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Heated humidified high-flow nasal cannula oxygen after thoracic surgery — A randomized prospective clinical pilot trial

Jason Brainard [a], Benjamin K. Scott [a], Breandan L. Sullivan [a], Ana Fernandez-Bustamante [a], Jerome R. Piccoli [b], Morris G. Gebbink [b], Karsten Bartels [a,*]

[a] Department of Anesthesiology, University of Colorado School of Medicine, 12401 E. 17th Avenue, Leprino Office Building, 7th Floor, MS B-113, Aurora, CO 80045, USA
[b] Department of Respiratory Care, University of Colorado Hospital, 12605 East 16th Avenue, MS F-764, Aurora, CO 80045, USA

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ABSTRACT

Background: Thoracic surgery patients are at high-risk for adverse pulmonary outcomes. Heated humidified high-flow nasal cannula oxygen (HHFNC O_2) may decrease such events. We hypothesized that patients randomized to prophylactic HHFNC O_2 would develop fewer pulmonary complications compared to conventional O_2 therapy.
Methods and patients: Fifty-one patients were randomized to HHFNC O_2 vs. conventional O_2. The primary outcome was a composite of postoperative pulmonary complications. Secondary outcomes included oxygenation and length of stay. Continuous variables were compared with *t*-test or Mann-Whitney-*U* test, categorical variables with Fisher's Exact test.
Results: There were no differences in postoperative pulmonary complications based on intention to treat [two in HHFNC O_2 ($n = 25$), two in control ($n = 26$), $p = 0.680$], and after exclusion of patients who discontinued HHFNC O_2 early [one in HHFNC O_2 ($n = 18$), two in control ($n = 26$), $p = 0.638$]. Discomfort from HHFNC O_2 occurred in 11/25 (44%); 7/25 (28%) discontinued treatment.
Conclusions: Pulmonary complications were rare after thoracic surgery. Although HHFNC O_2 did not convey significant benefits, these results need to be interpreted with caution, as our study was likely underpowered to detect a reduction in pulmonary complications. High rates of patient-reported discomfort with HHFNC O_2 need to be considered in clinical practice and future trials.

1. Background

Postoperative pulmonary complications are prevalent following major thoracic surgery with a risk up to 25% following lung resection [1]. Risk factors in this patient population include severe baseline pulmonary disease, smoking, lung collapse during surgery, resection of viable lung, and poor pain control after a thoracotomy incision. Development of postoperative respiratory failure following major surgery is associated with a mortality of up to 27%, compared to 1% in patients without respiratory failure [2]. Atelectasis formation is a key factor for the development of such postoperative pulmonary complications. Unfortunately, the occurrence of atelectasis is extremely common postoperatively, with an incidence of up to 85% [3] and it significantly increases the risk for pneumonia and acute hypoxic respiratory failure [4].

Non-invasive ventilation has emerged as a successful strategy for both the prevention and treatment of postoperative acute respiratory failure in high-risk surgical patients [5-9]. Non-invasive ventilation generates positive airway pressure, thereby improving atelectasis and systemic oxygenation [10]. For example, in patients with acute respiratory failure following lung resection, the use of non-invasive ventilation has been shown to decrease the incidence of re-intubation from 50% to 21% [11]. Non-invasive ventilation, however, has important limitations, such as the need for a face-mask that usually covers the nose and mouth possibly leading to claustrophobia, prevention of normal oral intake, possibly less effective clearance of secretions, and prevention of usual communication with family members and medical staff [12]. Furthermore, in thoracic surgery, the potential for positive pressure ventilation to increase stress on surgical suture lines as well as concerns for exacerbation of bronchopulmonary fistulas have tempered enthusiasm for the prophylactic use of non-invasive ventilation [13].

Heated humidified high-flow nasal cannula oxygen (HHFNC O_2) is an alternative to standard oxygen therapy and non-invasive ventilation. This therapy involves high flows of oxygen (up to 60 + L per minute) delivered through a modified nasal cannula. This treatment may provide many of the same respiratory advantages of non-invasive

Abbreviation: (HHFNC O_2), heated humidified high-flow nasal cannula oxygen.

* Corresponding author at: University of Colorado, Department of Anesthesiology, 12401 E. 17th Ave., Leprino Office Building, 7th Floor, MS B-113, Aurora, CO 80045, USA.
E-mail address: karsten.bartels@ucdenver.edu (K. Bartels).

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ventilation, without the significant drawbacks including patient discomfort, cost, and medical expertise [14]. Indeed, HHFNC O_2 has been used successfully to reduce rates of re-intubation in a low-risk mixed medical/surgical ICU population [15]. Similarly, it has been shown that HHFNC O_2 appears to be non-inferior to non-invasive ventilation in preventing re-intubation in high-risk ICU patients [16] – a finding that was also confirmed specifically in cardiothoracic surgery patients [17]. Here, we sought to test the hypothesis that prophylactic use of HHFNC O_2 in patients admitted to the ICU after thoracic surgery would have fewer postoperative pulmonary complications compared to patients treated with conventional O_2 therapy.

2. Methods

2.1. Trial design

This prospective randomized trial was conducted from August 2013 to June 2015 at an academic medical center in the United States. The institutional review board approved the study protocol before patient enrollment. Participants gave their written informed consent to participate in the trial. No incentive was paid for agreeing to participate. This study was reported using the CONSORT statement for the reporting of randomized clinical trials [18]. The trial was retrospectively registered at ClinicalTrials.gov on January 10, 2017 (NCT03024112).

