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Acute effects of different nutritional supplements on symptoms and functional capacity in patients with chronic obstructive pulmonary disease[1,2]

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ABSTRACT

Background: Use of nutritional supplements in depleted patients with chronic obstructive pulmonary disease (COPD) requires optimization between positive effects on outcome and potential acute adverse effects on metabolism and exercise performance.

Objective: The aim of this study was to investigate the acute effects of nutritional supplements on metabolism and exercise capacity in stable COPD patients.

Design: In part 1, the effects of 3 different energy loads (placebo, 1046 kJ, and 2092 kJ) with a normal distribution of macronutrients were investigated in 14 COPD patients. In part 2, the effects of a fat-rich compared with a carbohydrate-rich supplement (both 1046 kJ) were studied in 11 COPD patients. The study was performed in a randomized, double-blind, crossover fashion. Metabolic and ventilatory variables were measured postprandially and during a submaximal cycle endurance exercise test.

Results: Overall, no immediate negative effects of the supplements were found in part 1. A slight but significant postprandial increase in respiratory quotient was found after the 1046-kJ and 2092-kJ supplements compared with placebo. There was no significant difference in metabolism or exercise capacity after a fat-rich or carbohydrate-rich supplement. Surprisingly, the change in shortness of breath (postprandial compared with preprandial) was significantly greater after the fat-rich supplement.

Conclusions: An energy load up to 2092 kJ had no adverse immediate effect in COPD patients compared with placebo. The subjects who consumed the fat-rich supplement experienced more shortness of breath than did the subjects who consumed the carbohydrate-rich supplement. *Am J Clin Nutr* 2001;73:295–301.

KEY WORDS Nutrition, exercise, COPD, metabolism, chronic obstructive pulmonary disease, nutritional supplement

INTRODUCTION

The association between weight loss and chronic obstructive pulmonary disease (COPD) has long been recognized. In the 1960s, several studies reported that a low body weight and weight loss were negatively associated with survival in COPD (1). Adverse effects of weight loss and, in particular, loss of the fat-free-mass component on skeletal muscle function and exercise capacity were reported extensively (2). Weight loss results from an imbalance between dietary intake and energy expenditure. An elevated resting energy expenditure (3) is reported in COPD, as well as an elevated total daily energy expenditure (4). The latter is related to the increased oxygen cost of breathing and possibly also to a decreased mechanical and metabolic efficiency (5). Therefore, patients with COPD can lose weight despite an apparently normal dietary intake. Besides, symptoms that occur frequently, such as dyspnea and fatigue, as well as an elevated systemic inflammatory response, are reported in relation to a decreased appetite and dietary intake (6, 7). So when optimal adaptation of dietary habits fails to improve dietary intake to preserve body weight, nutritional supplements are commonly indicated. To improve functional capacity, nutritional support should be combined with an anabolic stimulus. Indeed, nutritional support as an integrated part of a pulmonary rehabilitation program results in improvements in muscle function, exercise capacity, and health status (8).

In supplemented COPD patients, potential adverse effects on the ventilatory system of the nutritional support strategy also have to be considered. Nutrition and ventilation are intrinsically related because oxygen is required for optimal energy exchange. Meal-related dyspnea and limited ventilatory reserves may restrict the quantity and composition of nutritional support in patients with respiratory disease.

It was suggested that carbohydrate-rich supplements would induce greater ventilation as a result of a higher respiratory quotient (RQ). In clinically stable patients with COPD, 3 studies (9–11) compared the acute effects of high-energy (3849 kJ) nutritional supplements with high and low carbohydrate contents, respectively, on immediate postprandial energy metabolism at rest and during exercise. For instance, Efthimiou et al (9) found adverse effects of supplements on exercise performance. However, the energy content of the supplements was even higher than that of a normal meal and would therefore be difficult to incorporate into the daily pattern of meal consumption without affecting spontaneous food intake.

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TABLE 1

Physiologic, pulmonary, and metabolic characteristics of the study group[1]

Characteristic	Part 1 (n = 14)	Part 2 (n = 11)
Age (y)	65 ± 11	62 ± 8
Weight (kg)	58.9 ± 6.1	66.5 ± 7.2[1]
BMI (km/m^2)	20.6 ± 1.4	22.6 ± 2.3[1]
FFMI (km/m^2)	16.0 ± 1.3	16.6 ± 1.8
FEV_1 (% of predicted)	36 ± 7	34 ± 12
IVC (% of predicted)	86 ± 16	90 ± 16
FVC (% of predicted)	82 ± 14	87 ± 19
TLC (% of predicted)	127 ± 24	125 ± 23
ITGV (% of predicted)	161 ± 24	166 ± 44
R_{aw} (% of predicted)	225 ± 82	230 ± 113
DL_{CO} (% of predicted)	45 ± 13	64 ± 42
P_aO_2 (kPa)	9.5 ± 1.4	10.1 ± 1.2
P_aCO_2 (kPa)	5.6 ± 1.2	5.5 ± 0.5
S_aO_2 (%)	94.7 ± 1.2	94.8 ± 1.7
*W*max (W)	61 ± 20	71 ± 30

[1] $\bar{x}$ ± SD. FFMI, fat-free mass index; FEV_1, forced expiratory volume in 1 s; IVC, inspiratory vital capacity; FVC, forced vital capacity; TLC, total lung capacity; ITGV, intrathoracal gas volume; Raw, airways resistance; DL_{CO}, diffusion capacity of carbon monoxide; P_aO_2, arterial oxygen pressure; P_aCO_2, arterial carbon dioxide pressure; S_aO_2, oxygen saturation; *W*max, maximal power on cycle ergometer test.

[2] Significantly different from part 1, $P < 0.001$ (independent Student's *t* test).

