Efficacy of different respiratory supports to prevent hypoxia during flexible bronchoscopy in patients of COPD: a triple-arm, randomised controlled trial

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ABSTRACT

Background Patients with chronic obstructive pulmonary disease (COPD) undergoing bronchoscopy for various reasons, and are at relatively higher risk of complications. This study evaluated the efficacy of non-invasive ventilation (NIV) and high-flow oxygen therapy (HFOT) compared with conventional oxygen therapy (COT) in patients with COPD undergoing bronchoscopy, to prevent hypoxia.

Methods It was a triple-arm, open-label, randomised controlled trial. Ninety patients with COPD were randomly assigned into three intervention arms in 1:1:1 ratio. The incidence of hypoxia, lowest recorded oxygen saturation measured by plethysmography (SpO2), ECG, patient vitals and comfort levels were assessed.

Results Mean age of the study population was 61.71±7.5 years. Out of 90 cases enrolled, 51, 34 and 5 were moderate, severe and very-severe COPD, respectively, as per GOLD (Global Initiative for Chronic Obstructive Lung Disease) classification. Rest of the baseline characteristics were similar. SpO2 during flexible bronchoscopy (FB) was lowest in COT group (COT: 87.03±5.7% vs HFOT: 95.57±5.0% vs NIV: 97.40±1.6%, p<0.001). Secondary objectives were similar except respiratory-rate (breaths-per-minute) which was highest in COT group (COT: 20.23±3.1 vs HFOT: 18.57±4.1 vs NIV: 16.80±1.9, p<0.001).

Whereas post FB partial pressure of oxygen in arterial blood was highest in NIV group (NIV: 84.27±21.6 mm Hg vs HFOT: 69.03±13.6 mm Hg vs COT: 69.30±11.9 mm Hg, p<0.001). Post FB partial pressure of carbon dioxide in arterial blood was similar in the three arms. Operator’s ease-of-performing procedure was least in the NIV group as assessed with Visual Analogue Scale (p<0.01). A higher number of NIV group participants reported nasal pain as compared with the other two arms (p<0.01).

Conclusion NIV and HFOT are superior to COT in preventing hypoxia during bronchoscopy, but NIV is associated with poor patient-tolerance and inferior operator’s ease of doing procedure.

Trial registration number CTRI/2021/03/032190.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity in patients undergoing diagnostic bronchoscopy. In view of common risk factors of age and smoking, COPD subjects are at higher risk of developing pulmonary malignancies and infections. In general, flexible bronchoscopy (FB) is a safe intervention with serious complications and mortality reported in only 0.08% and 0.01% cases, respectively.1 However, coexisting COPD predisposes such patients to higher risk of complications during bronchoscopy like hypoxia, hypercapnia, arrhythmias and need for periprocedural intubation.2 Apart from bronchoscopy itself, added procedures may increase the risk and severity of hypoxia like
bronchoalveolar lavage where around 100 mL of normal saline is instilled into the diseased segment, thereby hampering the gas exchange and endobronchial biopsy which has high chances of intrabronchial bleeding episodes. Oxygen supplementation during flexible bronchoscopy has been recommended to achieve oxygen saturation (SpO2) of at least 90%. Supplementation of oxygen during the procedure and the recovery period also reduces the risk of significant arrhythmias. Significant oxygen desaturation may still happen during the procedure despite the use of supplemental oxygen, likely due to coexisting pulmonary illness or sedation administered or both. Therefore, additional strategies like non-invasive ventilation (NIV) and high flow oxygen therapy (HFOT) may be able to prevent worsening of hypoxia and avoid complications.

Among patients with severe emphysema, bronchoscopy can lead to worsening of air trapping due to the increase in functional residual capacity especially when scope is inserted via transnasal route. Positive-pressure ventilation may counteract the intrinsic positive end-expiratory pressure. The utility of NIV during bronchoscopy has been evaluated previously by various investigators and was found to be associated with a lower incidence of complications. Majority of these studies have included cases who had high probabilities of periprocedural intubation, like hypercapnic patients with COPD, or patients with coexisting community-acquired pneumonia. NIV was found to be superior to conventional oxygen supplementation for preventing gas exchange deterioration during FB in patients with respiratory failure.

