

Clinical Research Progress of Treatment of Reflux Esophagitis by Integrated Traditional Chinese and Western Medicine

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Abstract: *In recent years, the incidence of reflux esophagitis has been increasing year by year. This article aims to summarize the literature on RE in recent years and elaborate on the etiology and treatment of RE from the perspective of integrated Chinese and Western medicine, and holds its pathogenesis of reflux esophagitis is still unclear. While utilizing targeted treatment with Western medicine, individualized treatment with traditional Chinese medicine can often be combined to reduce the recurrence rate of RE, reduce dependence on acid suppressants, and improve clinical efficacy and patient quality of life.*

Keywords: Reflux esophagitis, Western medicine therapy, TCM treatment, Literature review.

1. Introduction

Reflux esophagitis (RE) is a digestive disease in which the contents of the stomach and duodenum flow toward the pharynx or mouth, causing damage to the esophageal mucosa, with reflux, heartburn as the clinical manifestations, and is the most common type of gastroesophageal reflux disease (GERD), accounting for about 30-40% of GERD [1]. A large number of epidemiological studies have shown that the prevalence of GERD ranges from 18.1-27.8% in North America, 8.8-25.9% in Europe, 2.5-7.8% in East Asia, 8.7-33.1% in the Middle East, 11.6% in Australia, and 23.0% in South America [2]. In the past 20 years, the prevalence rate of GERD in China has increased from 6.0% to 10.6% [3]. Although the prevalence rate in China is lower than that in western countries, with the economic and social development, the incidence rate exists a rising trend year by year. The incidence rate of RE has been gradually increasing in recent years, and the intractability of its symptoms has a serious impact on the quality of life of patients, the economy, and the psyche. Therefore, how to prevent and treat this disease has become a hot research topic both domestically and internationally. This article aims to elaborate on the etiology and treatment of RE in recent years, hoping to provide some ideas for clinical diagnosis in the future.

2. The Pathogenic Factors of RE

2.1 Factors Associated with Pathogenesis in Western Medicine

The causative factors of this disease can be divided into the following factors: low education level, diet and lifestyle habits (including smoking, high-fat diet, alcohol, liking sweet or sour food, overeating, eating before bed, etc.), emotional factors (anxiety, depression), and so on. The studies have shown [4] that males, obesity, eating speed ≤ 10 min, smoking, hypertension, constipation, and NSAIDs are risk factors for RE. And some studies have shown that [5-6] centripetal obesity is an independent risk factor for RE, and a 1.73 relative risk of at least weekly in obese patients. With the

deepening of research, some scholars have suggested that the incidence of RE may be related to somatoform autonomic dysfunction and psychological factors. Hu Shuiqing et al. [7] concluded that there is a correlation between anxiety, depression and RE by analyzing the scales and questionnaires of RE patients and healthy individuals.

In addition, the pathological mechanism of RE is weakened defense mechanism, increased gastroesophageal junction compliance, esophageal motor dysfunction, and irritation of esophageal mucosa by refluxed substances, and so on. Patients with RE have esophageal dyskinesia, and most of them have reduced lower esophageal sphincter pressure (LESP), esophageal dysperistalsis and (or) low-amplitude distal esophageal peristalsis, and the greater the degree of esophageal injury, the more serious the dynamic abnormalities [8]. Although discovered relatively recently, *Helicobacter pylori* is known to have infected humans for at least 50000 years. *H. pylori* infection is a widely discussed influencing factor in clinical practice, and the relationship between the two is still controversial. Some literature has shown that *H. pylori* infection [9] may have a protective effect on reflux, while others believe that [10] eradication of *H. pylori* treatment can effectively improve clinical efficacy and reduce the recurrence rate of the disease.

2.2 The Etiology and Pathogenesis of Traditional Chinese Medicine

In the Chinese medicine, there is no corresponding name for RE, but according to its clinical manifestations such as acid reflux and heartburn, it can be attributed to the categories of "acid regurgitation", "heartburn", and "Esophageal ulcer". Its basic pathogenesis is stomach Qi rising, reverse ascending of Stomach-Qi; the reason is feeling external evil, improper diet, emotional maladjustment and Congenital deficiencies. The disease is located in the esophagus and is closely related to the liver, spleen, lung and stomach viscera. Suwen Xuanji Yuanbingshi is LIU Wan-su's representative work, it shows that the disease is closely related to the liver. "Danxi Xinfu" is ZHU Dan-xi's representative work, it shows that the disease

is closely related to lung qi. The Liver controlling dispersion, can dredge up the whole body of qi; The spleen and stomach are located in the middle-jiao, the former is the acquired foundation and the origin of qi and blood, governs movement and transformation, the latter is the sea of water valley, governs reception. spleen and stomach is the hub of the human air-lift. Liver failing to maintain normal flow of qi, spleen and stomach qi lifting disorder, then the birth of this disease. Upper-jiao and spleen are closely related, the lung in the upper-jiao, is the upper source of water, governs the qi. The lung and liver, regulat the whole body qi. The spleen is of the five elements of earth as the mother and the lungs are of the five elements of gold as the son; disorder of mother-organ involving its child-organ, disorder of the child-organ involving its mother-organ. The prevalence of the spleen affects the function of the lungs; at the same time, if the lungs have a problem in functioning, it will also affect the function of the spleen.

