Effect of carbohydrate rich versus fat rich loads on gas exchange and walking performance in patients with chronic obstructive lung disease

J Efthimiou, P J Mounsey, D N Benson, R Madgwick, S J Coles, M K Benson

Abstract

Background High calorie intakes, especially as carbohydrate, increase carbon dioxide production (V\textsubscript{CO\textsubscript{2}}) and may precipitate respiratory failure in patients with severe pulmonary disease. Energy obtained from fat results in less carbon dioxide and thus may permit a reduced level of alveolar ventilation for any given arterial blood carbon dioxide tension (P\textsubscript{ACO\textsubscript{2}}).

Methods Ten patients with stable chronic obstructive lung disease underwent a six minute walk before and 45 minutes after taking 920 kcal of a fat rich drink, an isocalorific amount of a carbohydrate rich drink, and an equal volume of a non-calorific control liquid on three separate days, in a double blind randomised crossover study. Borg scores of the perceived effort to breathe were measured at the beginning and end of each six minute walk. Minute ventilation (V\textsubscript{E}), V\textsubscript{CO\textsubscript{2}}, oxygen consumption (V\textsubscript{O\textsubscript{2}}), respiratory quotient (RQ), arterial blood gas tensions, and lung function were measured before and 30 minutes after each test drink.

Results Baseline measurements were similar on all three test days and the non-calorific control drink resulted in no changes in any of the measured variables. The carbohydrate rich drink resulted in significantly greater increases in V\textsubscript{E}, V\textsubscript{CO\textsubscript{2}}, V\textsubscript{O\textsubscript{2}}, RQ, P\textsubscript{ACO\textsubscript{2}}, and Borg score and a greater fall in the distance walked in six minutes than the fat rich drink (mean fall after carbohydrate rich drink 17 m v 3 m after fat rich drink and the non-calorific control). The increase in V\textsubscript{CO\textsubscript{2}} correlated significantly with the decrease in six minute walking distance and the increase in Borg score after the carbohydrate rich drink. The only significant change after the fat rich drink when compared with the non-calorific control was an increase in V\textsubscript{CO\textsubscript{2}}.

Conclusions Comparatively small changes in the carbohydrate and fat constitution of meals can have a significant effect on V\textsubscript{CO\textsubscript{2}}, exercise tolerance, and breathlessness in patients with chronic obstructive lung disease.

Introduction Patients with severe chronic obstructive lung disease possess little ventilatory reserve and disease possess little ventilatory reserve and are at risk of developing acute respiratory failure, with hypercapnia as a complication. The hypercapnia in these patients has generally been attributed to mechanical factors limiting ventilation and to reduced central respiratory drive. The potential adverse effects of carbohydrate loads in patients with chronic obstructive lung disease, particularly with regard to carbon dioxide production (V\textsubscript{CO\textsubscript{2}}), has received considerable attention recently.

The absorption and metabolism of carbohydrate loads in normal subjects causes an increase in V\textsubscript{CO\textsubscript{2}} and respiratory quotient (RQ). The increase in V\textsubscript{CO\textsubscript{2}} results from a shift in net whole body fuel utilisation from predominantly fat (metabolised with an RQ of 0·7) to predominantly carbohydrate (metabolised with an RQ of 1·0), as well as from the thermogenic effect of food itself. In addition, ingestion of carbohydrate in excess of energy requirements may result in lipogenesis, leading to a further increase in V\textsubscript{CO\textsubscript{2}}.

The increased load of carbon dioxide must be eliminated predominately by the lungs, and people with normal lungs do this easily. Patients with chronic obstructive lung disease, who are prone to hypercapnia, are less able to excrete this load, and the optimal management of these patients may involve a shift from a diet that is predominantly carbohydrate to one with a greater proportion of fat. The net effect of such a change should be a lower V\textsubscript{CO\textsubscript{2}} and a reduced tendency to hypercapnia, possibly with symptomatic benefit in terms of improved exercise tolerance.

This study was designed to compare the effect of carbohydrate and fat rich loads on V\textsubscript{CO\textsubscript{2}}, oxygen consumption (V\textsubscript{O\textsubscript{2}}), RQ, and exercise tolerance in patients with stable chronic obstructive lung disease, in a controlled double blind randomised crossover manner.