The argument in the favour of use of HFOT, to support respiration during FB, comes from its ability to generate a positive expiratory airway pressure based on its high delivery flow rate, size of the cannula in relation to the nostrils, decreased dead space and enhancing the alveolar ventilation. It has also been shown to improve secretion clearance and bronchoconstriction by using heated and humidified gas. In non-hypercapnic respiratory failure cases HFOT has superior tolerability compared with NIV. During FB or endobronchial ultrasound (EBUS) in at-risk patients, HFOT was associated with a significantly lower drops in oxygen saturation.

Both NIV and HFOT require additional equipment and expertise during the procedure. Additionally, the use of NIV and HFOT may be associated with significant discomfort to the patient and inconvenience to the operator. In spite of their prophylactic use in high-risk cases who are undergoing bronchoscopy, there is no head-to-head comparative evidence in support or against this practice.

Therefore, we designed a triple arm study to evaluate the utility of three modes of oxygenation/respiratory support among high-risk COPD cases undergoing flexible bronchoscopy as an outpatient procedure.

**MATERIAL AND METHODS**

**Study setting**

The study was conducted at the bronchoscopy suite of the Pulmonary and Critical Care Medicine Department at a tertiary care university teaching hospital of northern India from April 2021 to December 2021. The trial was registered at the Clinical Trials Registry of India.

**Patient and public involvement**

Patients and public were not involved in the study design.

**Study design**

It was a hospital-based triple arm, single centre, randomised control trial. Primary objective of the study was to compare the incidence of hypoxia defined as SpO2<94% (cut-off was chosen based on institutional practice) lasting for 10s or more measured non-invasively by continuous SpO2 (using Nellcor bedside pulse oximeter by Medtronic) monitoring, among the three arms, during the bronchoscopy in patients with COPD. Secondary endpoints included comparing of frequencies of cardiorespiratory adverse events during bronchoscopy (heart rate, blood pressure, arrhythmias, any evidence of ischaemia, respiratory rate), arterial blood gas parameters, both at baseline and immediate after bronchoscopy, patient-related comfort and operator’s ease-of-doing procedure during bronchoscopy.

**Participants**

All subjects between the age of 40 and 75 years, undergoing bronchoscopy were eligible for participation. Only diagnosed stable COPD cases who were planned for flexible bronchoscopy in the department were considered for screening. Diagnosis of COPD was made using spirometry criteria (presence of post-bronchodilator forced expiratory volume in 1 s/forced vital capacity (FEV1/FVC)<0.70) according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) 2021 guidelines with appropriate symptoms and exposure to noxious stimuli. Written informed consent was taken from all screened patients in a language they could understand. We excluded cases with nasal deformities, myocardial infarction in past 3 months, hypercapnia in baseline blood gas analysis. EBUS guided trans-bronchial needle aspiration (TBNA) cases were also excluded from the study as it required the placement of mouth guard for an oral access which interfered with the application of NIV mask. Additionally, we also excluded cases with central airway obstruction, haemodynamic instability and who were already on supplemental oxygen therapy at baseline.

**Randomisation**

All COPD cases undergoing bronchoscopy were screened for study participation. Those who satisfied the inclusion and exclusion criteria were enrolled after informed consent. Subsequently, patients were randomly assigned...
into one of the three intervention arms (conventional oxygen therapy (COT), NIV and HFOT group) in a ratio of 1:1:1. Randomisation was done in blocks of variable sizes, with a minimum size of three and a maximum size of nine with an increment value of one, in three arms with equal distribution. Randomisation sequence was computer-generated by an independent expert and kept at the study site in sealed opaque envelopes which were opened just prior to the procedure. All nurses and other research staff were blinded to the randomisation schedule and block sizes.

Due to the nature of the intervention, participants, operators doing bronchoscopy and assisting nursing staff could not be blinded to the group assignments.

Intervention
All bronchoscopies were performed while patients were in a semi-recumbent supine position. Lidocaine-spray (10%) and diluted lidocaine solution (2%) were used for topical anaesthesia of the nasopharynx and tracheobronchial tree, respectively. Bronchoscopy was performed using a flexible video bronchoscopy system (Olympus EVIS EXERA III model BF-1T180 video bronchoscope). Bronchoscopy was performed via the nasal route in all study participants. Short-term sedation was administered in all patients according to their respiratory and haemodynamic situations. Sedation and analgesia were induced using 1 mg midazolam and 50 mcg fentanyl at the beginning of the procedure and top-up boluses were given as per the orders of the operator. A Richmond agitation sedation scale score of –1 to –2 was targeted. All patients were monitored using standard monitoring and alarm systems which include SpO₂, blood pressure, heart rate and ECG.

