamyl transferase, iron, TSH in post-HD. There was a negative correlation only for creatine kinase and Mg in pre-HD and calcium in post-HD. In all groups, a positive correlation was found for urea, creatinine and a negative correlation was found for magnesium.
Conclusions: Our study showed higher salivary urea and creatinine levels in patient groups, consistent with serum levels. Based on these results, salivary urea and creatinine levels may be useful in the evaluation of azotemia in dialysis patients.

Keywords: end-stage renal failure, hemodialysis, peritoneal dialysis, analysis of saliva, serum

Kratak sadržaj

Uvod: Cilj ove studije je da se utvrdi da li analiza salive predstavlja alternativu rutinskim biohemijskim analizama i imunoesejima kod pacijenata podvrgnutih peritonealnoj dijalizi (PD) ili hemodijalizi (HD).
Metode: Grupu ispitanika činilo je 40 zdravih kontrolnih subjekata, 44 pacijenta na PD i 44 na HD. Mereni su rutinski biohemijski analiti, tireostimulišući hormon (TSH), slobodni T3, slobodni T4, vitamin B12, feritin i folna kiselina.
Rezultati: U poređenju sa stanjem pre HD, nivoi uree, kreatinina, mokraćne kiseline, kalijuma bili su niži posle HD, dok su nivoi kalcijuma, magnezijuma, vitamina B12 bili viši posle HD kako u salivi tako i u serumu. Pozitivne korelacije između salive i seruma nađene su za TSH i feritin u kontrolnoj grupi; ureu, LDH, K u PD; ureu, kreatinin, alkalnu fosfatazu pre HD, i gama-glutamil transferazu, gvožđe, TSH posle HD. Negativna korelacija je postojala samo za kreatin-kinazu i Mg pre HD i kalcijum posle HD. U svim grupama nađena je pozitivna korelacija za ureu, kreatinin, a negativna korelacija je nađena za magnezijum.
Zaključak: Naša studija je pokazala više nivoe uree i kreatinina u salivi u grupama pacijenata, koji su odgovarali serumskim nivoima. Ovi rezultati pokazuju da bi salivarni nivoi uree i kreatinina mogli biti korisni u proceni azotemije kod pacijenata na dijalizi.

Ključne reči: krajnji stadijum bubrežne insuficijencije, hemodijaliza, peritonealna dijaliza, analiza salive, serum

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Introduction

End-stage renal disease (ESRD) is an irreversible stage of advanced impairment of the renal excretory, synthetic, and regulatory functions. Rigorous laboratory follow-up is very important for the maintenance of homeostasis and improvement of patient quality of life for this disease which is known to affect all organ systems (1, 2). However, rigorous laboratory follow-up necessitates constant blood sampling. In most cases related to this disease decreased erythrocyte production is observed, hence constant blood sampling may worsen already existing anemia. Furthermore, constant blood sampling requires the use of special equipment and well trained personnel which makes the sampling process costly (3, 4). Saliva as a diagnostic fluid is more advantageous than serum, because it can be collected noninvasively by anyone with a moderate education and offers a cost-effective approach to screening large populations (5). Evaluation of saliva has been reported to be effective in the diagnosis and follow-up of cases of renal failure. In this light, various studies have been published aimed at analyzing saliva samples in patients with renal failure (6, 7).

In this study, we aimed to determine whether saliva analysis can be an alternative to blood analysis in patients with ESRD. In this regard, a healthy control group, a peritoneal dialysis (PD) group and a hemodialysis (HD) group were formed. In previous studies, saliva, urea, creatinine (Crea), and uric acid (UA), were investigated extensively in ESRD. We also examined in simultaneous analyses of a wide range of biochemistry test panels, thyroid function tests (thyroid stimulating hormone (TSH), free T3 (fT3), free T4 (fT4), vitamin B12 (vit B_{12}), folic acid and ferritin in blood and saliva samples. Furthermore, serum and saliva analysis were carried out before and after the HD procedure was conducted, so as to investigate the effect of HD on these analytes.

