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RESEARCH PROTOCOL

Effects of nasal continuous positive airway pressure compared with high flow nasal cannula on the coordination between swallowing and breathing in post-extubation patients, a randomized crossover study

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ABSTRACT:

Background: Coordination between swallowing and breathing is essential to prevent aspiration. Swallowing during expiration (E-E swallow) is considered the most protective pattern [1,2]. High-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP) may promote this pattern by increasing the proportion of E-E swallows [3-5], but their comparative effects in post-extubation patients remain unclear.

Objectives: To compare the effects of nasal CPAP and HFNC on swallowing-breathing coordination patterns in post-extubation patients and to identify factors influencing this coordination.

Methods: This randomized, controlled, crossover trial includes patients who received invasive mechanical ventilation for ≥ 48 hours and were extubated within 48 hours prior to enrollment. Patients with dysphagia (modified water swallowing test score < 4) were excluded. Eligible patients are randomly assigned to Group A (CPAP → HFNC) or Group B (HFNC → CPAP). Each intervention is applied for 5 minutes, followed by three continuous water swallowing tests. Swallowing and respiratory phases are recorded using surface EMG and ECG-derived respiration. A 5-minute washout with low-flow nasal oxygen is provided between interventions. Swallowing–breathing coordination is classified into four patterns: E–E, I–E, E–I, and I–I. The primary outcome is the percentage of E-E swallows. Secondary outcomes include other patterns, swallowing frequency, expiratory time, and respiratory rate. All outcomes are analyzed using linear mixed-effects models.

Hypothesis: CPAP and HFNC may differ in their effects on swallowing–breathing coordination, particularly in promoting the E–E pattern.

Conclusions: This study explores how nasal CPAP and HFNC affect swallowing–breathing coordination and their potential impact on airway protection after extubation.

Ethics and dissemination: Approved by the IRB, Faculty of Medicine, Chulalongkorn University. Results will be disseminated via peer-reviewed journals and conferences.

Trial registration: TCTR20210607003

Keywords: Continuous positive airway pressure; High flow nasal cannula; Coordination of breathing and swallowing; Post-extubation

INTRODUCTION

The coordination between swallowing and breathing is crucial for airway protection and preventing aspiration. This coordination can be categorized into four patterns depending on the respiratory phase occurring before and after swallowing. The most protective and predominant pattern is the exhale-swallow-exhale (E–E swallow) pattern, where swallowing is initiated during expiration and followed by expiration after the swallow. Other patterns include inhale-swallow-exhale (I–E swallow), exhale-swallow-inhale (E–I swallow), and inhale-swallow-inhale (I–I swallow). The resumption of respiration with expiration is seen as a mechanism to safeguard the airway by preventing inhalation of any residual material in the pharynx after swallowing [1,2].

Post-extubation dysphagia is characterized by impaired or unsafe swallowing of solids or liquids following endotracheal tube removal. It increases the risk of aspiration and is associated with adverse outcomes, including pneumonia, extended antibiotic use, reintubation, tracheostomy, longer ICU and hospital stays, and elevated mortality [6,7]. Therefore, understanding factors that influence swallowing-respiration coordination in this population is clinically important.

Previous studies have investigated the effects of noninvasive respiratory support on this interaction. CPAP has been shown to increase the rate of post-swallow expiration and reduce post-swallow inspiration in both healthy individuals and patients with COPD, potentially enhancing airway protection [3,4]. In contrast, BiPAP has been associated with increased post-swallow inspiration, which may elevate aspiration risk. While HFNC has not shown consistent effects in healthy volunteers [8], more recent evidence suggests that in post-extubation patients, HFNC may promote the E–E swallow pattern and improve coordination between swallowing and breathing compared to low-flow oxygen therapy [5].

Despite the widespread use of noninvasive ventilation and HFNC in post-extubation care to prevent respiratory failure and reintubation [9-12], their impact on swallowing-breathing patterns remains incompletely understood. In particular, no study has directly compared the effects of nasal CPAP and HFNC on this coordination during the post-extubation period.

To address this gap, we conducted a randomized, controlled crossover study to compare the effects of nasal CPAP and HFNC on swallowing-respiration coordination in recently extubated patients. By evaluating their impact on coordination patterns, this study aims to improve understanding of how different respiratory supports may influence airway protection mechanisms in the post-extubation setting.

OBJECTIVES

The primary objective is to compare the effects of nasal CPAP and HFNC on swallowing-breathing coordination patterns in post-extubation patients. The secondary objective is to identify factors influencing the coordination between swallowing and breathing in this population.