3. Treatment of RE

3.1 Western Medicine Treatment

3.1.1 General treatment

A good lifestyle, a reasonable diet and habits, and a stable mood can help alleviate the symptoms of reflux. For example, try to stay upright after meals, try not to eat before going to bed, lose weight, stop smoking, limit alcohol, raise the head of the bed when sleeping, try to choose low fat, low protein, low fiber food, and control the intake of caffeine, spicy, sweet and sour foods.

3.1.2 Medical treatment

At present, the drugs used to treat RE include proton pump inhibitors (PPI), H₂ receptor antagonists, potassium competitive acid blockers (P-CAB), mototropic drugs, gastric mucosal protective agents, etc. PPI is the first choice of drugs for this disease, including omeprazole, Rabeprazole, lansoprazole, etc. When drugs are used in the clinic, they can be used alone or in combination, and the effects vary with different combinations. Patients with mild esophagitis can be treated on demand, but long-term use of PPIs may cause a variety of complications, a Meta-analysis shown that PPIs can reduce bone density, leading to bone loss, which increases the risk of osteoporosis and fracture [11], and also lead to changes in histopathology, with the appearance of hyperplastic polyps, gastric fundus glandular polyps, etc. [12]. And long-term use can lead to increased intragastric PH, excessive bacterial reproduction, increasing the chance of Clostridium difficile infection. H₂ receptor antagonists are more suitable for mild and moderate patients, with short-term efficacy, adverse effects, and susceptibility to resistance, so their use in clinical practice needs to be cautious. P-CAB with its acid-suppressing effect, has the effect of healing the mucous membrane of esophagitis. Prokinetic drugs, including domperidone, mosapride, etopride, etc., can not only increase LES to prevent reflux, but also increase esophageal peristalsis and gastric emptying to enhance esophageal clearance. The clinical efficacy of the combination of PPI (rabeprazole) and prokinetic drugs (mosapride) for the treatment of GERD is even more significant [13]. For patients

whose symptoms still do not improve after routine clinical treatment such as acid suppression, combined use of anti-anxiety or depression drugs may be considered according to their situation to improve the quality of life of patients [14].

3.1.3 Surgical treatment

Surgical treatment mainly uses minimally invasive transabdominal surgery, including laparoscopic and robot-assisted anti-reflux surgery. The purpose of the operation is to reconstruct the anti-reflux structure of the gastroesophageal junction, mainly by establishing the anti-reflux valve to effectively reduce the reflux of gastric acid and restore its anti-reflux function. Laparoscopic fundoplication for the treatment of complex reflux esophagitis has been widely recognized [15]. PPI treatment failure is one of the indications for anti-reflux surgery, but surgical treatment is not recommended for non-acid reflux patients.

3.1.4 Endoscopic treatment

Endoscopic treatment has less trauma and better long-term clinical effect than surgical treatment. Including endoscopic radiofrequency ablation, transoral incisionless fundoplication (TIF), peroral endoscopic cardiac constriction (PECC), endoscopic anti-reflux mucosectomy (ARMS), etc. [16], aims to enhance the anti-reflux ability of the sphincter and reduce the frequency of antacid drug use, thereby improving the health status of patients. It is suitable for patients with the presence of pathological acid reflux and effective to PPI treatment, for patients with ineffective PPI, 24h esophageal PH impedance monitoring is required to confirm the presence of pathological acid reflux before considering endoscopic surgical treatment. Endoscopic treatment of reflux is less traumatic and more convenient than laparoscopic anti-reflux surgery when conditions permit, but the long-term efficacy is not yet certain, and large-sample, high-quality clinical case studies are needed to provide more clinical research evidence for its indications and contraindications, and better guide the clinic.

