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Relation between globus pharyngeus and OSA in patients examined simultaneously by PSG and pH monitor: A cross sectional study

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ABSTRACT

Objective: This was a first cross-sectional single-center study to research the relation between globus pharyngeus, OSA and GERD. Since previous clinical studies have demonstrated a relationship between globus phayrngeus and GERD, however, no reported study on the relation between globus pharyngeus, sleep disorders including OSA, and GERD.

Methods: Seventeen patients underwent general and otorhinolaryngological examinations and responded to several questionnaires (ESS, PSQI, HADS, and Globus pharyngeus VAS score) at their first visit, and underwent a gastroesophageal test for 24-h pH monitoring and in-laboratory PSG one to two months later.

Results: No significant differences were seen in ESS, PSQI, or HADS scores between the groups. The acid exposure time was not significantly different among the groups. The percentage of esophageal reflux time was higher than the percentage of laryngopharyngeal reflux time through the total time as well as the supine period. This indicated that GERD occurred more frequently than laryngopharyngeal reflux. The entire results showed concurrent OSA in 10 cases (59%) and concurrent GERD in 7 cases (41%). The cases with OSA were treated by CPAP or oral appliance, and those treatments were effective for globus pharyngeus.

Conclusion: Although the relation between OSA and globus phayngeus is still controversial, these findings suggest that OSA may be a previously undetected cause of globus pharyngeus. By improving OSA, it may offer an additional option of treatment for those globus pharyngeus cases combined with OSA.

1. Introduction

1.1. Poorly understood etiology

Globus pharyngeus, also described as globus sensation or globus hystericus is a poorly understood disease. It is commonly described as having a "lump in one's throat", with the persistent sensation of having phlegm or some other sort of obstruction in the throat even when none exists. Hippocrates first recorded globus pharyngeus approximately 2500 years ago [1]. The first accurate description of the condition was by Purcell [2] in 1707, who thought that globus resulted from pressure on the thyroid cartilage when the strap muscles of the neck contracted. In the past, globus was frequently associated with menopause or psychogenic factors, and thus the term "globus hystericus" has been used. Malcomson [3], noting that most patients experiencing

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globus did not have a hysterical personality, suggested the term "globus pharyngeus" in 1968. On the other hand, Riehl and Keefer believed that the two factors of visceral hypersensitivity and symptom hypervigilance were critical for esophageal symptoms, although the pathophysiology is likely multifactorial [4].

1.2. Relation between globus pharyngeus and GERD

Gastroesophageal reflux disease (GERD) is characterized by repeated overflow of gastric contents into the esophagus and clinical features, such as heartburn and regurgitation, during daytime and nighttime. Although there is still considerable debate about the causative role of GERD in patients with globus pharyngeus, gastroesophageal reflux has been suggested to be a major cause of this condition, potentially accounting for 23%–68% of globus pharyngeus patients [5–7]. Koufman [7] found that 58% of patients with globus had abnormal pH results, and Cherry et al. [8] demonstrated that 10 out of 12 subjects complained of globus when acid was infused into the distal esophagus. In a study with 24-h double probe pH monitoring of 25 patients with globus and hoarseness, 72% of the patients exhibited pathologic reflux [9] and the globus symptom score was significantly higher in patients with GERD than in those without [10]. Discordant data have also been reported [11,12]. However, it is clear that many patients with globus have concomitant GERD and that there is a true association between GERD and globus.

1.3. Relation between GERD and OSA

Sleep apnea is a sleep disorder characterized by pauses in breathing or periods of shallow breathing during sleep. Each pause can last for a few seconds to several minutes and they happen many times a night. Obstructive sleep apnea (OSA) is the most common category of sleep-disordered breathing. The muscle tone of the body ordinarily relaxes during sleep, and at the level of the throat the human airway is composed of collapsible walls of soft tissue which can obstruct breathing. Patients with OSA are known to have metabolic dysregulation and cardiovascular, cerebrovascular or neurocognitive complications [13].

Patients with OSA may have an increased risk of GERD, as evidenced by the frequent findings of gastrointestinal symptoms, esophageal pH monitoring, and endoscopic findings of esophagitis [14,15]. A high prevalence of GERD in OSA patients has been reported, but there are many confounding factors such as obesity, gender, and lifestyle [16]. There is little evidence for a causal relationship between GERD and OSA. Suzuki reported that among patients with reflux, the types of arousal differed significantly between those with mild-to-moderate versus severe OSA, and in patients with mild-to-moderate OSA, Laryngopharyngeal reflex induces more spontaneous than does GERD [17]. In addition, one published study suggested GERD might not be associated with OSA [18], and so this is still being debated.

1.4. First trial investigating relation between globus pharyngeus, OSA, and GERD

Globus pharyngeus may be caused by GERD, and GERD may be related to OSA, but these relations are unclear. The aim of this study was to evaluate whether there is an association between globus pharyngeus, OSA, and GERD. This was a cross-sectional study of globus pharyngeus patients in whom PSG and pH monitoring were examined simultaneously. This project required a research group composed of otolaryngologists who could diagnose and exclude other pharyngo-laryngeal diseases, sleep staff to organize fulltime polysomnography, and internal physicians who could operate a 24-h pH monitor. Because this overnight examination was complicated and time consuming, it was carefully explained to subjects and their informed consent was obtained. We limited it to one case per month as much as possible.

2. Materials and methods

2.1. Subjects

Patients who complained of globus pharyngeus symptoms, such as a lump in their throat with the persistent sensation of phlegm or some other sort of obstruction in the throat for more than three months, and who were refractory to medical management, were referred to us. The subjects were a sub-set of 17 of these patients (11 male and 6 female, mean age: 61.4 years, range: 36–80), who were diagnosed with globus pharyngeus and who underwent complete polysomnography (PSG) simultaneously with 24-h pH monitoring at the Good Sleep Center, Nagoya City University, Nagoya, Japan, from January 1, 2011 to December 31, 2016. None of them reported sleep disturbance as a chief complaint, and sleep disturbance was not brought up by any patients until they were asked about it specifically. Inflammatory findings in their upper airway, from nasal cavity to larynx, were not seen in endoscopic examination. Patients were excluded if they were currently taking over-the-counter or prescription medications for GERD that they were unwilling to stop for the duration of the study, or if they had any chronic medical condition, gastrointestinal conditions which might affect esophageal function or acid secretion, or previous surgery in the stomach and/or esophagus. Patients with any mental disorder or those who had been instructed to continue all medications that could influence sleep, such as benzodiazepines, were excluded as well.

2.2. Protocol

This was a cross-sectional single-center study. All patients received general and otorhinolaryngological examinations and responded to several questionnaires and instruments (ESS, PSQI, HADS, and globus pharyngeus VAS score) at their first visit, and underwent a gastroesophageal test for 24-h pH monitoring and in-laboratory polysomnography (PSG) one to two months later. Initially, all subjects underwent PSG for screening purposes to rule out sleep disorders other than OSA and to confirm the presence and severity of OSA. The apnea-hypopnea index (AHI, number of apneas and hypopneas per hour of sleep) was used to stratify participants into two groups: those with OSA− (AHI $<$ 15 events/h), and those with OSA+ (AHI $\geq$ 15 events/h). After the first 24-h pH monitoring and in-laboratory PSG, those patients who were diagnosed with mild

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