Conventional oxygen was delivered through the nasal cannula at the rate of 2–6 litres per minute (LPM) adjusted to maintain SpO₂ of ≥94%, starting 5 min before the procedure and continuing for 5–10 min after the procedure. During procedure titration was done as and when indicated.

Patients assigned to the NIV group were connected to the ventilator (Bellavista 1000 ICU NIV) through a clear full-face mask secured to the patient’s face with elastic straps. NIV was initiated at an inspiratory oxygen fraction (FiO₂) of 30%, starting 5 min before the procedure and continued for 5–10 min after the procedure. Ventilatory parameters were set at a positive end-expiratory airway pressure of 4 cm H₂O and pressure support of 8 cm H₂O, adjusted to maintain an SpO₂ of ≥94%. The bronchoscope was inserted through a dual-axis hole with rubber seal made in the mask, to prevent leaks (developed in-house).

HFOT was delivered via a dedicated high-flow delivery system (Bellavista 1000 ICU) having a heated humidifier system, with a medium-size adult nasal cannula as a patient interface, starting 5 min before and continued for 5–10 min after the procedure. Oxygen flow was started at the rate of 40 LPM, and FiO₂ was initiated at 30%. Both parameters were adjusted to maintain an SpO₂ of ≥94%.

Data collection
Prior to the randomisation all participants underwent a detailed history and physical examination, including demographic and anthropometric parameters measurement as well as routine baseline investigations like complete haemogram, coagulation profile, kidney function test, liver function test, random blood sugar, ECG and chest radiograph. Data with regards to COPD diagnosis and severity was also collected.

Blood samples for arterial blood gases were drawn from the radial artery at baseline and just after completion of bronchoscopy. Blood pressure, heart rate, respiratory rate and oxygen saturation were recorded by pulse oximetry (SpO₂) and constantly monitored throughout the procedure. Continuous ECG monitoring was done to record arrhythmias and cardiac complications. For the primary outcome, the number of episodes of hypoxia (SpO₂ <94%) lasting for 10 s or more were counted and recorded manually in paper format during bronchoscopy. To maintain safety, on recommendations of the institutional review board, all hypoxias with SpO₂ readings below 88% lasting for greater than 30 s were treated as rescue criteria. Such events were managed by increasing FiO₂ or the oxygen flow or both depending on the type of intervention.

To assess patient comfort and operator’s ease-of-doing-procedure with the intervention, Visual Analogue Scale of 0–100 points was used where higher points indicated maximum discomfort or least-ease. A questionnaire was also administered to all patients to evaluate acceptance and anxiety related to the procedure. All these assessments were conducted after about 2 hours of recovery to allow the effects of sedatives to wear off.

Statistical analysis
Using the definition of hypoxia to be SpO₂ <94%, it was estimated that 50% of the subjects with compromised lung functions undergoing bronchoscopy with COT will experience one or more events of hypoxia. Assuming that with the use of HFOT or NIV the incidence of hypoxia can be decreased to 20%, we calculated that 38 cases in each arm will be needed to achieve 80% power and 0.05 alpha error for detection of the dichotomous endpoint of hypoxia.

Data was initially collected in paper format and later entered and coded using Microsoft 365 office Excel, and statistical analysis was carried out using the statistical package for social sciences (SPSS) by IBM V.26.0. Continuous variables were summarised using summary statistics (mean, SD, median, IQR, minimum and maximum) by treatment groups. Categorical variables were presented using frequencies and percentages. The one-way analysis of variance method was used to compare the means for
continuous variables, and $\chi^2$ test was used to compare categorical variables among the three groups. A p value of <0.05 was considered as statistically significant.