KEY MESSAGES:

- Swallowing–breathing coordination plays a critical role in airway protection, particularly in the post-extubation period
- This randomized crossover trial compares the effects of nasal CPAP and HFNC on swallowing–breathing patterns in post-extubation patients
- The study investigates how each modality may influence the proportion of protective exhale–swallow–exhale (E–E) swallows
- The findings may contribute to optimizing respiratory support strategies to reduce aspiration risk in this population

MATERIALS AND METHODS

Trial design and setting

This study is a single-center, randomized, controlled, 2 x 2 crossover trial conducted at the Medical General Ward and ICU of King Chulalongkorn Memorial Hospital in Thailand.

Eligibility criteria

Inclusion criteria consisted of patients aged 18–80 years who were admitted to either a medical intensive care unit or a medical inpatient department, had undergone endotracheal intubation for at least 48 hours, and had been extubated within 48 hours prior to study enrollment, demonstrating clinical stability (defined as body temperature 36.5-37.5°C, respiratory rate 12-24 breaths per minute, heart rate 50-120 beats per minute, systolic blood pressure 90-180 mmHg, and oxygen saturation (SpO_2) ≥ 95% with low flow nasal oxygen cannula at 1-5 L/min). Eligible patients will undergo a modified water swallowing test [13]; those with a score below 4 indicating dysphagia will be excluded. Exclusion criteria encompass patients with delirium or alteration of consciousness (Glasgow Coma Score < 15), contraindications to oral intake, a history of dysphagia, diseases predisposing to dysphagia such as cerebrovascular or neuromuscular disorders, a history of head and neck pathology including cancer, surgery, or anatomical abnormalities, as well as conditions potentially interfering with electromyogram signals such as skin disease, permanent pacemakers, or automatic implantable cardioverter defibrillators. Written informed consent will be obtained from all eligible patients prior to enrollment.

Equipment and techniques

The patients will be in the upright position during the experiment. Surface electrodes are attached to the skin at both sides of the suprahyoid muscles, sternocleidomastoid muscles, 2nd intercostal muscles, diaphragms, and rectus abdominis muscles for recording the electromyogram (EMG) signal of swallowing and respiration mus-

cles (Trigno Wireless EMG sensors and Trigno Wireless Foundation System, Delsys, USA). ECG-derived respiration is used to record a phase of respiration. CPAP 5 cmH_2O is applied using a noninvasive artificial ventilator (V60, Philips Respironics, Murrysville, PA, USA) with a nasal mask. High-flow oxygen is applied through a specific nasal cannula (Optiflow, Fisher & Paykel Healthcare, Auckland, New Zealand) with a flow of 50 L/min and a temperature of 34°C. The FiO_2 was adjusted to maintain SpO_2 at ≥ 95%.

Study protocol

Eligible patients are randomized into two groups: the nasal CPAP first group or the HFNC first group, using concealed allocation based on a computer-generated block randomization sequence (blocks of four). In the first period, either nasal CPAP or HFNC is applied for 5 minutes according to the group assignment. After that, while still on the assigned device, patients are instructed to perform three consecutive water swallowing tests, each involving the ingestion of 10 mL of water delivered via a syringe pump through an extension tube over 1 minute (infusion rate: 10 mL/min). Swallowing and respiratory muscle activity, as well as respiratory phases, are recorded using surface electromyography (EMG) and ECG-derived respiration. Vital signs, including blood pressure, heart rate, respiratory rate, and oxygen saturation, are continuously monitored. After completing the three swallowing tests, patients in both groups receive low-flow oxygen (1-5 L/min) via nasal cannula (LFNO) to maintain SpO_2 at ≥ 95% during a 5-minute washout phase. In the second period, HFNC and nasal CPAP are applied for 5 minutes in the nasal CPAP first group and the HFNC first group, respectively. The swallowing test is performed again three times (Figure 1).

Swallowing–breathing coordination was evaluated by identifying the respiratory phase immediately before and after each swallowing event. The respiratory phase was determined using ECG-derived respiration signals. The inspiratory phase was defined as the interval from the ascending slope to the peak of the waveform, while the expiratory phase was defined as the interval from the peak to the next ascending slope. Swallowing events were detected via submental surface electromyography (EMG). Based on the respiratory phase immediately before and after each swallow, the coordination pattern was classified into one of four types:

1. E–E swallow: exhale–swallow–exhale
2. I–I swallow: inhale–swallow–inhale
3. I–E swallow: inhale–swallow–exhale
4. E–I swallow: exhale–swallow–inhale

For each continuous water swallowing test, the total number of swallows, the frequency of each coordination pattern, and the respiratory rate (breaths per minute) were recorded and analyzed.