Methods

Patients Ten patients (seven men, three women) with stable chronic obstructive lung disease were studied. Their clinical and physiological details are summarised in table 1. Their mean age was 69·2 (SD 3·8) years (range 63–75). Three patients had clinical and physiological evidence of emphysema with a carbon monoxide transfer factor (TL\textsubscript{CO}) corrected for alveolar volume (K\textsubscript{CO}) of less than 80% of predicted values, and two had a body weight less than 90% of predicted values. All had spirometric evidence of severe airflow obstruction with a mean forced
Table 1  Baseline clinical and physiological details of patients

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Weight (kg)</th>
<th>% pred</th>
<th>FEV₁ (l)</th>
<th>TLC (% pred)</th>
<th>VCO₂ (liters/min)</th>
<th>KCO (l/min/kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>52.5</td>
<td>85.6</td>
<td>0.42</td>
<td>16.9</td>
<td>5.8</td>
<td>1.1</td>
</tr>
<tr>
<td>2</td>
<td>73</td>
<td>M</td>
<td>69.5</td>
<td>94.2</td>
<td>0.67</td>
<td>17.7</td>
<td>6.1</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>69</td>
<td>F</td>
<td>59.9</td>
<td>90.3</td>
<td>0.74</td>
<td>34.3</td>
<td>8.7</td>
<td>1.6</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>M</td>
<td>80.3</td>
<td>117.2</td>
<td>0.82</td>
<td>27.7</td>
<td>6.0</td>
<td>2.7</td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td>F</td>
<td>65.3</td>
<td>97.7</td>
<td>0.73</td>
<td>48.6</td>
<td>5.6</td>
<td>1.9</td>
</tr>
<tr>
<td>6</td>
<td>68</td>
<td>M</td>
<td>58.7</td>
<td>95.3</td>
<td>0.80</td>
<td>37.0</td>
<td>6.7</td>
<td>2.1</td>
</tr>
<tr>
<td>7</td>
<td>63</td>
<td>M</td>
<td>71.2</td>
<td>105.8</td>
<td>1.05</td>
<td>68.0</td>
<td>3.2</td>
<td>4.7</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>F</td>
<td>64.8</td>
<td>99.1</td>
<td>0.50</td>
<td>26.4</td>
<td>6.6</td>
<td>1.5</td>
</tr>
<tr>
<td>9</td>
<td>75</td>
<td>F</td>
<td>54.4</td>
<td>88.0</td>
<td>0.74</td>
<td>33.6</td>
<td>5.9</td>
<td>1.3</td>
</tr>
<tr>
<td>10</td>
<td>67</td>
<td>M</td>
<td>67.5</td>
<td>104.4</td>
<td>0.50</td>
<td>23.1</td>
<td>6.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Mean</td>
<td>69.2</td>
<td></td>
<td>63.7</td>
<td>98.1</td>
<td>0.66</td>
<td>31.4</td>
<td>6.2</td>
<td>2.3</td>
</tr>
<tr>
<td>SD</td>
<td>3.8</td>
<td></td>
<td>8.4</td>
<td>9.8</td>
<td>0.19</td>
<td>10.2</td>
<td>1.1</td>
<td>0.8</td>
</tr>
</tbody>
</table>

FEV₁ = forced expiratory volume in one second; TLC = total lung capacity; KCO = carbon monoxide transfer factor; Pao₂ = arterial oxygen tension; PACO₂ = arterial carbon dioxide tension; COLD = chronic obstructive lung disease; % pred = percentage of predicted values.

Base metabolic rate determinations were made prior to collection of samples, and for each block of measurements expired gas was sampled for analysis of oxygen and carbon dioxide concentrations and ventilation. An Inspiration/Exhalation Ventilation Recorder (Gould Brush) was used to sample each breath through a mouthpiece, with the expiratory volume (VE) and carbon dioxide concentration (VCO₂) recorded. The respiratory exchange ratio (RQ) was calculated.

FEV₁ = force expiratory volume in one second; TLC = total lung capacity; KCO = carbon monoxide transfer factor; Pao₂ = arterial oxygen tension; PACO₂ = arterial carbon dioxide tension; COLD = chronic obstructive lung disease; % pred = percentage of predicted values.

AARCO, a computer program (Addison-Wesley, Reading, SL, UK) was used to calculate the mean values of each measured variable and to obtain regression analyses. Results are expressed as mean ± standard deviation.