3.2 Traditional Chinese Medicine Treatment

3.2.1 Syndrome differentiation and treatment

The expert consensus on Chinese medicine diagnosis and treatment of gastroesophageal reflux disease (2023) divides the disease into 7 syndromes, which are liver-stomach heat stagnation syndrom (Chai-hu Shu-gan powder plus Zuojin Pill), Gall bladder fire shangni syndrome (Xiao Chaihu Decoction plus Wendan Decoction), the syndrome of qi stagnation and phlegm obstruction. (Banxia Houpo decoction), hypofunction of Yang-Qi in chest syndrome (Zhishi Xiebai Guizhi Decoction), syndrome of deficient center and counterflow of qi (Xuanfu Daizhe Decoction plus LiuJunzi Decoction), spleen deficiency and damp-heat syndrom (Huang Lian Decoction), stomach Yin deficiency syndrome (Yiwei Decoction) [17].

3.2.2 Experience of various medical professionals

Clinically, for reflux esophagitis various medical doctors according to their own diagnosis and treatment experience,

syndrome differentiation and treatment, and all of them have achieved good curative effect. Prof. Wang Qingguo [18] believed that the basic pathogenesis of this disease was the dysregulation of the spleen and stomach and Cold-heat mixed. In clinical practice, He was used to Zhongjing's acrid-release and bitter-downbearing., and Banxia Xiexin Decoction plus Baihe Wubei Powder were selected to regulate the qi mechanism and calm the cold and heat, and the clinical effect was remarkable. Prof. Yang Chunbo [19] believed that qi mechanism disorder, stomach Qi rising were the basic pathogenesis, spleen deficiency and damp-heat and stagnation of blood-stasis in stomach collaterals were the common pathogenesis in the clinical syndrome, and taking clearing and eliminating dampness-heat and method of regulating qi and dispersing stasis as the treatment principles, in the administration of treatment is often evidence-based medicine, to the empirical formula "clearing drink" plus subtractions, and often get good results. Prof. Lin Tiandong [20] believed that the pathogenesis of this disease can be summarized as liver qi stagnation, spleen deficiency and qi stagnation, stomach heat upward reversal, in the process of treatment, focusing on regulating the liver qi, regulating the spleen to lower the reversal, and clearing the gastric heat, in order to dredge the liver and regulate the spleen, and to clear the stomach to lower the reversal as a rule of treatment, and self-proposed "Shugan Qingwei Decoction" to treat this disease, which has remarkable clinical effect. Prof. Li Tingquan [21] proposed according to the theory of "Zhizhonghe" that the disease was mainly caused by disharmony between the liver, spleen and stomach, and the combination of cold, dampness and heat. Banxia Xiexin Decoction was chosen as the base prescription for treatment, and Shunwei Jiangni prescription was prepared by himself to rationalize the qi mechanism, regulate the heat and cold, and harmonize the qi and blood, which has been clinically effective. Prof. Xu Jingfan [22] believed that the pathogenesis of reflux esophagitis always belongs to failure of stomach qi governing descending, disorder of qi movement, the location of the disease is in the esophagus, which is closely related to stomach, spleen and liver. In the treatment, emphasis should be laid on regulating the stomach, spleen and liver. The main therapeutic methods are descending method, harmonizing method and resolving method. Meanwhile, he original creates paste administration method with lying position to protect esophageal mucosa, clinically have obvious results.

3.2.3 Classic famous prescription

Clinically, the classical prescription used by various doctors in the treatment of reflux esophagitis is often effective. Yan Man [23] showed that Xuanfu Daizhe decoction and omeprazole in the treatment of liver-stomach depression RE had a higher efficiency in TCM syndrome, gastroscopy and liver and kidney function indexes of the treatment group were better than those of the control group ($P < 0.05$). Liu Dan [24] showed that Banxia Xiexin Decoction treated reflux esophagitis with intermingled cold and heat syndrome, the total clinical effective rate of the treatment group was higher than that of the control group, and the efficacy was satisfactory. At the same time, Banxia Xiexin Decoction combined with Sini powder or Zuojin Pill can also obtain obvious clinical effect on RE. Through systematic literature analysis, Li Juan et al. [25] showed that the application of

middle-invigorating Yang-lifting method and the addition or reduction of Buzhong Yiqi decoction in the treatment of RE had better clinical efficacy, and the therapeutic effect was better than that of conventional western medicine, with fewer adverse reactions. Cui Ya et al. [26] showed that the application of Liujunzi Decoction in combination with Xuanfu Daizhe Decoction in the treatment of Qi and reverse syndrome of RE could significantly improve clinical symptoms and reduce the recurrence rate of patients. The mechanism may be related to down-regulating the expressions of HIF-2 α , NF- κ B and TRPV1, improving hypoxic microenvironment under the condition of esophageal mucosal inflammation and re-duc-ing esophageal hypersensitivity.

