

Research Progress in Diagnosis and Treatment of Laryngopharyngeal Reflux Disease

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Abstract

Laryngopharyngeal reflux disease is a reflux of gastric contents (gastric acid, pepsin, bile acid, etc.) directly or indirectly into the upper esophageal sphincter in the form of liquid or gas, causing a series of symptoms and signs in the pharynx and larynx. In recent years, LPRD has attracted the attention of many clinical scholars, and its prevalence is increasing year by year. LPRD has no specific clinical manifestations, and its pathogenesis is complex and diverse. There is still a lack of unified diagnosis and treatment standards at home and abroad, and the diagnosis and treatment are not standardized in the process of clinical diagnosis and treatment. This article reviews the diagnosis and treatment of these diseases based on recent research.

Keywords: Laryngopharyngeal reflux disease; Diagnosis; Treatment

Introduction

In the early stages of research, many scholars thought that Laryngeal reflux (LPR) was only an extraesophageal manifestation of Gastroesophageal reflux disease (GERD), and that the two had similarities in their pathophysiology and pathogenesis. With the continuous research, the term Laryngopharyngeal reflux disease (LPRD) was officially included by the American Academy of Otolaryngology-Head and Neck Surgery in 2002 [1]. A number of experts and scholars in China jointly formulated the Expert Consensus on the Diagnosis and Treatment of Laryngopharyngeal Reflux Disease (2015) in 2016 to provide a clear definition of LPRD [2]. LPRD is one of the causative factors of many otorhinolaryngology-head and neck surgical diseases and the source of many diseases. There are great differences in the knowledge and management of LPRD at home and abroad, and clinical workers in the treatment process. There are cases of overdiagnosis and irregular treatment [3,4]. The research progress of LPRD diagnosis and treatment is reviewed.

Overview of LPRD

LPRD is an inflammatory reaction in the upper gastrointestinal tract and respiratory tract caused by reflux of gastric contents into the upper esophageal sphincter (including the pharynx, nasal cavity, trachea, etc.), which is usually accompanied by a series of symptoms such as foreign body sensation in the pharynx, hoarseness, persistent throat clearing, and laryngospasm. Epidemiological data show that there may be some correlation between the prevalence and country region, with the prevalence in the UK and Greek populations being about 34.4% [5] and 8.50%

[6]; there is also variability in the prevalence among regions in China, with the prevalence in Chongqing and Wuhan being about 11.90% [7] and 6.68% [8]. Geographical differences, population distribution, gender, and age can lead to different prevalence rates, and the prevalence rate has increased as people's dietary habits have changed substantially.

The pathogenesis of LPRD is not yet clear, and there are many different views both at home and abroad, mainly including: the weakened upper and lower esophageal sphincter and postural factors; the mechanism of mucosal damage in the pharynx; the mechanism of formation of symptoms and signs of pharyngeal reflux; the mechanism of vagal reflex; psycho-psychological factors and living and eating habits; and other factors (obesity, advanced age, increased intra-abdominal pressure, etc.) [9-12]. Some studies have shown that most patients with LPRD have cough, heartburn, chest pain and gastroparesis, or combined lesions of otitis media, allergic rhinitis, asthma and other related diseases [13,14], which shows that LPRD is the result of the interaction of multiple etiologies and mechanisms.

Diagnosis

Clinical symptoms and signs

The common symptoms of LPRD include persistent throat clearing, hoarseness, and foreign body sensation in the pharynx; the common signs under laryngoscopy include vocal cord edema, congestion, and white spots, and erythema and congestion in the laryngeal mucosa. In order to improve the accuracy of diagnosis, Belafsky, et al. [15,16] developed the RSI and RFS

scales based on the summary of previous studies. The RSI scales have been widely recognized by colleagues internationally, and both domestic and foreign studies have confirmed the clinical usefulness and accuracy of the RSI and RFS scales, which can be used as an auxiliary tool for the initial screening of diagnosis and the assessment of the efficacy of patients after treatment [17].

Salivary pepsin assay

According to the pathogenesis of LPRD, the detection of pepsin in a sample of saliva, sputum or nasal secretions indicates the presence of regurgitation of gastric contents into the pharynx, which means that the occurrence of LPR is determined. Knight, et al [18]. found that the sensitivity and specificity of a positive diagnosis of saliva or sputum pepsin were 100% and 89%, respectively. Meanwhile, Weitzendorfer, et al [19] and Zhang et al [20] confirmed that salivary pepsin assay is simple, noninvasive and has high specificity and sensitivity, and has high clinical diagnostic value by performing salivary pepsin assay in patients with LPRD. Enzyme-linked immunoassay is the most commonly used method to detect pepsin concentration in samples, which is simple, efficient and objective. Immunohistochemical methods to detect pepsin in the laryngeal mucosa have also been used, but this method is an invasive operation and has low patient acceptance, making it difficult to carry out widely in clinical work. In addition, Wu Mukun, et al [21] successfully developed salivary pepsin test strips using colloidal gold method in China, and confirmed through clinical studies that these test strips can be used as a new noninvasive diagnostic technique and widely used in clinical practice in combination with RSI and RFS scales. However, the content of pepsin in saliva or sputum varies greatly from time to time, and there is disagreement on when to take saliva or sputum as the test standard and what concentration can diagnose LPRD, and there is a lack of prospective studies with large samples, which are worthy of in-depth study.