Due to the clearly distinguishable interfaces and characteristics of the two devices, neither patients nor investigators can be blinded to group assignment; however, the assessor who interpreted the outcomes and the data analyst remain blinded to treatment allocation.

During testing, if a patient shows signs of aspiration—such as persistent coughing, respiratory distress following swallowing, oxygen desaturation ≥2%, or unstable vital signs—the procedure is immediately discontinued and standard medical care is provided.

OUTCOME MEASUREMENT

The primary outcome was the average proportion of exhale–swallow–exhale (E-E) swallows, expressed as a percentage of total swallows. Secondary outcomes included the average proportions of other swallowing–breathing coordination patterns (I–E, E–I, and I–I swallows), swallowing frequency, expiratory time within 1 minute, and respiratory rate. All outcomes were averaged across the three swallowing tests performed for each device. Another secondary outcome is the identification of factors influencing swallowing-respiration coordination.

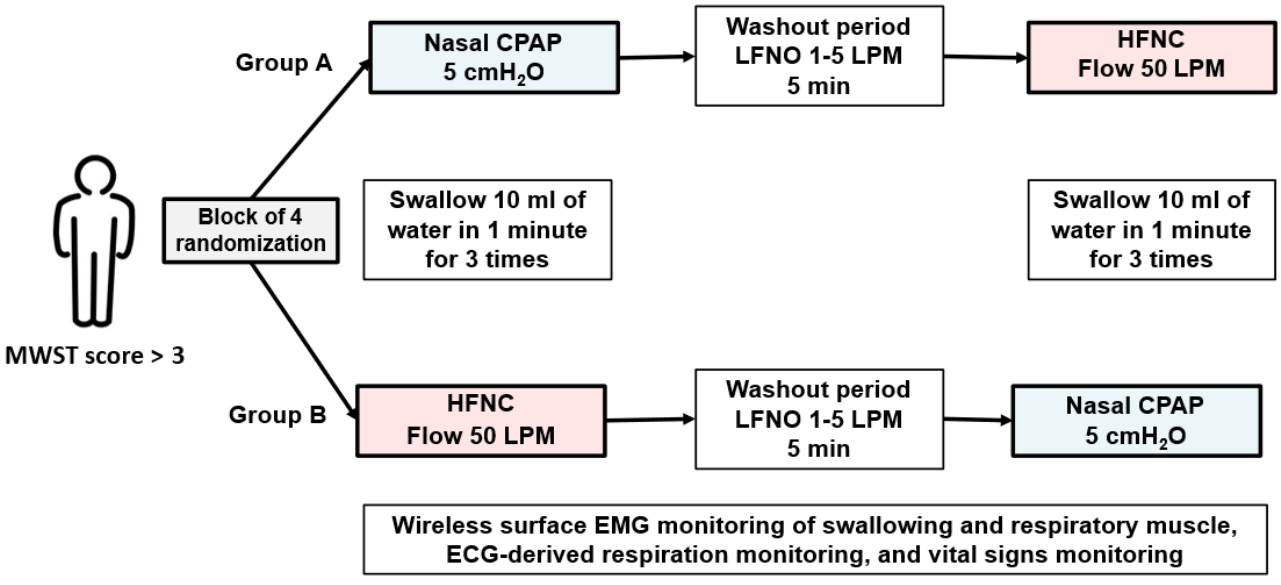

Figure 1. The study protocol.
Abbreviations: MWST: modified water swallowing test; EMG: electromyography; CPAP: continuous positive airway pressure; HFNC: high-flow nasal cannula; LFNO: low-flow nasal oxygen; ml: milliliters; min: minute; LPM: liters per minute.

DATA ANALYSIS PLAN

Sample size estimation

The formula for calculating sample size in a 2x2 crossover study comparing mean differences is as follows [12]:

$$n = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \sigma^2}{2\varepsilon^2}$$

Since it is not possible to obtain the values of the mean difference (ε) in the percentage of exhalation after swallowing between the two devices and the standard deviation (σ) from previous research, an effect size of 0.5 is estimated for this study, considered a moderate effect size. When this is used in the formula, 16 subjects will be needed for a type I error (α) of 0.05 and a power (β) of 0.8. Assuming a drop-out rate of 20%, the total sample size is 20 participants.

Statistical analysis

Continuous variables will be summarized as mean ± standard deviation (SD) or median [quartile 1, quartile 3], as appropriate, while categorical variables will be expressed as frequencies and percentages.

