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Measurement of Combined Oximetry and Cutaneous Capnography During Flexible Bronchoscopy

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Running title: Monitoring during bronchoscopy

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ABSTRACT

Aims: To assess the feasibility of measuring combined oximetry (SpO_2) and cutaneous carbon dioxide tension ($PcCO_2$) to monitor ventilation and quantify change in $PcCO_2$ during bronchoscopy.

Methods: Combined SpO_2 and $PcCO_2$ were measured at the ear lobe in 114 patients. In four patients the ear clip slipped and hence excluded. 11 patients had artifacts with SpO_2 recordings and hence SpO_2 was analyzed in 99 patients. Spirometry data were available in 77 patients. Multivariate analysis of covariance and logistic regression were used for statistical analyses.

Results: Mean baseline $PcCO_2$ was 36±8 mm Hg. Mean rise in the $PcCO_2$ during bronchoscopy was 9.5±5.3 mm Hg. Mean $PcCO_2$ at the end of bronchoscopy was 44±9 mm Hg. Baseline $PcCO_2$ and the lowest SpO_2 were significantly associated with peak $PcCO_2$ and the change in $PcCO_2$ during bronchoscopy. Risk of significant hypoxemia (≤90%) was lower for a higher baseline SpO_2. Peak $PcCO_2$ was directly associated with significant hypoxemia. There was no significant association in the baseline $PcCO_2$, peak $PcCO_2$, baseline SpO_2 or the lowest SpO_2 comparing patients with and without COPD.

Conclusion: It is feasible to measure combined oximetry and $PcCO_2$ effectively to monitor ventilation during flexible bronchoscopy.

INTRODUCTION

Flexible bronchoscopy under local anesthesia and sedation is widely performed to diagnose and manage a variety of lung diseases. The purpose of sedation is to facilitate examination of the tracheobronchial tree, carry out the necessary diagnostic or interventional procedures and provide patient comfort [1-4]. Oximetry measures the oxygenation of blood and can detect hypoxemia but it cannot detect hypercarbia and hence the adequacy of ventilation [5]. When bronchoscopy is performed under conscious sedation without supplemental oxygen, oxygen desaturation will occur rapidly giving a good indication of ventilatory status. It has been recently shown that pulse oximetry is a useful tool to assess ventilatory abnormalities, but only in the absence of supplemental inspired oxygen [6]. However, most centers routinely offer oxygen supplementation to patients during flexible bronchoscopy [7]. Due to the '*S*' shape curve of the oxygen dissociation curve, in such situations the alveolar carbon dioxide tension will have to rise further before significant hypoxemia is manifested [8]. The British Thoracic Society (BTS) guidelines recommend that oxygen supplementation should be used to achieve an oxygen saturation of at least 90% to reduce the risk of significant arrhythmias during the procedure and also in the postoperative recovery period [2]. Furthermore, they suggest that care should be taken, however, to be alert to signs of respiratory failure in patients on oxygen supplementation who may have "safe" oximetry readings but who may be developing carbon dioxide retention [2]. Therefore, a reliable surrogate of arterial

carbon dioxide tension measured non-invasively is required as it might enhance patient safety during flexible bronchoscopy.

In intubated patients or under stable conditions without oral leakage, end tidal carbon dioxide tension has a good correlation with arterial carbon dioxide tension [9, 10]. However, during endoscopy procedures under sedation, regular breathing is often disturbed by moving, coughing or changes between nose and mouth ventilation causing leakage and therefore artifacts or misinterpretation of data acquired with end tidal carbon dioxide measurements and these problems often restrict the use of side-stream capnography in clinical practice [10]. Measurement of cutaneous carbon dioxide tension ($PcCO_2$) with a digital sensor has been reported recently [11]. The $PcCO_2$ values have been shown to have a good correlation with arterial blood gas measurements [12, 13]. A rise in $PcCO_2$ measurement has been reported during medical thoracoscopy and colonoscopies [10, 13]. We undertook this study to assess the feasibility of measuring combined SpO_2 and $PcCO_2$ at the ear lobe to monitor ventilation and quantify the degree of change in $PcCO_2$ during flexible bronchoscopy under local anesthesia and sedation.

