Measurement of Resting Energy Expenditure in Patients With Chronic Obstructive Pulmonary Disease in a Clinical Setting

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ABSTRACT: There is a growing tendency to estimate energy requirements by means of the assessment of resting energy expenditure (REE) by indirect calorimetry. In this study a computerized open-circuit ventilated hood system is described that was constructed for assessing REE in a clinical setting. Measurement error of the device, tested by ethanol combustion was +2% for V\textsubscript{O}\textsubscript{2} and V\textsubscript{C}\textsubscript{O}\textsubscript{2} and <1% for respiratory quotient. To assess the within-patient variability of REE measurements performed in a daily clinical routine, we studied the following aspects of the measurements in several groups of patients with chronic obstructive pulmonary disease: (1) reproducibility, (2) the influence of routine physical activities before the measurement, (3) measurement duration, and (4) difference between measurements using a ventilated hood or a mouthpiece. Reproducibility of measurements with a 2-month interval in 12 weight-stable patients was good (1415 ± 128 and 1398 ± 138 kcal/day). Variations due to limited activities and different measurement durations (between 10 and 30 minutes) were not significant. Variations between measurements with a mouthpiece and ventilated hood were larger in patients than in healthy control subjects, but for both groups no systematic difference was established. REE can be assessed reliably by short-term measurements with a ventilated hood in stable chronic obstructive pulmonary disease patients on an outpatient basis, provided a short rest is taken before the measurement. (Journal of Parenteral and Enteral Nutrition 16:364-368, 1992)

The maintenance of body functions requires a constant expenditure of energy. Energy is expended for active transport processes, to keep chemical and electrical gradients across cellular membranes, for the synthetic processes, and for muscular contraction. Twenty-four-hour energy expenditure is composed of four components: the sleeping metabolic rate, energy cost of arousal, the thermic effect of food, and the energy cost of activity.\textsuperscript{1} Resting or basal energy expenditure, which comprises the sleeping metabolic rate and the energy cost of arousal, can be defined as the minimum rate of energy expenditure in an awake, relaxed person, lying on a bed, after an overnight fast.\textsuperscript{2} Resting energy expenditure (REE) is the major determinant amounting to about 70% in sedentary persons.\textsuperscript{2}

In the past, estimation of resting energy requirements of patients was mostly based on prediction formulas such as the Harris-Benedict equations.\textsuperscript{3} At present there is a growing tendency to estimate energy requirements using the assessment of REE by indirect calorimetry. Measurement of REE may be particularly valuable in patients with chronic obstructive pulmonary disease (COPD) for two reasons: (1) nutrition depletion is a common problem in these patients, and (2) several studies have demonstrated an increased REE in patients with COPD.\textsuperscript{4}

Determination of REE by using the principles of indirect calorimetry has been facilitated by the availability of a number of gas-exchange measurement devices.\textsuperscript{5} In this study a computerized open-circuit ventilated hood is described that was constructed for assessing REE in patients in a clinical setting.

Although REE is generally assumed to be relatively constant, few data exist with regard to the within-patient variability of REE measurements performed in a daily clinical routine. In this study we therefore addressed the following questions: (1) Is the REE measurement reproducible in stable COPD patients? If, indeed, the measurement is reproducible, it would imply that one measurement could be used to calculate a patient's energy requirements. (2) What is the influence of physical activity on the REE measurement? If REE is still increased a few hours after normal physical activities, it implies that REE cannot be measured on an outpatient basis. (3) Is there a difference in REE measurements using a ventilated hood or a mouthpiece? Brief measurements of energy expenditure with a mouthpiece and nose clips are an acceptable alternative to continuous measurement of gas exchange with a ventilated hood in healthy subjects who are adjusted to the technique.\textsuperscript{6} Because many COPD patients suffer from severe dyspnea, we studied whether the two methods give different results in patients with advanced COPD.

METHODS

The Ventilated Hood System

The principle of a ventilated hood system is that a stream of air is forced to pass across the face of a subject
and mixes with the expired air, which is collected by a transparent Plexiglas hood placed over the subject’s head. The rate of energy expended can be calculated by determining the amount of air flowing through the hood and by measuring the oxygen (O₂) and the carbon dioxide (CO₂) concentrations in the incoming and outgoing air. Figure 1 gives a schematic representation of the system.

