

Noninvasive Measurement of Carboxyhemoglobin in Cystic Fibrosis Patients by Pulse CO-oximeter

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Carboxyhemoglobin levels may be elevated by the inspiration of environmental carbon monoxide or as a result of its endogenous production by inducible heme oxygenase, which is a stress protein that breaks down heme. Heme breakdown products, including carbon monoxide, have antioxidant, anti-inflammatory, and cytoprotective effects. Increased exhaled carbon monoxide has been measured in active smokers, sepsis, and in a number of inflammatory pulmonary diseases including cystic fibrosis (CF). Carboxyhemoglobin can now be measured noninvasively by pulse CO-oximetry (SpCO) within a range of $\pm 2\%$ by the Rainbow-SET Rad-57 Pulse CO-Oximeter (Masimo Inc., Irvine, CA). To become familiar with this device, staff measured SpCO during routine outpatient visits at a Pediatric Pulmonary and Cystic Fibrosis Center. Among the outpatients were 48 patients with CF, who had an average SpCO of $7.1\% \pm 5$ [SD] (range 0–20). When SpCO was compared to the forced expiratory volume in 1 sec at the same visit, there was a moderate positive correlation ($r=0.67$, $p<0.001$). SpCO did not correlate with a history of active or passive tobacco smoke exposure in patients with CF. This report shows that carboxyhemoglobin levels may be measured by pulse CO-oximetry in patients with CF and suggests that elevated levels may correlate with better pulmonary function. Further controlled, prospective studies are needed to determine if this noninvasive test may be useful in evaluating the severity of CF or aiding in its treatment.

Introduction

CARBOXYHEMOGLOBIN CAN NOW be measured noninvasively by pulse CO-oximetry (SpCO) within a range of $\pm 2\%$ by the Rainbow-SET Rad-57 Pulse CO-Oximeter (Masimo Inc., Irvine, CA). To become familiar with this device, staff measured SpCO during routine outpatient visits at a Pediatric Pulmonary and Cystic Fibrosis Center. Expecting values within the normal range, the authors were surprised to find significant unexplained elevations in SpCO.

Methods

The Rainbow-SET Rad-57 Pulse CO-Oximeter¹ was placed on a finger, and when a reading was unchanged for 5–10 sec, SpCO and pulse oximetry were recorded. Measurements were made by the author (LEK) or trained clinic nurses. Cystic fibrosis (CF) patients were diagnosed using published criteria.² They were receiving standard CF treatment regimens including oral or inhaled antibiotics. No patient was acutely ill. Percent predicted of forced expiratory volume in 1 sec (FEV₁%) as part of routine clinic pulmonary function testing was performed by clinic respiratory therapists using either the Sensormedic VMax22 (Sensormedic Corp., Yorba Linda, CA) or the KoKo spi-

rometer (nSpire Health, Inc., Longmont, CO). Spirometric predicted values were based on those of Polgar³ for 4–6 years of age, Wang⁴ for 7–17 years of age, and NHANES⁵ for 18 years of age or older. SpCO and FEV₁% values were compared using the Pearson product-moment correlation coefficient.

As this study presents data collected retrospectively, this study was submitted to and exempted from review by the Upstate Medical University Institutional Review Board.

Results

Observations were made on 48 cystic fibrosis patients (24 males, average age 13.7 ± 5.0 years; 24 females, average age 10.7 ± 4.8 years). Average FEV₁% was $81.4\% \pm 27.2$ and average SpCO was $7.1\% \pm 5$ [SD]. Patient data are shown in Figure 1. The Pearson correlation coefficient was $r=0.67$, $p<0.001$. Five CF patients admitted to passive or active smoke exposure: three of these patients had an SpCO less than the sample mean of 7.1%, and two had values greater than 7.1%. Average SpCO results were compared to the following groups: 23 nonsmoking pediatric residents and clinic staff—SpCO was $0.08\% \pm 0.3$; 87 patients with well-controlled asthma (average age of $8.8 \text{ years} \pm 4.3$)—SpCO was $0.3\% \pm 0.8$; 21 patients with asymptomatic allergic

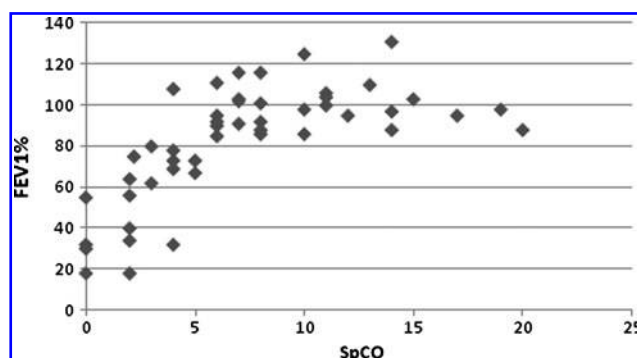


FIG. 1. SpCO compared to FEV1% for 48 outpatients with cystic fibrosis. There was a positive correlation between SpCO and FEV1% of $r=0.675$ ($p<0.0001$). SpCO, pulse CO-oximetry; FEV1%, forced expiratory volume in 1 second.

rhinitis (average age of $6.8 \text{ years} \pm 4.1$)—SpCO was $0.77\% \pm 1.5$; and seven non-CF patients with acknowledged passive smoke exposure at home or in the car—SpCO was $6.18\% \pm 3.7$.

Discussion

SpCO in CF patients varied from normal to surprisingly elevated levels that could not be explained by exogenous carbon monoxide exposure, and likely represent endogenous carbon production from heme oxygenase breakdown of heme.⁶ In CF, findings of elevated carbon monoxide in exhaled breath collection^{7–9} and of elevated carboxyhemoglobin in patients with iron deficiency anemia¹⁰ support this interpretation. The association of better lung function, as measured by FEV₁%, with higher SpCO in this study is intriguing. While controls were not matched, their SpCO results suggest that the CF SpCO results were not due to exogenous CO exposure from city traffic. Endogenous products of heme degradation by heme oxygenase, which are the result inflammation and oxidative stress, may also have anti-inflammatory, antioxidative, or cytoprotective functions.^{11–15} In an airway epithelial cell line, increased expression of inducible heme oxygenase resulted in the release of carbon monoxide and protection against *Pseudomonas aeruginosa* induced injury and apoptosis.¹⁶ Transfer of heme oxygenase complementary DNA to mice previously infected with *P. aeruginosa* attenuated neutrophil influx and decreased apoptotic bronchial epithelial cells caused by the infection.¹⁷ A recent study showed that certain inducible heme oxygenase polymorphisms may help maintain lung function in the presence of *P. aeruginosa* infection in CF.¹⁸ The potential here is that heme breakdown products may actually help to protect lung function in CF patients.

Conclusion

The observations herein reported show that a noninvasive pulse CO-oximeter can measure blood carboxyhemoglobin in CF. Well-designed prospective studies are needed to show whether this test may be of benefit in clinically evaluating patients with CF.

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Author Disclosure Statement

No conflicting financial interests exist.

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