PATIENTS AND METHODS

Combined oximetry and $PcCO_2$ (Sentec AG, Switzerland) were prospectively measured in 114 patients undergoing flexible bronchoscopy in an observational fashion. The combined cutaneous digital sensor was placed on earlobe of all patient's prior to the procedure and was removed when the patient left the bronchoscopy suite.

Flexible bronchoscopy was performed under local anesthesia and sedation. Combined sedation was achieved with intermittent boluses of intravenous midazolam and 5 mg of hydrocodone [1]. All patients received supplemental nasal oxygen at 2 to 4 liters per minute. Significant hypoxemia (spO2 ≤ 90%) during flexible bronchoscopy was successfully treated with jaw support or nasopharyngeal tube insertion [7]. The duration of bronchoscopy was calculated from the administration of sedation until the flexible bronchoscope was removed from the tracheobronchial tree. Bronchoalveolar lavage was performed in 57 patients, endobronchial biopsy in 32 patients, bronchial washings in 19 patients, transbronchial needle aspiration in 18 patients, transbronchial biopsy in 15 patients and bronchial brushings in 11 patients. Spirometry data prior to bronchoscopy was available in 77 patients. Patients with chronic obstructive pulmonary disease were defined as per the American Thoracic Society / European Respiratory Society guidelines [14].

Statistical analysis:

Data are presented as mean (± standard deviation). Multivariate analysis were performed using analysis of covariance to examine peak $PcCO_2$, change in $PcCO_2$ from baseline and change in $PcCO_2$ adjusted for baseline $PcCO_2$ during bronchoscopy as dependent factors versus patient age, dose of midazolam (mg/kg), baseline $PcCO_2$ and lowest oxygen saturation as independent factors. Only scatterplots are provided for the association of peak $PcCO_2$ and change in $PcCO_2$ with duration of procedure. Analysis of variance was used to examine the association between the type of sampling procedure during bronchoscopy with the change in $PcCO_2$. Logistic regression was used to examine independent factors associated with significant hypoxemia ($SpO_2 \leq 90\%$) and COPD. The students t test was used to compare significance between the baseline and peak $PcCO_2$ during bronchoscopy and $PcCO_2$ at lowest SpO_2 and the peak $PcCO_2$ during bronchoscopy.

RESULTS

The mean duration of the procedure was 19 minutes (±10). In four patients the ear clip slipped off from the earlobe due to patient movement and hence these patients were not included in the analysis as the equilibration had to be achieved again and there was loss of data recording points. Therefore data analysis was performed in 110 patients (M:F, 70:40; mean age 61 years [±15]). In 11 patients the oxygen saturation was not included in the analysis due to artifacts produced whilst recording by coughing or a low signal. Therefore, $PcCO_2$ measurements for the purposes of data analysis were available in 110 patients and both oximetry and $PcCO_2$ measurements in 99 patients. Therefore, for multivariate analysis only data from patients with both oximetry and $PcCO_2$ were used. Hypoxemia during the procedure was successfully treated with jaw support or nasopharyngeal tube insertion in all patients. None of the patients developed severe respiratory depression necessitating sedation reversal medication or abandoning the procedure half way without completion. The indications for bronchoscopy were suspected lung malignancy 42 (38%) patients; radiological infiltrates 31 (28%) patients, hemoptysis 9 (8%), suspected interstitial lung disease 9 (8%), suspected sarcoidosis 5(5%), post airway stent inspection 4 (4%), cough 3 (3%), post lung surgery 2 (2%) and evaluation of post tracheostomy tracheal stenosis, larngeal papilloma and mucociliary dyskinesia one patient each.