**Study Protocol**

Patients were asked to fast for 12 hours prior to their attendance at the laboratory. During this period, patients were given water ad libitum. On arrival, they were instructed to sit upright and rest quietly for 5 minutes, after which time expired gas samples were collected and analyzed for oxygen and carbon dioxide concentrations. After this period, patients were asked to inhale and exhale a predetermined volume of expiratory gas, which was subsequently sampled and analyzed for oxygen and carbon dioxide concentrations. The respiratory exchange ratio (RQ) was calculated.

**Discussion**

The results of the study showed that patients with chronic obstructive lung disease had reduced FEV₁ and TLC values, indicating airflow limitation. The mean predicted values were 85.6% for FEV₁ and 97.7% for TLC. The mean measured values of FEV₁ and TLC were 78.5% and 75.6%, respectively, indicating significant airflow limitation.

**Conclusion**

The study findings suggest that patients with chronic obstructive lung disease have reduced lung function, as evidenced by decreased FEV₁ and TLC values. These results highlight the importance of early diagnosis and intervention to prevent the progression of chronic obstructive lung disease.
Table 2  Mean (SD) values before and after each test drink in 10 patients with chronic obstructive lung disease

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>% Change</th>
<th>Before</th>
<th>After</th>
<th>% Change</th>
<th>Before</th>
<th>After</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-calorific drink</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V̇e (l/min)</td>
<td>9.5 (2.0)</td>
<td>9.4 (1.9)</td>
<td>-1.1</td>
<td>9.3 (2.1)</td>
<td>11.1 (2.8)</td>
<td>19.4</td>
<td>9.2 (1.9)</td>
<td>10.5 (2.4)</td>
<td>14.1</td>
</tr>
<tr>
<td>V̇CO₂ (l/min)</td>
<td>0.24 (0.03)</td>
<td>0.24 (0.03)</td>
<td>0</td>
<td>0.24 (0.03)</td>
<td>0.30 (0.05)</td>
<td>25.7</td>
<td>0.23 (0.03)</td>
<td>0.28 (0.04)</td>
<td>21.7</td>
</tr>
<tr>
<td>V̇O₂ (l/min)</td>
<td>0.28 (0.04)</td>
<td>0.27 (0.03)</td>
<td>-5.6</td>
<td>0.27 (0.03)</td>
<td>0.29 (0.04)</td>
<td>7.4</td>
<td>0.27 (0.03)</td>
<td>0.28 (0.04)</td>
<td>3.7</td>
</tr>
<tr>
<td>RQ</td>
<td>0.85 (0.05)</td>
<td>1.02 (0.06)</td>
<td>14.4</td>
<td>0.87 (0.05)</td>
<td>1.02 (0.06)</td>
<td>14.4</td>
<td>0.85 (0.05)</td>
<td>0.92 (0.05)</td>
<td>4.5</td>
</tr>
<tr>
<td>Pao₂ (kPa)</td>
<td>7.68 (0.58)</td>
<td>7.69 (0.57)</td>
<td>0.1</td>
<td>7.66 (0.59)</td>
<td>7.95 (0.60)</td>
<td>3.9</td>
<td>7.69 (0.57)</td>
<td>7.87 (0.58)</td>
<td>2.4</td>
</tr>
<tr>
<td>Paco₂ (kPa)</td>
<td>6.08 (0.85)</td>
<td>6.07 (0.96)</td>
<td>-0.2</td>
<td>6.06 (0.96)</td>
<td>6.13 (0.95)</td>
<td>1.3</td>
<td>6.09 (0.86)</td>
<td>6.07 (0.96)</td>
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<tr>
<td>6 MlW (m)</td>
<td>228 (57)</td>
<td>229 (56)</td>
<td>0.4</td>
<td>227 (58)</td>
<td>210 (57)</td>
<td>-8.2</td>
<td>225 (56)</td>
<td>222 (54)</td>
<td>-1.2</td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>0.66 (0.19)</td>
<td>0.66 (0.19)</td>
<td>0</td>
<td>0.65 (0.21)</td>
<td>0.64 (0.22)</td>
<td>-0.2</td>
<td>0.65 (0.18)</td>
<td>0.66 (0.19)</td>
<td>0.2</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>1.84 (0.48)</td>
<td>1.85 (0.47)</td>
<td>0.5</td>
<td>1.85 (0.90)</td>
<td>1.83 (0.50)</td>
<td>-1.2</td>
<td>1.85 (0.47)</td>
<td>1.81 (0.47)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*For the significance of differences between the changes in the measured variables between Ensure-plus and Pulmocare.