Material and Methods

Patient and control groups

The study was conducted at the Biochemistry Department of Ankara Training and Research Hospital, Ministry of Health, with the support of the Nephrology Clinic. The study was approved by the local Ethics Committee (Meeting No: 366, Date: 07/04/2010, Decision No: 2954) and conducted in accordance with the principles of the Declaration of Helsinki. All patients were informed of the study and signed a written approval.

The patient group included a total of 44 patients for PD and 44 for HD. The control group included 40 healthy subjects free from hypertension, diabetes mellitus, thyroid disease, liver and renal diseases, salivary gland disease, oral disease or any other known disease. Dialysis patients that had any salivary gland diseases and/or oral diseases were excluded from the study. Demographic properties of the patients are shown in *Table I*.

Blood and saliva samples

Blood and saliva samples were collected from patients of the HD group before and after dialysis, and from patients of the PD and control groups in the morning before meals. Blood samples were drawn into evacuated serum separator tubes containing clot activator (SST Vacutainer®, Becton Dickinson). All blood samples were centrifuged at 1500 g for 10 minutes during a 30 minute period. Serum samples obtained were collected into Eppendorf tubes (Eppendorf® Safe-Lock microcentrifuge tubes, Turkey) and stored in deep freeze at –80 °C.

An unstimulated saliva collection was carried out based on guidelines given by the University of Southern California School of Dentistry (8). The patients were asked to refrain from oral hygiene procedures like brushing with fluoridated toothpaste, at least 1 h prior to salivary sample collection. Drinking water was given to the subjects to rinse their mouths with. Five minutes after the oral rinse, unstimulated saliva was collected in 50 ml sterile plastic containers using the spitting method. The patients were then asked to swallow the saliva present in their mouths and then to remain still without moving their tongues or swallowing their saliva for 1 min. The patients were then asked to spit the saliva every 60 s for a total of 5 min into the container, until the day of the study was reached. The collected saliva samples were immediately transferred into plastic tubes, covered, and stored at –80 °C. Saliva samples were then defrozen at +4 °C and were later brought to room temperature on the day of the study. All saliva samples were centrifuged at 1500 g for 15 minutes after mixing with a vortex, and analyzed parallel with serum samples by separating the supernatant.

Devices used

Analysis of serum and saliva urea, creatinine, UA, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH), creatine kinase (CK), calcium (Ca^{+2}), magnesium ($Mg+^{2}$), inorganic phosphate (Phos), iron, total protein (TP) and albumin (ALB) levels was carried out with the original reagents in the Olympus AU 2700 (Mihsima Olympus Co. Ltd. JAPAN) analyzer using the spectrophotometric method. Sodium (Na^{+}), potassium (K^{+}), chloride (Cl^{-}) analytes of serum and saliva were measured in the same analyzer using the ion selective electrode method. TSH, fT3, fT4, vit B_{12}, folic acid, ferritin levels were measured with the original reagents using the chemiluminescence

Table I Descriptive characteristics of patient and control groups.

Patient group		Control	Peritoneal dialysis	Hemodialysis
Number of patients (n)		40	44	44
Gender	Female (%)	16 (40%)	18 (43.3%)	14 (33%)
	Male (%)	24 (60%)	26 (56.7%)	30 (67%)
Age (years)($\bar{x}\pm s$)		43.9±8.5	45.8 ±13.3	48.2±12.3
BMI (kg/m^2)($\bar{x}\pm s$)		27.7±3.7	29.7±3.9	28.7±4.1
Duration of initiating dialysis	<1year	–	8	7
	1–5 years	–	25	28
	5–10 years	–	11	9
Cigarette smoking (%)		9 (24%)	6 (13%)	2 (4%)
Disease information	Diabetes mellitus (%)	–	8 (18%)	5 (11%)
	Bone diseases (%)	–	5 (11%)	6 (13%)
	Cardiovascular diseases (%)	–	3 (8%)	2 (4.5%)
	Hypertension (%)	–	12 (27%)	14 (31%)
	Dyslipidemia (%)	–	6 (13%)	8 (18%)
	Thyroid diseases (%)	–	4 (9%)	–
Drugs used	Anti-lipidemic (%)	–	5 (11%)	9 (16%)
	Antihypertensive (%)	–	29 (65%)	17 (38%)
	T3 agonist	–	4 (9%)	–
	Folic acid derivative (%)	-	13 (29%)	35 (79%)
	Iron drugs	–	10 (22%)	38 (86%)
	Phosphate binding	–	13 (29%)	41 (93%)
	Recombinant erythropoietin	–	5 (11%)	33 (75%)
	Anti-aggregant drugs	–	3 (6.8%)	–