3.2.4 Acupuncture treatment

Acupuncture and moxibustion, as a unique treatment of traditional Chinese medicine, has been widely used in clinical practice and has gradually been accepted abroad. The clinical effect of acupuncture on RE is obvious and can effectively reduce the recurrence rate. Yi Yue et al. [27] used data mining technology to obtain the core acupoint combination for RE was "Zhongwan and Zusanli" and the core prescription was "Zhongwan, Zusanli, Weishu and Neiguan. According to the study of Xu Yin et al. [28], the effective rate of the "WANG's old ten needles" acupuncture treatment for reflux esophagitis was significantly better than that of the control group (oral omeprazole), and the difference was statistically significant ($P < 0.05$). Wen Na et al. [29] showed that acupuncture has preferable short and long term therapeutic effects for treatment of reflux esophagitis of heat stagnation of liver and stomach type. Liu Yusheng et al. [30] showed acupuncture of the Jianwei Liqi Hewei therapy was effective on reflux esophagitis.

3.2.5 Combined treatment of traditional Chinese medicine and western medicine

In recent years, various medical practitioners have clinically applied traditional Chinese medicine decoction, Chinese patent medicines, and acupuncture in combination with conventional western medicines to treat RE with clear efficacy, which is significantly better than that of western medicines alone, and can significantly improve the symptoms, alleviate the pain of the patients, effectively shorten the course of treatment, and slow down the economic pressure of the patients. patients' economic pressure. Qian Xiaopan et al. [31] applied Wuzhuyu decoction and Sini powder in combination with Western medicine to treat spleen-stomach deficiency cold and liver-stomach disharmony of RE, which was conducive to improving clinical symptoms and improving treatment efficiency. Yang Shujuan et al. [32] applied Xufu daizhe decoction to treat reflux esophagitis. The main symptom score, clinical symptoms and the effective rate of esophageal inflammation under gastroscopy in the treatment group were significantly higher than those in the control group, and the levels of serum motilin (MTL) and gastrin (GAS) in the patients were also increased. Sun Liwei et al. [33] showed that Prescription of Soothing Liver and Warming Stomach combined with Western medicine in the treatment of reflux esophagitis can significantly improve the curative effect, effectively improve clinical symptoms, improve sphincter function and esophageal contraction function and

reduce reflux frequency, worthy of clinical promotion. Que Renye et al. [34] showed that Shugan Hewei Decoction combined with Rabeprazole is effective and safe in clinic. And it optimizes the treatment plan of RRE. It is worth popularization and application. Yin Hongwei et al. [35] showed that Dalitong Granule combined with pantoprazole in the treatment of elderly patients with reflux esophagitis can effectively improve the clinical symptoms and endoscopic situation. It is safe and stable and worthy of clinical application. Meng Min et al. [36] showed that Ganhai Weikang Capsules combined with esomeprazole sodium has good clinical efficacy in treatment of reflux esophagitis, and can significantly improve clinical symptoms and esophageal mucosa status, and significantly improve mental and psychological status and life quality, which is worthy of clinical application. Zhu Zhiqiang et al. [37] showed that reflux esophagitis patients were randomly divided into acupuncture combined with Chinese herbs group (acupuncture + Xuanfu Daizhe Decoction combined with Zuojin pills) and western medicine group (omeprazole + mosapiride). Combination of acupuncture and medicine seems to have obvious curative effect, low recurrence rate and few adverse reactions in the treatment of reflux esophagitis.

4. Conclusion

Reflux esophagitis is one of the common digestive diseases in clinical practice. Its pathogenesis is still unclear, and it may be related to reduced pressure of lower esophageal sphincter, transient relaxation of lower esophageal sphincter, impaired function of esophageal mucosal barrier, and gastric emptying dysfunction. In clinical practice, Western medicine routinely uses PPIs, H2 receptor antagonists, P-CAB, gastric motogenic drugs, gastric mucosal protective agents and other drugs, and the efficacy is clear, but it is easy to relapse after drug withdrawal, and long-term medication has more adverse reactions. Traditional Chinese medicine treatment of this disease has its unique advantages, multi-target, multi-way, syndrome differentiation treatment, has achieved remarkable curative effect. Under the guidance of the theory of Chinese medicine, combined with the targeted treatment of Western medicine, the two complementary advantages can improve the clinical efficacy, reduce the recurrence rate, improve the quality of life of patients, reduce adverse reactions, shorten the course of treatment. The treatment of RE by integrated Chinese and Western medicine can be used as the first choice for clinical treatment and is worth further promotion and application. However, there is still a lack of unified drug use standards for its treatment. Therefore, in order to better promote and apply it, we should pay attention to large samples and high-quality clinical research, provide more theoretical basis and experimental evidence for clinical treatment, and better guide clinical practice.

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