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Analysis of symptoms and clinical signs of laryngopharyngeal reflux depending on pepsin in saliva

Analiza simptoma i kliničkih znakova laringofaringealnog refluksa, ovisno o koncentraciji pepsina u slini

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Summary

In the last fifty years, an epidemic of reflux disease has occurred as a result of poor eating habits, stress, and activities of the food industry. Part of this disease is laryngopharyngeal reflux, a disease characterized by the return of gastric contents to the throat and surrounding organs, leading to hoarseness, coughing, difficulty in swallowing and breathing, and ultimately the development of benign and malignant changes in the larynx.

This study is aimed to examine the symptoms and signs of laryngopharyngeal reflux in the study group before and after therapy and to compare the concentration of pepsin in saliva with the above. The prospective longitudinal cohort study included 50 subjects, divided into two groups. The first group consisted of 25 subjects with laryngopharyngeal reflux. The second group consisted of 25 healthy subjects without symptoms and signs of laryngopharyngeal reflux. Symptoms and signs before and after therapy were collected using RSI and RFS questionnaires. Pepsin in saliva was measured with Peptest before and after therapy. The most pronounced symptoms are hoarseness, postnasal drip, and a feeling of "a lump in the throat". The median RSI score after three months of therapy was reduced from 20 to 8. From the first group, 7 subjects had measurable levels of pepsin in saliva, and none after therapy. In the control group, no subjects were found to have pepsin in their saliva. Significant improvement was observed in clinical findings (subglottic edema, posterior commissure hypertrophy, vocal cord edema, dense endolaryngeal secretion) after three months of therapy in subjects with LPR. No association of pepsin with LPR symptoms was observed but there is a significant positive association between pepsin and the clinical finding of erythema/hyperemia.

In most cases, we start therapy with medication. It is, therefore, important to emphasize that laryngopharyngeal reflux treatment must always begin with a change in diet, lifestyle, and stress regulation. Treatment must be individual and should include a multidisciplinary team with a nutritionist, psychologist, and psychiatrist.

Key words: food habits, laryngopharyngeal reflux, peptest, pepsin, treatment, diagnosis

Sažetak

U posljednjih pedesetak godina javlja se epidemija refluksne bolesti kao posljedica loših prehrambenih navika, stresa i aktivnosti prehrambene industrije. Dio ove bolesti je i laringofaringealni refluks (LPR), bolest koju karakterizira vraćanje želučanog sadržaja u grlo i okolne organe, što dovodi do promuklosti, kašlja, otežanog gutanja i disanja, te u konačnici razvoja dobroćudnih i malignih promjena na grkljanu.

Cilj ove studije je ispitati simptome i znakove laringofaringealnog refluksa u ispitivanoj skupini prije i nakon terapije, te usporediti koncentraciju pepsina u slini s navedenim. U prospektivno longitudinalno kohortno istraživanje uključeno je 50 ispitanika, podijeljenih u dvije skupine. Prvu skupinu činili su ispitanici s laringofaringealnim refluksom, njih 25. Drugu skupinu činili su zdravi ispitanici bez simptoma i znakova laringofaringealnog refluksa, njih 25. Simptomi i znakovi prije i nakon terapije prikupljeni su pomoću RSI i RFS upitnika. Pepsin u slini je izmjeren pomoću Peptesta prije i nakon terapije. Prema spolu, 29 (58 %) je

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žena i 21 (42 %) muškarac. Od simptoma, najizraženiji su promuklost, postnazalno slijevanje i osjećaj "knedle u grlu". Medijan RSI rezultata nakon tromjesečne terapije snižen je s 20 na 8. Iz prve skupine 7 ispitanika je imalo mjerljivu razinu pepsina u slini, a niti jedan nakon provedene terapije. U kontrolnoj skupini nijednom ispitaniku nije detektiran pepsin u slini. Uočeno je značajno poboljšanje u kliničkim nalazima (subglotički edem, hipertrofija stražnje komisure, edem glasnica, gusti endolaringealni sekret) nakon tromjesečne terapije kod ispitanika s LPR. Nije uočena povezanost pepsina sa simptomima LPR-a, ali postoji značajna pozitivna povezanost između pepsina i kliničkog nalaza eritema / hiperemije.

