

Evaluation by ^{99m}Tc -pertechnetate scintigraphy of the effect of levocetirizine on salivary glands function, in allergic rhinitis patients

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Abstract

The purpose of this study was to assess the effect of levocetirizine (xyzal) on salivary glands function in patients with allergic rhinitis using technetium-99m pertechnetate (^{99m}Tc -P) salivary gland scintigraphy. *The study population consisted of 67 patients with allergic rhinitis and 31 healthy controls (14 males and 17 females, mean age 30.1 ± 6.8 years). The patients were divided into two groups: an untreated patient Group of 32 patients, 17 males and 15 females, mean age 29.9 ± 6.5 years and a levocetirizine-treated with $5\text{mg}\cdot\text{day}^{-1}$ for 4 weeks patient Group, consisted of 35 patients, 16 males and 19 females, mean age 33.5 ± 7.8 years. All patients and healthy controls underwent salivary glands scintigraphy. After the intravenous administration of 185MBq of ^{99m}Tc -P, dynamic salivary glands scintigraphy was performed for 25min. By the time-activity curves, the following glandular function parameters were calculated for the parotid and submandibular salivary glands: uptake ratio, maximum accumulation, and ejection fraction. *Our results showed:* All functional parameters obtained for the untreated patient Group were significantly lower than for the levocetirizine-treated patient Group and healthy controls ($P<0.05$). There was no significant difference in any functional parameters between the levocetirizine-treated patient Group and healthy controls ($P>0.05$). *In conclusion,* results of our study indicate that patients with allergic rhinitis treated with levocetirizine showed a significantly higher salivary glands function compared with untreated patients and healthy controls. Levocetirizine treatment showed no side effects on salivary glands function.*

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Introduction

Xerostomia, a subjective feeling of dry mouth, may arise from decreased production of saliva. Sjögren's syndrome, external radiation to the head and neck, chemotherapy, the anticholinergic effects of many drugs and various viral infections have been held responsible for inducing xerostomia [1-3].

Allergic rhinitis is an extremely common health problem with an incidence rate of approximately 10%-25% [4-6]. It is characterized by antigen-mediated inflammation of the nasal mucosa. It usually presents with sneezing, watery rhinorrhea, nasal congestion and itching, postnasal drip, and red watery, itchy eyes [7]. Nevertheless, patients with allergic rhinitis were found to have lower salivary flow rates [8].

Antihistamine drugs are a first-line treatment for allergic rhinitis. By blocking histamine H1 receptors, antihistamine drugs relieve most of the signs of allergic rhinitis such as sneezing, nasal itching, and rhinorrhea [9]. Levocetirizine, the active enantiomer of cetirizine, has twice the affinity for the H1 receptor compared with cetirizine [10-12]. In addition, levocetirizine provides effective selective H1 blockade without anticholinergic activity [13, 14].

Salivary gland scintigraphy with technetium-99m pertechnetate (^{99m}Tc -P) is a well accepted diagnostic tool for allergic rhinitis, it has a low dosimetry and does not interfere with normal physiology [15-18]. In addition, by using this method, quantitative data about the major functions of salivary glands can be obtained [3, 19, 20].

Review of the literature reveals that there is no report about the evaluation of salivary glands function using ^{99m}Tc -P salivary glands scintigraphy in allergic rhinitis patients treated with antihistamine drugs.

The aim of this study was to evaluate the effect of levocetirizine on salivary glands functions in allergic rhinitis patients using ^{99m}Tc -P salivary glands scintigraphy.

Materials and methods

Patients

The study population consisted of 67 patients with allergic rhinitis and 31 healthy controls. Healthy controls were 14 males and 17 females ranging in age from 20 to 46 years, mean age 30.1 ± 6.8 years. The patients were divided into two groups: an untreated patient Group of 32 patients, 17 males and 15 females ranging in age from 22 to 49 years, mean age 29.9 ± 6.5 years and a levocetirizine-treated patient Group of 35 patients, 16 males and 19 females ranging in age from 21 to 51 years, mean age 33.5 ± 7.8 years (Table 1). All patients in the treated Group received the standard clinically recommended oral dose of levocetirizine of $5 \text{ mg} \cdot \text{day}^{-1}$ (xyza[®], UCB, Slough, UK) for 4 weeks. The Ethics Committee of our university approved this study. All patients with allergic rhinitis had perennial nasal symptoms and a positive skin test to common inhalant allergens. None of the patients or healthy controls had a history of head or neck surgery or radiation treatment. None had a connective tissue or other systemic disease.

