Annals of Nuclear Medicine Vol. 16, No. 2, 117–120, 2002

# Salivary function in patients with chronic renal failure undergoing hemodialysis

Meryem KAYA,* Tevfik Fikret ÇERMİK,* Funda ÜSTUN,* Saniye ŞEN** and Şakir BERKARDA*

*Departments of *Nuclear Medicine and **Nephrology, Trakya University Medical Faculty, Edirne, Turkey*

***Purpose:*** The aim of this study was to evaluate the changes in salivary gland function in patients with chronic renal failure (CRF) undergoing hemodialysis. ***Methods:*** The group consisted of 23 patients with CRF (13 female, 10 male; mean age: 40 ± 13 yr) and 14 healthy control subjects (mean age: 40 ± 13 yr). All underwent dynamic salivary gland scintigraphy with gustatory stimulation. After intravenous administration of $^{99m}$Tc pertechnetate, first, perfusion images at 2 seconds per frame were acquired for 1 minute, then dynamic images at 1 minute per frame were acquired for 45 minutes. At 30 minutes after injection, 10 m*l* lemon juice was given for 15 minutes as a gustatory stimulus. We obtained time-activity curves derived from regions of interest centered over the four major salivary glands. The following functional indices were calculated for each gland: the time of maximum radioactivity ($T_{max}$) for the prestimulated period, the time of minimum radioactivity ($T_{min}$), as an indicator of velocity of secretion after stimulation, and the Lem $E_5$% value as an indicator of the secretion function. ***Results:*** When the patients with CRF undergoing hemodialysis were compared to the controls, there were statistically significant differences in $T_{max}$, $T_{min}$ and Lem $E_5$% values for bilateral parotid glands, and $T_{min}$ values for bilateral submandibular glands ($p < 0.05$), there were no statistically significant differences in $T_{max}$ and Lem $E_5$% values for bilateral submandibular glands. There were also significant differences in $T_{max}$ and Lem $E_5$% values for bilateral parotid glands between mild oral problems and severe oral problems in patients with CRF (undergoing hemodialysis). ***Conclusion:*** In this study, prolonged $T_{max}$ and $T_{min}$ values, and decreased Lem $E_5$% values for parotid glands and prolonged $T_{min}$ values for submandibular glands on salivary scintigraphy pointed out decreased parenchymatous and excretory function in patients with CRF undergoing hemodialysis.

**Key words:** chronic renal failure, salivary function, scintigraphy

## INTRODUCTION

UREMIA is the term generally applied to the clinical syndrome observed in patients suffering from profound loss of renal function. Although the cause(s) of the syndrome remain unknown, the term uremia was adopted originally because of the presumption that the abnormalities seen in patients with chronic renal failure (CRF) resulted from retention in the blood of urea and other end products of metabolism normally excreted into the urine.

Patients with CRF undergoing hemodialysis have clinical changes such as uremic odor, dry mouth, taste and salivary changes.[1] The concentration of Mg and $PO_4$ ions in parotid saliva is also high in patients with CRF.[2] In addition, Epstein et al.[3] showed that dialysis patients formed more heavy calculus, and an increased salivary urea concentration when undergoing hemodialysis.

Scintigraphy with $^{99m}$Tc pertechnetate is a readily available, non-invasive, diagnostic test used to evaluate salivary glands function. It has been used in diagnosis of a variety of salivary disorders, including Sjögren's syndrome,[4] Bell's palsy,[5] sialolithiasis, gland aplasia and duct obstruction.[6]

The aim of this study was to evaluate the changes in

Received June 22, 2001, revision accepted December 20, 2001.

For reprint contact: Meryem Kaya, M.D., Trakya Üniversitesi Tıp Fakültesi, Nükleer Tıp ABD, 22030 Edirne, TURKEY.