U većini slučajeva LPR terapiju započinjemo lijekovima. Stoga je bitno naglasiti da liječenje LPR uvijek mora započeti promjenom prehrane, načina života i regulacije stresa. Liječenje LPR-a mora biti individualno i treba uključivati multidisciplinarni tim s nutricionistom, psihologom i psihijatrom.

Ključne riječi: prehrambene navike, laringofaringealni refluks, peptest, pepsin, liječenje, dijagnoza

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Introduction

For more than 40 years, there has been a clinical entity in medical literature known as laryngopharyngeal reflux (LPR) or "silent reflux." According to the American Academy of Otorhinolaryngology and Head and Neck Surgery, gastric contents are returned to the laryngopharynx.[1] Leichen et al[2] concluded that the above definition of LPR is incomplete because the return of gastric contents, which contains pepsin, bile acid salts, and other gastroduodenal proteins, causes irritation not only of the laryngeal mucosa but also of the entire upper aerodigestive tract. Therefore, they defined LPR as inflammation of the upper aerodigestive tract tissues that occur directly or indirectly by gastric or duodenal reflux and cause morphological changes such as irritation and inflammatory conditions from mild to life-threatening. LPR is a common disease and today has the characteristics of an epidemic.[3,4] A 2010 study on the prevalence of LPR and gastroesophageal reflux (GER) in a sample of 656 US citizens shows that 40% of respondents have reflux, 22% GER, and 18% of LPR, or almost one in five Americans suffer from LPR. There was no statistically significant difference in the incidence of reflux concerning the age, gender, and geographical affiliation of the subjects. Unexpected and surprising data from the research is that almost 37% of subjects aged 21 to 30 have reflux.[5]

Despite this, it is still often unrecognized by both patients and physicians. It is often untreated or inadequately treated or interpreted as atypical GER. One of the reasons for its inadequate treatment stems from the fact that in most patients, "silent reflux" is not accompanied by symptoms of "loud reflux", heartburn and belching, and is manifested by symptoms that are non-specific and characteristic of several different diseases.[6] It is estimated that less than 50% of patients with LPR have gastroesophageal reflux disease (GERD), and about 32.8% of patients with GERD have laryngopharyngeal discomfort.[7,8] Most authors believe that pepsin plays a crucial role in developing changes in the larynx and other organs and developing symptoms, and its acidic medium serves to maintain proteolytic activity. However, other enzymes may also play a vital role in developing inflammatory reactions.[9,10] Stress and autonomic nervous dysfunction are also mentioned as possible reasons for the development of LPR. Autonomic nerve dysfunction may increase the frequency of opening the upper and lower esophageal sphincters, leading to more frequent LPR episodes. Recently, only a few authors have hypothesized that LPR patients have autonomic nervous system dysfunction, anxiety, or stress.[11,12]

Treatment of all forms of LPR should always begin with a change in diet, lifestyle, avoidance of stress, and only in cases of severe and life-threatening LPR drug treatment should be used that should not last long due to numerous short-term and long-term side effects.[13]

Unfortunately, in everyday clinical practice, we are witnessing that the treatment of LPR, regardless of the form of LPR, begins with medication, and changes in diet and stress regulation are often omitted. Patients are not referred to a nutritionist, psychologist, or psychiatrist.

This study is aimed to examine the symptoms and signs of laryngopharyngeal reflux in the study group before and after therapy and to compare the concentration of pepsin in saliva with the above. Also, we want to highlight nutritional therapy with stress regulation in the treatment of LPR, and the need to include a multidisciplinary team of a nutritionist, psychologist, and psychiatrist.

