Study Title: The Impact of High-flow Nasal Cannula on Swallow Function

Principal Investigator:

J. Brady Scott, MSc, RRT, RRT-ACCS, AE-C, FAARC, FCCP

Director of Clinical Education and Assistant Professor

Rush University, Department of Respiratory Care

Co-Investigator(s):

Lisa LaGorio, PhD, MPH, CCC-SLP

Assistant Professor

Rush University, Department of Communication Disorders and Sciences

Jie Li, MS, RRT-NPS-ACCS

Clinical Education Coordinator and Assistant Professor

Rush University, Department of Respiratory Care

Hibbah Alshuwaikhat

Respiratory Care Student

Rush University, College of Health Sciences

3/8/2018

Specific Aims

The primary aim of this research is to determine the impact of different flow rates of a high-flow nasal cannula on spontaneous swallowing frequency at rest and swallowing effort and timing while swallowing.

Introduction

High-flow nasal cannula (HFNC) is a non-invasive heated and humidified oxygen delivery device that is capable of delivering up to 60 L/min of flow.[1] It is a relatively new modality that has been introduced as an alternative to conventional oxygen therapy in patients with chronic obstructive pulmonary disease (COPD)[2,3], respiratory failure[4,5], obstructive sleep apnea (OSA)[6], post-extubation[7-10], and status asthmaticus.[11] The humidified gas preserves mucociliary function that prevents secretion retention and enhances patient's comfort. This feature allows prolonged use of HFNC in clinical sittings of up to 30 days.[12]

In addition to its ability to provide adequate humidification levels, HFNC has various respiratory physiological effects. These physiological effects include: alveolar recruitment, dead space washout, and decreased airway resistance.[12] The clinical value of the use of HFNC is not limited to its ventilation and oxygenation effects, it enables the patient to talk and is purported to permit oral feeding during oxygen therapy.[13]

Currently, despite the fact that patients are often permitted to eat while receiving HFNC therapy, there is insufficient evidence regarding the impact of HFNC on swallow function. The uncertainty of the effect of this oxygen delivery device on swallow function arises not only from the limited number of studies, but also the contradictory results. For example, Sanuki et al. reported that increasing the flow rates of the HFNC resulted in enhanced swallow function by reducing reflex latency.[14] Based on their findings, the researchers suggested that the use of HFNC should not affect the decision to start or resume feeding. Similarly, Lader et al. proposed that the use of high-flow nasal cannula should not delay oral alimentation.[15] On the contrary, Ferrara et al. conducted a study in neonates and concluded that providing feeding while using Nasal Continuous Positive Airway Pressure (nCPAP) increased the risk of aspiration.[16] These opposing outcomes support the need for further studies to obtain more definitive evidence.

Spontaneous Swallowing Frequency:

Spontaneous swallowing is an airway protection reflex and the measurement of its frequency is considered to be a sensitive indicator of swallow function. This index can sensitively identify dysphagia and other swallowing-related disorders. Furthermore, the reduction in this index is associated with increased level of secretions and chest infections.[17] One modality used to measure swallowing frequency is surface electromyography (sEMG), which records electric activity during swallow via an electrode placed on the skin under the chin. This non-invasive technology has been used for more than 20 years to record various aspects of swallowing physiology.[18,19] In this study, sEMG will be used because of its feasibility, accuracy, and ability to detect a swallow.

Swallowing Effort and Timing:

Swallowing effort via submental sEMG provides an objective measurement of lingual and sub-mental muscle activity during the act of swallowing. Measurements include muscle contraction amplitude and contraction timing/speed. Clinically, swallowing effort parameters have been used to document normative values in healthy individuals,[20] as well as to document the effects of a disease on swallowing.[21] Prior research has shown that both amplitude and timing are influenced by multiple factors including the volume and viscosity of the item (or bolus) being swallowed,[22,23] and the age and gender of the person swallowing.[24,25] However no study has investigated the effects of HFNC on either swallowing effort parameter.