V̇e = minute ventilation; V̇CO₂ = carbon dioxide production; VO₂ = oxygen consumption; RQ = respiratory quotient; Pao₂ = arterial oxygen tension; Paco₂ = arterial carbon dioxide tension; 6 MlW = six minute walking distance; FEV₁ = forced expiratory volume in one second; FVC = forced vital capacity.
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Relation between increase in carbon dioxide production (\(\dot{V}_{\text{CO}_2}\)) and fall in six minute walking distance after the carbohydrate rich drink Ensure-plus in 10 patients with chronic obstructive lung disease.

\(r = 0.56, p < 0.02\)

\(= 0.49, p < 0.05\) seen immediately before the six minute walk.

**DURATION OF CHANGES AFTER TEST DRINKS**

The increases in \(\dot{V}_{\text{CO}_2}\) of one subject (case 6, table 1) 30 minutes and one, two, and three hours after Ensure-plus were 24-7%, 20-3%, 11-9%, and 1-6% respectively and the equivalent values 30 minutes and one, two, and three hours after Pulmocare were 15-9%, 13-1%, 4-8%, and 0-3% respectively. The associated decreases in six minute walking distance at 30 minutes and one, two, and three hours after Ensure-plus were 7-1%, 5-7%, 1-3%, and 0-2% respectively and the equivalent values 30 minutes and one, two, and three hours after Pulmocare were 0-8%, 0-7%, 0-4%, and 0-1% respectively.

**EFFECT OF BRONCHODILATORS ON GAS EXCHANGE AND EXERCISE TOLERANCE**

Apart from small increases in \(\dot{V}_{\text{CO}_2}\) (2-1% at one hour, 1-7% at two hours) and \(\dot{V}_{\text{O}_2}\) (1-4% at one hour, 0-9% at two hours), there were no definite changes in gas exchange or six minute walking distance after the patient’s normal drug treatment, which consisted of nebulised salbutamol and oral slow release amino-phylline.

**EFFECT OF NON-CALORIFIC DRINK**

There were no significant changes in any of the variables following the non-calorific drink (table 2). The baseline values of all the variables were similar on the three test days.

**Discussion**

This study shows that carbohydrate rich loads may increase \(\dot{V}_{\text{CO}_2}\), \(\dot{V}_{\text{O}_2}\), RQ, and Paco2 and decrease exercise tolerance to a greater extent than fat rich loads of identical calorific value in patients with chronic obstructive lung disease. Gas exchange was measured 30 minutes after finishing the test drinks because (a) our preliminary studies showed that the peak \(\dot{V}_{\text{CO}_2}\) occurred around this time; (b) previous similar studies in normal subjects and patients with chronic obstructive lung disease used this protocol; (c) a previous study in cats showed that peak postprandial Paco2 occurred at this time; and (d) the peak RQ after an oral sugar load also occurs around 30 minutes postprandially.

The perceived effort to breathe (the Borg score) following a six minute walk also increased more after the carbohydrate rich than the fat rich load. The decrease in exercise tolerance and increase in Borg score both correlated with the increase in \(\dot{V}_{\text{CO}_2}\) after the carbohydrate rich load. In the patient who was studied for several hours after the carbohydrate rich load the changes in \(\dot{V}_{\text{CO}_2}\) and six minute walking distance persisted for at least two hours. Although the changes seen after the calorific drinks were generally small, in a few patients they were substantial and may have important clinical implications for the diet and timing of meals in such patients.

In the past decade several studies have showed that large carbohydrate loads in patients being ventilated, even without respiratory disease, can result in an increase in \(\dot{V}_{\text{CO}_2}\) and precipitate respiratory distress and rarely respiratory failure. Normal subjects given a carbohydrate load increase their \(\dot{V}_{\text{CO}_2}\), \(\dot{V}_{\text{O}_2}\), and RQ to a similar extent but unlike patients with chronic obstructive lung disease do not increase their Paco2 presumably because they are able to increase their ventilation accordingly. In patients with stable chronic obstructive lung disease a pure carbohydrate load is

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**Table 3 Mean (range) Borg scores before and after each test drink**

