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Editorial

Estimation of Clinical Predictive Factors in Treating Patients With Globus

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Article: Clinical predictors for response to proton pump inhibitor treatment in patients with globus
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Gastroesophageal reflux disease (GERD) may cause laryngopharyngeal reflux (LPR), which results in mucosal exposure of the pharynx, larynx or pulmonary system to the different components of the gastric refluxate, and so provokes symptoms including throat discomfort, hoarseness, globus pharyngeus and chronic cough. Of the LPR patients, 25% experience spontaneous resolution of symptoms and 50% have a chronic course of the disease with intermittent exacerbations and remissions.[1] There is no gold standard tool for establishing the association between GERD and extraesophageal symptoms of GERD because many of them may have a variety of etiologies. A recent study demonstrated that 52% of patients had laryngeal symptoms that were associated with GERD based on upper gastrointestinal endoscopy and/or on esophageal pH monitoring.[2]

Globus is usually long-lasting and difficult to treat in clinical field. Potential diverse causes can lead to globus. Recent data have focused on GERD, abnormalities of the upper esophageal sphincter, psychological and psychiatric disorders, and stress as major factors contributing to the globus sensation.[3] Since there is a lack of well-designed controlled studies on the treatment of globus, an empirical therapeutic trial with a proton pump inhibitor (PPI) twice daily for at least 3 months is recommended in patients with a clinically suspected reflux-related extraesophageal symptoms in Westerns.[4] In this issue of Journal of Neurogastroenterology and Motility, Jeon et al[5] investigated clinical predictors to short-term PPI treatment in 41 patients with globus treated with pantoprazole 40 mg daily for 4 weeks. Of them, 22 patients (53.7%) were classified as responders. They suggested that the presence of typical reflux symptoms was related to a higher response rate to 4-week pantoprazole treatment, which means globus is associated with GERD. On the contrary to this study, another study showed that typical reflux symptoms were not associated with improvement of globus symptoms in which patients with globus received rabeprazole 20 mg twice daily for 14 days.[6] Apart from relation of reflux, stress and psychological factors have often been thought to trigger the globus sensation. A psychological history should be considered and could be an important predictor for treatment outcome, because anxiety is related to poorer response to PPI therapy.[7] Authors also suggested that long symptom duration ($\geq$ 3 months) was associated with a

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lower response rate. It is dubitable whether the effect of good response in patients with short symptom duration would be due to the medication or placebo effect. Further study will be needed only in patients with long symptom duration ($\geq$ 3 months) excluding short duration, which will have much more significant results. This study is not a placebo controlled design, which makes the results difficult to apply in real clinical field. There were previous studies which were conducted as a prospective, randomized, double-blind, placebo-controlled trial. They have shown conflicting results.[8,9] A study showed that twice-daily PPI treatment for 3 months demonstrated a significantly greater improvement in laryngeal appearance and LPR symptoms,[8] while another study suggested that the patient with globus did not benefit from once-daily lansoprazole therapy for 3 months.[9] The difference between two studies is that participants with all other LPR symptoms as well as globus were included in the former study, and in addition, higher dose of PPI were used compared to the latter one.

Inadequate duration of treatment would be an issue, because at least 3 months of treatment has been suggested in patients with LPR in Westerns. There is no guideline in Easterns, and authors explained that 7-14 days is considered to be probably long enough to determine the effect of the PPI.[10] Limitations of the current study include not a placebo controlled study, its small sample size and without history of psychological factors. Follow-up data regarding natural course of patients with globus should be needed as well because responding with short-term therapy does not mean symptom free for long-term.

In summary, the cause of globus seems to be multifactorial. The lack of evidence still exists in association with GERD. This study showed globus is connected with GERD and suggested clinical predictors in treating globus symptom with PPI. A guideline to treat LPR patients would be drawn up through much more researches in Eastern.

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