学 位 論 文 の 要 旨

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学 位 論 文 名　Gastroesophageal Reflux During Enteral Feeding in Stroke Patients: A 24-Hour Esophageal pH-Monitoring Study

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論 文 内 容 の 要 旨

INTRODUCTION

Stroke is the major cause of neurogenic dysphagia, which is frequently complicated by the development of aspiration pneumonia. Patients receiving nasogastric tube or percutaneous endoscopic gastrostomy (PEG) feeding tend to have gastroesophageal reflux (GER). James et al. reported that stroke patients with PEG had a high prevalence (18%) of aspiration pneumonia, and their median survival was only 10 months. Several mechanisms could be involved in the development of GER, including transient lower esophageal sphincter relaxation, excessive acid reflux, and gastric acid hypersecretion. Nevertheless, the pathophysiology of GER after stroke has not been well documented. One previous study examined the relationship between GER and aspiration pneumonia in patients with various brain diseases, but the influence of lateralization and size of brain lesions after stroke on GER remains unclear. This study was designed to examine, by means of 24-hour pH monitoring, the incidence of GER in stroke patients under enteral feeding and the effects of hemispheric lateralization and lesion volume on GER in those patients.

MATERIALS AND METHODS

We selected 16 stroke patients aged 57 to 95 years (mean 83.2±9.2 years) who had been admitted to Shimane University Hospital and who were receiving PEG or nasogastric tube feeding. Six patients had stroke lesions in the right middle cerebral artery (MCA) territory and 10 had lesions in the left MCA territory. Exclusion criteria were severe illness including malignancy, history of gastroesophageal surgery, and lack of informed consent. The diagnosis of stroke was made clinically and lesions were confirmed by magnetic resonance

imaging (MRI). All patients had been treated with antiplatelet or antithrombin drugs in the acute stage of stroke. The diagnosis of aspiration pneumonia required 3 or more of the following characteristics: pulmonary infiltrates in chest radiography, fever, dyspnea, abnormal respiratory examination, and leukocytosis. Aphasia was diagnosed on the basis of disruption of sentence comprehension, sentence production, naming, and reading. Twenty-four–hour esophageal pH monitoring was performed using the Degitrapper pH400. The pH electrode was positioned 5 cm above the lower esophageal sphincter. The mean duration between stroke onset and the start of PEG or nasogastric tube feeding was 59±82 days. Each patient was given liquid-type nutrition 3 times a day during the study. The patients were kept in an upright position for 2 hours after each meal. The administration of H_2 blockers and/or proton pump inhibitors had been stopped 7 days before the study. All recorded data were transferred to a personal computer for analysis use. A gastroesophageal acid reflux episode was defined as the time for which the pH was below 4. Lesion volume was measured on T2-weighted axial magnetic resonance images using the MRIcron software. The study was approved by the Ethics Committee of Shimane University Hospital. As for statistical analysis, the Mann–Whitney U test, Chi-square test and Spearman correlation coefficient test were used. $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Four patients underwent PEG and 12 patients underwent nasogastric tube feeding. Nine patients (56%) were diagnosed with GER, which was defined on the basis that the number of acid reflex episodes was >25 per day and the cumulative reflux time was >4%. Ten patients (63%) developed aspiration pneumonia during enteral feeding. The rate of aspiration pneumonia was significantly higher in patients with GER (88.9%) than in those without GER (42.9%; $p=0.04$). However, the rate of aspiration pneumonia revealed no significant difference between patients with left lesions (70.0%) and those with right lesions (50.0%). The incidence of aspiration pneumonia was not affected by age, gender, feeding method, or duration after stroke onset. The 3 pneumonia patients without GER were diagnosed with infectious pneumonia after sputum culture. *Staphylococcus aureus* was detected in two cases, and *Klebsiella pneumoniae* was detected in one case. Ten patients with left hemispheric lesions had a significantly higher incidence of acid reflux than 6 patients with right hemispheric lesions (116±105 vs. 13±17 per day; $p=0.04$). No significant difference was seen in total time of acid reflux between left and right lesions (105.2±116.0 vs. 23.8±9.7 hours). The mean pH value was also similar for left and right lesions (6.0±0.7 vs. 6.2±0.7). There was no difference in the rate of aphasia between patients with and without GER (55.5% vs. 28.5%), or between patients with and without pneumonia (50.0% vs. 33.3%). There was no difference in lesion volume between patients with and without GER (47.8±49.3 vs. 64.3±30.6 cm^3) or between patients with and without

pneumonia (57.1±45.1 vs. 50.4±38.0 cm^3). The lesion volume was also similar between patients with left and right hemispheric stroke (60.9±45.4 vs. 45.1±36.5cm^3). The lesion volume was not correlated with any measures of GER (number of acid reflux episodes, total time of acid reflux, or mean pH value).

Aspiration pneumonia is a serious common complication in stroke patients. Dysphagia is often associated with stroke and may eventually lead to PEG feeding. Our study also yielded a similar incidence rate (56%) of GER in patients receiving enteral feeding. Furthermore, the incidence of aspiration pneumonia was very high (89%) in patients who had evidence of GER. GER is known to be observed with higher frequency in patients after stroke compared to normal subjects. The prevention of aspiration pneumonia is a critical issue for improvement of the prognosis of stroke patients on long-term enteral feeding. Our findings indicate that lesions in the left hemisphere are more prone to cause GER than right hemispheric lesions. While the right prefrontal cortex is normally dominant in the activation of stress-related systems, the left prefrontal cortex may work to inhibit stress-related emotional expression by means of interhemispheric inhibition. Therefore, patients with left hemispheric lesions could be susceptible to mental stress. In addition, aphasia is associated with left hemispheric stroke more often than with right hemispheric stroke. Aphasia could cause mental stress and might increase the secretion of gastric acid. Walsh et al. reported a case of aphasia after left hemisphere stroke associated with Cushing's ulcer and duodenal perforation caused by elevated gastrin level, and suggested that poststroke aphasia might cause ulceration via neurogenic stress. Patients with stress-related mucosal disease and ulcers have low intragastric and intramural pH values, which could be a cause of GER. Another mechanism leading to a high prevalence of pneumonia in patients with left hemispheric stroke might be related to cerebral asymmetry in the control of the immune system. Koch et al. found that patients with left hemispheric stroke had a higher variability in C-reactive protein and white blood cell measurements. Left-sided stroke may be considered a direct risk factor for infectious disease or immune deficits. Stroke patients with left hemispheric lesion are prone to develop GER, and in these cases clinicians should consider early treatment for GER and proper control of patients' body positioning. The present study did not find any relation between stroke lesion volume and GER or incidence of pneumonia. One reason for the absence of such a relationship may be the small number of patients in this study.

CONCLUSION

GER was a significant risk factor for aspiration pneumonia and was more prevalent in patients with left hemispheric lesions. These findings should be helpful in preventing the development of poststroke pneumonia.