Table 1. Characteristics of patients and healthy controls groups

Groups	N	Sex (male/female)	Mean age \pm SD (range) (years)
Untreated patients	32	17 / 15	29.9 ± 6.5 (22-49)
Levocetirizine-treated patients	35	16 / 19	33.5 ± 7.8 (21-51)
Healthy controls	31	14 / 17	30.1 ± 6.8 (20-46)

Salivary gland scintigraphy

After intravenous administration of 185 MBq of $^{99\text{m}}\text{Tc-P}$, dynamic salivary glands scintigraphy was performed using a single-head gamma camera with a parallel-hole, low-energy, high-resolution collimator (GE-Starcam 4000 XR/T, St Albans, Hertfordshire, UK). The photopeak was centered at 140 keV with a 20% window. A total of 25 frames of 60s each were acquired in the anterior position of the head and neck during the 25min study with a zoom of 1.33 and matrix of 128×128 . Salivary gland secretion was stimulated with 3mL concentrated lemon juice instilled orally with a syringe at 20min. All patients and healthy controls tolerated the 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 (Fig. 1). A background ROI was placed in the temporal region. A time-activity curve of each salivary gland was created. As shown in Figure 2, the following points were designated on the time-activity curve: a) representing vascular perfusion at 1 min; b) the maximum count before stimulation; c) the background count at the time of peak activity; d) the minimum count after stimulation.

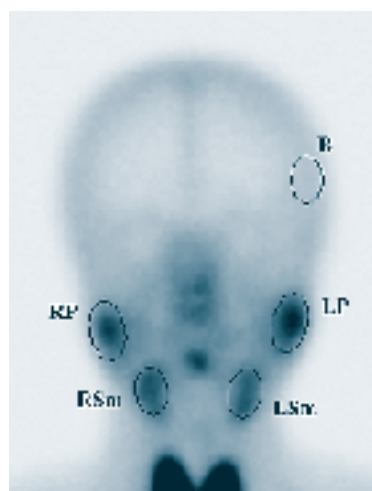


Figure 1. Regions of interest on the summation image, obtained by dynamic scintigraphy. RP, right parotid; LP, left parotid; RSm, right submandibular gland; LSm, left submandibular gland; B, background.

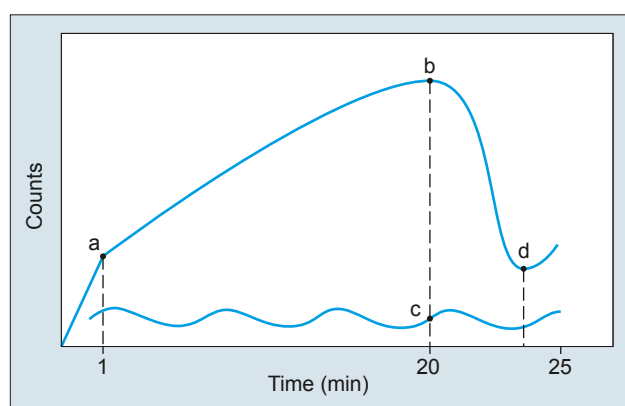


Figure 2. Schematic presentation of a time-activity curve, in a normal pattern of salivary gland scintigraphy. Points: a, representing a vascular perfusion at 1 min; b, the maximum count before stimulation; c, the background count at the time of peak activity; point d, the minimum count after stimulation.

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

$$\text{Uptake ratio (UR)} = b / c,$$

$$\text{Maximum accumulation (MA\%)} = (b - a) / b \times 100,$$

$$\text{Ejection fraction (EF\%)} = (b - d) / b \times 100$$

Statistical analysis

The Kolmogorov-Smirnov test of the normality of the distribution led to the use of the nonparametric method. The Mann-Whitney U test was used for comparison of healthy control group versus untreated patient group, healthy control group versus levocetirizine-treated patient group and untreated patient group versus levocetirizine-treated patient group. The Kruskal-Wallis test was used for comparison of all Groups with a Bonferroni correction. Differences with a P value less than 0.05 were accepted as significant. Data are presented as means \pm standard deviation (SD). The SPSS version 11.5 (SPSS Inc., Chicago, IL) software program was used for statistical analysis.

Results

In Table 2, the values for the UR, MA% and EF% calculated from parotid and submandibular glands are presented. Statistical analysis revealed that the UR, MA% and EF% values for bilateral parotids and submandibular glands obtained in untreated patients were significantly lower than those in levocetirizine-treated patients and healthy controls ($P < 0.05$) (Fig. 3a-3c). However, no significant difference was found for UR, MA% and EF% values of bilateral parotids and submandibular glands between levocetirizine-treated patients and healthy controls ($P > 0.05$).

Discussion

Allergic rhinitis, an inflammation of the upper airway mucous membranes, is mediated by binding antigens to specific immunoglobulin E antibodies. The most common symptoms are sneezing, sniffing, watery rhinorrhea, nasal congestion, and itching in patients with allergic rhinitis. However, there have also been reports of allergic conjunctivitis, characterized by red, watery, and itchy eyes [7]. Additionally, dryness of the mucous membrane in the nasal cavity has been described [8, 21]. Thus, after the allergic watery discharge, a dry mouth sensation may be expected. The anatomical proximity between the nasal cavity and the oral cavity may also lead to the patient's perception of dry mouth [22]. A lower salivary flow rate was found in patients with allergic rhinitis compared with healthy controls [8]. In this study, similar findings were observed and the differences were statistically significant.

