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Evaluation of gustatory functions in patients with laryngopharyngeal reflux

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Abstract

Objective: The aim of the study is to evaluate the gustatory functions in patients with laryngopharyngeal reflux (LPR).

Methods: The study population consisted of the control and the reflux groups. There were 50 patients in each group. Reflux symptom index and reflux symptom scoring system were used in the diagnosis of reflux group. These two groups were subjected to taste test described by Goins et al., and taste test was applied separately to the back, middle and anterior parts of the tongue and the results were compared.

Results: When the demographic characteristics of the groups were compared, there was no statistical difference in terms of sex, age and smoking habit. In our study, we found a statistically significant decrease in the perception of bitterness, sourness and salty taste at the back, mid- dle and 1/3 anterior part of the tongue in the LPR group when com- pared to the control group. There was no significant difference between groups in terms of sweet taste.

Conclusion: While laryngopharyngeal reflux disease affect negatively the salty, bitter and sour taste functions, we found the sweet taste as the most resistant taste to LPR. Histopathological examination in animal experiments may be useful in order to prove the hypothesis concerning loss of taste caused by LPR.

Keywords: Larynngopharyngeal reflux, loss of taste, reflux symptom index, reflux symptom score.

Gastroesophageal reflux (GER) is the backward escape of stomach contents into the esophagus without retching or vomiting.[1] However, it has been reported for the first time since the late 19th century that GER may also cause extraesophageal complications.[2] Clinically, typical form of GER is characterized by symptoms of retrosternal burning and regurgitation, which are caused by esophagitis involving lower esophageal segment. In atypical GER, in which typical symptoms are not predominant, clinical manifestations vary according to the system or organ in which the signs or symptoms are manifested.[3] In these atypical forms of the disease, also called extraesophageal clinical signs or supra- esophageal complications, symptoms and findings affecting the larynx, pharynx, oral cavity, nose, paranasal sinuses and lungs may be encountered.[4,5]

The forceful backward escape of the stomach contents through the upper esophageal sphincter without retching or vomiting is defined as extra-esophageal reflux (EER), supra- esophageal reflux or laryngopharyngeal reflux (LPR).[2] LPR is an atypical form of gastroesophageal reflux. With the identification of LPR that is among the laryngopharyngeal manifestations of GER, hundreds of studies on the diagnosis and treatment of LPR have been performed up to day.[6] With the development of diagnostic methods, the number of patients diagnosed with LPR has increased in recent years. Recent studies have shown that between 4% and 10% of the patients admitted to the otorhinolaryngology clinics are receiving the diagnosis of LPR.[7,8]

Taste is a chemical sense just like smell and plays an important role in one's quality of life.[5] Taste generally means

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recognizing and identifying the melted stimuli in the mouth. While receptors receiving sense of taste are present in the fetus and genetic factors play a role in the preference of taste, this preference generally occurs with experience and may vary according to the needs of the body.[5] Smell, touch and eyesight also affect this preference. Though taste disorders are frequently seen, it may be overlooked by the patient or skipped by a physician who considers these tests to be tedious and time-consuming. Many factors such as infection, drug use, genetics, and trauma lead to impairment of gustatory functions. However, these disorders need to be diagnosed accurately, as they can indicate a serious illness and may affect various aspects of patient's private life as nutrition, taste and personal hygiene.

Many studies have been conducted in the literature on the possible adverse effects of laryngopharyngeal reflux, but studies on gustatory functions seem to be inadequate. Our aim in this study is to investigate the effects of LPR disease on gustatory functions.

Materials and Methods

In order to perform this study, the approval of the Ethics Committee of Zonguldak Bülent Ecevit University Application and Research Hospital was obtained (date: 05. 20.2014, decision no: 2014/10).

This study was carried out on 100 patients as a prospective randomized clinical trial in Zonguldak Bülent Ecevit University Application and Research Hospital between April 1, 2014 and April 1, 2015 to evaluate the gustatory functions in LPR patients. Required information about informed consent was provided to all individuals who partic- ipated in the study and their consents were obtained. Then, relevant data were collected.

After ENT examination of the reflux group participated in the study was performed, reflux symptom index (RSI) and reflux symptom score (RSS) forms that evaluate LPR and developed by Belafsky and Koufman were filled out. Patients receiving more than 13 and 7 points from RSI and RBS tests, respectively, were considered to have LPR and taste tests were applied.

