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ORIGINAL ARTICLE

Coordination between respiration and swallowing during non-invasive positive pressure ventilation

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ABSTRACT

Background and objective: **The purpose of this study was to test the hypothesis that the risk of silent aspiration is increased in non-invasive positive pressure ventilation.**
Methods: **We analysed the coordination between respiration and swallowing, in 12 young volunteers and 10 elder volunteers, by simultaneously monitoring respiratory flow, laryngeal movement and swallowing sound in three different conditions: control, continuous positive airway pressure (CPAP), and bi-level positive airway pressure (BiPAP). A step-wise multiple regression analysis was performed with the occurrence rate of inspiration after swallows as the dependent variable and various correlated variables as the independent variables.**
Results: **In both subject groups, the occurrence rate of inspiration after swallow was greater with BiPAP compared with control and CPAP conditions. Repetitive saliva swallowing test count and swallow non-inspiratory flow occurrence rate were extracted as predictor variables for risk of inspiration after swallows during BiPAP treatment.**
Conclusion: **We found that the occurrence rate of inspiration after swallow is increased with BiPAP use irrespective of age. The results suggest that swallow non-inspiratory flow may trigger inspiratory support in the BiPAP mode, resulting in a risk of aspiration.**

Key words: non-invasive positive pressure ventilation, respiration, swallowing.

Abbreviations: BiPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; EPAP, expiratory positive airway pressure; RSST, repetitive saliva swallowing test; SNIF, swallow non-inspiratory flow; SW-I, inspiration after swallow.

SUMMARY AT A GLANCE

We evaluated the coordination between respiration and swallowing during non-invasive artificial ventilation in healthy subjects and found that the occurrence rate of inspiration after swallowing is increased while using BiPAP. The results suggest that SNIF may trigger inspiratory support during BiPAP treatment, increasing the risk of aspiration.

INTRODUCTION

Pneumonia is the third commonest cause of death in Japan, and most of the deaths are due to aspiration pneumonia. The coordination between respiration and swallowing is an important airway defensive mechanism for preventing aspiration.[1–3] In healthy subjects, expiration occurs after swallowing, which prevents aspiration. However, in patients with chronic respiratory failure, this coordination is impaired, which predisposes them to chronic aspiration.[4,5] The respiratory management in chronic respiratory failure patients should include the prevention of aspiration; however, little is known about swallowing function during artificial ventilation.

Recently, non-invasive artificial ventilation has become the preferred treatment in the management of acute phase respiratory failure.[6–8] The swallowing function during non-invasive artificial ventilation is thought to be relatively well preserved as compared with that during invasive (intubated) artificial ventilation; however, this has not been systematically studied yet. In the present study, we hypothesized that the risk of silent aspiration is increased with non-invasive positive pressure ventilation and tested the hypothesis by analysing the coordination between respiration and swallowing by simultaneously monitoring respiratory flow, laryngeal movement and swallowing sound.

METHODS

Study participants

Twelve healthy young volunteers (8 males and 4 females, 28.0 ± 11.5 years old) and 10 healthy elder volunteers (4 males and 6 females, 73.9 ± 5.8 years old) were enrolled in the study. They did not have a past history of aspiration pneumonia, cerebrovascular diseases or respiratory failure, and they were able to

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swallow more than three times per 30 s by repetitive saliva swallowing test (RSST). All participants gave written consent after they were informed about the purpose and methods of the study. They were also informed that they could leave the study at any time without any loss of benefit. The protocol of the study was approved by the Ethics Committee of Hyogo College of Medicine (No. 1579).

