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Face mask leak with nasal cannula during noninvasive positive pressure ventilation: A randomized crossover trial

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ABSTRACT

Background: Nasal cannula can achieve apneic oxygenation during emergency intubation. However, pre-procedure nasal cannula placement may be difficult in patients undergoing non-invasive positive pressure ventilation (NPPV) prior to intubation. Our objective was to compare mask leak during NPPV with versus without simultaneous application of nasal cannula. We hypothesized mask leak would be no worse with concomitant use of nasal cannula (non-inferiority design).

Methods: We performed a randomized crossover non-inferiority study of healthy volunteers. We randomized subjects undergoing 60 s trials of NPPV (10 cm H_2O continuous positive airway pressure) to either NPPV alone (NPPV-a) or NPPV with nasal cannula at 15 L/min (NPPV-nc). After a brief rest period, all subjects underwent the alternative intervention. The primary outcome was time averaged mask leak over 60 s (L/min). We defined a non-inferiority margin of 5 L/min.

Results: We enrolled 64 subjects. Mean time-averaged mask leak was 2.2 L/min for NPPV-a versus 4.0 L/min for NPPV-nc for a difference of 1.7 L/min (one-sided 95% CI −∞ to 3.2 L/min). NPPV-a resulted in higher mean minute volume received (13.5 versus 12.2 L) and higher mean respiratory rates (14.8 versus 13.5 breaths per minute).

Conclusion: The addition of nasal cannula during NPPV does not significantly increase mask leak. The simultaneous application of nasal cannula with NPPV may be a useful strategy to streamline airway management among patients undergoing NPPV prior to intubation.

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1. Introduction

1.1. Background

Preoxygenation techniques optimize intubating conditions during emergency airway management by prolonging time to desaturation [1]. Historically, the standard technique entailed administering a high fraction of inspired oxygen (FiO_2) via non-rebreather mask (NRB) for 3 min or eight vital capacity breaths to wash out nitrogen in the lungs and achieve preoxygenation [2]. However, these strategies may not be practical or sufficient in critically ill patients and may lead to peri-intubation hypoxia.

Another option to minimize peri-procedural desaturation is apneic oxygenation via standard nasal cannula placement during intubation [1]. This strategy can prolong safe apnea time, increase time oxygen saturations remain above 95%, and limit desaturations during intubation [3,4]. Apneic oxygenation via standard nasal cannula is associated with increased endotracheal intubation first pass success without hypoxemia in the Emergency Department (ED) setting [5].

Patients exhibiting shunt physiology may not achieve adequate oxygen saturations using these techniques alone. They may require pre-intubation non-invasive positive pressure ventilation (NPPV) to augment mean airway pressure, improving oxygenation and ventilation of shunted alveoli. Critically ill patients preoxygenated with NPPV have higher mean oxygen saturations prior to intubation and higher peri-intubation nadirs [6]. Pre-intubation NPPV has also been shown to benefit patients with primary lung disorders not involving shunt, such as asthma and COPD [7].

Patients requiring NPPV to improve oxygen saturations prior to intubation may benefit from continuation of passive oxygenation via nasal cannula during the intubation apneic period [8]. Rapid transition from preoxygenation to intubation is imperative in these critically ill patients. Hence, simultaneous application of nasal cannula during NPPV prior to intubation would be preferable to application of nasal cannula after discontinuing NPPV prior to initiating intubation. One potential concern with the simultaneous application of NPPV and nasal cannula is that the

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nasal cannula tubing may compromise the NPPV mask seal and therefore compromise delivery of positive pressure during preoxygenation.

1.2. Study objective

The objective of this study is to compare measured mask leak flow (L/min) while on NPPV in healthy volunteers with versus without the simultaneous use of a nasal cannula. We hypothesize that mask leak will not be significantly greater with the use of a nasal cannula versus not using a nasal cannula (non-inferiority design).

2. Methods

2.1. Study design and setting

We performed a randomized crossover non-inferiority study using healthy volunteers. The study setting was an urban academic tertiary care hospital. Our institutional review board reviewed and approved the study. We registered the study on ClinicalTrials.gov (NCT02743936).

2.2. Subjects

We recruited a convenience sample of staff members affiliated with our ED. Subjects included medics, nurses, residents, and attending physicians. Inclusion criteria consisted of healthy adult volunteers aged 18 years or older. Exclusion criteria included craniofacial abnormalities precluding the application of either nasal cannula or NPPV, inability to tolerate NPPV during the acclimation phase of the protocol, or active cardiac or pulmonary disease (including any respiratory infection).

We obtained written informed consent from all subjects. No subjects received compensation for participating. We documented subject flow in accordance with the Consolidated Standards for Reporting Trials (CONSORT) Statement (Fig. 1) [9].

