**Original Article**

Prolonged apnea/hypopnea during water swallowing in patients with amyotrophic lateral sclerosis

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**Abstract:** Purpose Swallowing difficulty is increased along with progression of respiratory disturbance in patients with Amyotrophic Lateral Sclerosis (ALS). To analyze the respiratory patterns during swallowing is important for the management of this disease. In this study, we evaluated apnea/hypopnea during water swallowing and the respiratory cycle at rest and after water swallowing.

Method We evaluated respiratory patterns in swallowing in 10 ALS patients (66.0 ± 7.1 years old), in 10 Myotonic dystrophy (MD) patients (46.5 ± 12.2 years old), and in 10 healthy volunteers as control subjects (61.7 ± 10.0 years old). The ALS and MD patients had consulted the Department of Neurology of Toneyama National Hospital or Tokushima National Hospital between April 2002 and July 2006. Respiratory patterns were evaluated by simultaneous recording of cervical swallowing sound in water swallow. A hypersensitive microphone measured cervical sound. A thermistor was used for pneumography. The means of four continuous respiratory cycles at rest and after swallow of 3 ml water were used for analysis. Respiration with amplitude of 1/2 or smaller than that of the pneumography at rest was defined as hypopnea, and the apnea/hypopnea duration was evaluated as the respiratory suppression time.

Statistical Analysis All analyses were performed using SPSS 11.0J (SPSS Inc., Chicago, IL).

Results In the ALS group, the respiratory cycle was 3.15 ± 0.76 sec (2.31-4.39 sec) at rest, while after swallowing, it was 2.78 ± 0.83 sec (1.77-4.80 sec) (p = 0.1). In the MD group, the respiratory cycle was 2.56 ± 0.46 sec (1.91-3.67 sec) at rest, while after swallowing, it was 2.94 ± 0.60 sec (2.03-4.29 sec). In the control group, it was 3.46 ± 0.57 sec (3.18-4.34 sec) at rest and 3.24 ± 0.50 sec (2.64-4.04 sec) after swallowing. The apnea/hypopnea duration during water swallow was 14.33 ± 8.89 sec (2.50-30.68 sec) in the ALS group, 3.66 ± 1.58 sec (1.78-6.42 sec) in the MD group, and 3.64 ± 1.00 sec (2.34-5.56 sec) in the control group. The apnea/hypopnea duration in the ALS group was significantly longer than that in MD and control groups (p = 0.005, p = 0.004 by the t-test). The ALS patients with severe respiratory failure or with aspiration in videofluoroscopy showed extended apnea/hypopnea duration.

Conclusion Prolonged apnea/hypopnea was observed during water swallowing in ALS patients. We speculate that this prolongation is caused by severe swallowing disturbance and respiratory failure, which increases the risk of aspiration. The respiration of ALS patients should be closely monitored during eating.

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**Introduction**

Amyotrophic lateral sclerosis (ALS) is an extremely severe and progressive neuromuscular disease. Respiratory insufficiency and dysphagia develop as the disease progresses. Swallowing difficulty is increased along with progression of respiratory disturbance in patients with ALS. Therefore,
Fig. 1 The cervical swallowing sound and the respiratory cycle simultaneously recording system.

Methods

We evaluated respiratory patterns during swallowing in 10 ALS patients, in 10 MD patients, and in 10 healthy volunteers. The ALS patients (66.0 ± 7.1 years old [range 57-77]), MD patients (46.5 ± 12.2 years old [range 26-60]), and control subjects (61.7 ± 10.0 years old [range 52-79]) had consulted the Department of Neurology of Toneyama National Hospital or Tokushima National Hospital between April 2002 and July 2006.

ALS was diagnosed according to the EL Escorial criteria and MD was diagnosed clinically. The control subjects had no cerebrovascular or neuromuscular disease, and did not exhibit choking (suggesting dysphagia), sputum sticking, or moist voice. No abnormalities were observed in this group during testing. Of the 10 ALS patients, 2 required supplemental tube feeding (ALS Functional Rating Scale swallowing part); FRSSw 0), 5 required a diet of better consistency (FRSSw 2), 2 occasionally choked (FRSSw 3), and 1 was able to swallow and eat normally (FRSSw 4).

The ethics committees of both institutions approved this study, and written consent was obtained from all subjects.

Measurements

Respiratory patterns in water swallow were evaluated by simultaneous recording of cervical swallowing sound and pneumography. A sensor, commonly used for measurement of sleep apnea, was used for pneumography because this is an established method for measuring respiratory curves without causing discomfort. Cervical sound was measured by a hypersensitive microphone.