Room air is drawn through the hood by negative pressure created by a pump downstream (Mijnhardt, Bunnik, The Netherlands). Airflow through the hood is measured in the outlet airstream by a dry gas meter (Ö6, Meterfabriek Schlumberger, The Netherlands). The dry gas meter used is calibrated with a Blakelee piston pump with mercury seals. A humidity sensor (Vaisala, Humicap, HMD20U, Helsinki, Finland), a temperature sensor (P. Schoffelen analog devices AD590), and an ambient pressure sensor (Mijnhardt, CX103 board) are incorporated. Gas temperature is measured in the gas meter and relative humidity after the gas meter. Flow readings of the gas meter are converted to standard temperature, pressure dry conditions. Downstream to the flow measurement a small quantity (0.1 L/min) of air is continuously withdrawn for gas analysis. Before gas analysis the sample is dried (Perma pure mini-dryer MD, Inacom Instruments BV, Veenendaal, The Netherlands) and sample pressure is stabilized for analysis. Through a system of computer-driven solenoid valves (Kühnke, Germany), a sample gas is obtained from either the ventilated hood, calibration gases, or room air upstream of the canopy. Gas analysis is performed with a paramagnetic O₂ analyzer (Mijnhardt Oxygen module, Bunnik, The Netherlands) with a full-scale range of 100%, modified to 0% to 25%, and an infrared CO₂ analyzer (Mijnhardt, CX103 module) with a modified full-scale range of 1%. The O₂ and CO₂ analyzers are accurate to 0.05% and 0.04% absolute, respectively. Accuracy is improved by linearizing the CO₂ analyzer data and by digitally filtering data in the computer. Both analyzers then are within 0.01% absolute accuracy. Analyzers are calibrated using two dry calibration gases. Zero settings are performed by passing 100% nitrogen through the analyzers (0.1 L/min). The span of the O₂ and CO₂ analyzers is set by passing a special gas mixture (0.8 ± 0.008% CO₂ and 19.0 ± 0.005% O₂ in N₂) through the analyzer. The equipment is calibrated with both calibration gases at the start and end of every experiment. Canopy gas is sampled continuously and data are produced every 10 seconds. Flow rates between 25 and 50 L/min, depending on body size, are used. The flow through the canopy is adjusted to keep CO₂ readings in the range of 0.40% to 0.80%, i.e., as near to the calibration gas CO₂ content as possible, for maximum accuracy. The hood has a volume of 30 L. The CO₂ concentration increases during exhalation and is mixed with air in the canopy. The flow is directed over the face of the subject through an air inlet in front and an air outlet at the top of the hood, to remove exhaled CO₂ immediately and avoid CO₂ buildup in the canopy. Further mixing takes place in the tubes and in the gas meter. Flow adjustments are made before the experiment is started. The flow is kept constant throughout the experiment.

A microcomputer (Apple IIe) controls the system and performs the calculations. Output voltage signals of the O₂ and CO₂ analyzers, and the humidity, pressure, and temperature sensors are measured and digitized by a data-acquisition interface (Applied Engineering) using a 16-channel, 12-bit AD converter. The gas meter pulse output is digitally counted in the computer giving a continuous flow measurement. O₂ and CO₂ concentrations of canopy air samples are measured continuously, and every 10 seconds a filtered value is recorded. The computer calculates and prints the values of O₂ consumed, CO₂ produced, the respiratory quotient (RQ), and the rate of energy expenditure throughout the experimental period.

Energy expenditure is calculated using the abbreviated Weir formula. This formula deletes the factor necessary to adjust for incomplete protein oxidation.

**Patients**

The study group consisted of COPD patients in stable clinical condition admitted to a pulmonary rehabilitation center. The healthy volunteers consisted of hospital staff members. A description of the study groups for the different experiments is given in Table I.

**Study 1: Variability and Accuracy of the Method**

The precision of the gas analyzers and the calibration procedure was measured throughout the study period by ethanol (Merck 983, Darmstadt, Germany) combustion tests of different durations ranging from 5 minutes to 60 minutes. To oxidize 1 g of ethanol 1.460 L of O₂ is needed and 0.972 L of CO₂ is produced (RQ = 0.686). When a known quantity of ethanol is combusted, the volumes of O₂ consumed and CO₂ produced, involved in the oxidation process, can be calculated. These calculated values are compared with the observed values. To calculate the variability of the method, the ethanol combusions were extrapolated to an ethanol combustion rate needed for the average sedentary individual with a RER of 1600 kcal/day. This would correspond to an ethanol combustion of 229 g, assuming an energetic equivalent of ethanol oxidation of 7 kcal. For the oxidation of 229 g of ethanol, 334 L of O₂ are needed and 222 L of CO₂ are produced.

