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Optimizing Oxygenation During Rigid Bronchoscopy: A Randomized Trial of High-Flow vs. Low-Flow Nasal Oxygen

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Abstract:

Background: The efficacy of high-flow nasal oxygenation (HFNO) in improving oxygenation is influenced by various factors, and its effectiveness is not consistently guaranteed. This study aimed to compare the effects of HFNO and standard low-flow nasal oxygenation during rigid bronchoscopy in apneic patients.

Methods: Patients undergoing rigid bronchoscopy under general anesthesia with full muscle relaxation were randomly assigned to receive either HFNO (HFNO group) or standard low-flow oxygenation (Standard group). Primary endpoints included the lowest peripheral oxygen saturation (SpO2), hypoxemia-related surgical interruptions (SpO2 ≤ 94%), and changes in arterial oxygen tension (PaO2) and carbon dioxide tension (PaCO2) during the apnea period.

Results: Fifty-three patients completed the study. No statistically significant differences were found between the HFNO and Standard groups in the lowest SpO2 levels (median [Q1, Q3]: 99 [98, 100]% vs. 98 [94, 100]%, P = 0.059) or the increase rate of PaCO2 (mean ± standard deviation [SD]: 1.6 ± 0.7 mmHg/min vs. 2.0 ± 0.8 mmHg/min, P = 0.064). However, the HFNO group experienced significantly fewer hypoxemia-related surgical interruptions (1 [3.8%] vs. 8 [29.6%], P = 0.024) and exhibited a significantly attenuated decline rate in PaO2 (median [Q1, Q3]: 4.6 [0.0, 7.9] mmHg/min vs. 10.5 [6.4, 12.9] mmHg/min, P = 0.005).

Conclusions: While HFNO did not significantly enhance the lowest SpO2 levels compared to standard low-flow oxygenation, it significantly reduced hypoxemia-related surgical interruptions and attenuated the decline in PaO2. Therefore, HFNO demonstrates considerable clinical efficacy for rigid bronchoscopy.

Keywords: Anesthesia, general; Bronchoscopy; Humans; Hypoxia; Oxygen inhalation therapy; Thoracic surgical procedures.

Introduction

Rigid bronchoscopy remains an indispensable tool for the diagnosis and management of various airway pathologies, including foreign body removal, airway stenting, and tumor debulking. However, the procedure inherently interrupts spontaneous ventilation, leading to

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periods of apnea and potential hypoxemia. Maintaining adequate oxygenation during these periods is paramount to patient safety and procedural success.

Traditional methods of oxygen supplementation during rigid bronchoscopy often involve standard low-flow nasal oxygenation. While effective in some cases, this technique may be insufficient to prevent hypoxemia, particularly in patients with compromised respiratory function or prolonged apneic periods. This limitation has prompted the exploration of alternative oxygenation strategies, with high-flow nasal oxygenation (HFNO) emerging as a promising option.

HFNO delivers heated and humidified oxygen at high flow rates, exceeding the patient's inspiratory flow demand. This technique offers several potential advantages over standard low-flow oxygenation, including improved oxygenation, reduced anatomical dead space, and positive airway pressure. These physiological effects may contribute to enhanced oxygenation during apneic periods, potentially reducing the incidence of hypoxemia and associated complications.

The efficacy of HFNO has been demonstrated in various clinical settings, including preoxygenation before intubation, post-extubation respiratory support, and management of acute respiratory failure. However, its application during rigid bronchoscopy remains relatively understudied. While some studies have suggested that HFNO can improve oxygenation during this procedure, the evidence is not conclusive, and the optimal oxygenation strategy remains a subject of debate.

Factors influencing the effectiveness of HFNO during rigid bronchoscopy include patient-specific characteristics, such as body mass index, lung function, and underlying comorbidities, as well as procedural factors, such as the duration of apnea and the complexity of the intervention. Furthermore, the variability in HFNO device settings and delivery techniques may also contribute to inconsistent results.