Experimental Design and methods

This is a prospective study designed to measure swallowing frequency and swallowing effort in fifty healthy adult volunteers (25 participants will be between 21 and 49 years old; and the other 25 above 50 years old). To recruit volunteer participants, an email will be sent via university internal email system to the faculty, students and employees in the departments of Respiratory Care and Speech Language Pathology. Snowball sampling (non-probability sampling) will also be utilized to recruit individuals outside of those departments. No compensation is offered to the participants. Enrolled participants are sub-categorized into two different age groups to

determine if there are any swallowing differences between the different age groups. Inclusion criteria include individuals who are older than 21 years of age and have no cognitive impairment. Exclusion criteria include individuals who are less than 21 years of age, have a history of dysphagia or disease/condition that may cause dysphagia, current use of medications that alter swallowing function, nasal obstruction, and the presence of a tracheostomy tube.

Upon meeting inclusion criteria, informed consent explaining the procedure and potential harm will be obtained and a copy will be given to the subject. Then, a unique identification code number will be assigned to protect the subject's identity.

HFNC:

The AIRVO 2 high-flow nasal cannula system (Fisher and Paykel Healthcare Limited, Panmure, Auckland, New Zealand) will be used. Nasal prongs sizes are chosen as per manufacturer recommendations. Participants will receive three levels of HFNC flow rates (30, 45, and 60 L/min) through nasal prongs. If a small-size nasal prong is used, the participant will receive 30, 45, and 50 L/min flow rates instead of 30, 45, and 60 L/min, as manufacturer recommendations state the maximum liter flow for a small-size nasal prong is 50 L/min. Oxygen concentration will be set at 21% and a temperature of 37 °C. First, individuals will be placed on the sEMG monitor. Following the application of the sEMG, each participant will sit quietly for 10 minutes, before being attached to the HFNC, so a baseline swallow frequency can be established. After the baseline swallow frequency is established, each participant will be asked to swallow 8 boluses: 2 trials of water at 2 volumes (5 and 10 mL) and 2 trials of applesauce at 2 volumes (5 and 10 mL). Participants will rest for 15 seconds after completing each swallow. This procedure will establish the participant's baseline swallowing effort measurements. Once these swallows have been completed, the participant will be placed on the HFNC. Each participant will be placed on three different flow rates (30, 45, and 60 L/min or 30, 45, and 50 L/min) in random order. The random order will be generated by an online random number tool (https://www.randomizer.org). The study participant will be subjected to each flow rate for 15 minutes. During the first 10 minutes, swallow frequency will be recorded. After 10 minutes at the given flow, the participant will complete the 8 aforementioned swallows. After completing all of the swallowing trials, the participant will be removed from the HFNC for a period of 10 minutes. This process will be repeated for all three

flowrates for a total of 32 boluses swallowed.

Swallowing Frequency:

Swallowing frequency is analyzed by sEMG signals recorded on the KayPentax Digital Swallow Workstation™ with integrated digital swallowing signals lab (DSW™, Model 7120, New Jersey). A three-sensor sEMG electrode (Uni-Patch™, Disk #7500, Covidien Corporation, Tyco Healthcare, Wabasha, MN) will be placed on the anterior neck skin under the chin, over the submental muscles above the hyoid bone. Each patch will include two recording electrodes and a third ground electrode. Spontaneous swallowing frequency is calculated as the number of swallows per minute (SPM) for 10 minutes on room air and then for each HFNC intervention. Swallows will be counted from the visual myographic waveform produced by the DSW.