Measurements

We monitored respiratory flow using a flow sensor cannula (Pro-Tech ProFlow cannula, Sleep Lab Products, Sterling Heights, MI, USA) and a differential pressure transmitter (KL-17, Nagano Keiki Co., Tokyo, Japan). Laryngeal motion and swallowing sound were simultaneously recorded using a custom-made piezo-electric pressure sensor placed on the skin surface around the thyroid cartilage. We verified that the piezo-electric sensor was able to pick up high-frequency peaks characteristic of swallowing sounds, even more clearly than the widely used laryngeal microphone. The sensor output was band-pass filtered to differentiate between laryngeal motion signal and sound signal. The analysis was made using MATLAB software (R2008b, Mathworks, Natick, MA, USA) on a Windows 8.1 computer. Swallows were detected by the laryngeal motion and the absence of respiratory flow (deglutition apnea, >400 ms). The sensitivity and specificity of the detection algorithm for experimental data that included 27 swallowing events and 60 non-swallowing behaviours (e.g. snoring, coughing, deep breathing and vocalization) were 100% and 86.36%, respectively.[9] In addition, we confirmed that each detected swallow-candidate period included an apneic episode within which a high frequency (>750 Hz) sound was audible; these are characteristics of swallowing activity.[10]

Continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP) ventilations were applied using a non-invasive artificial ventilator (V60, Philips Respironics, Murrysville, PA, USA). During non-invasive artificial ventilation, the airway pressure was monitored using an analogue output from the V60 ventilator and recorded at 10 kHz.

Protocols

The subjects underwent five series of repetitive saliva swallowing trials in three different conditions: control, CPAP (4 cmH2O) and BiPAP (respiratory rate 10 times per minute, IPAP 8 cmH2O and EPAP 4 cmH2O) conditions. The subjects were in the supine position with their head tilted upwards at 30°, and they wore a full-face mask during artificial ventilation. One series of repetitive saliva swallowing trials consists of three saliva swallows (one swallow per 10 s); the subjects underwent five trials, resulting in 15 swallows in total.

For RSST, subjects were instructed to swallow saliva as many times as possible within 30 s in the supine position with their head tilted upwards at 30°. The onset of each swallow was judged based on palpation of the laryngeal prominence by the examiner's finger, and the number of elevations of the laryngeal prominence was counted.[11] RSST is used as a screening test for dysphagia. An RSST count of less than three times in 30 s suggests suspected dysphagia, and the sensitivity and specificity of RSST to predict aspiration in video-fluoro-graphic examination are reported to be 0.98 and 0.66, respectively.[12]

The occurrence rate of swallow non-inspiratory flow (SNIF) during non-invasive ventilation was also measured. SNIF was previously defined as a slight inspiratory flow that occurs after deglutition apnea.[13] We first identified a respiratory pause associated with swallowing and subsequently detected SNIF using a custom-made analysis software. To estimate occurrence of SNIF during BiPAP, we counted both solitary SNIFs (Fig. 1a) and SNIFs that accompanied asynchronous inspiratory supports (Fig. 1b).

Respiratory phases after swallows were classified into three phases: inspiration, expiration and pause. Each occurrence frequency was expressed as a percentage of the total number of swallows.

In addition, we compared the phase in the respiratory cycle for initiating a swallow during CPAP and BiPAP. The phase in the respiratory cycle for initiating a swallow was represented by a timing from the onset of the preceding inspiration, normalized by the average duration of a single breath.

Statistical analysis

Occurrence rates of SNIF during control breathing, CPAP and BiPAP were compared using the Friedman test. Similarly, occurrence frequencies of each respiratory phase after swallow in these conditions were compared in young and elder subject groups using the Friedman test and *post hoc* multiple comparisons with Bonferroni's adjustment. Correlations between the occurrence rate of inspiration after swallow (SW-I) and RSST count, SNIF occurrence rate and age were evaluated by Spearman's rank correlation coefficient. Subsequently, step-wise multiple regression analysis was performed with the occurrence rate of SW-I as the dependent variable and various correlated variables as the independent variables. Phases in the respiratory cycle for initiating a swallow during CPAP and BiPAP were compared using the unpaired t-test. All data are presented as mean ± standard deviation. P values were two-sided, and $P < 0.05$ was considered as statistically significant. Statistical analyses were performed using IBM SPSS Statistics (version 22; IBM Corporation, Armonk, NY, USA).

