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Brief Reports

END-TIDAL OXYGEN SATURATION WITH NASAL CANNULA DURING NONINVASIVE POSITIVE PRESSURE VENTILATION: A RANDOMIZED CROSSOVER TRIAL

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☐ **Abstract—Background: Simultaneous use of nasal cannula (NC) with noninvasive positive pressure ventilation (NIPPV) may help streamline the transition from preoxygenation to intubation with apneic oxygenation in patients with deteriorating respiratory status, but may also compromise preoxygenation by impairing NIPPV mask seal. Objectives: To demonstrate that end-tidal oxygen (EtO_2) after NIPPV with NC is noninferior to that of NIPPV without NC. Methods: We conducted a randomized cross-over noninferiority study using healthy volunteers. All subjects underwent a 3-min trial of NIPPV with or without high-flow NC at 15 L/min of oxygen, followed by a 5-min washout period, and then a second 3-min trial of the opposite intervention. We randomized subjects to order of interventions. The primary outcome was postintervention EtO_2 as measured by immediate exhalation into an oxygen analyzer after the 3-min ventilation period. We compared this outcome between the two study arms using an absolute 5% noninferiority margin. Results: We enrolled 37 subjects, each of whom underwent both interventions of NIPPV alone and NIPPV with 15 L/min NC. The paired mean difference in EtO_2 between NIPPV with NC measurements vs. NC alone measurements was 0.5% (95% confidence interval -∞ to 2.7%). Analyses stratified by order of intervention yielded similar results. Conclusions: The mean difference confidence interval did not include the noninferiority margin. Hence, NIPPV with NC seems noninferior to NIPPV alone with regard to EtO_2. These results indicate that concomitant use of NC with NIPPV may be an appropriate preoxygenation strategy in anticipation of the potential need for transition to intubation. Published by Elsevier Inc.**

☐ **Keywords—airway management; oxygenation; preoxygenation; noninvasive positive pressure ventilation; nasal cannula; apneic oxygenation**

INTRODUCTION

Preoxygenation is a critical component of intubation procedures, particularly in the emergency department (ED) setting. Desaturation below 70% can increase the risk of significant morbidity and mortality, including hypoxic brain injury, cardiac arrest, and death (1). Patients undergoing emergent intubation are frequently at high risk for compromised respiratory effort and shunt physiology, which can make preoxygenation even more difficult. Physiologic shunts, such as pneumonia, atelectasis, pulmonary edema, and mucous plugging are common causes of hypoxia in the ED (2). Patients who present with compromised oxygenation due to shunt conditions will

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likely benefit from noninvasive positive pressure ventilation (NIPPV) (3). In addition, NIPPV may avert the need for intubation altogether in these patients by stabilizing their respiratory status.

In patients still requiring intubation, NIPPV may nevertheless prove useful for optimizing peri-intubation oxygen saturation. NIPPV can specifically improve shunt physiology and increase oxygen saturation prior to intubation through augmentation of mean airway pressure. In a study by Baillard et al., hypoxic intensive care unit (ICU) patients preoxygenated with NIPPV had higher mean oxygen saturations prior to intubation when compared with patients undergoing preoxygenation with nonrebreather mask (NRBM): 98% vs. 93% (3). Additionally, patients in the NIPPV group had significantly higher peri-intubation oxygen nadirs compared with the NRBM group: 93% vs. 81% (3).

Another method to prevent peri-intubation hypoxia is oxygen administration via nasal cannula (NC) at high flow rates during the apneic phase of intubation. During apnea, oxygen extraction continues to occur from the functional residual capacity of the lung, despite the lack of diaphragmatic movement (4,5). Apneic oxygenation via NC can increase the time to desaturation during apnea. In a study comparing apneic oxygenation with NC at 5 L/min vs. oxygenation by room air only, patients placed on NC had significantly prolonged time of saturations above 95%: 5.3 vs. 3.5 min (5). Whereas some literature calls into question the utility of apneic oxygenation in the ED, a recent meta-analysis found that apneic oxygenation decreases the risk of desaturation during emergency airway management (6,7).

Given the possible benefit of apneic oxygenation via NC during intubation, the ability to transition smoothly between the preoxygenation period and intubation would be beneficial in emergency airway management. There have been few studies looking at the simultaneous use of both NIPPV and high-flow NC as a preoxygenation strategy. Each modality has a distinct benefit among patients requiring emergent intubation. Patients with shunt physiology will likely benefit most from NIPPV during the apneic period to improve ventilation/perfusion mismatch (8). NC (both at flows of 15 liters per minute [LPM] and 60 LPM) during the apneic period has been shown to benefit patients at risk for critical desaturation and, unlike NIPPV, physicians may apply NC during an intubation procedure (5,8–10).

Combining these two modalities of oxygenation may prove a potent strategy for completing intubation without desaturation by facilitating the transition from preoxygenation to laryngoscopy. Conversely, using NIPPV alone would require removal of the NIPPV prior to intubation followed by NC placement, which would require another step and delay apneic oxygenation, at which time the patient could experience arterial oxygen desaturation. A potential objection to the placement of an NC underneath an NIPPV mask will disrupt the seal of the mask. Any such disruption of the mask seal could, in turn, lead to suboptimal ventilation and oxygenation by NIPPV. A previous study of healthy volunteers demonstrated mask leak with simultaneous use of NC and NIPPV to be noninferior to that of NIPPV alone (11).

The aim of this study is to expand upon this previous research by conducting a similar experiment, but instead, measure end-tidal oxygen (EtO_2). We again chose a noninferiority design given our specific objective to determine whether the concomitant use of NIPPV and NC, which offers the advantage of simplifying the transition to intubation, does not have less efficacy in achieving oxygenation as compared with NIPPV alone (12). In particular, the aim of this study is to compare EtO_2 concentration in healthy volunteers undergoing NIPPV, both with and without NC. We hypothesized that the use of high-flow NC with NIPPV would be noninferior to NIPPV without NC as measured by EtO_2.

METHODS

This study is a prospective randomized crossover noninferiority trial of healthy volunteers (12). We conducted this study in a nonpatient care area of an urban tertiary care academic hospital (13). Our hospital institutional review board reviewed and approved the study. We registered the study on ClinicalTrials.gov (NCT03093662). We report our results in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement (14).

We recruited a convenience sample of healthy volunteers for this study. Inclusion criteria were age > 18 years and self-reported overall good health. Subjects included emergency medicine attending physicians, physician assistants, emergency medicine residents at various levels of training, physician assistants in training, medical students, and residents of other specialties rotating in our ED. Exclusion criteria included known cardiac, pulmonary, or upper respiratory disease. We also excluded participants known to have an inability to tolerate NIPPV or high-flow NC (e.g., due to facial anatomy). After obtaining written informed consent, subjects reported their demographics on a hard-copy data collection form prior to participation.

All participants underwent both NIPPV with NC and NIPPV alone during this study. Given the nature of our study procedures, we were unable to blind subjects or investigators to study interventions (open label design). We randomized participants to initial intervention utilizing a randomization sequence with permuted blocks of four. We separated each intervention by a 5-min washout