Ultrasonic measurements of CO_2 during quiet breathing may diagnose degree of airway obstruction

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ABSTRACT

Patients with airway obstruction might be identified and categorized as to severity with measures of CO_2 and spirometric flow patterns during quiet breathing. Molar mass measures were compared to CO_2 measurements made with a mass spectrometer. Sixteen healthy subjects and twenty patients were tested in our pulmonary laboratory. They breathed quietly for 5 minutes on an ndd ultrasonic spirometer (ndd, Zurich Switzerland). CO_2 was simultaneously measured with a mass spectrometer (mspec) and estimated with molar mass (MM) determined from the ndd spirometer. Volume/time, %CO_2mspec and %CO_2MM were sampled at 200 Hz throughout each respiratory cycle. Composite capnograms (%CO_2mspec vs. Volume) and (%CO_2MM vs. Volume) were created for each subject by averaging the %CO_2mspec concentrations at matched exhalation volumes. Maximum slope and the volume where the maximum slope occurred were calculated from the composite curves for each subject. In addition, slope of phase III was calculated. Linear discriminate analysis was used to compare percentage of correct classifications using CO_2mspec data and the CO_2MM data. Additional analyses were performed using only the molar mass data and adding age and gender to the discriminate analysis. A final classification analysis was performed categorizing subset only into "Normal" or "Any Obstruction" using the molar mass data.

Results: The %CO_2MM measurements accurately tracked the %CO_2mspec. %CO2mspec data correctly categorized 72% of the subjects into their spirometric "Normal" or "Obstruction" category. Molar mass data correctly categorized 67% of the subjects. Adding Age and Gender, molar mass data correctly categorized 78% and finally molar mass data correctly classified 83% into either "Normal" or "Any Obstruction"

Conclusions: Molar mass measurements may provide an effort-independent test that will diagnose the presence of and degree of airway obstruction. Molar mass data may add additional information to traditional spirometry.

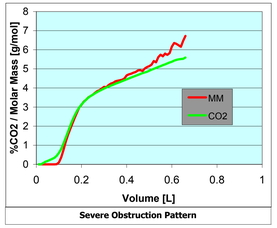
METHODS

Study Design

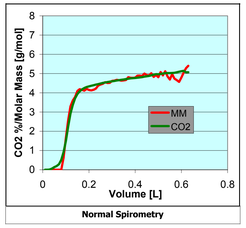
Patients and healthy volunteers at the pulmonary function laboratory at LDS Hospital in Salt Lake City, Utah, USA

N=65 (35 Men, 30 Women)
Mean Age: 48.4 (range 18 to 81)

Measurements:
- Spirometry (FVC, FEV1, PEF and FEV1/FVC ratio)
- DLCO (only in scheduled patients)
- Mass spectrometer (%CO_2 Measurements)
- Ultrasonic flow sensor (Volume, Molar Mass Measurements)



Severe Obstruction Pattern



Normal Spirometry

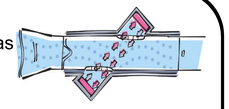
Protocol
- Subjects seated using nose clips
- Relaxed breathing for 5 minutes
- Slow vital capacity within first and last minute of testing
- Mass spectrometer calibrated prior to each test
- Signals digitized at 200 samples/sec
- Tidal breaths over 5 minutes are combined for analysis into two composite curves (CO_2 vs. Volume and Molar Mass vs. Volume)

Spirometry

Standard spirometry was done on all subjects, except one, prior to performing the quiet breathing on the ultrasonic molar mass device. PFT measurements of FVC and FEV1 and percent predicted values (using NHANES III reference equations) were obtained and used to categorize the subjects into normal, and mild, moderate or severe obstruction or restricted.

ANALYSIS

Molar mass & Volume



The speed of sound in a gas is proportional to the molar mass of the gas. Molar mass is directly measured from the average sound velocity. Accuracy of molar mass measurements is 0.034%. Table 1 shows an example of molar mass for room air.