RESULTS

SNIF waveforms during BiPAP

Representative flow and pressure signals of SNIF during BiPAP are shown in Figure 1. When SNIF did not trigger an inspiratory support, a small inward flow on the flow signal and a small negative-to-positive pressure swing on the pressure signal were observed (Fig. 1a). The small negative-to-positive pressure swing was conceivably due to expiratory positive airway pressure (EPAP) level control in response to SNIF. When SNIF triggered an inspiratory support, SNIF was still

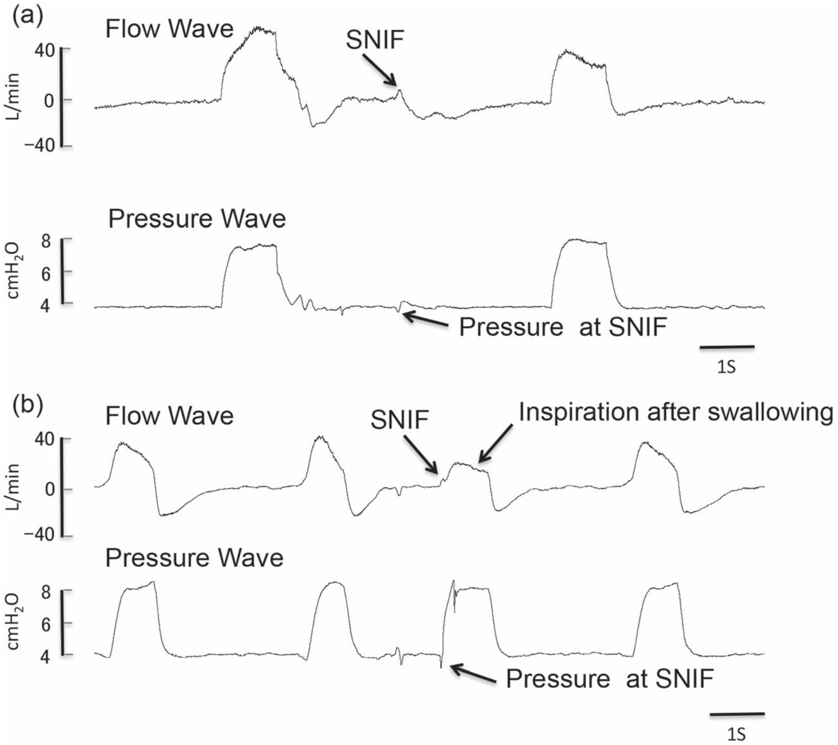


Figure 1 Swallow non-inspiratory flow (SNIF) waveforms during bi-level positive airway pressure (BiPAP). In both (a) and (b), the upper panel shows the flow signal and the lower panel shows the pressure signal. (a) A representative case in which SNIF did not trigger an inspiratory support. A standard SNIF waveform during BiPAP is characterized by a small inward flow on the flow signal and a small negative-to-positive pressure swing on the pressure signal associated with EPAP level control in response to SNIF. (b) A representative case in which SNIF triggered an inspiratory support. SNIF is observed as a negative pressure (0.4–0.8 cmH2O) on the pressure signal. Note a notch on the rising phase of the inspiratory flow signal and an overshoot of the inspiratory pressure, which indicates an asynchronous breathing different from a natural pressure-supported breathing.

observed as a negative pressure (0.4–0.8 cmH2O) on the pressure signal (Fig. 1b). An inspiratory flow triggered by SNIF is characterized by a notch on the rising phase of the inspiratory flow signal and an overshoot of the inspiratory pressure, which indicates an asynchronous breathing different from a natural pressure-supported breathing.

Comparison of SNIF during control, CPAP and BiPAP breathing

SNIF was observed during control breathing, CPAP and BiPAP in 68.3 ± 36.6%, 91.6 ± 8.1% and 86.7 ± 10.2%. There was no statistical difference between occurrence rates of SNIF (Friedman test, $P = 0.134$). Furthermore, there was no statistical difference between phases in the respiratory cycle for initiating a swallow during CPAP and BiPAP (CPAP 0.71 ± 0.28 and BiPAP 0.73 ± 0.26). Phases in the respiratory cycle for initiating a swallow were normally distributed (data not shown); thus, swallows most frequently occur at the mid-expiratory phase.