Subjects sat quietly without talking or moving for 5 minutes, while resting respiration was continuously recorded. The operator marked events such as dry swallows, coughing, and body movements, which were deleted from the respiratory trace before analysis. The mean of four continuous respiratory cycles at rest was used for analysis. The same process was used to measure the respiratory cycle after the subjects drank 3 mL of water 3 times at 20-second intervals. Because dry swallows or coughs sometimes occurred, a sequence of four respiratory cycles with the least noise obtained during the 3 water swallows was used for the analysis. Again, the mean of four continuous respiratory cycles after swallowing was used for analysis.

A thermistor, TR-711T (L type) by Nihon Koden, was used for pneumography in this study, but the temporal changes from exhalation to inhalation and apnea were slightly unclear. Therefore, respiration with an amplitude of 1/2 or smaller than that of the pneumography at rest was defined as hypopnea, and the apnea/hypopnea duration was evaluated as the respiratory suppression time.

Swallowing and Respiratory Monitoring Equipment (Fig. 1)

Cervical sound was measured by a hypersensitive microphone (Microphone UC-92H by Sound level meter Unit UN-04 RION).

For the pneumography recording, a thermistor (5-mm diameter) was placed near, but not in contact with, the nostril (to avoid body temperature changes). The thermistor was connected to a respiratory/plethymo coupler (DAT Data re-
corder RD-135T TEAC), and the cervical swallowing sound and the respiratory cycle were recorded simultaneously. Analysis was performed using the Multipurpose Bioelectric Signal Analysis Program BIMUTAS®II (Kissei Comtec Co., Ltd.).

Forced vital capacity was measured before the study.

Statistical Analysis
All analyses were performed using SPSS 11.0J (SPSS Inc., Chicago, IL). The t-test was used to compare the two data sets. The individual mean respiratory cycle of four respiratory cycles was used for analysis.

Results

Profiles of the ALS patients, the MD patients, and the control subjects are shown in Table 1. Fig. 2 shows the results of the swallowing sounds and pneumography in a control subject, an ALS patient and a MD patients.

Table 1 Profiles of the ALS patients, the MD patients, and the control subjects

| ALS Case 1 | 57 | M | 53 | oral phase disturbance |
| ALS Case 2 | 59 | F | 46 | unremarkable |
| ALS Case 3 | 59 | M | 81 | unremarkable |
| ALS Case 4 | 59 | F | 88 | unremarkable |
| ALS Case 5 | 66 | M | 24 | penetration |
| ALS Case 6 | 68 | F | 130 | unremarkable |
| ALS Case 7 | 69 | M | 80 | aspiration |
| ALS Case 8 | 73 | M | 35 | aspiration |
| ALS Case 9 | 73 | F | 34 | aspiration |
| ALS Case 10 | 77 | M | NIV | penetration |
| MD Case 1 | 27 | M | 82 | poor lingual movement |
| MD Case 2 | 30 | M | 47 | poor lingual movement |
| MD Case 3 | 33 | M | 61 | nd |
| MD Case 4 | 44 | F | 43 | aspiration |
| MD Case 5 | 50 | M | 26 | sever aspiration |
| MD Case 6 | 54 | F | 74 | nd |
| MD Case 7 | 54 | F | 38 | poor lingual movement |
| MD Case 8 | 56 | M | 32 | poor lingual movement, residue on pharynx |
| MD Case 9 | 57 | M | 60 | nd |
| MD Case 10 | 60 | M | 52 | poor lingual movement, aspiration |

Control 1 | 52 | F | nd | normal |
Control 2 | 53 | F | nd | normal |
Control 3 | 53 | F | nd | normal |
Control 4 | 55 | F | nd | normal |
Control 5 | 56 | F | nd | normal |
Control 6 | 58 | F | nd | normal |
Control 7 | 66 | F | nd | normal |
Control 8 | 70 | M | nd | normal |
Control 9 | 75 | M | nd | normal |
Control 10 | 79 | M | nd | normal |

FVC: forced vital capacity, VF: videofluoroscopy, nd: not done

The respiratory cycle is expressed as mean ± standard deviation (minimal value-maximal value) for each group. In the ALS group, the respiratory cycle was 3.15 ± 0.76 sec (2.31-4.39 sec) at rest, while after swallowing, it was 2.78 ± 0.83 sec (1.77-4.80 sec) (p = 0.1). In the MD group, the respiratory cycle was 2.56 ± 0.46 sec (1.91-3.67 sec) at rest, while after swallowing, it was 2.94 ± 0.60 sec (2.03-4.29 sec). In the control group, it was 3.46 ± 0.57 sec (3.18-4.34 sec) at rest and 3.24 ± 0.50 sec (2.64-4.04 sec) after swallowing (Fig. 3).

The apnea/hypopnea during water swallow was 14.33 ± 8.89 sec (2.50-30.68 sec) in the ALS group, 3.66 ± 1.58 sec (1.78-6.42 sec) in the MD group, and 3.64 ± 1.00 sec (2.34-5.56 sec) in the control group. The apnea/hypopnea duration in the ALS was significantly longer than that in MD and in control (p = 0.005, p = 0.004 by the t-test) (Fig. 4).

