Assessment of salivary gland function in patients after successful kidney transplantation using $^{99m}$Tc-pertechnetate salivary gland scintigraphy

Abstract
Chronic renal failure and its treatment can induce oral health problems and salivary glands dysfunction. The purpose of this study was to assess salivary glands function in patients with kidney transplantation using technetium-99m pertechnetate ($^{99m}$Tc-P) salivary glands scintigraphy. We prospectively studied 34 patients with kidney transplantation (30 males and 4 females, mean age 39.76±11.6 years) and 28 healthy controls (12 males and 16 females, mean age 36.1±9.5 years). Salivary gland scintigraphy was performed nearly 4.4±2.9 years after successful kidney transplantation. Dynamic salivary glands scintigraphy was performed during 25min after the intravenous administration of 185MBq of $^{99m}$Tc-P. Time-activity curves and glands functional parameters were calculated for the parotid and submandibular salivary glands: uptake ratio, maximum accumulation of the radionuclide, and excretion fraction. Statistical analysis of the functional parameters showed no significant differences between patients with kidney transplantation and healthy controls (P>0.05). In conclusion, this study showed that using $^{99m}$Tc-P salivary gland scintigraphy, salivary glands function of patients with successful kidney transplantation do not differ statistically from those in healthy controls.

Introduction
Kidney transplantation has been the best treatment option for patients who suffered from chronic end-stage kidney disease. The number of patients with kidney transplantation increases rapidly [1]. All transplant patients use immunosuppressant treatment to prevent allograft rejection. Some of them may suffer from systemic diseases and may also affect the oral health and salivary flow rate [2, 3]. It has been reported that the parenchymatous and excretory functions of salivary glands were decreased in patients with chronic renal failure undergoing haemodialysis or continuous ambulatory peritoneal dialysis [4-6]. Salivary gland scintigraphy is a useful method in the determination of the etiology and the degree of salivary dysfunction. Salivary glands scintigraphy is non-invasive with low dosimetry, does not interfere with normal physiology and can provide quantitative data about uptake ratio, concentration and excretion fraction of the salivary glands [7-9].

The purpose of this prospective study was to assess salivary glands function in patients kidney transplantation using technetium-99m pertechnetate ($^{99m}$Tc-P) salivary gland scintigraphy.

Materials and methods
Patients
The study population consisted of 34 patients with kidney transplantation (30 males and 4 females, mean age 39.76±11.6 years) and 28 healthy controls (12 males and 16 females, mean age 36.1±9.5 years). The salivary gland scintigraphy was performed approximately 4.4±2.9 (range 1 to 11) years after successful kidney transplantation. The levels of glomerular filtration rate (GFR) are higher than 60mL/min/1.73m² in all patients. Serum creatinine (Scr) and blood urea nitrogen (BUN) values of patients were 1.04±0.23mg/dL (normal range, 0.66-1.44mg/dL) and 15.39±3.16mg/dL (normal range, 6-22mg/dL), respectively. Patients with a history of head or neck, surgery or radiation treatment or patients with diabetes mellitus were excluded from the study. All patients gave their informed consent for the study. The study protocol was approved by the local ethics committee.
Salivary gland scintigraphy

Salivary gland scintigraphy was performed after intravenous administration of 185MBq of $^{99m}$Tc-P using a dual head gamma camera with a parallel-hole, low-energy, high-resolution collimator (Siemens E.CAM, Siemens Medical Systems, Inc. Hoffman Estates, IL 60195). The photopoint was centered at 140keV with a 20% window. A total of 25 frames of 60sec each were acquired in the anterior position of the head and neck during the 25min study with a zoom 1.33 and matrix of 128x128. Salivary glands secretion was stimulated with 3mL concentrated lemon juice instilled orally with a syringe at 20min similar protocols have been used by others [9, 10]. All patients tolerated the repeated study well.

Semi-quantitative analysis

For semi-quantitative analysis, regions of interest (ROI) were drawn around the right and left parotid glands and the right and left submandibular glands on summation images of dynamic scintigraphy. A background ROI was placed in the temporal region (Fig. 1). A time-activity curve of each salivary gland was created (Fig. 2).

The following points were designated on the time-activity curve: a) vascular perfusion, at 1min; b) the maximum count before stimulation; c) the background count at the time of peak activity; d) the minimum count after stimulation (Fig. 2).

The following glandular function parameters were calculated using the time-activity curves for each salivary gland:

\[
\text{uptake ratio (UR)} = \frac{b}{c}, \quad \text{maximum accumulation (MA)\%} = \frac{(b-a)}{b} \times 100, \quad \text{excretion fraction (EF)\%} = \frac{(b-d)}{b} \times 100.
\]

Statistical analysis

We used the SPSS software program for statistical analysis. All dates were calculated as mean±standard deviations. The normal distribution of data was analysed by the Kolmogorow-Smirnow test. Groups were compared using the Mann-WhitneyU test and Student’s t-test. Significance level for P was taken as <0.05.

