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The effects of high-frequency chest compression on end-tidal CO_2

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Abstract

Introduction: High-frequency chest compression (HFCC) is used for airway clearance, but may have other effects. We sought to determine if HFCC provides augmented ventilation.

Methods: During treatment, capnometry was measured with the HFCC vest set to 6-20 Hz. End-tidal CO_2 ($etCO_2$) was compared using generalized estimating equations.

Results: Twenty-four measurements were obtained from 15 subjects with mean age 15.2 ± 2.5 years and forced expiratory volume in one second (FEV_1) % predicted 70 ± 23. $EtCO_2$ decreased with HFCC at 6 Hz when compared with baseline ($P < .001$), with small changes with increasing oscillation frequency. Change in $etCO_2$ was not predicted by FEV_1, body mass index, age, or sex.

Conclusions: While HFCC has been shown to be a suitable method of airway clearance, investigators have failed to demonstrate differences between techniques. Assessment of these methodologies will become important as new airway clearance devices are proposed. Other outcome measures (besides FEV_1) may be needed to assess effects of airway clearance, and we propose that physiologic measures might be one such measure which deserves further exploration.

KEYWORDS

capnometry, cystic fibrosis, high-frequency chest compression, ventilation

1 | INTRODUCTION

Cystic fibrosis (CF) is characterized by increased sputum viscosity, defective mucociliary clearance and airway obstruction.[1] Airway clearance treatments including high-frequency chest compression (HFCC), are a mainstay of treatment of CF.[2,3] Comparisons between airway clearance methods are challenging.[3] HFCC is the most popular choice for patients with CF in the U.S., although less common in other countries.[4] We demonstrated that different HFCC frequencies have differing effects on volume and flow measured at the mouth.[5] We also observed increased changes in expiratory volumes with lower oscillation frequencies.[5,6] Thus we sought to determine if HFCC provides augmented ventilation (as assessed by end-tidal CO_2 [$etCO_2$]) and whether the degree of ventilation is related to oscillation frequency or other patient factors.

2 | METHODS

Patients with CF were recruited from the inpatient service at Children's Hospital of Pittsburgh if they were 6 to 21 years old, and admitted for pulmonary exacerbation. Subjects were excluded if they had pneumothorax, hypoxemia, or moderate/severe hemoptysis. Patients were offered the opportunity to repeat measurement in 7 days if they remained hospitalized. This study was conducted with the approval of the Institutional Review Board of the University of

Pittsburgh. Informed consent was obtained from the parents/patients before participation.

2.1 | Capnometry

During a HFCC treatment, a sampling cannula was placed within the nostrils and connected to a digital capnometer (Capnostream™ 35, Medtronics, Boulder, CO). Patients were asked to close their mouth and take three to five normal (tidal) breaths through their nose, and $etCO_2$ was recorded. The HFCC vest (The Vest, Hill-Rom, Chicago, IL) was set to a pressure of 7 out of 10, and frequency of 6 Hz. After 1 minute of treatment, $etCO_2$ was re-measured and the HFCC treatment continued for four additional minutes. The device was paused, the patient was asked to cough three to four times, and an additional $etCO_2$ measurement was collected with the patient breathing through their nose to document recovery to baseline. This procedure was repeated with different HFCC frequencies (8, 10, 16, 18, and 20 Hz), with treatment at each frequency lasting 5 minutes. Capnography with a baseline $etCO_2$ of <30 mm Hg or an unstable tracing was excluded.

Subject characteristics were abstracted from the chart including age, sex, body mass index (BMI), and most recent spirometry results normalized according to GLI2012 equations.[7]

2.2 | Analysis

Differences in $etCO_2$ and respiratory rate were compared with repeated measures analysis of variance with Tukey's multiple comparisons test, and generalized estimating equations using xtgee (STATA v15, StataCorp LLC, College Station, TX), adjusting for age, sex, BMI, forced expiratory volume in one second (FEV_1), and respiratory rate.

3 | RESULTS

3.1 | Subjects

Twenty subjects with CF were recruited, 15 (5 M/10 F) of whom produced usable capnography. Subjects had a mean ± standard deviation (range) age of 15.2 ± 2.54 (10.8-19.8) years, BMI of 50 ± 27 (0.98-90.6) percentile, and FEV_1 of 70 ± 23 (29-112) percent-of-predicted.