Some of the ALS and the MD patients with exhibiting inspiratory failure show the tendency of the extended apnea/hypopnea (Fig. 5). There was no significant relationship be-
Fig. 2  The results of the swallowing sound and pneumography in an ALS patient, in a MD patient and in a control subject.

Fig. 3  The respiratory cycle before and after water swallowing (Aws) in ALS, MD and control. In the ALS group, the respiratory cycle was decreased after swallowing (p = 0.1).

Fig. 4  The apnea/hypopnea (A/H) duration in the ALS was significantly longer than that in MD groups and in the control group (p = 0.005, p = 0.004 by the t-test).

between apnea/hypopnea and respiratory cycle after water swallow (Fig. 6).

Results of videofluoroscopy, which was done within 2 weeks, showed longer apnea/hypopnea times in ALS patients who had aspiration than in those without aspiration (p = 0.5) (Fig. 7).

Discussion

In this study, we evaluated apnea/hypopnea during water swallowing in patients with ALS, in patients with MD, and in control subjects; prolonged apnea/hypopnea was observed in ALS patients. In Hiest’s study, the respiratory cycle after swallowing was decreased in healthy elderly subjects in an upright position1. In our study, we found the trend of the reduction of post swallow respiratory cycle in ALS (p = 0.1), but could not find any significant change of respiratory cycle before and after water swallow in MD and control. Preiksatis compared one respiratory cycle immediately before swallow and one immediately after swallow, and showed the respiratory cycle in post swallow was slightly longer than that in pre swallow in younger subjects2,3. In supine position, Nishino4 found that the respiratory cycle did not change af-
Fig. 5  Relationship between apnea/hypopnea (A/H) duration and % forced vital capacity (%FVC) in ALS and MD patients. The apnea/hypopnea (A/H) duration was extended in some of the patients exhibiting respiratory failure.

Fig. 6  Apnea/hypopnea (A/H) & respiratory cycle after water swallow (Asw) in ALS & MD.

ter water swallow in comparison with that before swallow in normal subjects. The differences and disagreements described in post swallow respiratory cycle durations may be due to methodological factors such as volume of water, position, analysis duration of respiratory cycle.

We showed extremely prolonged apnea/hypopnea in ALS patients during water swallowing. Three mechanisms for apnea/hypopnea prolongation during water swallowing in the ALS patients were considered:

1) Respiration was depressed by aspiration or penetration during the swallow. Results of videofluoroscopy, which was done within 2 weeks, showed longer apnea/hypopnea times in ALS patients who had aspiration than those without aspiration (p = 0.5). But there was no significant difference in apnea/hypopnea times in MD patients with or without aspiration (Fig. 7).

2) Respiratory movement was reduced because of swallowing disturbance: Dysphagia has been reported to aggravate respiratory insufficiency, because the respiratory muscles are mobilized during swallowing. That could be a reason that apnea/hypopnea elongation occurs during water swallow with severe respiratory failure. Some of the ALS patients and the MD patients who had severely affected respiratory function (lower % FVC) showed longer apnea/hypopnea in our study.

3) Prolongation of oropharyngeal transit. Oropharyngeal transit time is longer in ALS patients than in MD patients with the same degree of respiratory function (personal study). Long oropharyngeal transit time could lead long respiratory suppression.

Hadjikoutis reported that the inhalation phase was likely to occur after swallowing in patients with motor neuron diseases. It has also been reported that prolonged apnea readily induced inhalation after swallowing. In another study, a high risk of aspiration during inhalation immediately after swallowing has been reported. We speculate that prolonged apnea after water swallowing, which leads to inhalation, also increases the risk of aspiration or silent aspiration. In other words, patients who have prolonged apnea are at greater risk of aspiration than those who do not.

This study had some limitations. First, because a thermistor was usually used to measure sleep apnea, the temporal changes from exhalation to inhalation and apnea/hypopnea
were slightly unclear. This limitation precluded evaluation of the occurrence rate of inhalation soon after swallowing. Second, only water was used to test swallowing. The pattern of breathing after a swallow assessed by a water bolus may not be the same as with a chew and swallow, such as semisolid or solid food. Respiratory cycles during and after swallowing have been reported to be irregular depending on the amount of swallowed water or food in the elderly and in patients with chronic obstructive respiratory insufficiency. Another limitation is that we did not evaluate pneumography and videofluoroscopy simultaneously during water swallowing. However, aspiration does not occur in each swallow. If aspiration induces elongation of apnea/hypopnea, averaged apnea/hypopnea in four swallow times should show the relationship to aspiration.

Conclusion

Prolonged apnea/hypopnea times were observed during water swallowing in ALS patients. We speculate that this prolongation is caused by severe swallowing disturbance and respiratory failure, which increases the risk of aspiration. The respiration of ALS patients should be closely monitored during eating.

References

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