enzyme immunoassay method via Advia Centaur (Diagnostic Products Corporation, Los Angeles, USA) analyzers according to the manufacturer instructions. These methods have been used for saliva in earlier studies (9, 10, 11).

Statistical analysis

Statistical analysis was performed using SPSS for Windows v15.00 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean ($\bar{x}$), standard deviation (SD), the smallest (min) and biggest (max) values. Distribution of the groups was evaluated using the Kolmogorov-Smirnov test. The groups were reported to show normal distribution. The difference between the control and patient groups was evaluated using the Student-t test. Comparison of analyte levels of serum and saliva collected before and after HD was made using the paired t-test. The Pearson correlation analysis was used to analyze all serum and saliva parameters. A *P*-value of <0.05 was considered statistically significant.

Results

The comparison and mean values of test results from serum and saliva samples of the healthy control group, PD group and HD group are shown in *Table II* and *Table III*.

When the control group and the PD group were compared, Na^+, Cl^-, ALP and LDH levels were found to be lower in the PD saliva measurements and there was a significant difference between these levels ($P<0.05$). The salivary measurements of HD patients compared with the control group, urea, Crea, AST,

Table II Comparison of the measured serum analytes in the study groups.

Analyte (unit)	Control		PD		Before HD		After HD	
	Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
Urea, mmol/L	13.8	3.25	37.1.	9.28	43.9	14.96	14.8	7.78
Crea, μmol/L	85.7	14.14	694.8[a]	259.89	640.1[a]	221.88	265.2[a,b,c]	94.58
UA, μmol/L	277.7	77.32	324.17[a]	57.7	335.5[a]	92.19	105.3[a,b,c]	55.91
ALP, U/L	76.1	25.8	139[a]	126	102[a]	78.5	121[a]	85.3
GGT, U/L	28.7	16.3	38.5	32.1	24.4	27.7	26.2	25.2
AST, U/L	28.4	42.7	16.2	5.51	14.6[a]	5.54	16.2	6.07
ALT, U/L	29.5	59.1	15.7	9.09	9.06[a,b]	3.61	9.68[a,b]	4.68
LDH, U/L	195	36.9	156[a]	71.8	210a	138	221[a,b]	74.2
CK, U/L	112	76.8	132	165	61.1[a,b]	54.2	62.7[a,b]	64.2
Na^+, mmol/L	140	7.25	137[a]	3.71	140b	7.10	137	2.88
K^+, mmol/L	4.30	0.63	4.19	0.68	5.18[a,b]	0.79	3.64[a,b,c]	0.42
Cl^-, mmol/L	107	5.20	101	2.55	99.1[a,b]	3.60	97.9[a,b]	3.36
Ca^{+2}, mmol/L	2.22	0.19	2.24	0.19	2.14[b]	0.20	2.86[c]	0.32
Mg^{+2}, mmol/L	0.41	0.05	0.45[a]	0.08	0.465[a]	0.08	0.41[b,c]	0.04
Phos, mmol/L	1.18	0.20	1.45[a]	0.43	1.78[a,b]	0.53	0.86[a,b,c]	0.29
Iron, μmol/L	12.96	6.98	11.29	3.62	11.99	7.05	13.75	11.01
TSH, μIU/mL	1.35	0.90	2.73[a]	2.62	1.45	1.13	1.40[b]	1.06
fT3, pg/mL	3.08	0.34	2.83[a]	0.52	2.25[a]	0.51	2.50[b,c]	0.47
fT4, ng/dL	1.02	0.47	0.98	0.20	0.99	0.26	1.18[b,c]	0.29
Folic acid, ng/mL	6.50	3.74	6.14	2.14	2.35	1.09	2.44[b]	1.48
Vit B_{12}, pg/mL	247	120	500[a]	303	368[a]	58.6	286	96.6
Ferritin, ng/mL	55.5	55.9	501[a]	192	869[a,b]	1070	1255[a,b]	612