Patients and methods

The prospective longitudinal cohort study included 50 subjects, who were divided into two groups of 25 subjects. All subjects were diagnosed with LPR based on a detailed history, filling in the reflux symptom index (RSI questionnaire). Furthermore, we made the diagnosis by performing flexible transnasal video-laryngoscopy and filling in the reflux finding score (RFS questionnaire). Inclusion criteria were: adult

subjects who agreed to participate in the study, subjects with LPR, and for the control group healthy subjects without symptoms and clinical signs of LPR or subjects with RSI <13 and RFS <7. Excluded from the study were all subjects who did not adhere to the recommended diagnostic-therapeutic procedures. All subjects signed a voluntary consent to participate.

The study group included all patients whose RSI sum of symptoms was greater than 13 and RFS sum of clinical findings greater than 7. The control group consisted of subjects without symptoms and clinical signs of laryngopharyngeal reflux or subjects with RSI <13 and RFS < 7.

We determined the concentration of pepsin in saliva at the beginning of the study in all subjects and patients with LPR and control subjects and the examined group after three months of therapy. The sample was collected after morning wakening and before brushing teeth and breakfast. In twenty-five subjects in the study group, treatment included changing lifestyle and eating habits, taking an antireflux oral suspension of alginate and carbonate, and taking alkaline water. The follow-up was after three months with re-completion of the RSI and RFS questionnaires according to Belafsky and determination of pepsin in saliva. Since the symptoms of LPR in patients occur periodically, in late autumn and early spring, the sample was collected from December 2019 to the end of March 2020.

The Belafsky RSI questionnaire includes the nine most common and characteristic LPR symptoms: hoarseness, clearing of the throat, feeling of secretion in the throat – postnasal secretion, feeling of a foreign body in the throat, difficulty swallowing, feeling of difficulty in breathing – choking, laryngospasm, cough. All these nine symptoms of the RSI questionnaire were quantified from 0 – no symptoms to 5 – the symptom is very pronounced. The RFS questionnaire includes eight characteristic findings on the larynx: pseudo-sulcus vocalis, ventricular obliteration, erythema and hyperemia, vocal cord edema, diffuse laryngeal edema, posterior commissure mucosal hypertrophy, postcricoid edema (tiger-stripe post cricoid edema), granulomas/ulcers/ulcers mucus. All eight clinical findings on the larynx were quantified from 0 – absent, 1 – mild, 2 – present, partial, moderate, 3 – moderate, 4 – complete, diffuse, polypoid, obstructive.

Statistical analysis

Category data are presented in absolute and relative frequencies. Differences of categorical variables were tested by χ^2 test. The normality of the distribution of numerical variables was tested by the Shapiro - Wilk test. Numerical data are described by the median and boundaries of the interquartile range. Differences in numerical variables between the control group and subjects with LPR were tested by the Mann-Whitney test. The differences in numerical variables in the group of subjects with LPR before and after three months of therapy were tested by the Wilcoxon test. The association score was expressed by the Spearman correlation coefficient (Rho). All P values are two-sided. The significance level was set to Alpha = 0.05. MedCalc Statistical Software version 18.11.3 (MedCalc Software, Ostend, Belgium; https://www.medcalc.org; 2019) was used for statistical analysis.

Results

The study included 50 subjects, divided into two groups of 25 (50%). In the first group were healthy subjects without symptoms and clinical signs of LPR, with RSI <13 and RFS <7 (control group), and the second group consisted of subjects who first appeared in the clinic with symptoms of laryngopharyngeal reflux. According to gender, 29 (58%) were women, and 21 (42%) were men, with no significant difference from the experimental groups. The mean (median) age of the subjects was 41 years (interquartile range of 30 to 56 years) with no significant difference compared to the groups.

According to the Belafsky questionnaire, the symptoms were rated from 0 – no symptoms to 5 – symptoms very pronounced. All subjects in the control group did not have any of the nine symptoms, while in subjects with LPR hoarseness was most pronounced, median 4 (interquartile range of 3 to 5, and postnasal dripping and feeling of a "dumpling" in the throat was rated as median 3 (interquartile range of 3) to 4), the least pronounced cough after eating or lying down, a feeling of suffocation and coughing fits. All RSI questionnaire symptoms comparing the control and group patients with LPR were statistically significant (Table 1).