RESULTS

Over a period of 9 months from April 2021 to December 2021, 205 patients underwent bronchoscopy of which 137 were diagnosed to have COPD. There were multiple interruptions in the bronchoscopy services due to second and third wave of COVID-19 pandemic. Ninety eligible consenting patients with COPD were randomised in either of the three arms (figure 1). Patients enrolled in the study had age ranging from 40 to 74 years with mean age of 61.71±7.5 years. Mean body mass index of the study participants was 20.81±3.1 kg/m². Eighty-one (90%) participants had a history of smoking, out of which 57 were current, and 23 were former smokers. Nine (10%) participants were never smokers; all of them were women having a history of biomass fuel exposure during household activities (table 1). Mean post-bronchodilator FEV1/FVC (%) was 58.91±8.3 (p=0.86). Of all the recruited cases 51, 34 and 5 had moderate, severe and very severe COPD, respectively. The most common indication for bronchoscopy was suspected lung cancer (n=42, p=0.39) followed by evaluation of haemoptysis (n=22, p=0.15), unexplained cough (n=14, p=0.91) and non-resolving pneumonia (n=12, p=0.13). Baseline vitals and blood gas parameters were comparable among study groups. Endobronchial biopsy was the most common procedure performed among the study population (endobronchial biopsy, 44 (48.9%) cases), followed by non-EBUS TBNA, (27 (30%) cases) and bronchoalveolar lavage (19 (21.1%) case) (p=0.015).

Baseline data of vitals and arterial blood gases (ABG) parameters were similar in the three groups. The mean of lowest recorded SpO2 value was least in COT group (COT: 87.03±5.7% vs HFOT: 95.57±5.0% vs NIV: 97.40±1.6%, p<0.001) (figure 2). The average heart rate
during bronchoscopy was similar in the three groups. The average respiratory rate during a bronchoscopy was 18.53±3.4 per minute (COT: 20.23±3.1, HFOT: 18.57±4.1, NIV: 16.8±1.9, p<0.01). Average mean blood pressure and systolic blood pressure during FB were similar in the three groups. Number of patients with hypoxia events (defined by SpO2<94% lasting for 10 s or more) was highest among COT group subjects (27, 90%), followed by HFOT group (7, 23.3%) and NIV group patients (2, 6.7%) (p<0.01). Post bronchoscopy PaO2 was numerically highest in NIV group subjects (COT: 69.30±11.9 mm Hg, HFOT: 69.03±13.6 mm Hg, NIV: 84.27±21.2 mm Hg, p<0.01). Post FB pH and partial pressure of carbon dioxide in arterial blood (PaCO2) was similar in the three groups (table 2).

Evaluation of secondary outcomes demonstrated that average time taken for the procedure was similar in the three groups (COT: 18.43±6.6 min, HFOT: 19.00±7.4 min, NIV: 16.87±5.4 min, p=0.42). For conscious sedation, HFOT group participants had received a higher dose of midazolam as well as fentanyl (p=0.008 and p=0.04, respectively) during the procedure (table 2).

The median score for patient discomfort was 0.00 with IQR of 0.0–10.0 for all study participants, which was not significantly different among study groups (COT: 0.00 IQR - 0.0–6.2, HFOT: 0.00 IQR - 0.0–0.0, NIV: 0.00 IQR - 0.0–0.0, p=0.67). The median score of participant’s anxiety was 2.5 with IQR of 0.0–15.0, which was also not significantly different among study groups (COT: 0.00 IQR - 0.0–15.0, HFOT: 0.00 IQR - 0.0–10.0, NIV: 0.00 IQR - 0.0–0.0, p=0.67). Operator’s ease-of-doing-procedure during bronchoscopy was lower in the NIV arm as compared with that in HFOT and COT arms (COT: 0.00 IQR - 0.0–0.0, HFOT: 0.00 IQR - 0.0–0.0, NIV: 17.5 IQR - 15.0–20.0, p<0.01) (table 3).

Nose pain during a bronchoscopy was assessed using an ordinal variable ((1) none (2) mild pain (3) moderate pain (4) severe pain). Majority of cases experienced no pain, but mild pain was reported at a higher frequency by participants of NIV group (COT: 4, HFOT: 2, NIV: 14 p<0.01). Severity of