Unless described differently in the experiments, measurements were performed in the early morning (between 8:30 and 9:30 AM) in a fasting state (for at least 10 hours) approximately 2 hours after the patients had received their maintenance medication. The patients were lying comfortable in a semi-recumbent position. The upper
body was elevated according to individual preferences. The patients were asked to remain completely quiet and did not watch television or listen to the radio. The investigators ensured that the subjects did not move or sleep. After initiating the measurements, time was allowed (±7 minutes) to adjust to the hood and to stabilize energy expenditure.

**Study 2: Effect of Activities of Daily Living**

The effect of light activities of daily living before the measurement was tested in 12 patients on 2 consecutive days. On the first day the patients were allowed to dress, wash, and walk to the metabolic ward. After lying down for 20 minutes, energy expenditure was measured over a 30-minute period. On the second day, the patients stayed on their beds until the investigator took them in a wheelchair to the metabolic ward. The two measurements were done while the patients were maintained in the same position because it has been shown that resting metabolic rate may vary at different body positions.⁶

**Study 3: Length of Measurement**

To assess the possibility to perform short-term experiments, measurements of different duration were compared. REE was calculated in the same group of patients and in 14 healthy control subjects (age 31 ± 8 years) after 5, 10, 15, 20, 25, and 30 minutes.

**Study 4: Reproducibility of the Measurement**

Reproducibility of REE measurements during a 2-month interval was established in 12 patients whose body weight remained stable throughout this period.

**Study 5: Ventilated Hood or Mouthpiece**

Paired measurements using both a ventilated hood and a mouthpiece were performed in 12 patients and 6 control subjects. Ethanol combustion tests were performed before every combined measurement. Subjects were randomly measured with hood or mouthpiece first. All patients were remeasured by the second system within 5 minutes so that the subject’s position and environment remained unchanged throughout both measurements. The patient’s expired air was collected via a mouthpiece attached to a Douglas bag. The initial 5 minutes of gas collection was discarded to allow for adjustment to the mouthpiece. The remaining 7 to 10 minutes of gas collection were analyzed. Because REE is primarily determined by VO₂,⁷ and to exclude differences in accuracy of different gas analyzers, the O₂ analyzer of the ventilated hood system was used to measure REE in both conditions. No VCO₂ measurements could be performed because the VCO₂ of the exhaled air from the Douglas bag was outside the span of the CO₂ analyzer of the ventilated hood.

**STATISTICS**

Comparisons between measurements under different circumstances were made using the statistical analysis of Bland and Altman.⁸ As emphasized by these authors, methods that yield estimates with a high correlation coefficient may not necessarily show a high degree of agreement. Therefore, in this analysis the differences in REE under different circumstances were plotted against the means of the two methods. This was then used to calculate the overall mean bias (mean difference) between the two methods, the associated limits of agreement (±2 standard deviations of the differences between methods), and the extent to which the mean bias changes with an increase in the mean of two measurements.

**RESULTS**

**Study 1**

Ethanol combustion tests revealed that the gain during the calibration was slight to high (2.2%) and that the deviation of measurements was 2.7% for O₂, 2.1% for CO₂, and 1.7% for RQ. The measurements were tolerated well. In only one patient the measurement had to be stopped, because the patient had a claustrophobic reaction.
Study 2

No significant differences were established between measurements performed after a complete rest and measurements done after light physical activities when a short rest was allowed before the measurement. This counted not only for calculated energy expenditure (1406 ± 238 kcal and 1431 ± 259 kcal/day) (Fig. 2) but also for RQ (0.82 ± 0.05).

Study 3

Calculated REE did not differ significantly between measurements of 5, 10, 15, 20, 25, and 30 minutes duration (Table II).

Study 4

The reproducibility after a 2-month interval was very good (Fig. 3). Average REE in the 12 weight-stable patients (64.7 ± 14.3 kg and 65.0 ± 14.9 kg) after 2 months (1415 ± 128 kcal/day) was not significantly different from the baseline value at admission to the center (1398 ± 138 kcal/day).