The mean dose of midazolam administered was 0.06 mg/kg (±0.03). The mean baseline $PcCO_2$ was 36 mm Hg (±8) and the mean peak $PcCO_2$ was 46 mm Hg (±9) ($p<0.0001$). The peak $PcCO_2$ during the procedure was recorded at a mean duration of 13 minutes (±7) minutes. The mean rise in the $PcCO_2$ during the procedure was 9.5 mm Hg (±5.3). The mean $PcCO_2$ at the end of the procedure was 44 mm Hg (±9) and at the time of removal of the sensor was 44 mm Hg (±9). A rise in $PcCO_2$ was observed in all patients except one. The baseline SpO_2 was 97% (±2). The lowest mean SpO_2 was 93% (±4). The lowest SpO_2 in patients who desaturated from their baseline SpO_2 measurement was recorded at a mean duration of 9 minutes (±6). The mean $PcCO_2$ measured at lowest SpO_2 was 44 mm Hg (±14) and the mean peak $PcCO_2$ recorded subsequently was 51 mm Hg (±13) ($p<0.0001$).

Factors associated with peak $PcCO_2$ and change in $PcCO_2$ during the procedure

The peak $PcCO_2$ during the procedure was significantly associated with the baseline $PcCO_2$ ($p<0.0001$) and lowest SpO_2 ($p=0.016$). A higher baseline $PcCO_2$ was associated with the peak $PcCO_2$ ($\beta = 0.8$). However, there was an inverse relationship of the lowest SpO_2 with the peak $PcCO_2$, thus, the manifestation of a lower SpO_2 was associated with the peak $PcCO_2$ ($\beta = -0.4$). Change in $PcCO_2$ (difference in baseline and peak $PcCO_2$) was also significantly associated with baseline $PcCO_2$ ($p=0.024$) and lowest SpO_2 ($p=0.016$). Both these factors had an inverse relationship with the change in $PcCO_2$, thus,

patients manifesting a lower SpO_2 (β = -0.4) and a lower baseline (β = -0.2) would have a higher change in $PcCO_2$. Similarly, the change in $PcCO_2$ divided by the baseline $PcCO_2$ (adjusting the change in $PcCO_2$ for baseline) was also significantly associated with baseline $PcCO_2$ ($p<0.0001$) and lowest oxygen saturation ($p=0.016$). These analysis highlight that the baseline $PcCO_2$ and the lowest SpO_2 are linked to the peak $PcCO_2$ as well as the rise in $PcCO_2$ during bronchoscopy. There was no significant relationship of age and midazolam dosage with the peak $PcCO_2$, change in $PcCO_2$ and the change in $PcCO_2$/baseline $PcCO_2$. There was also no association of peak $PcCO_2$ and change in $PcCO_2$ with the procedure duration (Figure 1A and B). This factor was not included in the multivariate analysis as there seem to be two groups of patients, one who have a higher peak $PcCO_2$ and change in $PcCO_2$ with a short duration of procedure and the other group of patients who have a higher peak and change in $PcCO_2$ with a longer duration of procedure. To assess the influence of procedure on change in $PcCO_2$ and change in $PcCO_2$/baseline $PcCO_2$, these were categorized as follows: a. transbronchial biopsy only and transbronchial needle aspiration only (n=10), b. bronchoalveolar lavage only (n=42), c. transbronchial biopsy, transbronchial needle aspiration, bronchoalveolar lavage in combination of two or more (n=16) and d. bronchial washings and/or endobronchial biopsy (n=42). There was no significant association between the procedures performed and change in $PcCO_2$ ($p=0.3$) and change in $PcCO_2$/baseline $PcCO_2$ ($p=0.2$) during bronchoscopy.