2.2. Participants

Eligible patients were ≥18 years of age undergoing thoracic surgery with scheduled admission to the intensive care unit postoperatively. Exclusion criteria were age < 18, pregnant or breastfeeding, a known diagnosis of obstructive sleep apnea, current or previous lung transplantation, previous pneumonectomy, home oxygen > 4 L/min, or inability to adhere to assigned treatment for the intended duration (48 h after surgery or until transfer to the floor, whichever occurred earlier). Baseline data and patient demographics were recorded and included age, gender, height, weight, American Society of Anesthesiologists physical status, smoking history, duration of surgery and one-lung ventilation, intraoperative fluids, Simplified Acute Physiology Score, as well as surgical procedure.

2.3. Interventions

After completion of surgery and upon arrival to the post-anesthesia care unit, a sealed envelope was opened by a member of the study team to determine if subjects had been randomized to the HHFNC O_2 versus the standard O_2 treatment group (1:1 allocation).

The intervention group received HHFNC O_2 at a set flow of 40 L/min. FiO_2 was titrated by respiratory therapists to maintain SpO_2 ≥ 90%. The HHFNC O_2 apparatus (MaxVenturi®, Maxtec, Salt Lake City, UT, USA) included: 1.) Air-Oxygen blender – capable of delivering 21–100% FiO_2 at flow rates up to 60 L/min, 2.) Heated Humidifier – providing active heating and humidification to the delivered air-O_2 blend, 3.) Nasal cannula – larger diameter, slightly elongated nasal cannula with single limb connection to humidifier, 4.) O_2 analyzer- routinely calibrated during the study. The standard O_2 treatment group received usual nasal cannula or face mask oxygen titrated by nurses as necessary to maintain SpO_2 ≥ 90%. Patients were recovered from anesthesia in the post-anesthesia care unit and then transferred to the ICU. Allocated therapy continued for a total of 48 h or until transfer from the ICU to the floor. Given the apparent differences in the technical apparatus to administer HHFNC O_2 versus standard oxygen therapy, blinding procedures could not be performed.

If patient intolerance to HHFNC O_2 developed as assessed clinically by nursing, respiratory therapy, or physician care team, HHFNC O_2 therapy was discontinued, and reasoning for discontinuation was recorded. If a patient developed impending or acute respiratory failure while enrolled in the study, allocated study treatment was discontinued, and treatment decisions for escalation of therapy (non-invasive ventilation, re-intubation) were be made by the patient's care team.

2.4. Outcomes

Primary study outcome was the occurrence of the composite of postoperative pulmonary complications defined as: severe hypoxemia (SpO_2 < 90% with FiO_2 ≥ 50%), acute respiratory failure (dyspnea at rest, respiratory rate > 25 breaths/min, active use of accessory respiratory muscles, PaO_2/FiO_2 ratio < 200), escalation of therapy to non-invasive ventilation, re-intubation, occurrence of hospital-acquired pneumonia, or re-admission to the ICU. Secondary outcomes included ICU length of stay, hospital length of stay, and postoperative oxygenation.

2.5. Statistical methods

Categorical variables including the primary outcome "postoperative pulmonary complications" were compared with Fisher's Exact test. Since we only assessed one primary outcome variable, no adjustment for multiple comparisons was made. After testing for normality of distribution within treatment groups using Shapiro-Wilk test, continuous variables were compared with independent *t*-test not assuming equal variances or Mann-Whitney-*U* test as appropriate. Statistical significance was assumed at a level of significance of $p < 0.05$ (one-sided for primary outcome, two-sided for other variables) using SPSS Version 24, Copyright IBM Corporation. Based on historical data from our institution from September 2011 until August 2012, the incidence of the primary outcome was expected to be 61%. Assuming a 58.4% relative reduction in the incidence of acute respiratory failure [11], a total sample size of 52 patients (26 per group) would have given us 81% power to detect a difference in the incidence of postoperative pulmonary complications using Fisher's Exact test with a one-sided tail and significance at $p = 0.05$. Power analysis was performed using G*Power 3.1 [19].

3. Results

A total of 51 patients were randomized in the trial. Seven patients allocated to the HHFNC O_2 arm of the trial did not tolerate the treatment, and HHFNC O_2 was therefore discontinued (Fig. 1). An additional four patients reported discomfort with the HHFNC O_2 device but continued treatment. Baseline characteristics of the study population are reported in Table 1.

Based on intention to treat, postoperative pulmonary complications, the primary outcome, was detected in two patients (8%) within the HHFNC O_2 group and two patients (8%) in the conventional O_2 group ($p = 0.680$). Following exclusion of seven patients who discontinued HHFNC O_2 early due to discomfort, postoperative pulmonary complications occurred in one patient within the HHFNC O_2 group and two patients in the conventional O_2 group (Table 2). No patient from the control cohort required escalation from conventional O_2 to HHFNC O_2 therapy. One patient was diagnosed intra-operatively with a condition that required a separate surgery at a later date. Following the second surgery, this patient was again admitted to the ICU postoperatively. This admission to the ICU was not counted as an ICU readmission for the purpose of this study. Analysis of secondary outcomes revealed no difference between groups except for the number of hourly measurements of SpO_2 ≤ 93% 12–24 h postoperatively (Table 2).

4. Discussion

Major postoperative pulmonary complications rarely occurred in both the conventional and the HHFNC O_2 groups included in this pilot study. There were no statistically significant differences for the primary outcome of postoperative pulmonary complications in patients treated with HHFNC versus conventional O_2. Of the secondary outcomes, only