In subjects with LPR, there was a significant improvement in the overall scale after three months of therapy compared to the initial measurement, where the overall symptom score decreased from a median of 20 (interquartile range of 18 to 22) to a score of 8 (interquartile range of 8 to 10). (P <0.001) (Table 2).

The clinical finding also included completing RFS, which includes eight characteristic clinical findings on the larynx. All findings were quantified with grades from 0 – absent to 4 – complete, diffuse, polypoid, obstructive. Before treatment, there were no significant differences between the control group and subjects with LPR concerning erythema/hyperemia and granuloma, while the other six clinical findings were significantly worse in the group of subjects with LPR (Table 3).

Table 1 Assessment of RSI questionnaire symptoms before therapy
Tablica 1. Procjena simptoma RSI upitnika prije terapije

RSI questionnaire before therapy *RSI upitnik prije terapije*	Median (interquartile range) *Srednji (interkavrtilni raspon)*		P value* *P vrijednost*
	Control group *Kontrolna grupa*	Patients with LPR *Pacijenti sa LPR*	
Hoarseness/*Promuklost*	0 (0 - 0)	4 (3 - 5)	**<0,001**
Cleansing – clearing the throat *Čišćenje – pročišćavanje grla*	0 (0 - 0)	4 (4 - 4)	**<0,001**
Postnasal drainage *Postnazalna drenaža*	0 (0 - 0)	3 (3 - 4)	**<0,001**
Swallowing problems *Problemi kod gutanja*	0 (0 - 0)	1 (0 - 2)	**<0,001**
Cough after eating or lying down *Kašalj nakon jela ili ležanja*	0 (0 - 0)	0 (0 - 1)	**0,01**
Feeling of suffocation *Osječaj gušenja*	0 (0 - 0)	0 (0 - 2)	**<0,001**
Cough attacks *Napadi kašlja*	0 (0 - 0)	0 (0 - 1)	**<0,001**
Feeling of a "lump in the throat" *Osjećaj "knedle u grlu"*	0 (0 - 0)	3 (3 - 4)	**<0,001**
Heartburn, chest pain *Žgaravica, bol u prsa*	0 (0 - 0)	2 (2 - 3)	**<0,001**
Total/ *Sveukupno*	0 (0 - 0)	20 (18 - 22)	**<0,001**

*Mann Whitney U test. Bold denotes statistical significance / *Podebljano označava statističku značajnost*

Table 2 RSI questionnaire values in subjects with LPR before and after three months of therapy
Tablica 2. RSI vrijednosti upitnika u ispitanika s LPR prije i nakon tri mjeseca terapije

RSI questionnaire *RSI upitnik*	Median (interquartile range) in subjects with LPR *Medijan (interkvartilni raspon) u ispitanika s LPR*		P value* *P vrijednost*
	Before therapy *Prije terapije*	After therapy *Poslije terapije*	
Hoarseness/*Promuklost*	4 (3 - 5)	2 (2 - 3)	**<0.001**
Cleansing – clearing the throat *Čišćenje – pročišćavanje grla*	4 (4 - 4)	2 (1 - 2)	**<0.001**
Postnasal drainage *Postnazalna drenaža*	3 (3 - 4)	1 (1 - 2)	**<0.001**
Swallowing problems/ *Problemi kod gutanja*	1 (0 - 2)	0 (0 - 1)	**0.001**
Cough after eating or lying down *Kašalj nakon jela ili ležanja*	0 (0 - 1)	0 (0 - 0)	**0.03**
Feeling of suffocation *Osječaj gušenja*	0 (0 - 2)	0 (0 - 0)	**0.003**
Cough attacks *Napadi kašlja*	0 (0 - 1)	0 (0 - 0)	**0.003**
Feeling of a "lump in the throat" *Osjećaj "knedle u grlu"*	3 (3 - 4)	2 (1 - 2)	**<0.001**
Heartburn, chest pain *Žgaravica, bol u prsa*	2 (2 - 3)	1 (1 - 1)	**<0.001**
Total/ *Sveukupno*	20 (18 - 22)	8 (8 - 10)	**<0.001**