Regional taste test described by Goins et al. was used. The control group was also subjected to ENT examination and the same taste test. In both groups (reflux and control groups), patients with chronic sinonasal infections, allergic rhinitis, active upper respiratory tract infections, septum deviations, nasal polyps, chronic otitis media, history of ear surgery for any indication and/or head trauma, patients who have lost their gustatory sensation after upper respiratory tract infection, patients with malignancies related to intracranial and taste pathways, patients receiving RT due to head and neck malignancies, individuals who had drug use history due to chronic diseases, patients who lost their sense of smell for any reason and those with psychiatric or neuro- logical diseases were excluded from the study.

Regional Taste Test application

The taste test used in this study is a regional taste test developed by Goins et al. to assess cranial nerves receiving taste sensation. The solutions were prepared with sterile deionized water and stored at +4°C. The solutions were applied to the 3 regions of the tongue (anterior, middle and posterior parts) with sterile cotton tipped applicator. Sodium chloride (saline, 0.32 molar), sucrose (sweet, 1.2 molar), caffeine (bitter, 0.041 molar), citric acid (sour, 0.041 molar) were used as stimulants. Stimuli were applied from midline to anterior, middle and posterior regions of the tongue. Stimuli to each region were applied at 1 minute intervals. Then the patient was asked to compare the gustatory senses he/she perceived at anterior, middle and posterior parts of the tongue Scoring was done to assess the sense of taste of the groups. Individuals who did not perceive any sense of taste and those that lightly perceived received 1+ point. Patients who per- ceived the taste moderately or strongly received 2+ and 3+ points, respectively. Before application of each stimulus, the mouth was rinsed with water. The patients were asked not to eat, drink, smoke or use a toothbrush for one hour before the taste test.

Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v19 (SPSS Inc., Chicago, IL, USA). A normal distribution of the quantitative data was checked using Shapiro-Wilk test. Parametric tests were applied to data of normal distribution and non-parametric tests were applied to data of questionably normal distribution. Continuous data were presented as mean±standard deviation or median [minimum-maximum], as appropriate. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

Results

A hundred patients who applied to ENT Clinic of Bulent Ecevit University Medical Faculty Hospitals between 01.04.2014 and 01.04.2015 were included in our study. The

patients were divided into two groups. Each group consisted of 50 patients. The control group consisted of 25 (50%) female and 25 male (50%) patients. Reflux group comprised of 29 (58%) female and 21 (42%) male patients. There were no gender differences between the groups (p=0.422). The mean ages of the participants included in the study were 38.1±10.4; 37.72±10.38 (range: 20 to 59) and 38.56±10.54 (range: 17 to 60) years in the control and reflux groups, respectively. No statistically significant difference was found between the groups (p=0.712). Twenty (40%) out of 50 patients in the control group were smokers and 30 patients (60%) were non-smokers. Of the 50 patients in the reflux group, 19 (38%) were smokers. The remaining 31 patients (62%) were non-smokers. No statistically signifi- cant difference was found when the groups were examined in terms of smoking habit (p=0.838).

Intergroup differences regarding the perception of tastes according to the tested part of the tongue are shown in Table 1. When the levels of salty taste perceived at the posterior 1/3, middle 1/3 and anterior 1/3 parts of the tongue were compared between the groups, a statistically significant difference was found (p=0.001, p=0.002 and p<0.001, respectively). A statistically significant intergroup difference was not found when the sweet taste levels per- ceived at the posterior 1/3, middle 1/3 and anterior 1/3 parts of the tongue were compared (p=0.160, p=0.815 and p=0.096, respectively). A statistically significant intergroup difference was found when the bitter taste levels perceived at the posterior 1/3, middle 1/3 and anterior 1/3 parts of the tongue were compared (p<0.001, p<0.001 and p<0.001, respectively). A statistically significant difference was found when the sour taste levels perceived at the posterior 1/3, middle 1/3 and anterior 1/3 parts of the tongue were com- pared (p<0.001, p=0.002 and p<0.001, respectively).

Discussion

Although the symptoms of LPR are considered to be voice distress, throat clearing, night-choking sensation, post-nasal discharge, earache, chronic cough and swallowing difficulty, many of these symptoms are non-specific and often they should be correlated with laryngoscopic evaluation to suspect a diagnosis.[9,10] Among laryngoscopic findings, interarytenoid erythema, edema, pseudosulcus, ventricular obliteration and postcricoid hyperplasia are more prominent.[10] In our study, complaints of throat clearing were detected in 32 (64%), feeling of postnasal discharge in 11 (22%), hoarseness in 7 (14%), swallowing difficulty in 14 (28%), choking sensation in 4 (8%) and chronic coughing in 6 (12%) patients. Endoscopic examination revealed interarytenoid edema in 38 (76%), erythema in 29 (58%), posterior commissure hypertrophy in 24 (48%) and vocal cord edema in 17 (54%) patients.