Factors associated with significant hypoxemia (SpO_2 ≤ 90%) and COPD

Fifteen patients had significant hypoxemia during bronchoscopy. A lower baseline SpO_2 (p=0.003, odds ratio 0.6) and the peak $PcCO_2$ (p=0.041, odds ratio 1.1) were significantly associated with significant hypoxemia. This means that with a higher baseline SpO_2 the risk of significant hypoxemia is lower and the peak $PcCO_2$ is directly associated with significant hypoxemia. Patient age, duration of procedure, midazolam dose and baseline $PcCO_2$ were not associated with significant hypoxemia. There were 25 patients with COPD. The mean FEV1% in patients with mild COPD was 90 ± 10% (n=4), moderate COPD was 64 ± 8% (n=13), severe COPD was 39 ± 5% (n=6), and very severe 25 ± 3% (n=2). There was no significant association in the baseline $PcCO_2$, peak $PcCO_2$, baseline SpO_2 or the lowest SpO_2 comparing patients with and without COPD.

DISCUSSION

Recently, $PcCO_2$ measurements using the device used in this study have been shown to have a good correlation with arterial carbon dioxide values when more than 100 samples were compared (R=0.95) [13]. The findings of our study show that ventilation can be effectively monitored during flexible bronchoscopy using combined oximetry and $PcCO_2$ measurement. In a study of 22 patients, an increase in $PcCO_2$ has been shown to occur during flexible bronchoscopy [5]. However, the authors concluded that the technology that they used for $PcCO_2$ monitoring was complex [5]. Measurement of $PcCO_2$ in the current study was simple and did not lead to a delay in the start of the procedure or any complications related to the equipment. The potential complication with the use of this device is skin burn as the sensor is warmed to a temperature of 42 degrees Celsius. The recommended maximum duration for which a sensor can be placed cutaneously at 42 degrees Celsius is 8 hours [15]. None of the patients in this study manifested a skin burn. The BTS guidelines caution to monitor signs of respiratory failure in patients undergoing flexible bronchoscopy on oxygen supplementation who may have safe oximetry readings but may be developing carbon dioxide retention. Patients with a higher baseline $PcCO_2$ are at a greater risk of developing a higher peak $PcCO_2$. Furthermore, the peak $PcCO_2$ was significantly associated with the lowest SpO_2 during bronchoscopy. The results of our study show that it is feasible to measure continuous $PcCO_2$ during bronchoscopy, which has been shown to be a good surrogate of arterial carbon

dioxide tension [2, 12, 13]. Based on the findings of our study, no specific trend was observed in the association between peak $PcCO_2$ and change in $PcCO_2$ with procedure duration, as both, a short as well as a longer procedure duration were associated with the peak $PcCO_2$ and change in $PcCO_2$. The ability to effectively measure $PcCO_2$ is an important step in patient monitoring as diagnostic bronchoscopies are performed using sedation routinely and also drugs like propofol which are considered as general anesthetics are being increasingly used also in the absence of a trained anesthetist [16-19].

The mean duration to the manifestation of lowest SpO_2 was earlier than the mean duration to the peak $PcCO_2$. Therefore, it seems not possible to predict occurrence of lowest SpO_2 based on rising $PcCO_2$ values. The lowest SpO_2 manifested was significantly associated with peak $PcCO_2$. The hypothesis for this observation is that hypoventilation during flexible bronchoscopy performed under sedation with oxygen supplementation is multifactorial and not due to only central respiratory depression in which case a rise in $PcCO_2$ would precede significant hypoxemia due to the nature of the oxygen dissociation curve. Hypoventilation during flexible bronchoscopy is therefore due to a combination of upper airway obstruction, alveolar hypoventilation caused by sedative medication and the procedure itself [7]. The effective treatment of hypoxemia with jaw support or nasopharyngeal tube insertion supports the role of upper airway obstruction leading to acute hypoxemia during flexible bronchoscopy [7]. The rise in $PcCO_2$ manifested thereafter reflects alveolar hypoventilation, which is likely due to the

combined effect of sedatives (central respiratory depression) as well as the procedure itself potentially leading to ventilation perfusion mismatch. The findings of our study show that after effective treatment of upper airway obstruction, there continues to be a rise in $PcCO_2$ reflecting hypoventilation. Therefore, SpO_2 alone is not sufficient to monitor the complete ventilation status of the patient during bronchoscopy, thus highlighting the value of combined oximetry and cutaneous capnography during bronchoscopy.

