Resting energy expenditure in cryptogenic fibrosing alveolitis

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ABSTRACT: A proportion of patients with chronic airflow limitation appear to have a raised resting energy expenditure (REE). This has been suggested as the reason for weight loss which may occur in these patients. A previous study found an increased REE in patients with interstitial lung disease of mixed aetiology. We were interested in studying REE in a more homogeneous group, with cryptogenic fibrosing alveolitis (CFA).

Twenty patients with CFA were studied. They were compared with 18 controls matched for age, sex, weight and height. REE was measured by indirect calorimetry. Fat-free mass (FFM), was estimated by anthropometry. Patients had respiratory function tests performed, disability related to breathlessness was assessed by the St George’s Respiratory Questionnaire.

Mean REE in the CFA group was not different from the control group: 5.20 (0.56) versus 5.12 (0.51) kJ·h⁻¹·kgFFM⁻¹. REE was elevated to greater than 110% of the value predicted by the Harris-Benedict equation in one CFA patient and in no control subjects. There was no correlation of REE with weight, pulmonary function tests, arterial oxygen saturation or activity score.

The prevalence of a raised resting energy expenditure in cryptogenic fibrosing alveolitis patients with low transfer factor and relatively preserved vital capacity is low, and is less than that reported previously in a group of patients with interstitial lung disease of mixed aetiology.


A proportion of patients with chronic obstructive pulmonary disease (COPD) or chronic asthma have a raised resting energy expenditure (REE), both when compared to values given by prediction equations and when compared to matched controls [1]. The elevation in REE has been proposed as a possible cause of the weight loss seen in some patients. The mechanism of the elevated REE is not known but it has been proposed that it may, in part, be secondary to an increased work of breathing. If this were the case, patients with other respiratory disorders that caused an increase in the work of breathing would also be expected to have a raised REE. The work of breathing is increased in conditions that cause pulmonary fibrosis [2]. Fitting et al. [3] studied 12 patients with interstitial lung disease of mixed aetiology and found their mean REE to be significantly elevated. We were interested in examining the prevalence of hypermetabolism in a more homogenous group of patients with interstitial lung disease, and to see whether there was any relationship between REE and respiratory physiology, body composition and symptom score.

Methods

Patients and study design

Twenty patients with cryptogenic fibrosing alveolitis (CFA) were recruited. The diagnosis was made on the basis of a typical history of progressive breathlessness, physical examination revealing bibasal fine inspiratory crackles and finger clubbing, bilateral interstitial shadowing on chest radiography, no coexisting connective tissue disease and no history of exposure to known fibrogenic agents, including asbestos, drugs or other agents known to cause allergic alveolitis. There was no evidence of coexisting cardiac or systemic disease. In addition, the diagnosis was confirmed by transbronchial or open lung biopsy and/or high resolution computed tomography (HRCT) showing typical appearances of basal peripheral lung fibrosis plus areas of ground-glass appearance. Patients with evidence of other disease, particularly emphysema and pleural disease, were excluded. The HRCT scans were all interpreted by one experienced respiratory radiologist.

All patients attending our respiratory out-patients department were screened for possible inclusion and the patients included were sequential patients who met the inclusion criteria, except for one patient who did not want to take part in the study. The patients were studied when they were in a stable clinical state. Respiratory function tests were carried out in a regional lung function laboratory by experienced technicians. Spirometry was measured with a dry wedge spirometer (Vitalograph Ltd, Bucks, UK), lung volumes using a modified water-filled Collins spirometer (Warren E. Collins, MA, USA), and carbon monoxide transfer factor with the adapted Collins spirometer using the single-breath technique. Normal values were taken...
from the report of the working party for the European Coal and Steel Community [4]. Arterial blood gas values at rest breathing room air were measured from the radial artery in 14 patients (Radiometer, Copenhagen, Denmark). Eighteen healthy control subjects matched to the patients with regard to age, sex, height and weight were included in this study and underwent the metabolic study and anthropometric measures. The control subjects were matched to the patients with regard to age, sex, height and weight, had never smoked, and had no respiratory symptoms.

**REE, body composition, and quality of life**

REE was measured by open-circuit indirect calorimetry using a Datex Deltrac Metabolic Monitor (Datex Instrumentarium Ltd, Helsinki, Finland). This comprises a plastic canopy, which is placed over the head while the subject lies semi-reclined, relaxed and still. Room air is drawn into the canopy by a constant flow-rate generator. The flow-rate is checked monthly by nitrogen gas infusion and remains stable at 42.9 L·min⁻¹. A paramagnetic oxygen analyser and an infra-red carbon dioxide analyser sample continuously from the canopy and a microprocessor calculates oxygen consumption (V'O₂) and carbon dioxide production (V'CO₂). A read out of average values is given at 1 min intervals. Sampling is continued until six steady-state readings (<5% variation) are obtained. This usually takes about 15–20 min. The cumulative variance by this method for V'O₂ and V'CO₂ in the physiological range as checked by "dummy gases" was <2%. Each time the metabolic monitor was used, the gas analysers were calibrated by means of a commercial calibration gas mixture (Electrochem Ltd, Stoke on Trent, UK), which was independently checked by the Haldane technique.

Measurements were made in the morning after an overnight fast and when the patient was in a stable clinical state. The patients were brought to the laboratory by taxi to minimize exertion that morning. They collected an overnight timed urine sample. On arrival they rested while a quality of life questionnaire, the St George's Respiratory Questionnaire (SGRQ), was administered [5]. REE was measured as described above, and then anthropometric measures were made. These consisted of height, weight, mid-arm circumference (MAC), triceps skinfold (TSF), taken midway between the acromium and the olecranon using skin callipers (John Bull, British Indicators Ltd, Burgess Hill, UK), and handgrip strength (HGS), using a handgrip dynamometer (C.H. Sterling Co., Chicago, USA). A second REE measurement was then made and the results of the two were averaged.