Given the potential benefits of HFNO in improving oxygenation during rigid bronchoscopy, a thorough evaluation of its efficacy is warranted. This randomized controlled trial aims to compare the effects of HFNO and standard low-flow nasal oxygenation on oxygenation parameters during rigid bronchoscopy in apneic patients. We hypothesize that HFNO will provide superior oxygenation, as evidenced by higher peripheral oxygen saturation (SpO2), attenuated declines in arterial oxygen tension (PaO2), and a reduced incidence of hypoxemia-related surgical interruptions, compared to standard low-flow oxygenation. The findings of this study will provide valuable insights into the optimal oxygenation strategy during rigid bronchoscopy and contribute to improved patient safety and procedural outcomes.

Materials and Methods

Ethics:

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This prospective, open-label, randomized controlled trial was conducted in accordance with the Declaration of Helsinki, 2013. The study was approved by the Institutional Review Board (IRB no. 1-2019-0005, March 2019) and registered at ClinicalTrials.gov (NCT03892408, March 27, 2019) before patient enrollment (April 21, 2019). Written informed consent was obtained from all patients. This manuscript adheres to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Study Design and Patients:

In this prospective, open-label, randomized controlled trial, patients undergoing general anesthesia for rigid bronchoscopy procedures (stent placement/removal, bougienage, biopsy, foreign body/mass removal) between April 2019 and August 2022 were enrolled. Inclusion criteria were: age ≥19 years and American Society of Anesthesiologists (ASA) physical status II–IV. Exclusion criteria were: dementia/cognitive impairment, pregnancy, extracorporeal membrane oxygenation (ECMO), active nasal hemorrhage/obstruction/trauma/surgery, maxillofacial trauma/basal skull fractures, rigid bronchoscopy within one month, and inability to provide informed consent.

Randomized Allocation:

Patient allocation sheets were generated by N.K. using a random number generator (Microsoft Excel 2016®) with a fixed block size of four and a 1:1 allocation ratio. Patients were assigned to the high-flow nasal oxygenation (HFNO) or standard low-flow nasal oxygenation (Standard) group by K.L. Due to the visible nature of HFNO application, blinding was not feasible; therefore, the study was conducted as an open-label trial.

Anesthesia Protocol:

Patients were monitored with electrocardiography, non-invasive blood pressure, pulse oximetry, and bispectral index (BIS). Glycopyrrolate (4 µg/kg, max 0.2 mg) was administered intravenously, and patients received 100% oxygen via mask for ≥3 minutes. Anesthesia was induced and maintained with propofol (3–4 µg/mL) and remifentanil (2–4 ng/mL) using target-controlled infusion. Rocuronium (0.6–1.0 mg/kg) was administered after loss of consciousness, followed by mask ventilation with 100% oxygen. Train-of-four (TOF) stimulation was performed to confirm neuromuscular blockade. A supraglottic airway (i-gel®) was inserted, and an arterial catheter was placed for real-time arterial pressure monitoring. Patients with dental instability were intubated. Initial ventilator settings were: tidal volume 6 mL/kg ideal body weight (IBW), respiratory rate 16 breaths/min, and positive end-expiratory pressure (PEEP) 0 cmH2O. Respiratory rate was adjusted to maintain end-tidal CO2 (EtCO2) 30–40 mmHg. Dexamethasone (0.2 mg/kg, max 10 mg) was administered. An Optiflow® device (HFNO group) or standard nasal cannula (Standard group) was applied, but oxygen delivery was withheld until apnea onset.

Apnea onset was defined as supraglottic airway/endotracheal tube removal. Baseline EtCO2 and arterial blood gas analysis (ABGA) were recorded. At apnea onset, HFNO group received 100% oxygen at 70 L/min, and Standard group at 5 L/min. Upon rigid bronchoscope insertion, ventilator circuit was connected with settings: tidal volume 12 mL/kg IBW, respiratory rate 30 breaths/min, PEEP 0 cmH2O, and oxygen flow 18 L/min (volume-controlled ventilation).

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Intraoperative BIS was maintained at 40–60. Hypotension was managed with fluids or vasopressors. TOF was monitored every 20 seconds, and rocuronium 10 mg was administered if TOF count was 1. Hypoxemia-related surgical interruption (SpO2 ≤94%) involved pausing the procedure and sealing the multifunctional head of the bronchoscope. If SpO2 ≤90%, rigid bronchoscope was removed, and rescue ventilation was provided. Surgery resumed if SpO2 >94% for ≥10 seconds. The study was terminated if recovery did not occur within 5 minutes or if arrhythmias developed.