Antihistamine drugs are a standard treatment for moderate allergic symptoms. The first-generation antihistamines are not specific for any of the histamine receptors, and suffer the disadvantage of having cholinergic adverse effects such as urinary retention, constipation, drying of the mucus membranes, sedation, and impaired coordination [23, 24]. Levocetirizine, one of the recently used second-generation antihistamines, is a potent, selective antagonist of the peripheral H1 receptor, and furthermore is devoid of cholinergic activity [13, 14].

The salivary glands can be evaluated through computerized tomography and sialography. However, neither computerized tomography nor sialography allow quantification of the salivary gland function and obstruction [20]. Furthermore, in the diagnosis of functional obstruction by sialography, can-

Table 2. Comparison of scintigraphic parameters in patients and healthy controls groups

Parameter	Gland	Untreated patients (n = 32)	Levocetirizine-treated patients (n = 35)	Healthy controls (n = 31)
UR	RP	3.99 ± 1.44	8.52 ± 3.18	9.24 ± 2.12
	LP	4.67 ± 1.69	7.88 ± 2.63	8.74 ± 2.10
	RSm	2.49 ± 1.26	5.49 ± 1.26	6.20 ± 2.06
	LSm	2.44 ± 1.03	4.82 ± 1.41	5.77 ± 1.71
%MA	RP	53.61 ± 9.07	61.30 ± 7.70	64.91 ± 9.49
	LP	54.38 ± 10.53	61.39 ± 6.26	63.68 ± 9.27
	RSm	27.55 ± 10.11	37.60 ± 11.22	42.46 ± 9.26
	LSm	24.74 ± 10.20	39.95 ± 8.27	43.13 ± 8.64
%EF	RP	51.55 ± 9.80	62.79 ± 9.22	66.50 ± 9.01
	LP	53.34 ± 11.87	62.89 ± 7.60	65.40 ± 8.37
	RSm	39.57 ± 10.83	47.30 ± 9.53	50.47 ± 9.30
	LSm	38.47 ± 11.16	48.95 ± 8.71	52.09 ± 9.97

UR, uptake ratio; %MA, maximum accumulation; %EF, ejection fraction; RP, right parotid; LP, left parotid; RSm, right submandibular; LSm, left submandibular. Data are expressed as mean ± SD.

nulization of all four salivary glands ducts is difficult and often painful for the patients [20]. On the other hand, salivary glands scintigraphy enables a functional evaluation of the salivary glands, as a valuable tool. Salivary glands scintigraphy can be performed easily and quickly, and is non-invasive. It is well tolerated by patients because it has a low dosimetry and does not interfere with normal physiology [15-18]. A review of previous reports on quantitation of salivary glands function showed that most functional indices such as percent uptake, concentration and excretion fractions were derived from individual salivary gland time-activity curves generated from dynamic study [2, 3, 19, 20]. Booker et al. (2004) studied a variety of uptake ratios, maximum accumulation and ejection fraction in a group of 83 patients with xerostomia, including a subset of 40 patients with Sjogren's syndrome, and a group of 26 healthy volunteers [2]. Others performed salivary gland scintigraphy to obtain reference values of major salivary glands uptake and excretion fraction, in 50 healthy volunteers [3].

In conclusion, results of our study indicate that patients with allergic rhinitis treated with levocetirizine showed a significantly higher salivary glands function compared with un-

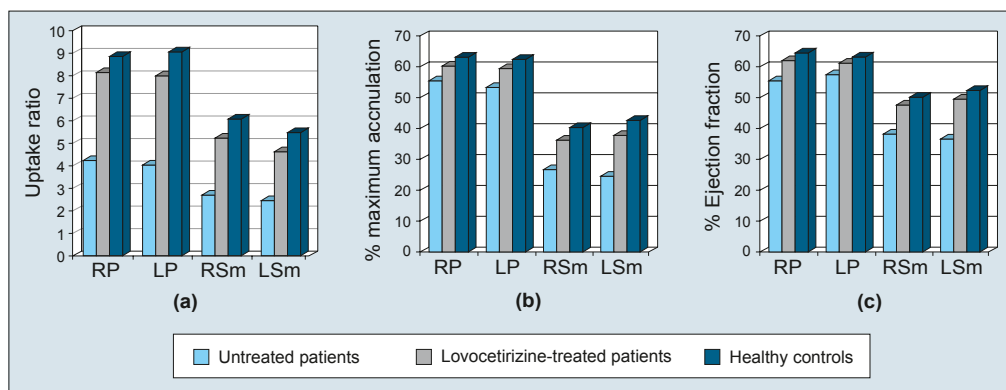


Figure 3. Calculation of uptake ratio (a), maximum accumulation percentage (b) and percentage ejection fraction (c) for patients and healthy controls. RP: right parotid; LP: left parotid; RSm: right submandibular gland; LSm: left submandibular gland.

treated patients and healthy controls. Levocetirizine treatment showed no side effects on salivary glands function.

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