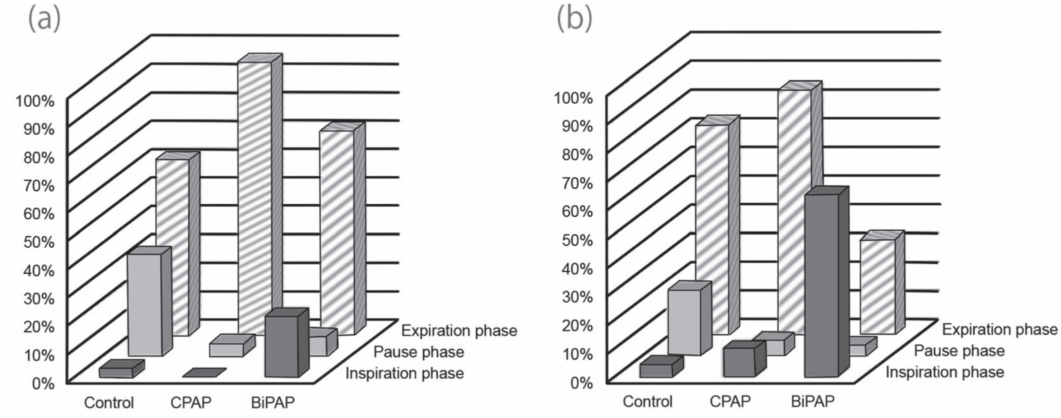
SW-I, RSST counts, SNIF rate and age

In both subject groups, the occurrence rate of SW-I was greater with BiPAP compared with control and CPAP conditions (Fig. 2). The occurrence rate of SW-I in BiPAP condition was significantly correlated with RSST count ($\rho = 0.490$), SNIF occurrence rate ($\rho = 0.626$) and age ($\rho = -0.557$), respectively (Table 1, Fig. 3a,b,c). There was a negative correlation between age and RSST count ($\rho = -0.631$) (Fig. 3d). The occurrence rate of expiration after swallow with BiPAP was correlated significantly with SNIF occurrence rate ($\rho = -0.624$) and age ($\rho = 0.558$), respectively (Fig. 4). Step-wise multiple regression analysis was performed with the occurrence rate of SW-I as the dependent variable and RSST count, SNIF occurrence rate and age as independent variables. As the result, RSST count and SNIF occurrence rate were extracted as predictor variables ($R = 0.815$, $R^2 = 0.664$, adjusted $R^2 = 0.628$, $P < 0.05$; Table 2).

DISCUSSION

In the present study, we investigated the coordination of respiration and swallowing during non-invasive ventilation. We found that the occurrence rate of SW-I is increased during BiPAP irrespective of age. We also identified that RSST count and SNIF occurrence rate predict the rate of SW-I. Expiration after swallow is increased with CPAP treatment irrespective of age.

Generally speaking, swallows most frequently occur during expiration, and after swallows, respiration is reinitiated with expiration. However, the occurrence rate of SW-I increases with age.[14] Kijima *et al.* found that respiratory loading in healthy subjects increased the respiratory frequency and disrupted the coordination of swallowing and the phases of respiration.[15] When respiration is reinitiated with inspiration, it predisposes aspiration of food residue around the laryngeal orifice, and thus, the SW-I pattern may increase the risk of aspiration. The SW-I pattern is also increased in patients with chronic obstructive pulmonary disease (COPD), which may be one of mechanisms causing exacerbation.[16–18] An inspiratory event may predispose subjects to penetration or aspiration of the passing bolus tail.[2]



(a)

	Control	CPAP	BiPAP
Inspiration phase	3.0%**	0.0%**	21.5%
Pause phase	35.6%	4.4%	6.6%
Expiration phase	61.4%	95.6%*	71.9%

*: P<0.05, **: P<0.01

(b)

	Control	CPAP	BiPAP
Inspiration phase	4.3%**	9.8%**	63.6%
Pause phase	22.8%*	5.2%	3.5%
Expiration phase	72.9%**	84.9%**	32.9%

*: P<0.05, **: P<0.01

Figure 2 Phase of respiration after swallowing in three different conditions. (a) Elderly volunteers and (b) young volunteers.