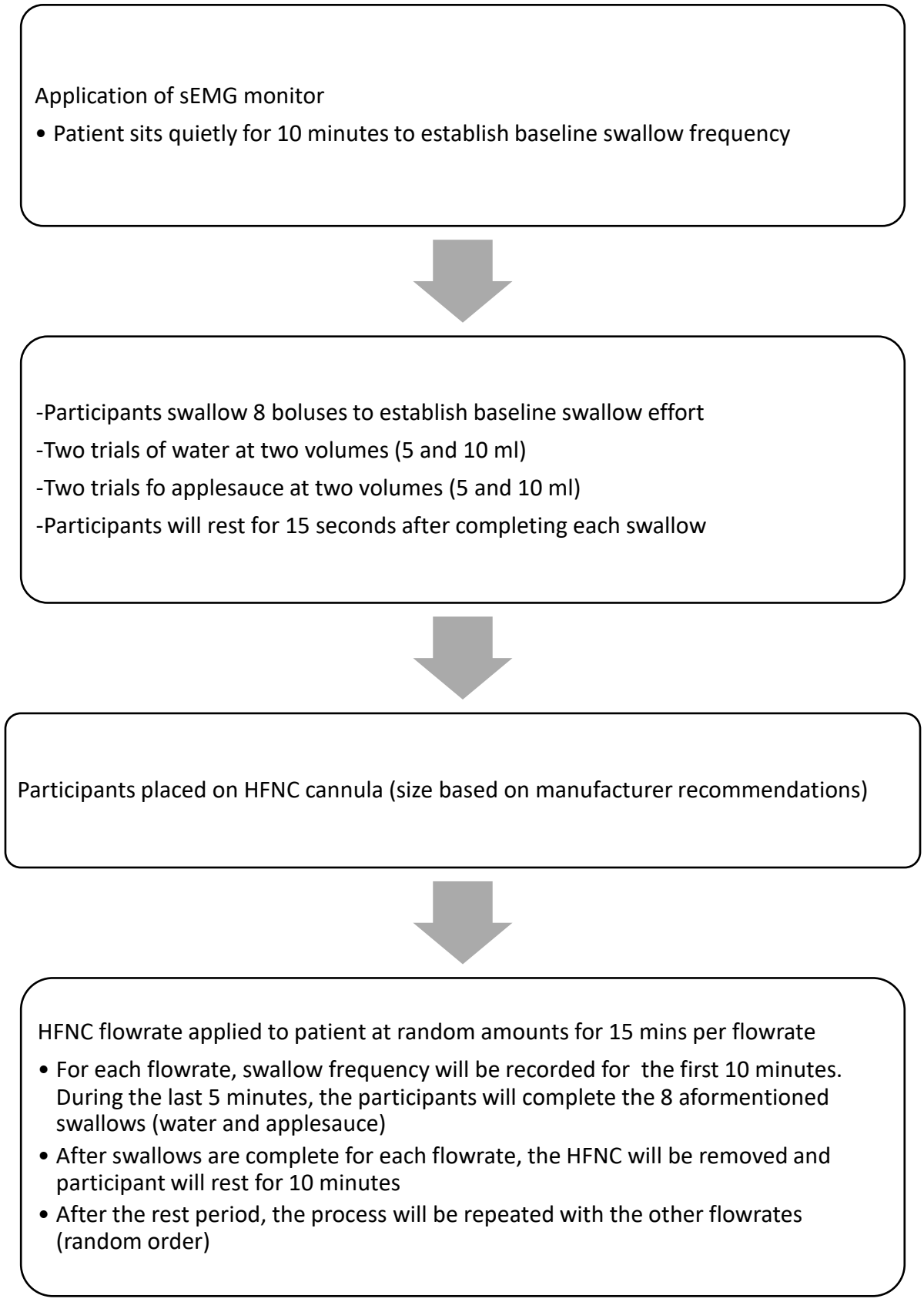
Swallowing Effort:

Both swallowing amplitude and timing parameters will be obtained by analyzing the individual graphic waveforms produced by the DSW algorithm. Measures will be obtained for each of the 8 swallows, at each of the HFNC flow rates.

Procedures Done for Research Purpose

- The use of HFNC with three levels of flow (30, 45, and 60 L/min or 30, 45, and 50 L/min [for small-size nasal prongs]).
- Swallow frequency measurement through sEMG.

Swallowing effort measurement through sEMG – participants will swallow measured amounts of water and applesauce. Presentation of the different volumes and viscosities will be done in pre-determined random order.


Application of sEMG monitor
• Patient sits quietly for 10 minutes to establish baseline swallow frequency
-Participants swallow 8 boluses to establish baseline swallow effort
-Two trials of water at two volumes (5 and 10 ml)
-Two trials fo applesauce at two volumes (5 and 10 ml)
-Participants will rest for 15 seconds after completing each swallow
Participants placed on HFNC cannula (size based on manufacturer recommendations)
HFNC flowrate applied to patient at random amounts for 15 mins per flowrate
• For each flowrate, swallow frequency will be recorded for the first 10 minutes. During the last 5 minutes, the participants will complete the 8 aformentioned swallows (water and applesauce)
• After swallows are complete for each flowrate, the HFNC will be removed and participant will rest for 10 minutes
• After the rest period, the process will be repeated with the other flowrates (random order)

Subject Population

Fifty healthy adult volunteers above the age of 21 will be assessed.

