The effect of antiallergic treatment with desloratadine-montelukast on salivary glands function in allergic rhinitis

Abstract
The aim of this study was to evaluate the possible favorable effect of desloratadine-montelukast combination on salivary glands (SG) function in patients with allergic rhinitis (AR) using SG scintigraphy. The study population consisted of 64 patients with AR and 28 healthy controls: 14 males and 14 females, with mean age 32.3±8.6 years. The patients were divided into two groups: the untreated patients group of 32 patients, 16 males and 16 females, mean age 28.5±5.4 years and the treated group, who received the standard clinically recommended oral dose of montelukast 10mg/d and desloratadine 5mg/d for 6 weeks. This group consisted of 32 patients, 16 males and 16 females, mean age 38.3±8.4 years. All patients and healthy controls underwent SG scintigraphy. After the intravenous injection of technetium-99m pertechnetate, (99mTc-P), dynamic SG scintigraphy was performed for 25min. Using the time-activity curves, the following glandular function parameters were calculated for the parotid and the submandibular SG: uptake ratio, maximum accumulation and ejection fraction. Results showed SG hypofunction. All functional parameters obtained for the untreated patients and for the desloratadine-montelukast treated patients were significantly lower than those in healthy controls (P<0.05). There was no statistically significant difference between treated and untreated patients (P>0.05).

In conclusion, our study showed that hypofunction of SG was present in all patients with AR. This hypofunction, as tested by semi-quantitative SG scintigraphy, and also the quality of life did not improve after treatment with montelukast and desloratadine.

Introduction
Allergic rhinitis (AR) is an extremely common health problem affecting 10% to 25% of the population [1, 2]. It is a chronic inflammatory disease that impairs quality of life due to both nasal symptoms, like rhinorrhea, itching, and sneezing and eye signs, like redness and itching [3, 4]. Salivary flow rates are often found to be significantly decreased [5, 6].

The second-generation antihistamine drug, desloratadine has been recommended as first line treatment for AR and its decongestant effect has been shown in previous reports [7, 8]. Montelukast, a leukotriene receptor antagonist has significantly improved day-time and night-time symptoms in patients with AR [9]. Recent studies in rats have shown that montelukast had potential protective effect on salivary glands (SG) function against I-131 induced damage [10]. Combination of both drugs has shown a synergistic effect in treating AR and improving patients’ quality of life [4].

Salivary glands scintigraphy with technetium-99m pertechnetate (99mTc-P) has been used for the functional assessment of the major SG both qualitatively and semi-quantitatively in multiple diseases or for appraising side effects of certain medications affecting SG [11-13].

A similar study showed that the same combined treatment has improved in perennial AR both the quality of life and nasal obstruction [4], but did not study SG function. The purpose of this prospective study was to evaluate the possible favorable effect of combined desloratadine and montelukast treatment on SG function in AR patients using 99mTc-P SG scintigraphy.

Subjects and methods
Patients
The study population consisted of 64 patients with AR and 28 healthy controls. Healthy controls were 14 males and 14 females ranging in age from 22 to 47 years old, mean
The patients were divided into two groups: an untreated patient group of 32 patients, 16 males and 16 females ranging in age from 23 to 46 years old, mean age 28.5±5.4 years old and a patients’ group treated with desloratadine-montelukast, which consisted of 32 patients, 16 males and 16 females ranging in age from 22 to 53 years old, mean age 38.3±8.4 years old (Table 1). All patients in the treated group received the standard usually recommended oral dose of montelukast and desloratadine (DESMONT®, Nuvomed, Istanbul, Turkey) once daily for 6 weeks. Each tablet contains desloratadine 5mg and montelukast sodium 10mg. The Ethics Committee of our university approved this study.

All patients had perennial nasal symptoms such as rhinorrhea, itching, sneezing fits, and nasal congestion and a positive skin test to common inhalant allergens such as mite, pollen and mold. None of the patients or healthy controls had a connective tissue or other systemic disease, interfering with SG function or a history of head or neck surgery or of radiation treatment.