E-mail: meryemk@trakya.edu.tr

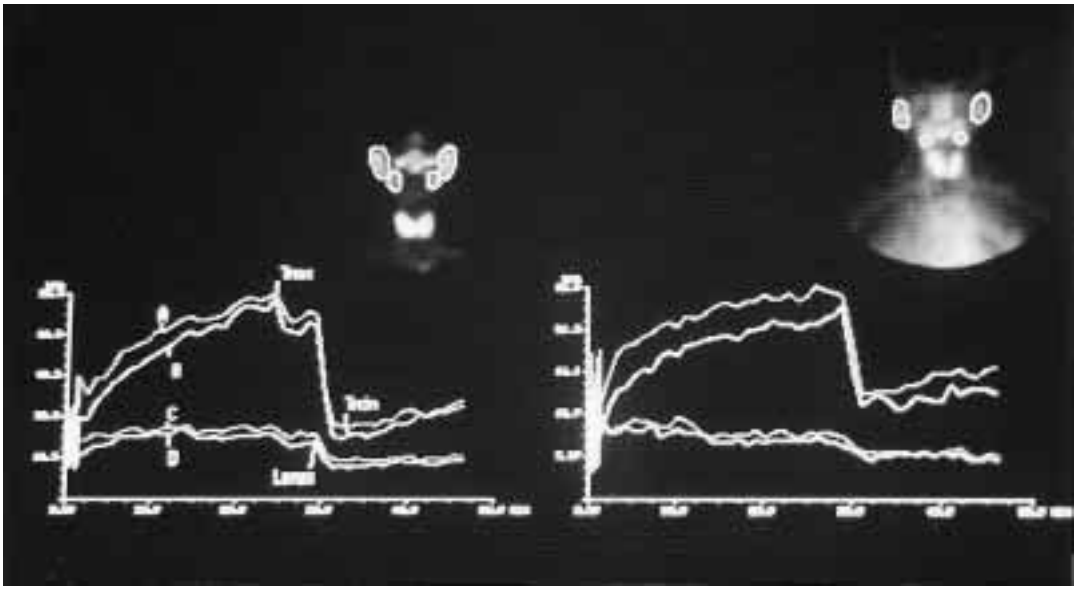

**Fig. 1** The figure on the left side illustrates the time-activity curves of a patient with CRF and the figure on the right side illustrates the time-activity curves of a normal control. Time-activity curves derived from ROIs over right parotid (A), Ieft parotid (B), right submandibular (C) and left submandibular (D) glands. $T_{max}$ and $T_{min}$ values, and the time of lemon juice stimulation were showed on the time-activity curves.

**Table 1** Comparison of scintigraphic parameters in normal controls and patients with chronic renal failure undergoing hemodialysis

| Parameter | Gland | Control (n = 14) Mean ± s.d. | Patients with CRF (n = 23) Mean ± s.d. | p value |
|---|---|---|---|---|
| $T_{max}$ (min) | RP | 21.14 ± 2.85 | 24.85 ± 5.95 | 0.036 |
| | LP | 20.71 ± 3.40 | 24.02 ± 5.20 | 0.04 |
| | RS | 19 ± 5.52 | 17.76 ± 6.11 | ns |
| | LS | 19.46 ± 5.06 | 18.07 ± 7.42 | ns |
| $T_{min}$ (min) | RP | 31.93 ± 0.58 | 33.61 ± 1.54 | 0.0004 |
| | LP | 31.68 ± 0.54 | 33.36 ± 2.42 | 0.015 |
| | RS | 31.82 ± 0.66 | 35.26 ± 3.87 | 0.002 |
| | LS | 31.57 ± 0.62 | 34.5 ± 3.23 | 0.02 |
| Lem $E_5$% | RP | 58.41 ± 17.2 | 48.16 ± 17.43 | 0.042 |
| | LP | 60.75 ± 16.4 | 46.92 ± 14.7 | 0.013 |
| | RS | 71.45 ± 5.03 | 69.21 ± 15.77 | ns |
| | LS | 70.63 ± 4.5 | 70.27 ± 16.19 | ns |

RP: Right parotid, LP: Left parotid, RS; Right submandibular, LS: Left submandibular, ns: not significant.

**Table 2** Comparison of the scintigraphic parameters in group 1 and group 2 patients with chronic renal failure undergoing hemodialysis

| | Group 1 (n = 9) | Group 2 (n = 14) | p values |
|---|---|---|---|
| RP $T_{max}$ | 18.5 ± 3.81 | 28.93 ± 2.28 | 0.00001 |
| RP Lem $E_5$% | 58.98 ± 17.17 | 41.21 ± 14.12 | 0.013 |
| LP $T_{max}$ | 19.50 ± 3.32 | 26.93 ± 3.98 | 0.0001 |
| LP Lem $E_5$% | 58.19 ± 14.28 | 40.05 ± 11.32 | 0.003 |

salivary gland function in patients with CRF undergoing hemodialysis.

## MATERIALS AND METHODS

*Patients*

Twenty-three individuals (10 male and 13 female; age range: 18–66 yrs; mean age 40 ± 13 yrs) with CRF undergoing hemodialysis and age-matched healthy control group were enrolled in this study. The glomerular filtration rate of all patients with CRF was 20 to 25 percent below normal, and they have received hemodialysis routinely (mean duration of hemodialysis 14 ± 7.2 months). The causes of renal failure were chronic pyelonephritis in nineteen patients, and chronic glomerulonephritis in four patients. Patients with CRF were taking only routine medications for renal failure and hemodialysis. Patients who had a history of smoking, or endocrine, collagen vascular disease, or any medication except for renal failure were excluded. All patients were examined for both subjective and objective oral problems. Group 1 (n = 9) patients had mild oral problems such as uremic odor, mild dry mouth and taste changes. Group 2 (n = 14) patients had severe oral problems such as petechia and/or ecchymosis, tongue coating, oral ulceration, stomatitis, increased plaque and calculus. The control group consisted of 14 healthy volunteers (5 male, 9 female; mean age 40 ± 13 yrs) who were not being treated for any systemic illness, or taking any prescribed medication. Controls were also free of xerotomic symptoms.