The permissible level of $PcCO_2$ rise during bronchoscopy is not known. The BTS guidelines state that the use of sedation in patients with severe COPD has increased risks relating to potential carbon dioxide retention [2]. The findings of our study show that patients with COPD who are not in hypercapnic respiratory failure are at an equal risk of hypercapnia as well as hypoxemia compared to patients without COPD. Based on the findings of our study (mean rise in $PcCO_2$ of 10 ± 5 mm Hg) , we speculate that a rise of 15 mm Hg in $PcCO_2$ from baseline may be an indication to limit further administration of sedatives and needs to be confirmed in future studies.

To summarize, our study demonstrates the feasibility of measuring combined oximetry and cutaneous capnography effectively to monitor ventilation during flexible bronchoscopy. Patients with COPD who are not in hypercapnic respiratory failure have a similar risk of hypoxemia and hypercapnia compared to those without COPD during bronchoscopy. The peak $PcCO_2$ is higher in patients

with a higher baseline $PcCO_2$ and is associated with lowest SpO_2 during bronchoscopy. Significant hypoxemia is associated with the peak $PcCO_2$ and baseline SpO_2. With the current study results, it is not possible to predict and select accurately a group of patients who should undergo capnography during bronchoscopy. Patients with elevated baseline arterial carbon dioxide tension or a low baseline SpO_2 will have the benefit of better monitoring of ventilation using such a device. Specifically, patients with a longer duration of procedure did not show a different rise in $PcCO_2$ compared to the others. Furthermore, we expected an association of the sedative dose with rise in $PcCO_2$, but that was also not the case. Therefore, future studies have to analyse the different patient groups with regards to the baseline $PcCO_2$ to potentially limit the application of cutaneous capnography to only a specific group of patients.

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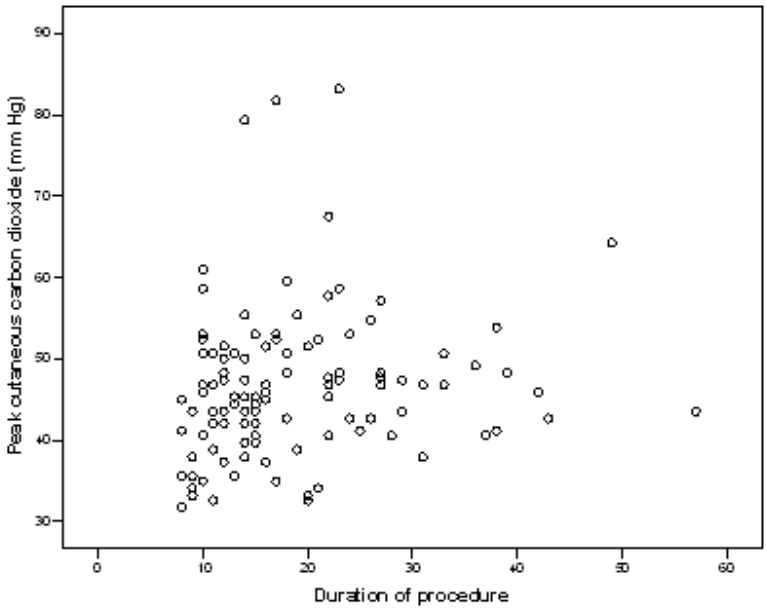
Legends for Figures

1 A Scatter plot of peak cutaneous carbon dioxide and duration of procedure



1 B Scatter plot of change in cutaneous carbon dioxide and duration of Procedure