**Table 1. Comparison of scintigraphic parameters in patients with kidney transplantation and healthy controls groups**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Salivary Glands</th>
<th>Healthy Controls (n=28)</th>
<th>Patients (n=34)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>8.55±2.41</td>
<td>8.49±4.77</td>
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<tr>
<td>LP</td>
<td>8.07±2.48</td>
<td>7.76±3.78</td>
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<tr>
<td>RSbm</td>
<td>5.30±2.36</td>
<td>4.25±0.97</td>
<td>0.087</td>
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<tr>
<td>LSbm</td>
<td>4.93±2.11</td>
<td>4.14±0.78</td>
<td>0.107</td>
<td></td>
</tr>
<tr>
<td><strong>%MA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>63.93±10.42</td>
<td>58.62±12.70</td>
<td>0.079</td>
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<tr>
<td>LP</td>
<td>62.86±9.67</td>
<td>57.32±13.55</td>
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<tr>
<td>RSbm</td>
<td>43.33±10.92</td>
<td>40.38±7.07</td>
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<tr>
<td>LSbm</td>
<td>44.28±10.70</td>
<td>41.24±5.82</td>
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</tr>
<tr>
<td><strong>%EF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>61.80±12.15</td>
<td>58.82±12.69</td>
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<tr>
<td>LP</td>
<td>60.93±11.69</td>
<td>59.22±9.10</td>
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<tr>
<td>RSbm</td>
<td>47.28±11.20</td>
<td>43.96±9.73</td>
<td>0.216</td>
<td></td>
</tr>
<tr>
<td>LSbm</td>
<td>46.90±13.14</td>
<td>44.56±10.60</td>
<td>0.442</td>
<td></td>
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</tbody>
</table>

Data are expressed as mean±SD. UR: uptake ratio, MA: maximal accumulation, EF: excretion fraction, RP, LP: right, left parotid glands, RSbm, LSbm: right, left submandibular glands.

**Results**

Thirty-four (30 males and 4 females) patients with kidney transplantation and 28 healthy controls (12 males and 16 females) were included in this study. In Table 1, the values for the UR, MA% and EF% calculated from parotid and submandibular glands are presented. When comparing the patients with kidney transplantation and healthy controls, there were no statistically significant differences in the UR, MA% and EF% for bilateral parotid and submandibular salivary glands (P>0.05) (Table 1).
Discussion

Chronic renal failure (CRF) affects most body systems such as hematological, cardiovascular, neurological and gastrointestinal. Also oral complications may occur as a result of CRF or its treatment such as dialysis and transplantation [3]. In a study a high prevalence of xerostomia was found in patients both on dialysis and after kidney transplantation [11]. Other researchers reported that salivary flow rate per minute decreased at the end stage renal disease of patients having Scr 9.05mg/dL and undergoing hemodialysis and also in patients’ peritoneal dialysis undergoing and having Scr 8.95mg/dL [12, 13]. Others reported that by using $^{99m}$Tc-P salivary gland scintigraphy, salivary gland function was impaired among the CRF patients treated with continuous ambulatory peritoneal dialysis compared with healthy controls by [6]. It was also reported that salivary flow rate increased in kidney transplantation patients compared with salivary flow rate before transplantation. This situation may mean an effect in the quality of life of patients with end stage renal disease [14]. Our study has demonstrated for the first time that salivary glands functions in patients with kidney transplantation measured by $^{99m}$Tc-P salivary gland scintigraphy after successful kidney transplantation were normal and almost as good as of healthy controls. Patients’ Scr during the study time was 1.04±0.23mg/dL (normal range, 0.66-1.44mg/dL) and BUN was 15.39±3.16mg/dL (normal range, 6-22mg/dL). Recovery in salivary gland function after kidney transplantation may be associated with restoration of physiological kidney function as for water and electrolytes distribution [14]. Other researchers reported in a two years follow-up study that decreased salivary function is reversible and is restored by kidney transplantation [14].

The salivary glands can be evaluated with computerised tomography (CT) and sialography but these techniques do not allow quantification of the salivary glands function. Furthermore, with sialography, which can diagnose functional obstruction, cannulisation of salivary glands ducts is difficult and painful for the patients [9]. Salivary glands scintigraphy enables a functional evaluation of the salivary glands, does not interfere with normal physiology, can be performed easily, quickly, is well tolerated by the patients, is non-invasive and has a low dosimetry [15-19]. Previous studies have reviewed the quantitation of salivary glands function, and of functional indices such as percent uptake, concentration and excretion fractions derived from salivary gland time-activity curves, as we have used [6-8, 20]. Other researchers studied a variety of uptake ratios, maximum accumulation and ejection fraction in a group of patients with xerostomia caused by various autoimmune diseases [7].

In conclusion, the results of our study indicated that salivary glands function prospectively studied in patients after successful kidney transplantation and in healthy controls using $^{99m}$Tc-P salivary gland scintigraphy did not differ statistically. Larger studies are required to evaluation of salivary gland functions in patients with kidney transplantation.

Bibliography