*Salivary Gland Scintigraphy*

After an overnight fast, patients were placed in a supine position with the neck slightly extended prior to intravenous injection of tracer. A gamma camera (Philips, Holland) with a low-energy high-resolution parallel hole collimator was used. After an intravenous bolus injection of about 370 MBq $^{99m}$Tc pertechnetate, perfusion images were obtained every 2 seconds for 1 minute and followed by acquisition dynamic images every minute for 45 minutes. At 30 minutes post-injection salivary excretion was stimulated with 10 m*l* of lemon juice administered orally. Images were collected into a $64 \times 64$ matrix in word mode with a zoom factor of 2. The energy window around the 140 keV photon peak of $^{99m}$Tc was 20%.

*Data Analysis*

For data analysis, four regions of interest (ROI) were drawn manually around the parotid and submandibular glands on summation images. A time-activity curve of each salivary gland was created (Fig. 1). On the basis of the time-activity curves, the following functional parameters were calculated for each salivary gland. $T_{max}$ was the maximum count before oral stimulation from 1 minute after injection. $T_{min}$ was the time until the minimum count after oral stimulation from 1 minute after injection. Lem $E_5$% value was calculated as the counts at the 5th minute after stimulation divided by the counts at the 30th minute the beginning of the study and multiplied by a hundred.

*Statistical Analysis*

All values are expressed as the mean ± standard deviation (SD). Statistical analysis was performed by means of the Mann-Whitney U test or Spearman rank test of correlation between groups. The Mann-Whitney U test was used for comparison of scintigraphic parameters for normal controls and patients with CRF undergoing hemodialysis. The Spearman rank correlation test was used for comparison of scintigraphic parameters and oral problems, and the duration of hemodialysis. Values of $p < 0.05$ were considered statistically significant.

## RESULTS

The scintigraphic parameters such as $T_{max}$, $T_{min}$, and Lem $E_5$% values for patients with CRF undergoing hemodialysis and healthy control subjects were compared (Table 1).

There were statistically significant differences in $T_{max}$, $T_{min}$, and Lem $E_5$% values for bilateral parotids, and $T_{min}$ for bilateral submandibular glands. There were no statistically significant differences at $T_{max}$ and Lem $E_5$% values for bilateral submandibular glands compared with healthy control subjects.

When comparing the patients with CRF undergoing hemodialysis in groups 1 and 2, there were statistically significant differences in $T_{min}$ and Lem $E_5$% values for both parotid glands (Table 2). There were no significant differences between groups 1 and 2 in $T_{min}$ values for parotid glands, and also all scintigraphic indices for submandibular glands in groups 1 and 2 were not significantly different. We did not find any relationship between the scintigraphic indices and the duration of hemodialysis.

## DISCUSSION

Salivary gland scintigraphy is a particularly valuable tool because it produces a dynamic, objective, and quantitative measurement of the major salivary gland functions. It is characterized both by an excellent intraobserver variability and reproducibility that allows the detection of changes in parenchyma function in a range about as low as 5–10%.[7] This enables not only early detection of Sjögren's syndrome, as compared with other imaging methods, and also detection of parenchyma impairment of salivary glands after low-dose radioiodine therapy.[8]

Normal salivary function is important for oral and dental health. Patients with CRF undergoing hemodialysis often have a decreased salivary flow rate and oral problems such as dry mouth, oral infection and dental problems. In previous studies, Kho et al.[1] showed that patients with end-stage renal disease (ESRD) requiring hemodialysis had lower flow rates of both unstimulated and stimulated parotid saliva than those of the controls. Gavalda et al.[9] showed that hemodialysis patients had significantly higher plaque and calculus indices, and lower salivary secretion than healthy controls. Kao et al.[10] used quantitative salivary scintigraphy for the evaluation of salivary function in patients with ESRD requiring hemodialysis. Patients with ESRD with oral manifestations had significantly poorer salivary function than patients with ESRD without oral manifestations and healthy controls.