<table>
<thead>
<tr>
<th>Before drink</th>
<th>After drink</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before 6 MW</td>
<td>After 6 MW</td>
</tr>
<tr>
<td>Non-calorific drink</td>
<td>11-2 (9-12)</td>
<td>16-0 (14-18)</td>
</tr>
<tr>
<td>Ensure-plus</td>
<td>11-2 (9-13)</td>
<td>16-1 (14-19)</td>
</tr>
<tr>
<td>Pulmocare</td>
<td>11-4 (19-13)</td>
<td>16-2 (14-18)</td>
</tr>
</tbody>
</table>

6 MW = six minute walk.

*p < 0.01 for difference between change in Borg score after Ensure-plus and change after Pulmocare; p < 0.001 also for change after Ensure-plus vs change after non-calorific drink.
known to increase $\dot{V}CO_2$ and decrease exercise tolerance, as assessed by a 12 minute walk. In our patients a carbohydrate rich meal (53% carbohydrate) resulted in a greater increase in $\dot{V}CO_2$ and a greater fall in exercise tolerance as determined by a six minute walk than did a fat rich meal (28% carbohydrate). The fall in exercise tolerance after the carbohydrate rich meal correlated with the increase in $\dot{V}CO_2$, suggesting an important association between the change in gas exchange and change in functional capacity.

Maximal exercise capacity, as measured by incremental cycle ergometry, decreases after a pure carbohydrate load and after a carbohydrate rich load of identical calorific value. The results of our study show that forms of exercise other than the maximal stress imposed by cycle ergometry may also be impaired and that such submaximal exercise may be more relevant to the abilities and normal exercise tolerance of severely limited patients. Moreover, the reduction in exercise tolerance was significantly worse after the carbohydrate rich than the fat rich load. This suggests that even relatively small changes in the constitution of meals in terms of carbohydrate and fat, may have significant effects on exercise tolerance and breathlessness in patients with severe chronic obstructive lung disease.

There are several possible mechanisms by which a carbohydrate load may decrease exercise performance. Changes in the proportion of fat and carbohydrate metabolised will alter respiratory gas exchange and ventilation, with carbohydrate loads causing an increase in both $\dot{V}CO_2$ and $RQ$. We suggest that the decrease in walking distance in our patients occurred because ventilation at any given walking pace increased more, with a greater rise in $\dot{V}CO_2$ after the carbohydrate rich meal than the fat rich meal. Although ventilation during the six minute walk was not measured in our study, consistently greater increases in resting ventilation occurred immediately before the six minute walk after the carbohydrate rich meal. Significant increases in $V$E have been reported during cycle ergometry after a pure carbohydrate meal.

The Borg score of the perceived effort to breathe increased significantly more at the end of the six minute walk after the carbohydrate rich meal than after the fat rich meal. In addition, the increase in Borg score was significantly correlated with the increase in both resting $V$E and $\dot{V}CO_2$ after the carbohydrate rich but not the fat rich meal. The Borg score correlates well with minute ventilation during exercise, both in patients with chronic obstructive lung disease and in normal subjects and our findings are consistent with this. Although the changes in exercise tolerance and breathlessness in our patients were generally small (maximum fall in six minute walking distance 15%, maximum increase in Borg score 14%), the combination of feeling more breathless and attaining a lower level of exercise may in some patients be of substantial clinical importance.

Various drugs used in the treatment of patients with chronic obstructive lung disease, including $\beta$ agonists and methylxanthines, can increase $\dot{V}CO_2$ and $VO_2$ but there was only a small and insignificant increase in these measurements in our patient two hours after taking his normal treatment. Such small changes are unlikely to have contributed to the substantial changes seen after the caloric drinks. All drug treatments were taken at the same time before each study, further reducing the risk of any drug effect.

Several studies have emphasised the frequency of malnutrition in patients with chronic obstructive lung disease, as well as its adverse effects on the respiratory system. As a result, there has been much interest in trying to replete malnourished patients with the disease. Our results show that vigorous attempts to treat malnutrition in patients with chronic obstructive lung disease, particularly with large carbohydrate rich meals, may produce adverse effects on respiratory gas exchange, exercise tolerance, and breathlessness, and we suggest that such factors should be carefully monitored in these patients. Physicians attempting nutritional support in patients with chronic obstructive lung disease should be aware that even comparatively small changes in the constitution of their meals, in terms of both total calories and the proportions of carbohydrate and fat, may have important effects. Further work should attempt to establish the optimal and safest feeding regimens for patients with and without carbon dioxide retention in both stable and acute conditions.


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