a: Significant comparison between control and PD
b: Signicifiant comparison between control and HD
c: Signicifiant comparison between before HD and after HD

CK, K^-, Phos, iron, vit B_{12} and ferritin levels were higher and LDH, Ca^{+2} and Mg^{+2} levels were significantly lower ($P<0.05$). These values are demonstrated in *Table III*.

When all study groups were included, there was a significant positive correlation for urea. However, there was a weak positive correlation for Crea, GGT, K^-, vit B_{12}, and a weak negative correlation for Mg^{+2}. Other results of the correlation analysis between serum and saliva values are shown in *Table IV*.

In our study comparison of serum and saliva analytes before and after HD, urea, Crea, and UA levels in serum and saliva were found to be significantly lower after HD than before HD. These low values

Table III Comparison of the measured saliva analytes in the study groups.

Analyte (unit)	Control		PD		Before HD		After HD	
	Mean	S.D	Mean	S.D	Mean	S.D	Mean	S.D
Urea, mmol/L	21.2	11.21	36.41[a]	20.74	44.9[a,b]	21.10	24.7[b,c]	12.42
Crea, µmol/L	37.2	26.52	44.2	39.78	58.4[a]	45.08	38.1[c]	21.21
UA, µmol/L	69.0	51.15	89.81	38.6	90.41	56.51	36.88[a,c]	16.1
ALP, U/L	4.24	3.30	3.72	1.40	4.00	1.72	4.98	2.61
GGT, U/L	7.15	5.07	9.77	8.48	9.45	8.31	8.09	5.92
AST, U/L	20.8	23.9	61.3[a]	116	69.6a	64.1	65.8	40.5
ALT, U/L	8.67	12.9	24.4	70.9	29.4	37.1	27.9	53.5
LDH, U/L	238	146	70.4[a]	26.6	104	81.1	82.7[a]	57.6
CK, U/L	4.70	4.45	8.86[a]	6.74	8.72a	7.50	5.92	5.84
Na^+, mmol/L	22.0	7.96	18.0[a]	5.77	21.7b	7.41	19.7	4.86
K^+, mmol/L	20.3	5.22	21.0	8.02	27.3[a,b]	6.75	22.9[c]	5.22
Cl^-, mmol/L	31.9	13.2	21.6[a]	11.6	31.5[b]	10.4	25.1[a,c]	7.97
Ca^{+2}, mmol/L	0.83	0.55	0.33[a]	0.19	0.38[a]	0.42	0.73[b,c]	0.59
Mg^{+2}, mmol/L	0.11	0.08	0.04[a]	0.025	0.06[a]	0.05	0.11[b,c]	0.08
Phos, mmol/L	6.40	2.37	5.33	2.90	7.53[b]	2.63	6.94[b]	2.78
Iron, µmol/L	0.65	0.51	1.16[a]	1.42	0.84	1.00	0.57[b]	0.74
TSH, µIU/mL	0.007	0.003	0.007	0.005	0.009	0.013	0.007	0.006
fT3, pg/mL	0.83	0.28	0.86	0.30	0.96	0.38	0.79[c]	0.32
fT4, ng/dL	0.41	0.13	0.41	0.11	0.58	0.80	0.47	0.15
Folic acid, ng/mL*	–	–	–	–	–	–	–	–
Vit B_{12}, pg/mL	165	68.3	173	122	285[a]	79.1	377[c]	177
Ferritin, ng/mL	27.5	52.9	10.8	7.57	34.9[a]	22.2	61.1	58.0