The primary outcome is the average percentage of E-E swallows. The secondary outcomes include the average percentages of other swallowing-breathing coordination patterns, swallowing frequency, expiratory time within 1 minute, and respiratory rate. All outcomes will be averaged across the three swallowing tests conducted per device. Outcomes will be analyzed using linear mixed-effects models (LMM) to identify significant differences between treatments. These models include treatment (nasal CPAP vs. HFNC), sequence (Group A: nasal CPAP followed by HFNC vs. Group B: HFNC followed by nasal CPAP), and period (first or second period) as fixed effects. Participant ID is included as a random effect to account for between-subject variability. A p-value < 0.05 is considered statistically significant. Potential carryover effects will be assessed by including sequence and period as fixed effects in the models, and their significance will be tested to validate the crossover design.

To further explore factors influencing swallowing–breathing coordination, multivariable linear mixed-effects models (LMMs) will be constructed by including additional covariates: age, BMI, APACHE II score, and duration of mechanical ventilation. Due to the small sample size, which limits the inclusion of multiple covariates in a single model, each covariate will be individually added to the base model in separate sensitivity analyses to evaluate its potential influence on the outcomes.

All statistical analyses will be conducted using IBM SPSS Statistics (Version 29.0, IBM Corp., Armonk, NY, USA).

DATA MANAGEMENT AND DATA MONITORING

Data collection

The baseline characteristic data recorded at the time of inclusion, such as age, sex, body mass index (BMI), underlying diseases, diagnosis upon admission, indication for intubation, duration of intubation, use of sedatives and/or neuromuscular blocking agents, and APACHE II score on the day of the study, as well as vital signs such as body temperature, blood pressure, heart rate, respiratory rate, and oxygen saturation, are collected by the investigators from patients' medical records. All data, including baseline characteristics and outcomes, will be recorded in the case record form.

Data management

The principal investigator is accountable for supervising the study data to maintain its authenticity, integrity, and confidentiality throughout the research process.

DISCUSSION

This study investigates the impact of nasal CPAP compared to HFNC on the coordination patterns of swallowing and breathing during the post-extubation period, with a particular focus on the exhale-swallow-exhale (E-E) pattern, a recognized airway protective mechanism. A previous study in post-extubation patients demonstrated a higher prevalence of the E-E swallow pattern with HFNC than with low-flow nasal oxygen, suggesting improved synchronization between swallowing and breathing [5]. While CPAP has been observed to increase expiration after swallowing in healthy adults [3] and COPD patients [4], its effect on swallowing–breathing coordination in post-extubation patients has not been previously investigated.

The physiological characteristics of CPAP and HFNC may contribute differently to their impact on coordination. CPAP delivers a constant positive airway pressure throughout the respiratory cycle, which may stabilize the pharyngeal airway but potentially interfere with dynamic neuromuscular processes involved in swallowing. In contrast, HFNC generates a fluctuating nasopharyngeal pressure that drops toward zero during inspiration, potentially allowing for more physiologic timing of the swallow reflex.

The strength of this study lies in being the first to directly compare nasal CPAP and HFNC in terms of their effects on swallowing–breathing coordination in post-extubation patients. Improvements in this coordination may reduce aspiration risk during this vulnerable period.

However, there are some limitations to this study. It included only medical patients without preexisting dysphagia and used continuous water infusion to assess coordination. Therefore, the findings may not be generalizable to individuals with dysphagia or other conditions affecting swallowing or those consuming food boluses. Blinding of participants and investigators was not feasible due to the distinct appearance and interface of the devices; however, outcome assessors and data analysts were blinded to group allocation. Although swallowing–breathing coordination is a critical component of airway protection and may influence aspiration risk, future studies should evaluate these interventions in broader populations, including patients with dysphagia, and assess clinically meaningful outcomes such as aspiration events, reintubation rates, and pneumonia. Moreover, studies with larger sample sizes are needed to validate these findings and further explore factors influencing the observed effects.

CONCLUSION

This study aims to provide additional insight into the effects of nasal CPAP and HFNC on swallowing–breathing coordination. The findings may help improve understanding of how different forms of respiratory support influence airway protection mechanisms in the post-extubation setting.

ETHICS

The study protocol was devised by the investigators and received approval from the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (COA No. 235/64). Additionally, it has been registered on www.thaiclinicaltrials.org (TCTR20210607003).

CONFIDENTIALITY

All data will be recorded in case record form using a code number as the patient's identification. Names, hospital numbers, or any other data that can identify the patients will not be recorded in the form or disclosed.

DISSEMINATION POLICY

The findings of this study will be disseminated through presentations at national or international conferences and submitted for publication in peer-reviewed journals.

ACKNOWLEDGEMENT

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SUPPLEMENTARY MATERIALS

None

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