*Wilcoxon test. Bold denotes statistical significance / *Podebljano označava statističku značajnost*

Table 3 RFS questionnaire concerning the groups before the therapy
Tablica 3. RFS upitnik u odnosu na grupe prije terapije

RFS questionnaire before therapy ***RFS upitnik prije terapije***	Median (interquartile range) *Medijan (interkvartilni raspon)*		P value* *P vrijednost*
	Control group *Kontrolna grupa*	Patients with LPR *Ispitanici s LPR*	
Subglottic edema/*Subglotski edem*	0 (0 - 0)	1 (0 - 2)	**0.005**
Ventricular obliteration *Ventrikularna obliteracija*	0 (0 - 0)	2 (2 - 2)	**<0.001**
Erythema / hyperemia/*Eritem / hiperemija*	2 (2 - 2)	2 (2 - 2)	0,06
Swelling of the vocal cords *Oticanje glasnica*	0 (0 - 0)	1 (1 - 2)	**<0.001**
Diffuse laryngeal edema *Difuzni edem larinksa*	0 (0 - 0)	1 (0 - 2)	**<0.001**
Posterior commissure hypertrophy *Hipertrofija stražnje komisure*	0 (0 - 1)	2 (2 - 2)	**<0.001**
Granuloma/*Granuloma*	0 (0 - 0)	0 (0 - 0)	> 0,99
Dense endolaryngeal secretion *Gusta endolaringealna sekrecija*	0 (0 - 0)	2 (2 - 2)	**<0.001**
Total/*Sveukupno*	2 (2 - 3)	11 (10 - 13)	**<0.001**

*Mann Whitney U test. Bold denotes statistical significance / *Podebljano označava statističku značajnost*

After three months of treatment, subjects with LPR significantly improved subglottic edema, vocal cord swelling, diffuse laryngeal edema, posterior commissure hypertrophy, and decreased endolaryngeal secretion, while no significant changes were observed in ventricular obliteration, erythema/hyperemia, and granuloma. (Table 4).

Table 4 RFS questionnaire values in subjects with LPR before and after three months of therapy
Tablica 4. RFS vrijednosti upitnika u ispitanika s LPR prije i nakon tri mjeseca terapije

RFS questionnaire ***RFS upitnik***	Median (interquartile range) in subjects with LPR *Medijan (interkvartilni raspon) u ispitanika s LPR*		P value* *P vrijednost*
	Before therapy *Prije terapije*	After therapy *Poslije terapije*	
Subglottic edema/ *Subglotski edem*	0 (0 - 2)	0 (0 - 0)	**0.008**
Ventricular obliteration *Ventrikularna obliteracija*	2 (2 - 2)	2 (2 - 2)	0.32
Erythema / hyperemia *Eritem / hiperemija*	2 (2 - 2)	2 (2 - 2)	0.32
Swelling of the vocal cords *Oticanje glasnica*	1 (1 - 2)	1 (0 - 1)	**<0.001**
Diffuse laryngeal edema *Difuzni edem larinksa*	1 (0 - 2)	0 (0 - 1)	**<0.001**
Posterior commissure hypertrophy *Hipertrofija stražnje komisure*	2 (2 - 2)	1 (1 - 1)	**<0.001**
Granuloma/*Granuloma*	0 (0 - 0)	0 (0 - 0)	> 0.99
Dense endolaryngeal secretion *Gusta endolaringealna sekrecija*	2 (2 - 2)	2 (1 - 2)	**0.01**
Total/*Sveukupno*	11 (10 - 13)	7 (6 - 7)	**<0.001**

*Wilcoxon test. Bold denotes statistical significance / *Podebljano označava statističku značajnost*

All subjects in the control group had a pepsin concentration of 0, and subjects with LPR had a concentration of 0 (interquartile range from 0 to 16) in the range from 0 to a maximum of 41, and after three months of therapy, all subjects had a value of 0, which is a significant decrease (Wilcoxon test, P = 0.01) (Table 5).