### Table 1 Baseline anthropometric, clinical and procedural characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>COT n=30</th>
<th>HFOT n=30</th>
<th>NIV n=30</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) mean±SD</td>
<td>59.93±8.7</td>
<td>62.50±7.4</td>
<td>62.70±6.4</td>
<td>0.29</td>
</tr>
<tr>
<td>Sex n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (86.7)</td>
<td>24 (80.1)</td>
<td>26 (86.7)</td>
<td>0.71</td>
</tr>
<tr>
<td>Female</td>
<td>4 (13.2)</td>
<td>6 (20.1)</td>
<td>4 (13.2)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²) mean±SD</td>
<td>20.26±2.7</td>
<td>20.49±2.6</td>
<td>21.69±3.7</td>
<td>0.15</td>
</tr>
<tr>
<td>Comorbidities n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0 (0)</td>
<td>2 (6.6)</td>
<td>1 (3.3)</td>
<td>0.36</td>
</tr>
<tr>
<td>Systemic HTN</td>
<td>1 (3.3)</td>
<td>0 (0)</td>
<td>3 (9.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>CAD</td>
<td>2 (6.6)</td>
<td>2 (6.6)</td>
<td>2 (6.6)</td>
<td>1.0</td>
</tr>
<tr>
<td>Smoking history n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>19 (63.3)</td>
<td>20 (66.6)</td>
<td>18 (60)</td>
<td>0.72</td>
</tr>
<tr>
<td>Former smoker</td>
<td>8 (26.4)</td>
<td>7 (23.1)</td>
<td>9 (30)</td>
<td>0.79</td>
</tr>
<tr>
<td>Never smoker</td>
<td>3 (9.9)</td>
<td>3 (9.9)</td>
<td>3 (9.9)</td>
<td>1.0</td>
</tr>
<tr>
<td>Smoking index (number of bidi/cigarettes smoked per day multiplied by number of years smoked)</td>
<td>1339.44±597.1</td>
<td>1199.63±489.3</td>
<td>1305.56±602.1</td>
<td>0.64</td>
</tr>
<tr>
<td>PFTs FEV1/FVC post BDR</td>
<td>59.38±9.9</td>
<td>59.10±7.2</td>
<td>58.26±7.9</td>
<td>0.87</td>
</tr>
<tr>
<td>FEV1 observed (L)</td>
<td>1.48±0.5</td>
<td>1.59±0.5</td>
<td>1.48±0.5</td>
<td>0.62</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>52.10±14.5</td>
<td>54.73±10.9</td>
<td>53.27±14.2</td>
<td>0.74</td>
</tr>
<tr>
<td>Baseline SpO2</td>
<td>97.56±2.0</td>
<td>97.28±1.9</td>
<td>98±1.6</td>
<td>0.84</td>
</tr>
<tr>
<td>Clinical presentation n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>5 (16.5)</td>
<td>6 (19.8)</td>
<td>11 (36.6)</td>
<td>0.15</td>
</tr>
<tr>
<td>Unexplained chronic cough</td>
<td>5 (16.5)</td>
<td>5 (16.5)</td>
<td>4 (13.2)</td>
<td>0.91</td>
</tr>
<tr>
<td>Non-resolving pneumonia</td>
<td>7 (23.1)</td>
<td>2 (6.6)</td>
<td>3 (9.9)</td>
<td>0.13</td>
</tr>
<tr>
<td>Suspected lung cancer</td>
<td>13 (43.2)</td>
<td>17 (56.7)</td>
<td>12 (39.9)</td>
<td>0.39</td>
</tr>
<tr>
<td>Type of procedure n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EBB</td>
<td>16 (53.4)</td>
<td>10 (33.3)</td>
<td>18 (60)</td>
<td>0.015</td>
</tr>
<tr>
<td>Non-EBUS TBNA</td>
<td>7 (23.1)</td>
<td>16 (53.4)</td>
<td>4 (13.2)</td>
<td></td>
</tr>
<tr>
<td>BAL</td>
<td>7 (23.1)</td>
<td>4 (13.2)</td>
<td>8 (26.7)</td>
<td></td>
</tr>
</tbody>
</table>

BAL, broncho-alveolar-lavage; BDR, bronchodilator response; BMI, body mass index; CAD, coronary artery disease; COT, conventional oxygen therapy; EBB, endobronchial biopsy; EBUS, endobronchial ultrasound; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; HFOT, high flow oxygen therapy; HTN, hypertension; NIV, non-invasive ventilation; PFTs, pulmonary function tests; SpO₂, oxygen saturation measured by plethysmography; TBNA, transbronchial needle aspiration.
cough frequency during a bronchoscopy was also statistically similar in the three groups ($p=0.37$) (table 3).