Table 1 Correlation among age, RSST count, occurrence rate of SNIF and occurrence rate of specific respiratory phases after swallowing (n = 22)

	Age	RSST	%SNIF	Inspiration	Expiration
Age	1.000				
RSST	−0.631**	1.000			
%SNIF	−0.347	0.016	1.000		
Inspiration	−0.557**	0.490*	0.626**	1.000	
Expiration	0.558**	−0.394	−0.624*	-0.947**	1.000

*$P < 0.05$. **$P < 0.01$ by Spearman's rank correlation coefficient.
RSST, repetitive saliva swallowing test; SNIF, swallow non-inspiratory flow; %SNIF, SNIF occurrence rate.

Non-invasive ventilation is the preferred treatment for respiratory failure in acute exacerbation of chronic obstructive pulmonary disease, in part because the risk of ventilator-associated pneumonia is less compared to intubated artificial ventilation.[19–21] However, we infer that the risk of silent aspiration during sleep due to saliva aspiration is increased with BiPAP, because the occurrence rate of SW-I is increased. Because the occurrence rate of expiration after swallow is increased in CPAP mode, it could be considered to switch to CPAP or nasal high flow from BiPAP at the earliest timing of treatment of an acute exacerbation. It has been suggested that nasal CPAP has an influence on the deglutition function during sleep and levator veli palatini muscle activity.[22,23] However, as nasal CPAP suppresses the swallowing reflex in proportion to the applied positive pressure,[24,25] care must be taken to determine an optimal pressure setting.

In the present study, the SW-I rate was correlated with SNIF, implying that the SW-I is caused by inspiratory pressure support triggered by SNIF. However, the most comfortable phase in the respiratory cycle for initiating a swallow might be the end expiration where the intraoral pressure is the lowest; then SW-I could be a natural consequence of trying to swallow while on BiPAP rather than being a result of inappropriate triggering by SNIF. However, when evaluating the phase in the respiratory cycle to initiate swallowing with CPAP and BiPAP, we found that swallows most frequently occur at the mid-expiratory phase with both treatments. Because there was no statistical difference in occurrence frequency of SNIF during CPAP and BiPAP and the occurrence rate of SW-I was greater during BiPAP, it suggests that inspirations after swallow during BiPAP were at least partially triggered by SNIF. In addition, we found that SNIF accompanies an asynchronous flow pattern (a notch on the rising phase of the inspiratory flow signal), further supporting the case that SNIF can trigger an inappropriate inspiratory support.

The SW-I rate was also positively correlated with RSST count. No previous study documenting such correlation, and we do not know the precise physiological mechanisms involved. RSST count of less than three

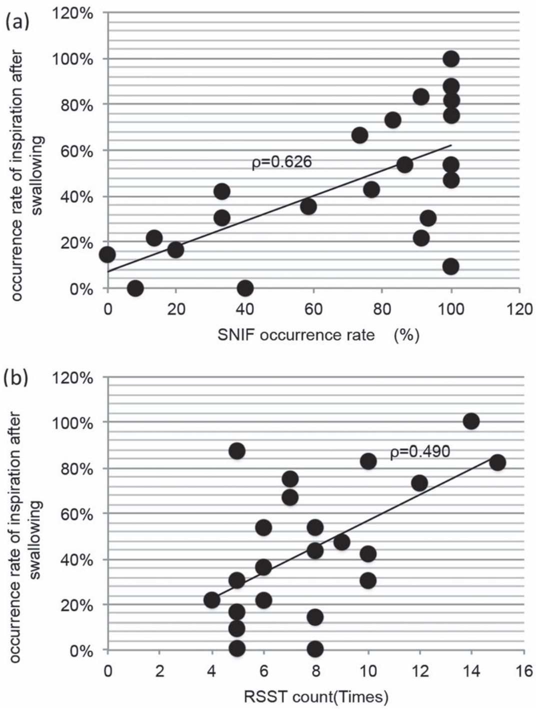


Figure 3 Correlations between the occurrence rate of inspiration after swallowing during bi-level positive airway pressure (BiPAP) and repetitive saliva swallowing test (RSST). (a) count, (b) swallowing non-inspiratory flow (SNIF) occurrence rate and (c) age. The occurrence rate of inspiration after swallow in BiPAP condition was significantly correlated with repetitive saliva swallowing test (RSST) count ($P < 0.05$, $\rho = 0.490$), SNIF occurrence rate ($P < 0.01$, $\rho = 0.626$) and age ($P < 0.01$, $\rho = -0.557$), respectively. (d) Correlations between age and RSST count. RSST count was significantly correlated with age ($P < 0.001$, $\rho = -0.631$).