In our study, we showed that the time-activity curve calculated from the salivary gland uptake of technetium 99m pertechnetate included the following phases: (1) the first phase until 1 minute after injection, representing a vascular perfusion of the salivary glands, (2) the second phase, which started at 1 minute and lasted until the time of maximum uptake ($T_{max}$) as an index of parenchymatous function, (3) the third phase represented the velocity of secretion after oral stimulation ($T_{min}$) and the quantity of secretion after oral stimulation (Lem $E_5$%). We found that patients with CRF undergoing hemodialysis had significantly prolonged $T_{max}$ and $T_{min}$ values and decreased Lem $E_5$% values for parotid glands compared to healthy control subjects. Submandibular glands the patients with CRF undergoing hemodialysis had also significantly prolonged $T_{min}$ values, but there were no significant differences in $T_{max}$ and Lem $E_5$% values, compared with healthy control subjects. In view of these results, the differences between the function of parotid and submandibular glands may be reveal that the function

of the parotid glands was affected more severely than the function of the submandibular glands.[11,12] In addition, all excretory function tests were more seriously affected in the parotid glands than in the submandibular glands. This may be due to the higher concentration of serous acinar cells in the parotid glands. In the present study, $T_{min}$ values as a parameter of secretion function were affected earlier than the parenchyma function of submandibular glands in patients with CRF undergoing hemodialysis. Moreover, our results indicated that the patients with severe oral problems had more significantly prolonged $T_{max}$ values and decreased Lem $E_5$% values than the patients with mild oral problems. But we did not find any correlation between the scintigraphic indices and the duration of hemodialysis. The scintigraphic evaluation of salivary gland function will contribute to the early diagnosis and treatment of oral and dental problems in patients with CRF undergoing hemodialysis.

In this study, it was indicated that prolonged $T_{max}$ and $T_{min}$ values, and decreased Lem $E_5$% values for parotid glands and prolonged $T_{min}$ values for submandibular glands on salivary scintigraphy pointed out decreased parenchymatous and excretory function of salivary glands in patients with CRF undergoing hemodialysis.

## REFERENCES


1. Kho HS, Lee SW, Chung SC, Kim YK. Oral manifestations and salivary flow rate, pH, and buffer capacity in patients with end-stage renal disease undergoing hemodialysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; 88: 316–319.
2. Earlbaum AM, Quinton PM. Elevated divalent ion concentrations in parotid saliva from chronic renal failure patients. *Nephron* 1981; 28 (2): 58–61.
3. Epstein SR, Mandel I, Scopp IW. Salivary composition and calculus formation in patients undergoing hemodialysis. *J Periodontol* 1980; 51: 336–338.
4. Kohn WG, Ship JA, Atkinson JC, Patton LL, Fox PC. Salivary gland $^{99m}$Tc-scintigraphy: a grading scale and correlation with major salivary gland flow rates. *J Oral Pathol Med* 1992; 21: 70–74.
5. Yamashita T, Ino C, Tomoda K, Kumazawa T. Prognostic determination and submandibular function in Bell's palsy. Dynamic testing with technetium Tc 99m. *Arch Otolaryngol* 1985; 111: 244–248.
6. van den Akker HP, Busemann-Sokole E. Absolute indications for salivary gland scintigraphy with $^{99m}$Tc-pertechnetate. *Oral Surg Oral Med Oral Pathol* 1985; 60: 440–447.
7. Bohuslavizki KH, Brenner W, Klutmann S, Hübner RH, Lassmann S, Feyerabend B, et al. Radioprotection of salivary gland by Amifostine in high-dose Radioiodine therapy. *J Nucl Med* 1998; 39: 1237–1242.
8. Bohuslavizki KH, Brenner W, Wolf H, Sippel C, Tonshoff G, Tinnemeyer S, et al. Value of quantitative salivary gland scintigraphy in the early stage of Sjögren's syndrome. *Nucl Med Commun* 1995; 16: 917–922.
9. Gavalda C, Bagan J, Scully C, Silvestre F, Milian M, Jimenez Y. Renal hemodialysis patients: oral, salivary, dental and periodental findings in 105 adult cases. *Oral Dis* 1999; 5 (4): 299–302.
10. Kao CH, Hsieh JF, Tsai SC, Ho YJ, Chang HR. Decreased salivary function in patients with end-stage renal disease requiring hemodialysis. *Am J Kidney Dis* 2000; 36 (6): 1110–1114.
11. Umehara I, Yamada I, Murata Y, Takahashi Y, Okada N, Shibuya H. Quantitative evaluation of salivary gland scintigraphy in Sjögren's syndrome. *J Nucl Med* 1999; 40: 64–69.
12. Liem IH, Olmos RA, Balm AJ, Keus RB, van Tinteren H, Takes RP, et al. Evidence for early and persistent impairment of salivary gland excretion after irradiation of head and neck tumours. *Eur J Nucl Med* 1996; 23: 1485–1490.