3.2 | Capnometry data

A total of 24 measurements were gathered from the 15 subjects. No complications occurred during testing. Changes in $etCO_2$ and respiratory rate with varied oscillation frequencies are depicted in Figure 1. All frequencies had lower $etCO_2$ compared with vest off ($P < .0001$), and $etCO_2$ at 20 Hz was lower than at 6, 8, and 10 Hz ($P < .05$). After adjusting for patient age, sex, BMI, baseline FEV_1, and respiratory rate, modeled $etCO_2$ decreased significantly with application of HFCC at 6 Hz when compared with baseline (−4 mm Hg at 6 Hz vs baseline, $P < .0001$). Increasing frequencies produced a significant but very small slope in $etCO_2$ (−2 mm Hg at 20 Hz vs 6 Hz). Change in $etCO_2$ was not associated with baseline FEV_1, BMI, age or sex. Respiratory rate was associated with lower $etCO_2$ (−0.12 mm Hg per breath/minute, $P = .022$), but there were no differences in rate between baseline and any frequencies ($P = .57$).

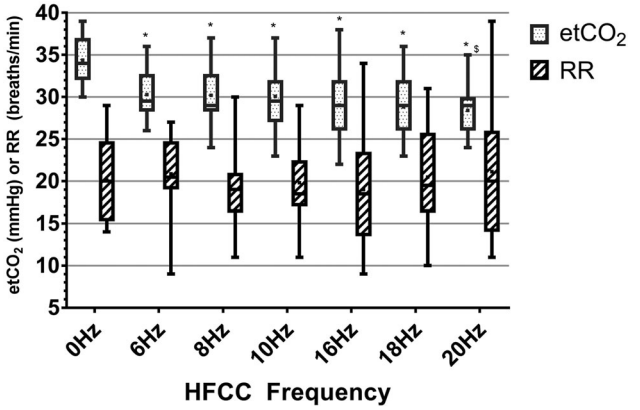

FIGURE 1 $EtCO_2$ (dotted bars, mm Hg) and respiratory rate (hatched bars, breaths per minute) measured during a treatment with high-frequency chest compression at a variety of oscillation frequencies from 6 to 20 Hz. Median values represented by horizontal bar, mean values by X. $EtCO_2$ at each frequency was lower ($P < .05$, *) than with vest off (0 Hz), and $etCO_2$ at 20 Hz was lower ($P < .05$) than at 0, 6, 8, and 10 Hz ($). $EtCO_2$, end-tidal CO_2; HFCC, high-frequency chest compression

4 | DISCUSSION

The main finding of our study is that HFCC results in augmented ventilation as assessed by a lower $etCO_2$. HFCC is a suitable method of airway clearance and sputum production in patients with CF similar to conventional physiotherapy,[8] but most investigators have failed to demonstrate significant differences between HFCC and positive expiratory pressure devices for treatment of CF.[4]

Interestingly, we found that all frequencies lowered $etCO_2$ compared with "vest off", but a relatively small difference in $etCO_2$ between frequencies. This was not predicted based on prior observations[5,6] that lower frequencies tended to result in greater changes in exhaled volume and higher frequencies tended to result in greater changes in airflow rate. Subjects in the current study were experiencing an acute exacerbation of their obstructive lung disease, while patients in the other studies were studied when well, and this could contribute to this finding.

Al-Saady analyzed external high-frequency oscillation (EHFO) and CO_2 in 20 healthy adult subjects and five adult subjects with respiratory failure wearing a cuirass ventilator. $EtCO_2$ was measured in healthy subjects, and arterial pCO_2 in subjects with respiratory failure at oscillation frequencies ranging from 1 to 5 Hz. EHFO significantly decreased $etCO_2$ or $PaCO_2$ at all frequencies, maximally from 38 to 27 mm Hg. In patients with respiratory failure, EHFO was

shown to increase PaO_2 and decrease $PaCO_2$. Is it difficult to relate their findings to ours, as their study differed in the patient population, use of arterial pCO_2, the methods of chest wall oscillation (cuirass vs inflatable vest), and the oscillation frequencies (much lower than ours).

Studies of airway clearance techniques have often used spirometry outcome measures. As FEV_1 tends to change relatively slowly,[9] studies to detect differences in airway clearance methodologies using this outcome would require a large sample size or a prolonged follow-up period. Additionally, some studies may use markers, such as sputum weight, which may be unfeasible in a pediatric population. Rigorous assessments of these methodologies may be increasingly important as new devices,[10-12] including portable devices lacking clinical evidence, are proposed for patient use.