24-hour multichannel intraluminal impedance-pH (MII-pH) monitoring

The 24-hour dynamic esophageal pH monitoring technique has high sensitivity and specificity, can do quantitative analysis of reflux and detect changes in H⁺, and is currently considered the gold standard for the diagnosis of LPRD [2]. Multichannel intraluminal impedance (MII) technique can identify the nature of the regurgitant and can differentiate regurgitation from swallowing. The combination of the two techniques has led to the development of the MII-pH technique, which combines the advantages of both: the ability to monitor acidic and non-acidic reflux; the ability to differentiate between reflux components; the ability to differentiate between reflux and swallowing; and the ability to monitor the reflux height of reflux. However, both pH monitoring and MII monitoring are invasive operations, which are not well accepted by patients because of the long monitoring time, high cost and tedious operation.

Pharyngeal pH (Dx-pH) monitoring

Dx-pH monitoring is an objective, noninvasive test that directly reflects pharyngeal reflux and is easy to perform and well tolerated by patients. Studies have shown that the detection of pepsin in saliva and pharyngeal pH monitoring reflect different reflux agents and that the combined use of both methods is important for diagnosis [22]. However, there are no uniform criteria for the diagnosis of Dx-pH monitoring technique, controversies about its specificity and sensitivity, disagreements about the consistency of the threshold values for normal and abnormal, and lack of prospective studies with large samples, all of which are to be addressed in further studies in the future. However, Dx-pH monitoring can be recommended as a new minimally invasive technique for diagnosis and pre- and post-assessment of anti-reflux therapy.

Diagnostic PPI treatment

PPI is currently a more internationally recognized clinical first-line drug for the treatment of LPRD, and some scholars have explored the therapeutic effect and safety analysis of PPI on LPRD through Mate analysis, which confirmed the significant effect of PPI in improving the symptoms of LPRD patients [23]. Currently, patients with suspected LPRD (RSI > 13 and/or RFS > 7) are treated with PPI for 8 weeks and diagnosed with LPRD if the treatment is effective. Visual analogue scale (VAS) scoring can also be used. There are controversies about the course and dose of PPI, but compared with 24-hour upper gastrointestinal pH monitoring, PPI diagnostic treatment is simple, non-invasive, and sensitive, which improves the diagnostic efficiency.

Treatment

General treatment

The main measures include: low-fat, low-acid, high-protein, high-fiber diet, avoiding the intake of foods that inhibit gastrointestinal motility function (citrus fruits, carbonated beverages, etc.), quitting smoking and alcohol, losing weight, and avoiding eating between midnight and before bedtime. Expert consensus clearly points out the importance of improving life and dietary habits in patients with reflux [2], and some studies have shown that treatment with anti-reflux medication supplemented by improvement of life and behavioral habits has achieved good therapeutic results in patients with LPRD. Therefore, changing poor dietary and lifestyle habits to prevent and stop reflux of gastric contents into the pharynx is of great significance for the occurrence and treatment of LPRD.

Acid-suppressing drug therapy

Acid suppression therapy is the most commonly used treatment modality, mainly including PPI, H₂ receptor blockers, and gastrointestinal stimulants, among which PPI is currently recognized as the drug of choice. 2005 American Academy of Otolaryngology, Head and Neck Surgery and 2008 American

Gastroenterological Association have recommended PPI acid suppression therapy as the preferred strategy for LPRD. The expert consensus proposed PPI as the first-line drug and formulated the corresponding treatment plan. In addition, the efficacy of PPI combined with gastrointestinal stimulants is better than that of single PPI drugs, and H₂ receptor blockers can be used as acute treatment and maintenance therapy for patients who cannot tolerate PPI or. In contrast, long-term use of PPI can lead to many adverse effects and increase the risk of gastrointestinal infection, hypomagnesemia, osteoporosis, myocardial infarction, vitamin deficiency and electrolyte shifts, as well as the development of dementia [24]; and for the reasonable dosage dose and time of PPI, there is still a great controversy at home and abroad, which deserves in-depth research to solve.

Surgical treatment

Surgical treatment mainly refers to esophageal fissure repair plus fundoplication. Surgical treatment can be considered for patients who have recurrent relapses after stopping medication or who have failed medical treatment, or who have persistent life-threatening complications. The success rate of surgical treatment is uncertain because of the wide variation in inclusion and exclusion criteria and treatment outcomes, the surgery itself is invasive, and there are mostly short-term postoperative complications such as dysphagia. Therefore, clinicians should fully assess the condition preoperatively and master the surgical indications and points in order to thereby achieve the desired surgical outcome [25].

Summary

In recent years, LPRD has gradually received attention and research work closely related to otorhinolaryngology has been widely carried out, and there are many diagnostic and therapeutic methods for LPRD that are worthy of clinical promotion and use, but there are still no unified standards for the standardized treatment of LPRD, and there are many problems that need to be explored in both diagnosis and treatment. In addition, the pathogenesis of LPRD has not been clearly established, and is currently considered to be the result of the action of multiple mechanisms. Therefore, further clarification of the etiology and pathogenesis of LPRD can help to understand its development and help to better diagnose and treat this type of disease in clinical work.

Author contributions

This research was finished by all the authors. Xin He and Hao Yang conceived the research project together. Xin He drafts the manuscript. Hao Yang revised and further processed the manuscript. All the authors read and approved the final manuscript.

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