a: Significant comparison between control and PD
b: Significant comparison between control and HD
c: Significant comparison between before HD and after HD
*: >24 ng/mL (higher than the limit of measurement)

were demonstrated as 45% for urea, and as 34% and 71% for Crea and UA, respectively. Percentage differences for serum analytes were 66% for urea, 58% for Crea, and 69% for UA. On the other hand, the mean decrease rate after HD of saliva Na^+, K^+, Cl^- was found to be 9.2%, 16.2%, and 19.3%. Results of our study show that saliva Ca^{+2} levels after HD were higher than the levels before HD ($p<0.001$). Saliva Ca^{+2} levels demonstrated an increase of 94% compared to values before HD was carried out. Similarly, serum Ca^{+2} levels after HD were found to be significantly higher ($P<0.05$). On the other hand, the increased rate of after HD serum Ca^{+2} levels was found to be 6.4%.

Table IV Significant correlation values of measured analytes in serum and saliva.

Group	Analyte	r	p	n
Control group	TSH	0.31	0.04	40
	Ferritin	0.55	<0.001	40
PD	Urea	0.31	0.03	44
	LDH	0.55	<0.001	44
	K^+	0.36	0.01	44
Before HD	Urea	0.25	0.009	44
	Crea	0.35	0.01	44
	ALP	0.38	0.009	44
	CK	–0.32	0.03	44
	Mg^{+2}	–0.30	0.04	44
After HD	Urea	0.62	<0.001	44
	GGT	0.70	<0.001	44
	Ca^{+2}	–0.40	0.006	44
	Iron	0.40	0.007	44
	TSH	0.33	0.02	44
HD Patients	Urea	0.58	<0.001	88
	Crea	0.38	<0.001	88
	GGT	0.25	0.020	88
	K^+	0.39	<0.001	88
	Ca^{+2}	–0.21	0.046	88
	Mg^{+2}	–0.34	0.001	88
	Iron	0.23	0.031	88
All groups	Urea	0.55	<0.001	172
	Crea	0.46	<0.001	172
	GGT	0.17	0.02	172
	K^+	0.36	<0.001	172
	Mg^{+2}	–0.24	0.02	172
	Vit B_{12}	0.16	0.035	172

Note: In this table significant correlations are presented.

Discussion

Laboratory follow-up is of utmost importance for patients with ESRD. Rigorous blood sampling can be discomforting for the patients, and may lead to the worsening of already existing anemia. Moreover, the risk of infection is very high during blood sampling, and the need for special equipment and well trained personnel makes the sampling process very expensive. However, the problems encountered in blood sampling are not observed during the analysis of saliva. Saliva analysis can be an alternative to blood analysis, since saliva contains the most blood analytes. In this study, we used a large test panel and evaluated routine biochemistry analytes, thyroid function tests, ferritin and vit B_{12} from serum and saliva of patients who were having follow-ups for ESRD, in order to determine whether saliva markers could be an alternative to blood markers. We investigated the relationship of saliva analytes with serum analytes, and their differences in healthy individuals and in patients with ESRD. In our study, most results of saliva analytes did not reflect serum values. There was a relative difference between the groups only in regards to the nitrogen compound (urea, crea, UA), in patients who underwent HD and PD.