Study 5

The difference between measurements with mouthpiece and ventilated hood was larger in patients than in control subjects, but no systematic difference could be established between both devices in either group. The

![Fig. 2. Difference against mean resting energy expenditure (REE) measured at complete rest and after light physical activities. Mean REE = (REEmouth + REEactivity)/2.](image)

![Fig. 3. Difference against mean of repeated resting energy expenditure (REE) measurements with a 2-month interval. Mean REE = (REEbaseline + REEmonths)/2.](image)

![Fig. 4. Difference against mean resting energy expenditure based on VO2 measured using a mouthpiece and a ventilated hood. Mean REE = (REEmouth + REEhood)/2. O---, patients; +---, control subjects.](image)

**TABLE II**

<table>
<thead>
<tr>
<th>Time</th>
<th>Patients</th>
<th>Control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 min</td>
<td>1420 ± 242</td>
<td>1510 ± 237</td>
</tr>
<tr>
<td>10 min</td>
<td>1410 ± 226</td>
<td>1505 ± 224</td>
</tr>
<tr>
<td>15 min</td>
<td>1410 ± 237</td>
<td>1514 ± 225</td>
</tr>
<tr>
<td>20 min</td>
<td>1414 ± 239</td>
<td>1521 ± 229</td>
</tr>
<tr>
<td>25 min</td>
<td>1428 ± 243</td>
<td>1531 ± 229</td>
</tr>
<tr>
<td>30 min</td>
<td>1436 ± 245</td>
<td>1535 ± 231</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The ventilated hood system appears to be a comfortable method to measure REE in patients with severe COPD. The ethanol combustion tests revealed that when properly maintained, calibrated, and interfaced to the patient, the device is very accurate.

Standard measurements were performed in the early morning after an overnight fast, at least 2 hours after the patients received their maintenance medication. Drug treatment in the majority of patients includes β2-agonists and theophylline, both potentially capable of increasing metabolic rate. The precise influence of these drugs was not measured because withdrawing treatment might exacerbate the condition. On the other hand, bronchodilating treatment itself may reduce the work of breathing. As suggested by others, the obtained REE is thus reflective of the "best case" ventilatory conditions.
A considerable number of patients were dyspneic at rest or suffered from severe exercise impairment. Washing, dressing, and shaving are activities that require frequent use of respiratory muscles. In patients with a severe air-flow obstruction, oxygen consumption of the respiratory muscles may increase to 40% of total \( V_O_2 \). Nevertheless, in agreement with findings in patients not suffering from COPD, we found that limited physical activity had no measurable effect on REE when a short rest was taken before the assessment.

Because subjects can breathe spontaneously in a ventilated canopy, it is possible to perform measurements requiring longer duration in a supine position with minimal discomfort. However, for a reliable assessment of REE, it is not necessary to perform long experiments or to strictly standardize the actual duration of the measurement, provided that a period is used (in our studies, 7 minutes) to adjust to the hood. Based on the experiments and to obtain an optimum between sample frequency and acceptability of the measurement, we changed the duration of our standard REE experiments from 30 to 15 minutes. Reproducibility of two measurements with the ventilated hood performed under the same standard conditions with an interval of 2 months was excellent and comparable with findings in healthy subjects.

A disadvantage of face masks, excluding full-face masks with diluted air stream, and mouthpieces is that it is nearly impossible to prevent air leaks. These are eliminated with a ventilated hood system because the hood is at a pressure slightly below barometric. Furthermore, the discomfort associated with masks, nose clips, and mouthpieces can alter breathing pattern, create anxiety, and prevent the achievement of the resting state.

On the other hand, a hood may create claustrophobic reactions. Although in some patients measurements with a mouthpiece and a ventilated hood indeed varied substantially, no systematic difference was established in patients or control subjects.

The following implications for the clinical measurement of resting metabolic rate can be drawn from these results. REE measurements using a ventilated hood are highly reproducible, suggesting that one measurement will suffice to characterize resting metabolic rate at a certain time point in patients with stable COPD. Because it seems justified to neglect variations in light physical activities, REE in patients with severe COPD can be measured on an outpatient basis providing a rest is taken before the measurement. Because the assessment of REE by indirect calorimetry has been facilitated by modern technology it opens possibilities for the future as a routine test to contribute information to aid in determining calorific requirements and/or to mark metabolic status. Ethanol combustion is a useful test to determine accuracy of the device, and should be performed on a regular basis.

REFERENCES