2.3. Study protocol

We randomized subjects to one of two initial study arms, NPPV alone (NPPV-a) or NPPV with nasal cannula (NPPV-nc). In both study arms, subjects underwent NPPV using a Respironics V60 non-invasive ventilator with a Respironics AF531 EE headgear and mask (Phillips Healthcare, Andover, MA). This is a facemask NPPV system that covers the patient's nose and mouth. Investigators determined subject mask sizes using standard sizing charts accompanying each mask. For the NPPV-nc arm only, subjects underwent NPPV with the simultaneous use of an AirLife standard nasal cannula (CareFusion, San Diego, CA). After screening, consent, and enrollment, we allocated subjects to their initial study arm using a randomization sequence with permuted blocks. Both subjects and investigators were aware of the subject allocation (open label design).

We administered continuous positive airway pressure (CPAP) at 10 cm H_2O for NPPV in both study arms. We added nasal cannula with 15 L/min oxygen flow in the NPPV-nc arm. For the NPPV-a arm, subjects underwent NPPV only without placement of a nasal cannula.

Prior to the start of each intervention investigators fit the NPPV facemask. In the NPPV-nc arm we placed a nasal cannula in the standard fashion before placing the NPPV facemask. We instructed subjects to relax and breathe naturally. At the start of both interventions, subjects underwent 2 min of acclimation to facilitate spontaneous restful ventilation and ensure appropriate mask fit. Subjects tolerating the acclimation period continued spontaneous restful ventilation for the 60 s data collection period. We made no adjustments to mask fit during the 1 min of data collection. All subjects underwent a two-minute rest (washout period) before proceeding to the alternate intervention (Fig. 1).

2.4. Measurements

Investigators obtained video recordings of the Respironics V60 ventilator data output including measurements of time-averaged mask leak flow (L/min) and tidal volume (L) for each breath. The recordings allowed accurate data collection and transcription of these parameters for every breath taken by each study subject during the trial period. The V60 ventilator measures flow rate and pressure at the machine output and patient mask, comparing both ends of the patient circuit to calculate measurements and perform automatic leak compensation. Regarding mask leak flow, the V60 ventilator compares end-exhalation actual flow of each respiratory cycle and the original baseline flow to estimate unintentional leak at each end-exhalation (reported in L/min), assuming that any discrepancy is due to mask leak. Regarding tidal volume, the ventilator compares delivered expiratory and inspiratory tidal volumes and assumes discrepancies represent mask leak [10]. We situated the ventilator monitors such that the subjects could not see and use the monitor output as real-time feedback to adjust breathing or positioning.

After undergoing both interventions, investigators asked subjects to rate their discomfort associated with the NPPV with and without nasal cannula using a verbal numerical rating scale (VNRS). This scale ranged from 0 ("no discomfort") to 10 ("maximal discomfort"). Investigators recorded these responses onto hard-copy data collection forms.

The primary outcome measure was time-averaged mask leak flow (L/min). Secondary outcomes included received minute volume over the minute-long NPPV period (L), respiratory rate (breaths per minute), the percentage of breaths with any mask leak, and subject discomfort as reported by VNRS (0 − 10).

2.5. Data analysis

We based our sample size estimate upon the primary outcome of time-averaged mask leak for which we assumed normally-distributed data. We planned a non-inferiority analysis. Specifically, the null hypothesis was that mask leak would be at least 5 L/min (non-inferiority margin) higher in the NPPV-nc arm compared to the NPPV-a arm. The alternative hypothesis was that we would observe no such difference in mask leak. Given our non-inferiority design, we planned one-sided inferential statistical testing and so assumed $\alpha = 0.025$ as is the convention for non-inferiority testing instead of $\alpha = 0.05$ as is the convention in superiority testing [11,12]. We anticipated standard deviation in mask leak measurements of 9 L/min based on preliminary data. Given these assumptions, enrollment of 63 subjects would achieve 80% power using one-sided to reject the null hypothesis (that mask leak is greater with NPPV-nc compared to NPPV-a) when the alternative is true. Rejecting the null hypothesis would lead to the conclusion that NPPV-nc is non-inferior (in terms of greater mask leak) compared to NPPV-a.

Investigators double entered all video recording and hard-copy form data into a secure Excel database (version 14; Microsoft, Redmond, WA). We exported all data into SPSS for statistical analysis (version 22; IBM, Armonk, NY). We calculated descriptive statistics to report patient characteristics. We compared the primary outcome of mean mask leak by calculating the one-sided 95% confidence interval (CI) of the difference in mean mask leak between NPPV-a versus NPPV-nc (equivalently a 97.5% confidence interval given our assumption that $\alpha = 0.025$). If the upper bound of the one-sided 95% CI was less than the inferiority margin (5 L/min) then we rejected inferiority. We chose 5 L/min as the non-inferiority margin based upon consensus between the investigators that this value represents the minimal clinically significant difference. We repeated these analyses of the primary outcome stratified by intervention sequence. We performed similar one-sided analyses of secondary outcomes including the percentage of breaths with any mask leak, mean minute volume received, mean respiratory

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