Apnea termination was defined as supraglottic airway/endotracheal tube reinsertion. ABGA was performed immediately before mechanical ventilation (MV) resumption, and EtCO2 of the third breath was recorded. Heart rate, systolic/diastolic blood pressure, and SpO2 were documented at baseline, apnea onset, apnea termination, and lowest SpO2 during apnea. Extubation was performed per hospital protocol, and sugammadex was administered. Postoperative nosebleeds and nasal skin breakdown were assessed.

Study Endpoints:

Primary endpoint: lowest SpO2. Secondary endpoints: hypoxemia-related surgical interruptions (SpO2 ≤94%), PaO2 change rate, and PaCO2 change rate during apnea.

Sample Size Calculation:

Based on a previous study, a sample size of 25 patients per group was calculated to detect a 4.4% difference in lowest SpO2 (α=0.05, β=0.20). Accounting for 10% attrition, 28 patients per group were required (n=56).

Statistical Analysis:

Data analysis included patients with complete lowest SpO2 data. Baseline imbalances were assessed using absolute standardized difference (ASD >0.54). Continuous variables were analyzed using t-tests or Mann-Whitney tests (normality assessed by Shapiro-Wilk). Categorical variables were analyzed using chi-square or Fisher's exact tests. PaO2 and PaCO2 change rates were analyzed for the entire cohort and the subgroup without hypoxemia-related interruption. Statistical analyses were performed using SPSS 26® and R 4.3.1®. Significance was set at $P<0.05$.

Results:

Results Of the 59 patients screened for eligibility, 56 were enrolled in the study. Of the enrolled patients, two withdrew consent and one patient was excluded because of a change in the surgical plan. None of the patients were excluded because of their inability to recover oxygen saturation or the development of new arrhythmias during apnea. Consequently, 53 patients (26 in the HFNO group and 27 in the Standard group) completed the study (Fig. 1). Tables 1 and 2 present preoperative baseline characteristics and operative data, respectively. Despite the higher proportion of female patients in the HFNO group (57.7% vs. 22.2%, standardized mean difference = 0.777), the age, BMI, comorbidity profiles, and types of surgery were similar

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between the groups. Moreover, no significant between-group differences were found in HR, SBP, and DBP values immediately upon entry into the operating room, at the start of apnea, and at the end of apnea. Additionally, the anesthesia time, apnea duration, and volume of administered fluids were similar between the groups. No significant differences were found between the HFNO and Standard groups in terms of the lowest SpO2 levels (99 [98, 100]% vs. 98 [94, 100]%, P = 0.059) (Table 3). However, fewer patients in the HFNO group experienced hypoxemia-related surgical interruptions (1 [3.8%] vs. 8 [29.6%], P = 0.024), with a relative risk (95% CI) of 0.13 (0.02–0.97) (Fig. 2). Additionally, ABGA revealed an attenuated decrease in oxygen tension (4.6 [0.0, 7.9] mmHg/min vs. 10.5 [6.4, 12.9] mmHg/min, P = 0.005) during apnea in the HFNO group, compared to the Standard group (Fig. 3). This difference remained significant even when patients with hypoxemia-related surgical interruptions were excluded from the analysis. However, the rate of increase in carbon dioxide tension

Discussion:

This study demonstrated that HFNO was not beneficial for the lowest oxygen saturation during the apneic period for rigid bronchoscopy. However, hypoxemia-related surgical interruptions at a saturation level of 94% as a primary safety measure occurred less frequently with HFNO. Additionally, although the application of HFNO did not significantly alter the rate of carbon dioxide tension accumulation, it attenuated the decrease in arterial oxygen tension during the apneic period. The underlying mechanisms of HFNO include delivery of a high concentration of inspired oxygen, reduction of anatomical dead space, and generation of PEEP in the oropharyngeal cavity [10]. Among these, PEEP generation significantly depends on the respiratory state (apneic, passive, or spontaneous ventilation) and whether the mouth is open or closed [4,11,12]. Despite the lower efficacy of PEEP generation with an open mouth than that with a closed mouth [4], HFNO can still enhance oxygenation in patients with an open mouth. In patients undergoing endobronchial ultrasound and those receiving dental treatment under sedation with an open mouth, HFNO resulted in higher minimum oxygen saturation levels than standard oxygenation at 10 L/min delivered through a bite block or nasal cannula oxygenation at 5 L/min [7,13]. These two studies involved sedated but spontaneously breathing patients with open mouths. Considering that the generation of PEEP in patients with paralyzed apnea with an open mouth is negligible [4,11], the effect of PEEP is expected to be even less significant in our setting. However, disregarding the effects of PEEP, several studies have reported that HFNO aids in maintaining saturation in patients with an open mouth in an apneic state [14–16] that is not consistent with our findings; no benefit in the lowest SpO2 in the HFNO group. To enhance patient safety, we halted the procedure at an SpO2 of 94%, sealed the porthole facing the surgeon’s direction, and attempted ventilation through the side port. This approach may explain the minimal between-group difference in the lowest oxygen saturation, suggesting that the implemented safety measures could have introduced a potential bias in the primary outcome. geons. This trend was also observed in sedated dental patients, potentially influencing surgeon satisfaction [13]. Thus, despite not being a primary endpoint, this finding is clinically relevant. The rate of decrease in arterial oxygen tension during the apneic period varied with HFNO [14,17]. In a study on apneic oxygenation with HFNO in patients with morbid obesity [17], arterial oxygen tension exhibited a nonlinear decline during the apneic period, initially decreasing rapidly and then slowly. Additionally, the slope and

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inflection points varied significantly among patients. An additional factor to consider is that our study administered oxygen through a ventilating side port of the rigid bronchoscope simultaneously, and the combined effect of oxygenation with HFNO can be complex. Therefore, presenting quantitative values for the rate of decrease in arterial oxygen tension in our study may not have been clinically significant. Nevertheless, our study was conducted as a randomized controlled trial and demonstrated similar apnea durations between the groups. Therefore, the conclusion that HFNO application reduces the rate of decrease in the oxygen tension remains valid. HFNO may assist in carbon dioxide removal in patients experiencing apnea [14,18], presumably through the flow-dependent washout effect of the dead space [2,18]. However, although HFNO may effectively meet the oxygen demand in patients with apnea, it seems less capable of suppressing CO2 elevation. Compared with spontaneous breathing in adults, the use of HFNO in patients with apnea results in a doubling of CO2 accumulation over 30 min under tubeless anesthesia, indicating limited efficacy [19]. HFNO was not beneficial in reducing the PaCO2 accumulation in adult patients with morbid obesity [17], and two pediatric studies also showed no benefit in the rate of transcutaneous CO2 increase [16,20]. These two groups, characterized by high CO2 production or relatively large dead space, are populations in which the effects of CO2 flushing can be maximized. Nevertheless, because these studies did not consider the impact of CO2 as the primary outcome, there are concerns that the sample size may have been too small to detect a significant effect. Similarly, our study did not show a clear benefit with respect to CO2 clearance, probably for the same reason. Notably, a recent non-inferiority study comparing oxygen flow applications from 0.25 L/min to 70 L/min demonstrated comparable increases in the PaCO2 levels [21]. Our study has some limitations. First, the intervention was performed at an SpO2 of 94% that could have unevenly affected the lowest SpO2 between the groups. However, it is part of the standard anesthesia procedures conducted at our institution to ensure patient safety. Second, the small sample size may have led to underestimation of the effects of HFNO on CO2 accumulation. Nevertheless, our research findings can assist in calculating the sample sizes for future related studies. Third, in conventional research methodology, an ASD > 0.1 is generally considered indicative of imbalance. However, following Austin's suggestion [8], we set the ASD threshold above 0.54 to evaluate discrepancies in baseline characteristics between the two groups that may be questioned for exceeding the conventional 0.1. Nonetheless, the items in Table 1 with an ASD of 0.1 or above, including those exceeding 0.54, are unlikely to influence the study's outcomes substantially. In conclusion, in settings equipped with safety measures during mild hypoxia, HFNO was not associated with better minimum oxygen saturation levels than conventional low-flow nasal oxygenation. However, it significantly reduces hypoxemia-related surgical interruptions and thus has considerable clinical efficacy. Moreover, it attenuates the decline in PaO2 and thus has potentially greater utility for prolonged periods of apnea. Nevertheless, caution is advised regarding CO2 levels. Our research expands the operational scenarios for HFNO. The accumulation of PaCO2 in settings of prolonged apnea needs to be clarified in future studies.

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