In the study of Bibi et al. (9) in ESRD and predialysis patients TP, ALB, LDH, UA, Na^+, K^+, Cl^-, Ca, Phos levels from saliva samples were evaluated; TP, ALB, Na^+, K^+, Cl^- Ca^{+2}, P levels of dialysis patients were found to be similar to those of PD patients, whereas LDH and UA levels were found to be significantly lower in PD patients. Seethalakshmi et al. (10) demonstrated a significant correlation between the results of serum and saliva samples for urea, Crea, K^+ and Phos, in HD patients; however, no correlation was found with regards to Na levels. Nandan et al. (11) also demonstrated a correlation between urea levels of serum and saliva in HD patients and patients who underwent renal transplantation. In another study, the serum and saliva levels of Crea in healthy subjects and HD patients were compared; saliva Crea analysis did not reflect serum levels (12). In the study by Thomas et al. (13), it was demonstrated that saliva Crea levels of HD patients were higher, compared to saliva samples from healthy subjects. In the said study, urea, Na^+, K^+ and amylase levels of HD patients were also found to be higher than those of healthy individuals. Xia et al. (14) showed that there was a high correlation rate of urea (r=0.918), Crea (r=0.932) and UA (r=0.810) levels of saliva and serum samples collected from healthy control and from ESRD patients with different stages of the disease; the saliva urea, Crea and UA levels were found to be higher than in healthy controls. In another study by Cheng et al. (15) a high correlation among urea (r=0.979), Crea (r=0.973) and UA (r=0.948) levels from saliva and serum samples of ESRD patients was reported, with a significant decrease in saliva and serum urea, Crea and UA levels after hemodialysis. Another study showed a strong correlation between urea (r=0.958) and Crea (r=0.931) levels of serum and saliva in patients with chronic renal failure, diabetes, and hypertension (16). Contrary to these studies, Lalisi et al. found significant but weak correlations between saliva and serum levels of Crea and urea (r=0.69 and r =0.51, p<0.001) (17). In a study carried out by Renda et al. (18), it was found that urea and Crea concentrations were higher in children with CKD, but there were no urea concentrations found in patients and control groups. In our study, a significant correlation was found between the serum and saliva urea and Crea levels in the patient and control groups

($r=0.58$, $r=0.46$, $p<0.001$). On the other hand, saliva urea levels of the patient groups were found to be higher than in control subjects. These results were found to correlate with those of other studies, in regards to saliva urea and Crea which reflected serum levels. Evaluation of azotemia from this condition demonstrates that uric acid levels were inadequate compared to urea levels.

Ca^{+2}, Mg^{+2} and Phos levels are known to be important in the follow-up of bone mineral diseases in ESRD patients. In our study, the comparison of patients with the control group showed that saliva Ca^{+2} and Mg^{+2} levels were lower in the patient groups. Although saliva Ca^{+2} levels were shown to reflect serum Ca^{+2} levels, our results explain why no correlation was found between serum and saliva Ca^{+2} levels. Similarly, saliva Mg^{+2} and Phos levels were found to be independent of the changes in serum values. Literature reports show different results of Ca^{+2}, Mg^{+2} and Phos levels (19–21). The difference in results obtained can be attributed to the different methods used in measuring these ions, difference in the manner of obtaining saliva (stimulated, non-stimulated), and the different properties of patients and healthy controls enrolled in the study.

In our study, LDH levels in the patient group were found to be lower compared to the control group. The comparison of the saliva-serum LDH correlation demonstrated that there was a significant positive correlation only in the PD group. In the study conducted by Goll et al. (22) on HD patients, it was demonstrated that there was no relationship between saliva LDH levels and serum. The fact that saliva analysis in patients showed lower values than in the control group can be attributed to suppression of LDH activity by uremic toxicity. Results of the other saliva enzyme measurements in our study demonstrated that the levels of saliva enzymes correlated with those of serum enzymes. Hence, it was shown that saliva enzyme levels changed independently from serum enzyme levels.

In this study, TSH, fT3, fT4, vit B12, folic acid, ferritin and iron parameters in saliva were frequently used in the diagnosis and management of both thyroid diseases and anemia in patients with renal insufficiency. There are no literature studies investigating TSH, fT_3, fT_4, vit B_{12}, folic acid, ferritin and iron levels in the saliva of patients with chronic renal failure. Putz et al. (23) performed simultaneous analysis on only total T_4 levels in serum and saliva samples. Results of their study showed increased T_4 levels in thyrotoxic patients, and decreased levels in patients with hypothyroidism, and demonstrated that saliva analysis could be a useful marker for the assessment of thyroid function. In our study, saliva levels of fT_3, fT_4, vit B_{12}, ferritin and iron analytes did not reflect serum levels; this supports the absence of a correlation between serum and saliva values. Furthermore, TSH concentrations were found to be lower than the limit of measurement, and folic acid concentrations were detected to be higher than the limit measured in saliva. There are no studies in literature about the hormonal properties of saliva in patients with renal insufficiency. Our work will contribute to the literature in this area.