According to the literature, two mechanisms are held responsible for the pathophysiology of LPR. First one is the irritation caused by gastric acid in the esophagus stimulates the vagal reflex, which in turn leads to cough and bron- chos-

Table 1. Distribution of tastes, regions of the tongue and taste scores in patients with and without reflux (the values given in the Table are expressed as number of persons and percentages).

		Control, n (%)			Reflux, n (%)			
		3+	2+	1+	3+	2+	1+	p-value
Salty taste	Posterior 1/3	26 (52%)	20 (40%)	4 (8%)	15 (30%)	15 (30%)	20 (40%)	0.001
	Middle 1/3	22 (44%)	16 (32%)	12 (24%)	8 (16%)	15 (30%)	27 (54%)	0.002
	Anterior 1/3	29 (58%)	18 (36%)	3 (6%)	11 (22%)	20 (40%)	19 (38%)	<0.001
Sweet taste	Posterior 1/3	25 (50%)	22 (44%)	3 (6%)	24 (48%)	17 (34%)	9 (18%)	0.160
	Middle 1/3	20 (40%)	18 (36%)	12 (24%)	22 (44%)	15 (30%)	13 (26%)	0.815
	Anterior 1/3	34 (68%)	13 (26%)	3 (6%)	25 (50%)	16 (32%)	9 (18%)	0.096
Bitter taste	Posterior 1/3	20 (40%)	24 (48%)	6 (12%)	7 (14%)	8 (16%)	35 (70%)	<0.001
	Middle 1/3	22 (44%)	16 (32%)	12 (24%)	7 (14%)	13 (26%)	30 (60%)	<0.001
	Anterior 1/3	28 (56%)	14 (28%)	8 (16%)	4 (8%)	9 (18%)	37 (74%)	<0.001
Sour taste	Posterior 1/3	21 (42%)	25 (50%)	4 (8%)	5 (10%)	15 (30%)	30 (60%)	<0.001
	Middle 1/3	23 (46%)	19 (38%)	8 (16%)	10 (20%)	17 (34%)	23 (46%)	0.002
	Anterior 1/3	29 (58%)	16 (32%)	5 (10%)	8 (16%)	13 (26%)	29 (58%)	<0.001

pasm; and the second one is the direct destructive effect of gastric acid which passes over the upper esophageal sphincter and reaches the laryngeal pharynx resulting in adverse effects of acid and activated pepsin on the mucosa.[9] Direct effect of reflux acid on the laryngeal mucosa is more destructive than its effect on the esophageal mucosa. This is because the laryngeal mucosa lacks the protective effect of the carbonic anhydrase enzyme. Some animal studies have shown that reflux acid has a destructive effect on the laryn- geal mucosa even within a few days.[8] In addition to direct effect of gastric acid on cells, gastric pepsin, which has high protease properties, is also responsible from this direct effect. Pepsin has an optimum effect between pH 2–3.5, and pepsin shows a rapid destructive protease activity within this interval.[11]

In a study investigating the histopathological effects of LPR, a mixture of acid and pepsin prepared in laboratory conditions was administered using an apparel to the ani- mal models with induced vocal cord damage and local ulcerative lesions and granulation formation were observed in vocal cords after 4 weeks. In the same study, it was stated that the inflammation score was higher in the reflux acid-exposed cord and the collagen fibrin was increased in the lamina propria of cords exposed to reflux acid.[12] In a study conducted by Johnston et al., laryngeal tissue biopsy was obtained from 9 patients with LPR dur- ing pH monitoring and 12 control subjects and pepsin lev- els were found to be statistically higher in the LPR-detect- ed group than the control group.[13] In an animal model study performed by Little et al., the researchers reported that reflux caused subglottic stenosis and formation of lesions on laryngeal mucosa.[14]

Habesoglu et al. induced an experimental reflux model in 18 rats, and microscopic examination of soft palate of the animals exposed to reflux revealed a significant difference between the control and study groups in terms of the hyperplasia, inflammation, subepithelial edema, muscular atro- phy, vascular dilatation and dilated secretory gland channels in submucous glands. In the background of histopathologi- cal evaluations, they thought that these findings could show the relationship between LPR and upper respiratory obstruction.[15]

In the literature, many clinical studies have discussed the relation of LPR with larynx, pharynx, sinuses and middle ear pathologies.[16,17] Among them, predominantly chronic cough, laryngitis, recurring croup, subglottic stenosis, globus, laryngeal carcinoma, sinusitis, adenoid hypertrophy, laryngomalacia, recurrent ear pain and otitis media with effusion are seen.[3,9,18–20]