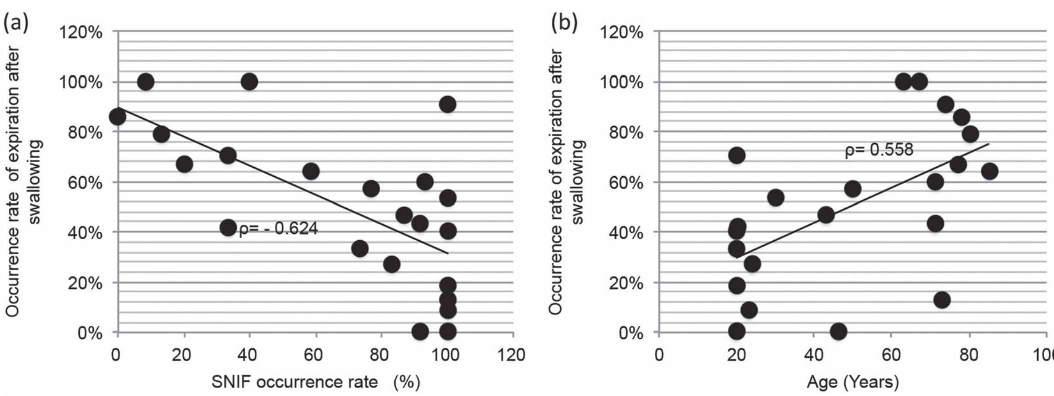


Figure 4 Correlations between the occurrence rate of expiration after swallowing during bi-level positive airway pressure (BiPAP) and swallowing non-inspiratory flow (SNIF). (a) occurrence rate and (b) age. The occurrence rate of expiration after swallow in BiPAP condition was significantly correlated with SNIF occurrence rate ($P < 0.05$, $\rho = -0.624$) and age ($P < 0.01$, $\rho = 0.558$), respectively.

Table 2 Factors that affect inspiration after swallowing during BiPAP

	R	Multiple *R*-squared	Adjusted *R*-squared	Partial regression coefficient	Standard error	*P*-value
	0.815	0.664	0.628			
Constant				−0.274	0.128	0.045
%SNIF				0.005	0.001	0.000
RSST				0.049	0.013	0.002

BiPAP, bi-level positive airway pressure; RSST, repetitive saliva swallowing test count; %SNIF, swallow non-inspiratory flow occurrence rate times in 30 s suggests suspected dysphagia.[12] Therefore, the positive correlation implies that the inspiratory event is likely to occur when the swallowing function is normal. We infer that pharyngeal constriction associated with swallowing is strong in healthy subjects, and consequently, the negative pressure generated upon the release of pharyngeal constriction is also strong and thus might cause SNIF and SW-I patterns. Therefore, the SW-I rate may increase with the improvement of swallowing function. This may be explained as follows: as the swallowing function improves, the strength of pharyngeal muscle contraction increases, and more negative pressure is generated when muscles are relaxed; and SNIF is exaggerated, and eventually, the chance for SNIF to trigger the inspiratory support increases. From these considerations, when the ventilatory condition and swallowing function improve, we recommend that the patient is weaned from the non-invasive ventilator.

This study was conducted in healthy volunteers in stable condition. The occurrence rates of SNIF and SW-I needs to be validated in patients with chronic respiratory failure during non-invasive positive pressure ventilation and BiPAP. Further studies are necessary to elucidate the coordination between respiration and swallowing during non-invasive artificial ventilation in patients with chronic respiratory failure.

In summary, the results of our study on the coordination between respiration and swallowing during non-invasive artificial ventilation in healthy volunteers suggest that SNIF may trigger inspiratory support in BiPAP mode, increasing the risk of aspiration. Care should be taken to observe the swallowing function during BiPAP ventilation.

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