Analysis of variance showed no difference between the first and the second V'O₂ and V'CO₂ measurement on the same day. Urinary nitrogen was assayed by the Kjeldhal technique to give an estimate of nonprotein respiratory quotient using the equations of FRAYN [6]. REE was then estimated and fuel oxidation rates were calculated Muscle mass was estimated from height, TSF and MAC using the equations of BLAQUE-BILAB et al. [3]. Total body fat, (IBW) was calculated according to the equation of HARRIS and BENEDICT [9]. REE was also expressed as kilojoules per hour per kilogram of fat-free mass, (kJ·h⁻¹·kg⁻¹FFM) and as a percentage of the predicted value given by the equation of FITTING et al. [3], which is related to FFM (%REE-FFM).

The SGRQ is a validated standardized questionnaire, which gives a score for activity, symptoms and impact, plus an overall score in relation to respiratory disease. It has been used primarily for patients with chronic airflow obstruction but the activity score is relevant for other patients with respiratory dysfunction. Scores are given as a percentage, and a higher score indicates more severe impairment. In our experience, normal controls score 0–11%, therefore we did not measure symptom scores on the control subjects. Further details are given in the Appendix.

The study was approved by the Leeds Eastern Health Authority Clinical Research Ethics Committee.

**Data analysis**

Data are presented as mean (SD), with 95% confidence intervals (95% CI) given. Differences between groups were analysed using the unpaired two tailed t-test. Statistical significance was taken at the 0.05 level. The relationship between variables was examined using linear regression. It was estimated that the power of the study to detect a difference in REE of 10% was 0.9 (α set at 0.05).

**Results**

Twenty patients (five females and 15 males) were studied, together with 18 matched controls (five females and 13 males). Fifteen of the patients were receiving maintenance oral prednisolone therapy (mean dose 12.8 mg), of which one in addition was on a regimen of weekly intravenous methylprednisolone. Seven patients were taking nonsteroidal immunosuppressive therapy (five cyclophosphamide, one azathioprine and one cyclosporine). The mean age of the patients was 62 yrs (range 37–79 yrs). The mean age of the control group was 57 yrs (range 32–71 yrs). A summary of the respiratory function and SGRQ activity scores of the patients is presented in table 1. Overall, they had relatively well-preserved lung volumes with a mean forced expiratory volume in one second (FEV₁) of 77% predicted and mean total lung capacity (TLC) of 84% pred. However, there was severe impairment of gas exchange, with both the transfer factor of the lung for carbon monoxide (TL;CO) and the gas transfer corrected for lung volume (KCO) being less than 45% pred. Most of the patients had high activity scores on the SGRQ, indicating significant restriction of their activity due to breathlessness.
Body composition

The patients were well-matched with controls for weight and height, as is shown in table 2. The mean (SD) weight of patients was 115 (15)% of IBW. One patient was significantly underweight, at less than 90% IBW. Mean (SD) muscle mass estimated from TSF and MAC was 29.9 (4.3) kg in the CFA patients and 31.9 (7.0) kg in the controls (difference nonsignificant (ns)). There was a very strong correlation between the muscle mass estimated from the TSF and MAC and FFM estimated by TSF according to the equation of DURNIN and WORMERSLEY [8] (p<0.0001, Pearson's correlation coefficient). FM and FFM were present in similar proportions in patients and controls. HGS was similar in both groups.

REE

There was no significant difference in REE between the patient and control group, as shown in table 3 and figure 1. The mean (SD) REE of the CFA patients was 98 (10)% of the value predicted by the Harris Benedict equation, and only one patient had a REE significantly higher than expected, at 111%. For the control group, mean (SD) REE was 97 (6)% (95% CI for the difference, -4.7%). REE expressed per kilogram of FFM was 5.20 (0.56) kJ·h⁻¹·kg⁻¹ in the patients, and 5.12 (0.51) kJ·h⁻¹·kg⁻¹ in the controls (95% CI for the difference -0.28–0.43). The equation of FITTING et al. [3] was used for estimation of predicted REE per kilogram FFM based on 46 normal male subjects; and it was found that %REEFFM of the CFA patients was 104 (12)% predicted and for controls was 102 (9)% (95% CI -4.4–9.6%) (fig. 2). There was no correlation between REE and %FFM, TLC, CO, vital
In conclusion, we found a low prevalence of elevation of resting energy expenditure in a group of well-nourished patients with cryptogenic fibrosing alveolitis with severe impairment of gas transfer and preserved lung volumes. Before it can be concluded that metabolic rate is raised in patients with other interstitial lung diseases, further studies in particular disease categories are required.

Appendix

Activity Section of St George's Respiratory Questionnaire

This consists of seven activities that may make a person feel breathless and nine activities that may be affected by
a person's breathing. The respondent is required to give a positive response if affected. The questions are weighted and the score is expressed as a percentage, with high scores indicating greater disability. Examples of representative scores are given below:

Usually breathless when sitting or lying still and takes a long time to get washed or dressed=100%

Breathless walking around the home and finds that jobs such as housework take a long time=72%

Breathless after walking up a flight of stairs and has to stop or slow down if hurries or walks fast=41%

Breathless walking up hills and finds light gardening, dancing, playing bowls difficult due to breathing=29%

Only really becomes breathless playing sports or games and would find it difficult to run, cycle or swim fast=11%

(In our experience, normal subjects score 0–11%)

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References


