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**New treatment for gastroesophageal reflux disease: Traditional Chinese medicine Xiaochaihu decoction**

Xu LY *et al*. Xiaochaihu decoction for GERD

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**Abstract**

Gastroesophageal reflux disease (GERD) has a high prevalence worldwide. Li *et al* performed a well-designed study on the efficacy of modified Xiaochaihu decoction (MXD) for GERD, which showed that MXD is an optional therapy for GERD beyond proton pump inhibitors (PPIs). The herbal granule administration mode minimized the bias from traditional herbal formula in clinical trials. One limitation of that study was that it lacked records of side effects and rescue medication. As a chronic disease with recurrent symptoms, GERD rehabilitation requires prolonged observation of the clinical course with MXD therapy.

**Key Words:** Gastroesophageal reflux disease; Xiaochaihu decoction; New treatment; Traditional Chinese medicine; ModifiedXiaochaihu decoction; Chronic disease

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**Core Tip:** Modified Xiaochaihu decoction (MXD) has been applied for gastroesophageal reflux disease (GRED) for thousands of years in Asian countries. Li *et al* proved that MXD is an ideal optional therapy for GERD. The drug selection of herbal granule makes double-blind research achievable. Side effects of MXD should be noted. As a chronic disease, GERD rehabilitation requires prolonged observation of the clinical course with MXD therapy.

**TO THE EDITOR**

We read with interest a clinical study by Li *et al*[1]. The researchers performed a prospective, double-blinded, and double-simulation study on the efficacy of modified Xiaochaihu decoction (MXD) for gastroesophageal reflux disease (GERD) and its effect on esophageal motility. The study enrolled 288 participants with GERD, and then divided them into the treatment and control groups, receiving MXD plus omeprazole simulation and omeprazole plus MXD simulation, respectively, for 4 wk. The GERD-Q scale score and esophageal manometry were evaluated. The results showed that MXD had a similar ability to increase the pressure at the lower esophageal sphincter and reduce ineffective swallowing, compared with omeprazole in mild-to-moderate GERD. The recurrence rate was significantly lower than that of the control group within 3 mo at follow-up visits. We greatly appreciate the dedication of the authors towards studying the effect of MXD on GERD as an optional therapy.

As we all know, GERD has a high global prevalence with limited therapeutic options, and its incidence is increasing annually. Patients with GERD present with a variety of symptoms including heartburn, effortless regurgitation, dyspepsia, bloating, and abdominal pain or discomfort, as well as cough and laryngitis, which severely impact their quality of life[2]. Since the 1990s, proton pump inhibitor (PPI) therapy has evolved as the standard treatment of choice for GERD[3]. However, it has become evident that symptoms attributed to GERD remain despite ongoing PPI treatment in up to 40% of patients[4], and PPI therapy increases the risks of infections, osteoporosis, hepatic failure, pancreatitis, jaundice, and persistent gynecomastia[5-7]. Therefore, multivariable treatment beyond PPIs is urgently required.

Traditional Chinese medicine theory believes that the herb Chaihu could regulate qi-flow to harmonize digestive disorders. The formula Xiaochaihu decoction, which has demonstrated therapeutic effects such as for nausea, poor appetite, and epigastric distension, has been used in treating GERD for thousands of years in Asian countries. However, high-level evidence-based traditional Chinese medical research is still lacking and is restricted by many factors. For instance, the herb formula is customized according to patient characteristics including severity of disease, gender, and age. Besides, pharmaceutical effects may be influenced by the way that Chinese herbs are decocted. Thus, it is hard to provide the same drug dose for each patient. In this research, drug selection of herbal granules makes double-blind research achievable. For the concealed allocation, herbal granules were supplied instead of traditional decoction, which greatly reduced the bias from herb treatment.

A limitation of this study was a lack of record keeping of the side effects and rescue medications. With the growing popularity of traditional Chinese medicines, reports of herbal side effects are common. Bupleurum, the main component of MXD, was found to increase the risk of chronic hepatotoxicity[8,9]. Meanwhile, Itoh *et al*[10] reported that long-term oral administration of MXD caused cholestatic liver injury, interstitial pneumonia, and even death[10]. Therefore, medical safety evaluation tests, such as liver and kidney function indices, should be assessed. Rescue medication or treatment for these adverse events should also be considered.

Besides, although the sample size was well calculated according to previous literature reports and formula, the sample size for esophageal manometric indicators, which was from 7–52, was relatively small.

The authors mainly focused on the efficiency of MXD therapy for a short duration. As we know, GERD is generally a chronic disease with recurrent symptoms and requires long-term management[11]. Further studies are needed to evaluate the effects of prolonged MXD therapy on GERD rehabilitation.

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