Among the analysis of adverse events, none was reported at significantly different frequencies among the three groups (table 4). No grade 3 or higher adverse event was reported. None of the study subjects required hospitalisation due to respiratory failure. We also conducted a subgroup analysis considering only severe and very severe COPD cases, lowest recorded SpO$_2$ was least in the COT group (COT: 84.60±5.8, HFOT: 97.00±2.3, NIV: 97.80±0.63, $p<0.001$) and the number of subjects experiencing hypoxia events were more in

![Box plot presenting lowest recorded SpO$_2$ values (y axis) during the bronchoscopy procedure for the three arms (x axis). FOB, Fiber-optic bronchoscopy; SpO2, oxygen saturation measured by plethysmography.](image)

**Table 2** Primary and secondary endpoints of the study, expressed as mean and SD

<table>
<thead>
<tr>
<th>Descriptive variables</th>
<th>COT n=30</th>
<th>HFOT n=30</th>
<th>NIV n=30</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest SpO$_2$ (%)</td>
<td>87.03 (84.9–89.16)</td>
<td>95.57 (93.7–97.4)</td>
<td>97.40 (96.8–98.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HR (per minute)</td>
<td>104.63 (96.8–112.5)</td>
<td>97.97 (91.1–104.8)</td>
<td>98.97 (95.1–102.8)</td>
<td>0.27</td>
</tr>
<tr>
<td>RR (per minute)</td>
<td>20.23 (19–21.4)</td>
<td>18.57 (17.0–20.1)</td>
<td>16.8 (16.1–17.5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BP (mean) mm Hg</td>
<td>104.20 (98.5–109.9)</td>
<td>98.07 (91.0–105.1)</td>
<td>96.23 (92.1–100.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>Systolic BP mm Hg</td>
<td>137.20 (129.8–144.6)</td>
<td>133.37 (123–143.8)</td>
<td>131.30 (123.5–139.1)</td>
<td>0.61</td>
</tr>
<tr>
<td>PaO$_2$ (mm Hg) baseline</td>
<td>70.63±12.1</td>
<td>69.80±9.0</td>
<td>68.90±8.6</td>
<td>0.80</td>
</tr>
<tr>
<td>PaCO$_2$ (mm Hg) baseline</td>
<td>34.73±6.4</td>
<td>34.93±5.4</td>
<td>36.50±5.4</td>
<td>0.43</td>
</tr>
<tr>
<td>PaO$_2$ (mm Hg) post-bronchoscopy</td>
<td>69.30 (64.8–73.7)</td>
<td>69.03 (64–74.1)</td>
<td>84.27 (76.4–92.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PaCO$_2$ (mm Hg) post-bronchoscopy</td>
<td>42.73 (37.8–47.6)</td>
<td>40.47 (36.0–44.9)</td>
<td>40.33 (37.1–43.6)</td>
<td>0.66</td>
</tr>
<tr>
<td>FB duration (minutes)</td>
<td>18.43 (16–20.9)</td>
<td>19.00 (16.2–21.8)</td>
<td>16.87 (14.8–18.9)</td>
<td>0.42</td>
</tr>
<tr>
<td>Midazolam (mg)</td>
<td>1.57 (1.3–1.9)</td>
<td>1.87 (1.5–2.2)</td>
<td>1.20 (1.0–1.4)</td>
<td>0.008</td>
</tr>
<tr>
<td>Fentanyl (mcg)</td>
<td>66.67 (56.8–76.6)</td>
<td>81.83 (69.3–94.3)</td>
<td>64.17 (54.8–73.6)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

BP, blood pressure; COT, conventional oxygen therapy; FB, during flexible bronchoscopy; HCO$_3^-$, post procedure bicarbonate levels in arterial blood; HFOT, high flow oxygen therapy; HR, heart rate; NIV, non-invasive ventilation; PaCO$_2$, post procedure partial pressure of carbon dioxide in arterial blood; PaO$_2$, post procedure partial pressure of oxygen in arterial blood; RR, respiratory rate; SpO$_2$, oxygen saturation measured by plethysmography.
COT arm as compared with the HFOT and NIV arms (COT=15, HFOT=2, NIV=0, p<0.001).

Following the final analysis, it was explored whether the intervention was hampering the yield of the procedure. As it was not a prespecified outcome we did a retrospective analysis of the records to find the number of participants requiring repeat procedures. Seven cases required one or more non-bronchoscopic intervention whereas 16 underwent repeat FB. Number of cases with failed first FB procedure was highest in NIV arm (NIV: 8, HFNC: 5, COT: 3, p=0.203) as compared with the other two groups.