Although histopathological and functional effects of LPR on many organs have been investigated, there is insufficient study of the effects of LPR on the tongue and taste sensation. Taste is a chemical sense just like smell and plays an important role in one's quality of life. There are approximately 7900 taste receptors in human mouth, separated by subclasses according to their location, mor- phology and innervations. Taste buds are mainly concen- trated on the tongue. However, they are also found at the palate, pharynx, epiglottis and upper end of the esophagus. Papilla fungiformis is intensely settled at the tongue tip and is responsible for sweet tastes. Papilla foliata are con- centrated on the edges of the tongue and are rather responsible for sour tastes. The papilla circumvallata is located in front of the sulcus terminals and is mainly responsible for the bitter and sour taste in the 2/3 posteri- or part of the tongue. There are about 2400 taste buds in the human body.[21]

Clinical investigation of taste disorders is difficult because most of the patients with olfactory disorders also complain of loss of taste. The reason is that 80% of the flavor of the aroma in the meals is perceived together with olfactory stimulants.[22] Any mucosal disease, infections and mucosal changes due to radiotherapy in the oral cavity and bad oral hygiene affect the sense of taste. A decrease in taste perception is observed in patients receiving RT directed at the head and neck region. The mechanism of this loss of taste has not been fully explained. Since the loss of taste after irradiation of parotid is observed, it is stated that this situation is especially related to xerostomia. However, within a few months after the end of the thera- py, the taste sensation slowly recovers.[23] Zheng et al. eval- uated the patients' taste sensations during radiotherapy in a prospective study of 40 patients with head and neck can- cer. They examined the relationship between the degree of taste disorder and time. They hypothesized that taste disorders that occur during radiotherapy may be due to damage to the taste buds in the area of radiotherapy.[24] The taste sensation may also be affected iatrogenically. Among them, taste disorders due to damage to the tym- panic cord after ear surgery are the most frequently known functional disorders. Another one is taste disorder due to injury to the glossopharyngeal nerve or lingual branch of this nerve developed after tonsillectomy or uvu- lopalatopharyngoplasty.[25]

Various methods are being used to evaluate the gustato- ry functions. Some of them are regional taste tests. In a study by Landis et al.,[26] the authors used the taste test described by Mueller et al. to evaluate taste functions

in patients with chronic otitis media and cholesteatoma. This test was performed by applying the taste strips containing 4 different concentrations of sweet, salty, sour and bitter tastes to the tongue. In our study, we used the regional taste test described by Goins et al.[27]

In our study, the reduction in the perceptions of salty, bitter and sour taste may be due to neuroepithelial effects exerted on taste receptors as a result of mucosal changes developed secondary to LPR. Chronic exposure of the larynx, pharynx and oral mucosa to acid and pepsin can also lead to deterioration of the salivary secretion, which may result in decreased taste perception. In addition, impaired taste and impaired oral hygiene after chronic exposure to acid and pepsin may also contribute to this reduction. In our study, we detected the sweet taste as the most resistant of the four main taste senses to acid. The resistance of sweet taste to acid may be due to the high concentration of the receptors or the less anatomical exposure of the tongue tip to the acid. In this study, we showed that LPR has negative effects on gustatory functions. However, there is a need for further study on the level of involve- ment of taste receptors.

Conclusion

In this study, we showed that LPR disease affects 4 major taste perceptions adversely including the salty, bitter and sour taste functions. In our study, we detected sweet taste as the most resistant taste to LPR. In this study, we believe that histopathological examination in animal experiments will be useful in order to prove our hypothesis about the pathogenet- ic mechanism of reflux that leads to taste loss.

Conflict of Interest: No conflicts declared.