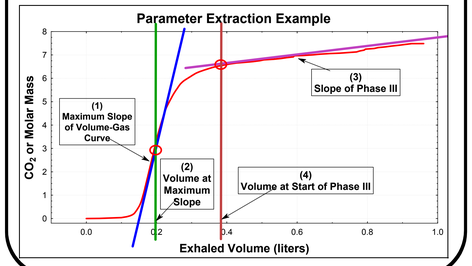
Table 1: Examples of calculation of molar mass (room air & typical alveolar gas)

Gas	Concentration	Molar Mass [g/mol]	Concentraion x MM
Nitrogen	0.781	28	21.8680
Oxygen	0.2093	31.99	6.6955
Carbon Dioxide	0.0003	44	0.0132
Argon	0.0094	39.95	0.3755
	1		
		Mean Molar mass of Air at 0% Humidity	28.95
End Tidal Gas From The Lungs			
		Mean Molar mass of alveolar gas	29.78

Volume measurements are made simultaneously using the transit time differences between ***upstream*** and ***downstream*** ultrasound pulses. The difference in the transit times is initially used to measure mean gas velocity in the breathing tube. Flow is calculated as velocity (cm/sec) x cross-sectional area (cm^2) of the tube and gives flow (cm^3/sec) or (ml/sec). Finally, flow is integrated to obtain volume measures.

Parameters extracted from composite curves

P1: Maximum slope of the volume-gas curve
P2: Volume where the maximum slope occurs
P3: Slope of phase III of the volume-gas curve
P4: Volume at beginning of Phase III



RESULTS/CONCLUSIONS

Statistical Analysis

Linear Discriminant Analysis
1. Compare % Classification using Volume-%CO_2 parameters vs. Volume-Molar Mass parameters to categorize subjects
2. Incorporate Age, Gender in addition to Molar Mass parameters to categorize subjects
3. Categorize to "Normal" or "Any Obstruction"

Results

Average values for FEV1 and FEV1/FVC in each disease category are listed in table 2, along with mean parameter values. There is excellent correlation between the parameters (1-4) derived from the mass spectrometer measured %CO2 vs. volume curves and the ultrasonic measured molar mass vs. volume curves. Correlations for P1: r^2 = 0.909, P2: r^2 = 0.961, P3: r^2 = 0.729, P4: r^2 = 0.960.

Table 3: Discriminate analysis using only CO2 measurements from mass spectrometer

	% Correctly Classified with Mass Spec %CO2	% Correctly Classified with Molar Mass
Spirometry: Normal	68.8	78.1
Spirometry: Any Obstruction	90.0	80.0
Overall: Correctly Classified	79.0	79.0

The information contained in the molar mass derived parameters can correctly categorize 79% of pulmonary patients. When age and gender are added to the discriminante analysis 82% of the patients were correctly classified.

Table 2	Normal	Mild	Moderate	Severe
FEV1 (L)	3.39	2.45	1.65	1.47
FEV1/FVC (%)	79.2	62.3	51.5	44.4
MAX Δ %CO2/L	55.2	42.4	44.3	35.4
Volume at Max Δ %CO2/L	0.122	0.162	0.123	0.142
Slope Phase III	1.97	3.95	4.73	4.49
Volume at Phase III	0.174	0.225	0.176	0.197

In the table 3 are the separate discriminate analyses. Almost 80% of the patients were separated into normal or disease. Overall, no difference was found between the mass spectrometer %CO2 vs. volume parameters and the molar mass vs. volume parameters to correctly classify patients into the simple "normal" or "any obstruction" groups. The MM parameters were more consistent in their classifications.

Classifying patients into their correct level of obstruction was less accurate. For %CO2 and molar mass about 60% of the patients were classified into their correct obstructed level (mild, moderate or severe) or normal groups.

There were only three restricted patients and the discriminant analysis generally categorized these into a normal pattern.

CONCLUSIONS

1. Molar mass measurements are simple and correlate well with traditional measures of CO2
2. Molar mass measurements may provide an effort-independent test that will diagnose the presence and degree of airway obstruction
3. In the future, these may add additional information to traditional spirometry from the shape of the molar mass vs. volume curves