Other outcome measures might be used to assess effects of airway clearance.[13] These include imaging techniques (eg, ^{3}He-MRI,[14] nuclear medicine clearance scans[15]) or other pulmonary function measures (eg, multiple breath washout[16,17]). We propose that physiologic measures, such as changes in ventilation that we observed may also allow for comparisons between airway clearance methods.

There are several limitations with this study. First, our sample size was relatively small. Although we attempted to allow $etCO_2$ to return to baseline, we cannot exclude a degree of carryover effect between oscillation frequencies, the order of which was not randomized. Other factors, such as the coughing maneuvers may also have contributed to changes in $etCO_2$. Additionally, $etCO_2$ may underestimate blood pCO_2 due to leak around the cannula, although there is no reason for such leak to be consistently higher after the baseline $etCO_2$ measurement.

In summary, HFCC mildly increases minute ventilation in patients with CF. The clinical implications of this observation, and its potential use to compare devices, deserve further exploration.

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REFERENCES

1. Ratjen F, Bell SC, Rowe SM, Goss CH, Quittner AL, Bush A. Cystic fibrosis. *Nat Rev Dis Primers*. 2015;1:15010.
2. van Winden CMQ, Visser A, Hop W, Sterk PJ, Beckers S, de Jongste JC. Effects of flutter and PEP mask physiotherapy on symptoms and lung function in children with cystic fibrosis. *Eur Respir J*. 1998;12(1):143-147.
3. Wilson LM, Morrison L, Robinson KA. Airway clearance techniques for cystic fibrosis: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev*. 2019;1:CD011231.
4. Osman LP, Roughton M, Hodson ME, Pryor JA. Short-term comparative study of high frequency chest wall oscillation and European airway clearance techniques in patients with cystic fibrosis. *Thorax*. 2010;65(3):196-200.
5. Luthy SK, Marinkovic A, Weiner DJ. Resonant frequency does not predict high-frequency chest compression settings that maximize airflow or volume. *Pediatr Pulmonol*. 2011;46(6):604-609.
6. Milla CE, Hansen LG, Warwick WJ. Different frequencies should be prescribed for different high frequency chest compression machines. *Biomed Instrum Technol*. 2006;40(4):319-324.
7. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J*. 2012;40(6):1324-1343.
8. Arens R, Gozal D, Omlin KJ, et al. Comparison of high frequency chest compression and conventional chest physiotherapy in hospitalized patients with cystic fibrosis. *Am J Respir Crit Care Med*. 1994;150(4):1154-1157.
9. Konstan MW, VanDevanter DR, Sawicki GS, et al. Association of high-dose ibuprofen use, lung function decline, and long-term survival in children with cystic fibrosis. *Ann Am Thorac Soc*. 2018;15(4):485-493.
10. Cantin AM, Bacon M, Berthiaume Y. Mechanical airway clearance using the frequencer electro-acoustical transducer in cystic fibrosis. *Clin Invest Med*. 2006;29(3):159-165.
11. Dingemans J, Eyns H, Willekens J, et al. Intrapulmonary percussive ventilation improves lung function in cystic fibrosis patients chronically colonized with Pseudomonas aeruginosa: a pilot cross-over study. *Eur J Clin Microbiol Infect Dis*. 2018;37(6):1143-1151.
12. Natale JE, Pfeifle J, Homnick DN. Comparison of intrapulmonary percussive ventilation and chest physiotherapy. *Chest*. 1994;105(6):1789-1793.
13. Tidden HAWM, Puderbach M, Venegas JG. Novel outcome measures for clinical trials in cystic fibrosis. *Pediatr Pulmonol*. 2015;50(3):302-315.
14. Mentore K, Froh DK, de Lange EE, Brookeman JR, Paget-Brown AO, Altes TA. Hyperpolarized HHe 3 MRI of the lung in cystic fibrosis. *Academic Radiol*. 2005;12(11):1423-1429.
15. Corcoran TE, Thomas KM, Myerburg MM, et al. Absorptive clearance of DTPA as an aerosol-based biomarker in the cystic fibrosis airway. *Eur Respir J*. 2010;35(4):781-786.
16. Subbarao P, Stanojevic S, Brown M, et al. Lung clearance index as an outcome measure for clinical trials in young children with cystic fibrosis. A pilot study using inhaled hypertonic saline. *Am J Respir Crit Care Med*. 2013;188(4):456-460.
17. Grosse-Onnebrink J, Mellies U, Olivier M, Werner C, Stehling F. Chest physiotherapy can affect the lung clearance index in cystic fibrosis patients. *Pediatr Pulmonol*. 2017;52(5):625-631.

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