References

1. Akiyama J, Kuribayashi S, Baeg MK, et al. Current and future per- spectives in the management of gastroesophageal reflux disease. Ann N Y Acad Sci 2018 May 16 [Epub ahead of print]. doi: 10.1111/nyas.13850
2. Napierkowski J, Wong KH. Extraesophageal manifestations of GERD. Am J Med Sci 2003;326:285–99.
3. Koufman JA, Aviv JE, Casiano RR, Shaw GY. Laryngopharyngeal reflux: position statement of the committee on speech, voice and swallowing disorders of the American Academy of Otolaryngology– Head and Neck Surgery. Otolaryngol Head Neck Surg 2002;127: 32–5.
4. Kendall KA. Controversies in the diagnosis and management of laryngopharyngeal reflux disease. Curr Opin Otolaryngol Head Neck Surg 2006;14:113–5.
5. Gyawali CP, Azagury DE, Chan WW, et al. Nonerosive reflux disease: clinical concepts. Ann N Y Acad Sci 2018 May 15 [Epub ahead of print]. doi: 10.1111/nyas.13845
6. Mendelsohn AH. The effects of reflux on the elderly: the problems with medications and interventions. Otolaryngol Clin North Am 2018 Apr 23. pii: S0030-6665(18)30054-9. [Epub ahead of print]. doi: 10.1016/j.otc.2018.03.007
7. Katz PO. State of the art: extraesophageal manifestations of gas- troesophageal reflux disease. Rev Gastroenterol Disord 2005;5: 126–34.
8. Vaezi MF. Extraesophageal manifestations of gastroesophageal reflux disease. Clin Cornerstone 2003;5:32–8.
9. Koufman JA. The otolaryngologic manifestations of gastroe- sophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experi- mental investigation of the role of acid and pepsin in the develop- ment of laryngeal injury. Laryngoscope 1991;101(4 Pt 2 Suppl 53):1–78.
10. Vaezi MF, Hicks DM, Abelson TI, Richter JE. Laryngeal signs and symptoms and gastroesophageal reflux disease (GERD): a crit- ical assessment of cause and effect association. Clin Gastroenterol Hepatol 2003;1:333–44.
11. Schreiber S, Garten D, Sudhoff H. Pathophysiological mecha- nisms of extraesophageal reflux in otolaryngeal disorders. Eur Arch Otorhinolaryngol 2009;266:17–24.
12. Roh JL, Yoon YH. Effect of acid and pepsin on glottic wound healing: a simulated reflux model. Arch Otolaryngol Head Neck Surg 2006;132:995–1000.
13. Johnston N, Knight J, Dettmar PW, Lively MO, Koufmann JA. Pepsin and carbonic anhydrase isoenzyme III as diagnostic mark- ers for laryngopharyngeal reflux disease. Laryngoscope 2004;114: 2129–34.
14. Little FB, Koufman JA, Kohut RI, Marshall RB. Effect of gastric acid on the pathogenesis of subglottic stenosis. Ann Otol Rhinol Laryngol 1985;94:516–9.
15. Habesoglu TE, Habesoglu M, Sürmeli M, et al. Histological changes of rat soft palate with exposure to experimental laryn- gopharyngeal reflux. Auris Nasus Larynx 2010;37:730–6.
16. Fraser-Kirk K. Laryngopharyngeal reflux: a confounding cause of aerodigestive dysfunction. Aust Fam Physician 2017;46:34-9.
17. Weaver EM. Association between gastroesophageal reflux and sinusitis, otitis media and laryngeal malignancy: a systematic review of the evidence. Am J Med 2003;115 Suppl 3A:81S–9S.
18. El-Serag HB, Gilger M, Kuebeler M, Rabeneck L. Extraesophageal associations of gastroesophageal reflux disease in children without neurologic defects. Gastroenterology 2001;121:1294–9.
19. Carr MM, Poje CP, Ehrig D, Brodsky LS Incidence of reflux in young children undergoing adenoidectomy. Laryngoscope 2001; 111:2170–2.
20. Velepic M, Rozmanic V, Velepic M, Bonifacic M. Gastroesophageal reflux, allergy and chronic tubotympanal disor- ders in children. Int J Pediatr Otorhinolaryngol 2000;55:187–90.
21. Altundag A, Cayonu M, Salihoglu M, et al. Laryngopharyngeal reflux has negative effects on taste and smell functions. Otolaryngol Head Neck Surg 2016;155:117–21.

22. Clark MP, O'Malley S. Chorda tympani nerve function after mid- dle ear surgery. Otol Neurotol 2007;28:335–40.
23. Bhide SA, Miah AB, Harrington KJ, Newbold KL, Nutting CM. Radi- ation-induced xerostomia: pathophysiology, prevention and treatment. Clin Oncol (R Coll Radiol) 2009;21:737–44.
24. Zheng WK, Inokuchi A, Yamamoto T, Komiyama S. Taste dys- function in irradiated patients with head and neck cancer. Fukuoka Iqaku Zasshi 2002;93:64–76.
25. Dawes PJ. Early complications of surgery for chronic otitis media. J Laryngol Otol 1999;113:803–10.
26. Landis BN, Beutner D, Frasnelli J, Hüttenbrink KB, Hummel T. Gustatory function in chronic inflammatory middle ear diseases. Laryngoscope 2005;115:1124–7.
27. Goins MR, Pitovski DZ. Posttonsillectomy taste distortion: a sig- nificant complication. Laryngoscope 2004;114:1206–13.

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