Spearman's correlation coefficient was used to assess pepsin concentration association before treatment with the symptom questionnaire (RSI) and clinical findings (RFS). In our sample, we did not observe any association of symptoms with pepsin concentration. Simultaneously, in the group of clinical findings, there was a significant positive association of pepsin concentration with only erythema/hyperemia. Hyperemia/ erythema was more pronounced at higher pepsin concentrations (Rho = 0.595 P = 0.002). (Table 6).

Table 5 Pepsin concentration before and after three months of therapy in subjects with LPR
Tablica 5. Koncentracija pepsina prije i nakon tri mjeseca terapije u ispitanika s LPR

	Median (interquartile range) in subjects with LPR *Medijan (interkvartilni raspon) u ispitanika s LPR*		P value* *P vrijednost*
	Before therapy *Prije terapije*	After therapy *Poslije terapije*	
Pepsin	0 (0 – 16)	0 (0 – 0)	**0.01**

*Mann Whitney U test. Bold denotes statistical significance / *Podebljano označava statističku značajnost*

Table 6 Spearman correlation coefficient of pepsin concentration with RSI and RFS questionnaire
Tablica 6. Spearmanov koeficijent korelacije koncentracije pepsina s RSI i RFS upitnikom

Patients with LPR ***Pacijenti s LPR***	Pepsin concentration before therapy *Koncentracija pepsina prije terapije*
RSI before therapy / *RFS prije terapije*	
Hoarseness / *Promuklost*	-0.004 (0,98)
Cleansing – clearing the throat / *Čišćenje – pročišćavanje grla*	0.108 (0,61)
Postnasal drainage / *Postnazalna drenaža*	-0.259 (0,21)
Swallowing problems / *Problemi kod gutanja*	-0.203 (0,33)
Cough after eating or lying down / *Kašalj nakon jela ili ležanja*	0.031 (0,88)
Feeling of suffocation / *Osjećaj gušenja*	0.370 (0,07)
Cough attacks / *Napadi kašlja*	0.082 (0,70)
Feeling of a "lump in the throat" / *Osjećaj "knedle u grlu"*	-0.103 (0,62)
Heartburn, chest pain / *Žgaravica, bol u prsa*	0.170 (0,42)
RFS before therapy / *RFS prije terapije*	
Subglottic edema / *Subglotski edem*	-0.197 (0,35)
Ventricular obliteration/ *Ventrikularna obliteracija*	-0.126 (0,55)
Erythema / hyperemia / *Eritem / hiperemija*	**0.595 (0.002)**
Swelling of the vocal cords / *Oticanje glasnica*	-0.189 (0.37)
Diffuse laryngeal edema / *Difuzni edem larinksa*	-0.341 (0.09)
Posterior commissure hypertrophy / *Hipertrofija stražnje komisure*	0.002 (> 0.99)
Granuloma / *Granuloma*	-
Dense endolaryngeal secretion / *Gusta endolaringealna sekrecija*	-

Bold denotes statistical significance / *Podebljano označava statističku značajnost*