Salivary glands scintigraphy

After the intravenous injection of about 185MBq of $^{99m}$Tc-P, dynamic SG scintigraphy was performed using a double-head gamma camera (Siemens E.CAM, Siemens Medical Systems, Inc. Hoffman Estates, IL 60195, USA) equipped with a parallel-hole, low-energy, high-resolution collimator. The photopeak was centered at 140keV 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 128x128. Secretion of the SG was stimulated with 3mL concentrated lemon juice instilled orally with a syringe at 20min. The intervention and diagnostic procedure were well tolerated by all patients and healthy controls.

Parameters studied, statistical semi-quantitative analysis

For semi-quantitative analysis, regions of interest (ROI) were manually drawn over each of the four major SG on the summation images of dynamic scintigraphy. A background ROI was placed in the temporal region (Fig. 1). Time-activity curves were generated for each SG (Fig. 2). The following points were assigned 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 and d) the minimum count after stimulation (Fig. 2). The following glandular function parameters were calculated using the above a-d, the time-activity curves for each SG: uptake ratio (UR)=b/c, maximum accumulation (MA%)=(b—a) / bx100, excretion fraction (EF%)=(b—d) / bx100.

The One Way Anova post-hoc Duncan’s multiple comparison test was used for comparison of scintigraphic parameters between patients with AR and healthy controls. Differences with a P-value less than 0.05 were accepted as significant, with data in the text presented as mean±standard deviation (SD). Statistical Package for the Social Sciences (SPSS version 20.0) software program was used for statistical analysis.

Results

In Table 2, the mean±SD values for the UR, MA% and EF% for the parotid and submandibular glands are presented. Statistical analysis revealed that the UR, MA% and EF% values for the right and left major SG obtained in untreated and in desloratadine-montelukast treated patients were significantly lower than those in healthy controls (P<0.05) (Fig. 3). There was no statistically significant difference between desloratadine-montelukast treated and untreated patients (P>0.05).

Table 1. Characteristics of healthy controls and of the two groups of patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Gender (male/female)</th>
<th>Mean age±SD (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy controls</td>
<td>28</td>
<td>14/14</td>
<td>32.3±8.6</td>
</tr>
<tr>
<td>Untreated patients</td>
<td>32</td>
<td>16/16</td>
<td>28.5±5.4</td>
</tr>
<tr>
<td>Treated patients</td>
<td>32</td>
<td>16/16</td>
<td>38.3±8.4</td>
</tr>
</tbody>
</table>

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Table 2. Comparison of mean±SD values of scintigraphic parameters in healthy controls and in the two patients’ groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy controls</th>
<th>Untreated patients</th>
<th>Treated patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>UR</td>
<td>9.16±1.19</td>
<td>4.04±0.76</td>
<td>3.64±0.41</td>
</tr>
<tr>
<td>LP</td>
<td>8.71±1.19</td>
<td>4.59±0.67</td>
<td>3.82±0.68</td>
</tr>
<tr>
<td>RSM</td>
<td>6.27±1.03</td>
<td>2.34±0.57</td>
<td>2.56±0.45</td>
</tr>
<tr>
<td>LSM</td>
<td>5.86±0.74</td>
<td>2.30±0.60</td>
<td>2.52±0.65</td>
</tr>
<tr>
<td>% MA</td>
<td>65.09±5.55</td>
<td>54.30±5.04</td>
<td>52.20±6.11</td>
</tr>
<tr>
<td>LP</td>
<td>63.84±5.34</td>
<td>55.51±6.03</td>
<td>52.89±7.55</td>
</tr>
<tr>
<td>RSM</td>
<td>42.76±5.17</td>
<td>26.37±5.53</td>
<td>26.34±6.83</td>
</tr>
<tr>
<td>LSM</td>
<td>43.51±8.29</td>
<td>23.56±6.66</td>
<td>26.17±7.45</td>
</tr>
<tr>
<td>% EF</td>
<td>66.41±7.16</td>
<td>53.07±8.78</td>
<td>49.73±6.68</td>
</tr>
<tr>
<td>LP</td>
<td>65.21±6.51</td>
<td>54.52±7.30</td>
<td>50.99±6.17</td>
</tr>
<tr>
<td>RSM</td>
<td>50.79±6.31</td>
<td>39.59±6.52</td>
<td>34.26±6.28</td>
</tr>
<tr>
<td>LSM</td>
<td>52.24±8.03</td>
<td>38.37±7.69</td>
<td>34.78±9.58</td>
</tr>
</tbody>
</table>