Inclusion criteria:

- Age >21 y/o
- Functional cognition as determined by the participant's ability to follow verbal directions; no formal cognitive test will be administered. Anyone not able to follow 1-step directions will be withdrawn from the study.
- Eat a "general/regular consistency" diet—determined by scoring a 6 or 7 on the Functional Oral Intake Scale (FOIS).[24]

Exclusion criteria:

- Age < 21 y/o
- Allergy to applesauce
- History of dysphagia or disease/condition that may cause dysphagia such as:
  - Achalasia
  - Diffuse spasm
  - Esophageal tumors or scar tissue
  - Esophageal rings
  - Gastroesophageal reflux disease (GERD)
  - Eosinophilic esophagitis
  - Scleroderma
  - Radiation therapy
  - Neurological disorders (multiple sclerosis, muscular dystrophy and Parkinson's disease)
  - Neurological damage (from a stroke or brain or spinal cord injury)
  - Pharyngeal diverticula
- Use of medications that alter swallowing function
  - Benztropine mesylate (Cogentin)
  - Oxybutynin (Ditropan)

  - Propantheline (Pro-Banthine)
  - Tolterodine (Detrol)
- The presence of tracheostomy tube.
- Nasal obstruction.

Recruitment and Consent Procedures:

- Recruitment will be based on the inclusion and exclusion criteria.
- Emails will be used to inform potential participants.
- Snowball sampling (non-probability sampling) will be utilized to recruit individuals outside of the Respiratory Care and Speech Language departments
- Informed consent explaining the procedures and potential harm will be obtained from all individual participants in the study.

Compensation:

- There will be no compensation provided to participants for participation in this study.

Risk to subject:

- Risks include aspiration of water or applesauce when swallowing on the HFNC. Discomfort and dryness of mouth or nose due to the use of the high flow. Also, since the swallowing measurement device is applied through patch to skin, allergic reaction may occur. Participants will be closely monitored by the study investigators and if any signs of aspiration (coughing, shortness of breath), discomfort, or allergic reaction occurs, the session will be terminated and the participant will be withdrawn from the study.

Special Precautions:

- All study material will be coded to de-identify participants and a separate list will be kept with the participant's ID and name.

Confidentiality:

- The study investigators, along with the IRB, will have access to the individual participant's results. Neither names nor personal information will be recorded or included in the data analysis. The investigators will strictly adhere to IRB guidelines to ensure that participant's confidentiality is maintained.

Plans for Data Analysis:

- The data collected will include swallow frequency (calculated as swallows per minute), peak effort amplitude (the highest amplitude of swallowing effort), and swallowing speed (the difference between the onset and offset of muscle contraction). Simple 1-way repeated measures ANOVA will be used to determine significant differences in swallowing frequency between oxygen flow rates ($p < .05$). A 4-way mixed methods repeated measures ANOVA (HFNC x volume x viscosity x age) will be used to determine significant differences in amplitude and timing ($p < .05$).

References:

1. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S. Use of High-Flow Nasal Cannula for Acute Dyspnea and Hypoxemia in the Emergency Department. Respir Care 2015;60(10):1377-1382.
2. Braunlich J, Kohler M, Wirtz H. Nasal highflow improves ventilation in patients with COPD. Int J Chron Obstruct Pulmon Dis 2016;11:1077-1085.
3. Braunlich J, Seyfarth HJ, Wirtz H. Nasal High-flow versus non-invasive ventilation in stable hypercapnic COPD: a preliminary report. Multidiscip Respir Med 2015;10(1):27-015-0019-y. eCollection 2015.
4. Ou X, Hua Y, Liu J, Gong C, Zhao W. Effect of high-flow nasal cannula oxygen therapy in adults with acute hypoxemic respiratory failure: a meta-analysis of randomized controlled trials. CMAJ 2017;189(7):E260-E267.
5. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 2015;372(23):2185-2196.
6. Joseph L, Goldberg S, Shitrit M, Picard E. High-Flow Nasal Cannula Therapy for Obstructive Sleep Apnea in Children. J Clin Sleep Med 2015;11(9):1007-1010.
7. Huang HW, Sun XM, Shi ZH, Chen GQ, Chen L, Friedrich JO, et al. Effect of High-Flow Nasal Cannula Oxygen Therapy Versus Conventional Oxygen Therapy and Noninvasive Ventilation on Reintubation Rate in Adult Patients After Extubation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Intensive Care Med 2017:885066617705118.
8. Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F, et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. Am J Respir Crit Care Med 2014;190(3):282-288.
9. Fernandez R, Subira C, Frutos-Vivar F, Rialp G, Laborda C, Masclans JR, et al. High-flow nasal cannula to prevent postextubation respiratory failure in high-risk non-hypercapnic patients: a randomized multicenter trial. Ann Intensive Care 2017;7(1):47-017-0270-9. Epub 2017 May 2
10. Hernandez G, Vaquero C, Gonzalez P, Subira C, Frutos-Vivar F, Rialp G, et al. Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. JAMA 2016;315(13):1354-1361.
11. Baudin F, Buisson A, Vanel B, Massenavette B, Pouyau R, Javouhey E. Nasal high flow in management of children with status asthmaticus: a retrospective observational study. Ann Intensive Care 2017;7(1):55-017-0278-1. Epub 2017 May 22

12. Ricard JD. High flow nasal oxygen in acute respiratory failure. Minerva Anestesiol 2012;78(7):836-841.
13. Maury E, Alves M, Bige N. High-flow nasal cannula oxygen therapy: more than a higher amount of oxygen delivery. J Thorac Dis 2016;8(10):E1296-E1300.
14. Sanuki T, Mishima G, Kiriishi K, Watanabe T, Okayasu I, Kawai M, et al. Effect of nasal high-flow oxygen therapy on the swallowing reflex: an in vivo volunteer study. Clin Oral Investig 2017;21(3):915-920.
15. Leder SB, Siner JM, Bizzarro MJ, McGinley BM, Lefton-Greif MA. Oral Alimentation in Neonatal and Adult Populations Requiring High-Flow Oxygen via Nasal Cannula. Dysphagia 2016;31(2):154-159.
16. Ferrara L, Bidiwala A, Sher I, Pirzada M, Barlev D, Islam S, et al. Effect of nasal continuous positive airway pressure on the pharyngeal swallow in neonates. J Perinatol 2017;37(4):398-403.
17. Crary MA, Carnaby GD, Sia I, Khanna A, Waters MF. Spontaneous swallowing frequency has potential to identify dysphagia in acute stroke. Stroke 2013;44(12):3452-3457.
18. Crary MA, Carnaby Mann GD, Groher ME. Identification of swallowing events from sEMG Signals Obtained from Healthy Adults. Dysphagia 2007;22(2):94-99.
19. Crary MA, Sura L, Carnaby G. Validation and demonstration of an isolated acoustic recording technique to estimate spontaneous swallow frequency. Dysphagia 2013;28(1):86-94.
20. Vaiman M, Eviatar, E., & Segal, S. Surface electromyographic studies of swallowing in normal subjects: A reivew of 440 adulats. Report 2. Quantitavie data: Amplitude measures. Otolaryngology-Head and Neck Surgery 2004; 131:773-780.
21. Lazarus CL, Logemann JA, Rademaker AWet al. Effects of bolus volume, viscosity, and repeated swallows in nonstroke subjects and stroke patients. Arch Phys Med Rehabil 1993; 74:1066-1070
22. Reimers-Neils L, Logemann J., Larson, C. Viscosity effects on EMG activity in normal swallow. Dysphagia 1994; 9:101-106.
23. Logemann JA, Pauloski, B. R., Rademaker, A. W., Colangelo, L. A., Kahrilas, P. J., Smith, C. H. Temporal and biomechanical characteristics of oropharyngeal swallow in younger and older men. J Speech Lang Hear Res 2000; 43:1264-1274.
24. McKee GJ, Johnston BT, McBride GB, Primrose WJ. Does age or sex affect pharyngeal swallowing? Clin Otolaryngol Allied Sci 1998; 23:100-106.
25. Crary JA, Carnaby Mann GD, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil 2005; 86:1516-20.