Discussion

In most patients, pepsin plays a crucial role in developing changes in the larynx and other organs, and its acidic medium serves to maintain proteolytic activity. In addition to pepsin, bile acid salts and other gastroduodenal proteins may play a role in developing inflammatory changes in the upper aerodigestive tract's mucosa. In this study, we compared the pepsin concentration with the RSI and RFS questionnaire before starting therapy. Our study has not detected an association between salivary pepsin and symptoms but there is a significant positive connection between pepsin and clinical sign erythema/hyperemia. There is a more significant association between RSI questionnaire symptoms and high levels of pepsin in saliva, so there is a clear correlation between symptoms such as clearing of the throat, cough, and feeling of a "lump in the throat" and higher values of pepsin concentrations.[14] Pepsin is a potential marker for LPR, has occupied the essential item of this study in which the concentration of the same in saliva before and after therapy was examined in the group of subjects and the control group. In subjects suffering from laryngopharyngeal reflux, 7 of them had a measurable concentration of pepsin in saliva before therapy, and after treatment, no subject was measured pepsin in saliva, which was a significant statistical difference. Also, none of the subjects in the control group had measurable levels of pepsin in saliva. Accordingly, in a 2017 study, a group of authors analyzed existing literature that used pepsin as an appropriate LPR marker. It was shown that in 10 of the 12 studies included in the analysis, a statistically significant difference was found between LPR cases and healthy controls. In patients with LPR, pepsin was detected in saliva in contrast to healthy subjects.[15] LPR therapy depends on the severity of symptoms (mild, moderate, severe). However, all three forms of the disease must include nutritional therapy, weight loss, maintaining a desirable body mass index, smoking cessation, not wearing tight clothing, avoiding exercise after meals, avoiding lying down 3-4 hours after a meal, raising the headboard, avoiding alcohol consumption and increasing physical activity. Nutritional therapy must identify foods and beverages that cause disturbances, high risk of reflux and try to replace them with similar foods that do not cause unwanted LPR symptoms.[16] In the treatment of LPR, patients must understand that proper nutrition is a crucial factor in the short-term and long-term treatment of LPR. Also, patients need to be further informed and educated about the need to treat stress and anxiety as both can lead to autonomic nervous dysfunction and occasional relaxation of the esophageal sphincters.

The proposal of nutritional therapy in people with LPR must be individual, based on evidence and recognized nutritional guides, and expressed in the form of serving foods that are present in the environment of people with LPR, adapted to age, health, physiological condition, daily level physical activity, level of education, religious and cultural characteristics.[17] Due to the proteolytic action of pepsin on the mucosa of the aerodigestive system and the fact that any source of hydrogen ions, including acidic foods and beverages, can prolong the time (days or weeks) of proteolytic activity, changing diets, especially diets with less acidic foods, is fundamental to treatment success. Consuming high-fat, low-protein, sweet and sour foods, and drinks increases the frequency of reflux episodes in the throat.[18]

Among the drugs in the first place are drugs that suppress acid secretion: proton pump inhibitors (PPI) in a double dose and blockers of H2A receptors for nocturnal reflux or occasional use when the symptoms of reflux are more pronounced pepsin reduce activity and enhance sphincter tone. However, PPIs are not recommended for practical use but only in proven acid and pepsin reflux, and it is recommended to take the drug as soon as possible. In our study, significant improvement was observed in clinical findings (subglottic edema, posterior commissure hypertrophy, vocal cord edema, dense endolaryngeal secretion) after three months of therapy in subjects with LPR. The short-term and long-term side effects of taking PPIs are well known. Lechien et al. showed a slight superiority of PPI over placebo and indicated the great importance of nutritional therapy. Nutritional therapy with the Mediterranean diet and alkaline water is more effective than PPI treatment.[19] It is important to note that little attention is paid to non-acidic, weakly acidic, or mixed gastric reflux that can enter the airways and is not insignificant. It would be advisable to determine the characteristics of the reflux that causes the disturbance before applying nutritional therapy. With acidic LPR, and in patients without GERD, there is a higher percentage of non-acidic or mixed LPR.[20] Non-acidic or weakly acidic and mixed LPR requires the use of alginates that control the alkaline component of reflux.[21-24] Changing diet and lifestyle with stress regulation must be the first step in treating all forms of LPR. Treatment must be individual, and a multidisciplinary team must be involved in LPR treatment, which must include a nutritionist, psychologist, and psychiatrist.

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