Allergic rhinitis is an inflammatory disorder of the nasal mucosa, induced by an immunoglobulin E (IgE)-mediated reaction [14] and is associated with systemic inflammation [15]. Allergen exposure leads to symptoms such as nasal itching, sneezing, rhinorrhea, and nasal congestion [3]. In addition, dry mouth signs have been described [16]. Reduced salivary flow rate was reported by using sialometry and salivary scintigraphy in patients with AR [17]. In our study, the difference in the saliva flow rate between AR and health controls was statistically significant, similar to previous reports [5, 17].

Monotherapy with montelukast and combination treatment with montelukast and desloratadine induces improvement in the quality of life, in patients suffering from persistent AR [18]. Montelukast has been shown to have secondary anti-inflammatory properties, apparently unrelated to conventional antagonism of leukotriene receptors [19]. Furthermore, a protective effect of montelukast on SG has been reported [10]. Oral antihistamines are recommended as first choice medications for AR [20]. The first generation antihistamines such as diphenhydramine, block histaminic and muscarinic receptors, and are recognized as having clinically significant anticholinergic adverse effects. Dry mouth, constipation and urinary retention are attributed to the antimuscarinic effects of these drugs [21]. The second generation antihistamines mainly block histaminic receptors. Desloratadine, a second generation antihistamine, is effective in the treatment of AR either intermittent or persistent [22]. Although antimuscarinic effects have not been reported with most of the second generation antihistamines, it is indicated that desloratadine has higher anticholinergic selectivity as compared to diphenhydramine and this may be the cause for dry mouth [23, 24]. It has also been reported that desloratadine is effective for itching and rhinorrhea in AR, but less effective for nasal congestion [25].

Other researchers have reported that montelukast could reduce nasal congestion in persistent AR and that combined treatment with desloratadine and montelukast is more effective than monotherapy with montelukast for improvement of nasal congestion [26]. Combined desloratadine and montelukast treatment on SG functions in AR patients using $^{99m}$Tc-P SG scintigraphy has not been reported in the literature. As for xerostomia and its negative effects on the quality of life, although not mentioned in our results, it is our impression that this treatment did not improve xerostomia.

Accurate assessment of SG function is important in patients with AR suffering from symptoms like xerostomia because subjective symptoms can differ from the results of an objective analysis [27]. Several methods have been suggested to evaluate SG function such as CT, sialography, SG ultrasonography, and labial SG biopsy. Nevertheless, these methods are either invasive or do not allow semi-quantitative measurements [22]. SG scintigraphy offers a semi-quantitative evaluation. Due to its low radiation dose, scintigraphy is also safe for these patients [28].

There have been few studies using SG scintigraphy for estimating SG function in AR [5, 17]. A lower salivary flow rate was reported in patients with AR compared to healthy controls [17]. In SG scintigraphy, no significant difference was found in their functional parameters between AR patients treated with levocetirizine—a third generation antistaminic and healthy controls [5]. AR patients have hypofunction of SG before treatment. Since only this 3rd generation drug was effective, we studied the combination of the 2 other drugs to see a possible treatment effect on SG functions using SG scintigraphy for the first time. We found no difference among patients treated with desloratadine and montelukast as compared to patients left untreated. The reason may be related to the daily use of montelukast sodium 10mg for 6 weeks that has insufficient protective effect on SG functions in patients with AR. Further comparative studies are needed.

In conclusion, our study showed that hypofunction of SG was present in all our patients with AR. Furthermore, combined treatment with montelukast and desloratadine did not improve SG functions as tested by semi-quantitative SG scintigraphy.

The authors declare that they have no conflicts of interest.
Bibliography