Effects of Hemodialysis

Goll et al. (22) demonstrated that there was a significant decrease in urea, Crea and UA levels in saliva after HD compared to levels before HD. It has also been reported that saliva Crea and UA levels correlated with serum levels in patients with CRF and HD (before and after). Bots et al. (24) collected saliva samples from HD patients to evaluate changes in urea levels during dialysis. They reported that saliva urea levels decreased by 60% during dialysis. In another study conducted by Blicharz et al. (25) saliva analyte levels before and after HD were compared and it was demonstrated that saliva UA levels decreased after HD. The authors reported that the decrease in urea levels, which is considered as a golden standard in the evaluation of the efficacy of dialysis, correlated with the decrease in saliva UA concentration, and suggested that the measurement of uric acid was valuable during HD follow-ups. Results of our study correlated with literature studies and demonstrated that saliva urea, Crea and UA levels decreased after HD, as compared to levels before HD. In our study, changes in the serum levels of urea, Crea and UA after HD were found to be similar to those of saliva analytes. Similar to the study by Goll et al. (22), we demonstrated that saliva urea and Crea levels before HD correlated with the serum levels. However, unlike in the said study, we demonstrated that after HD only saliva urea levels correlated with the serum values.

Carla et al. (26) in their study compared stimulated and non-stimulated saliva electrolytes before and after HD and reported that Na^+ levels increased after HD. Another study also demonstrated that HD had no effect on saliva Na^+ and Cl^- levels (20). Goll et al. (21) reported that saliva Na^+, K^+ and Cl^- levels decreased after HD. However, no relationship was found between saliva and serum levels. In our study, saliva K^+ and Cl levels were found to be decreased after HD. Although Na levels decreased after HD, this decrease was not found to be statistically significant. Very few literature studies have reported saliva analysis in HD patients. These studies have demonstrated various differences in the effect of HD on saliva electrolytes levels. These differences have been attributed to differences in age, gender, medication used, and in oral and systemic diseases observed among the patients enrolled in the study (26).

In the study conducted by Goll et al. (22) no differences were reported in saliva Ca^{+2} levels after HD;

however, there was a decrease in saliva Phos levels, which did not reflect in serum levels. The decrease in saliva P levels was reported as 13%, whereas decrease in serum levels was 43%. Carla et al. (26) compared values before and after HD and demonstrated that saliva Mg^{+2} levels decreased by 50%, while Phos levels decreased by 40%. Unlike in other studies, our study showed that there was an increase in saliva Ca^{+2} levels after HD, compared to values before HD. Our study showed an increase in saliva Ca^{+2} levels of 94% and serum Ca^{+2} levels of 6.4%, compared to values before HD. Furthermore, unlike in the study by Carla et al. (26), we demonstrated an increase in saliva Mg^{+2} levels after HD. However, serum Mg^{+2} levels were found to have decreased after HD. Comparison of saliva vit B_{12} levels before and after HD demonstrated that there was an increase in vit B_{12} levels after HD. This increase in vit B_{12} levels was found to be 32.3%. However, unlike these results, serum vit B_{12} levels after HD were found to be decreased.

Conclusion and Suggestions

In our study, most analytes of saliva results did not reflect serum values. There was a relative difference between the groups only with regards to the nitrogen compound (urea, Crea, UA), in patients who underwent HD and PD. As a result, saliva urea, Crea and UA measurements may be valuable in the follow-up of these patients. However, saliva UA values were lower than the values in serum; as a result, methods with high analytic sensitivity should be used for UA measurements. On the other hand, standardization is known to be difficult during saliva analysis. Although sampling does not involve invasive interventions, problems associated with mouth and teeth health may affect results. For this reason, analyses with serum have been generally suggested to be more reliable.

Conflict of interest statement

The authors stated that they have no conflicts of interest regarding the publication of this article.

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