**DISCUSSION**

In this study we compared three different modes of respiratory support for COPD cases undergoing bronchoscopy and found that NIV and HFOT are associated with significantly lower episodes of hypoxia, but NIV was associated with lower operator’s ease-of-doing-procedure.

Bronchoscopy is known to be associated with several risk factors for hypoxia like bronchospasm, bleeding, cough and laryngospasm. Additionally, procedures done during bronchoscopy like endobronchial biopsy,
bronchoalveolar lavage and transbronchial lung biopsy further worsen the gas exchange. The impact of these factors is disproportionately elevated in cases with coexisting COPD. To overcome the risk of hypoxia and hence the cardiac complications like arrhythmias, COT is advised but despite this hypoxia has been reported in up to 32% cases, depending on the definition of hypoxia chosen. Indian guidelines on diagnostic flexible bronchoscopy advice for the use of NIV to overcome the risk of hypoxia in cases with acute respiratory distress syndrome. It also mentions that COPD cases are at higher risk of desaturations during the procedure but no recommendations with regards to the use of NIV or HFOT have been made in this regard.

In this first head-to-head comparison of the three modalities, we demonstrated that NIV is associated with significantly lower risk of hypoxia, but at the same time it is accompanied with poor operator’s ease-of-doing procedure which can limit its generalisability, procedure yield and patient safety. One of the factors contributing to the higher failure rates in NIV arm could have been the fact that it is technical challenging to insert bronchoscope from channel of the face mask and manipulate it to the patient’s nostril. Also, the assessment of patient discomfort or sedation level is difficult with mask on. HFOT, in this regard, was found to be superior to COT in terms of hypoxia-events and also performed better over NIV in terms of operator’s ease. Our findings also support the use of HFOT over NIV in COPD cases due to the better procedure yield with HFOT as subjects in NIV arms were subjected to higher number of repeat procedures and additional procedures further augment the risk of complications, cost and hospital visits and delay in treatment.

Most study participants suffered from moderate to very severe COPD and the most frequent procedure done was endobronchial biopsy which itself is associated with higher risk of bleeding and hypoxia, as compared with other procedures like bronchoalveolar lavage. This improves the generalisability of the study. Despite the theoretical risk of hypercapnia in COPD cases, especially during sedation, none of our patient had any clinically significant elevation in the levels of PaCO₂, these findings are similar to the previous studies.

Time taken for the procedure was also similar in the three groups which increases the applicability of the modalities, more so in outpatient procedures like FB. All the procedures in our study were performed with the use of conscious sedation and analgesia to improve patient acceptance and comfort. Even though the dose of sedative agents used was higher in the HFOT group, the comfort levels did not differ among the three arms.

Higher incidence of nose pain reported in the NIV group could have been due to need of manipulation of the scope to reach up to the nostrils from the sealed opening of the face mask. None of the other adverse events reported in our study was significantly different in the three groups, which probably is due to intensive screening, and monitoring of the cases.

Despite the novelty and design of the study there were some significant limitations with our study. First, it was a single centre experience and the practices at other centres might vary. Second, we were not able to reach up to the estimated sample size. COVID-19 pandemic had repeatedly halted the routine bronchoscopy services as majority of times the procedure room was closed, or the oxygen supply was directed to high dependency units but despite this we were able to demonstrate a statistically significant difference in the primary outcome. Third, we used an in-house modified NIV mask to perform the procedure and maintain the air seal, but it was not standardised or externally validated. But as we did not face any ventilatory issues or major leaks during the procedure, it suggests the NIV mask being in-house had an insignificant impact on the overall outcome. Last the measurement of real time capnometry during the procedure might have added value to the data collected which we did not do as the instrument required for the same was not available at the study site. We did use pre-procedure and post-procedure ABG values to account for the same. Additionally, the number of comorbidities reported in our study are less for a cohort of COPD subjects. One of the important contributing factors towards this could have been that we did not systematically screen for other comorbidities and lack of awareness is common among the Indian rural population to which most of the study subjects belonged.

In conclusion, NIV and HFOT were found to be superior to conventional oxygen therapy for oxygen supplementation during bronchoscopy procedures in patients with COPD, but NIV is associated with poor operator’s ease-of-doing procedure. HFOT may be recommended to prevent hypoxia without compromising on the patient’s comfort or the operator’s ease. Multicentric randomised controlled trials with a larger sample size may be needed to further strengthen our research findings.
REFERENCES