It is important in daily clinical practice to find out the optimal disease-related nutritional support strategy that improves muscle function but interferes minimally with symptoms and activity patterns. The first aim of the present study was therefore to examine the effects of liquid oral nutritional supplements with different, but clinically applicable, energy contents on symptoms and exercise capacity. The second aim was to compare the effects of a carbohydrate-rich with a fat-rich supplement, at the most optimal energy load, on symptoms and exercise capacity in patients with COPD.

SUBJECTS AND METHODS

Study population

The study group consisted of patients with COPD participating in an inpatient pulmonary rehabilitation program. The patients were in clinically stable condition; patients with signs of an airway infection were excluded. Other exclusion criteria were cardiovascular, neurologic, or endocrine diseases or locomotor limitations and a resting arterial oxygen tension <7.3 kPa, or the need for oxygen supplementation. In part 1, 14 patients (10 men) and in part 2, 11 patients (9 men) participated in and completed the study. Patient characteristics are summarized in **Table 1**. No subject participated in both studies. All subjects were fully informed of the aims and the procedures of the study and gave written informed consent. The ethical committee of Maastricht University approved the study. The procedures followed were in accord with the Helsinki Declaration of 1977, as revised in 1983.

Study design

The first aim of the study was to test the effects of 2 different clinically applicable energy loads (1046 and 2092 kJ compared with placebo) on symptoms, lung function, and exercise capacity (part 1). Second, the effects of a high-carbohydrate compared with a high-fat supplement on symptoms, lung function, and exercise capacity were investigated at the most optimal energy load (1046 kJ) (part 2). The nutritional supplements were administered in a randomized, double-blind, crossover fashion. The composition of the nutritional supplements, which were given as drinks with an equal volume of 200 mL, are shown in **Table 2**. The placebo was a mixture of coffee creamer and lemon syrup with an energy load of 209 kJ. There was not more than 1 d between the study days. The measurements were done within 2 wk after the patients completed an incremental bicycle ergometer test. The administration of medication was standardized on the study days. Also, a breakfast with the same composition was given every study day at the same time (0730). The study design for both studies is shown in **Figure 1**.

Part 1

The experiment started 2 h after breakfast at 0930. Patients had to ingest the supplement in 15 min. Fifteen minutes after the supplement was consumed pulmonary function was measured and 30 min after the supplement was finished the exercise test began.

Part 2

The procedure followed in part 2 was exactly the same as that in part 1, except that blood glucose was analyzed as well. Furthermore, the patients had to ingest the supplement in 5 min because differences in gastric emptying might have influenced the results if patients drank the supplements at different speeds.

Assessments

Pulmonary function

The flow-volume curve was measured by using a flow screen (Masterlab; Jaeger, Wurzburg, Germany). Forced expiratory

TABLE 2

Energy profile and composition of the different supplements

	Part 1		Part 2	
Composition	Normal[1]	Normal[2]	Carbohydrate rich[3]	Fat rich[4]
Energy (kJ)	1046	2092	1046	1046
Protein (% of energy)	21	21	20	20
Fat (% of energy)	34	36	20	60
Carbohydrate (% of energy)	45	43	60	20

[1] 154 g Nutridrink (energy-rich nutritional supplement, Nutricia, Zoetermeer, Netherlands), 10 g Protifar (protein powder, Nutricia).

[2] 117 g Nutridrink, 35 g Protifar, 40 g maltodextrin-fat mixture (Nutricia).

[3] 179 g Respifor (energy-rich nutritional supplement for chronic obstructive pulmonary disease patients; Nutricia).

[4] 90 g Pulmocare (fat-rich nutritional supplement, Abbott Company, Abbott Park, IL), 12 g Protifar, 17 g Solagen (soy-emulsion, SHS, Liverpool, United Kingdom).

Time	0945	1000	1030	1045	1115	1125	1145	Recovery
Flow-volume measurement	x	supplement	x					
Symptoms by VAS	x		x	x				x
Oxygen Saturation	every minute							
$\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$				every minute				
Heart rate				every minute				
Glucose				x	every 10 min			x
Lactate				x	every 2 min			x
Peak work rate					**50% of *W*max**	**70% of *W*max**		

FIGURE 1. Study design. VAS, visual analogue scale; $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production; V_E, minute ventilation.

volume in 1 s, inspiratory vital capacity, forced vital capacity, mean expiratory flow, and peak expiratory flow were calculated from the flow-volume curve. The highest value of ≥3 measurements was used for analysis. The values were expressed as a percentage of the reference value (12).

Symptoms

Using a visual analogue scale, the patients reported the following symptoms: shortness of breath, satiety, and pain in the legs. The severity of the symptoms was assessed before and after administration of the supplements and before and after the exercise test. The symptom of pain in the legs was scored only before and after the exercise test.

Oxygen saturation

During the study, transcutaneous oxygen saturation was measured with a pulse oxymeter. The electrode was placed around a finger of the left hand of the subject. Measurements were done with an SaO_2 monitor (Fastrac; Sensormedics, Anaheim, CA), which is attached to a printer that automatically registers the lowest measured oxygen saturation value every minute.

Submaximal cycle ergometer test

Submaximal exercise testing was performed on an electrically braked cycle ergometer (Examiner 400; Lode, Groningen, Netherlands). Patients began to exercise at 50% of the maximal cycled load (*W*max) for 10 min. When the patients had performed this exercise, the workload was increased to 70% of *W*max (13). The patient cycled as long as possible but for a maximum of 30 min. Mechanical efficiency was calculated by using this submaximal exercise testing protocol. The maximal endurance time was also noted. The mean values of oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) during the last 3 min at 50% of *W*max were taken to calculate the net mechanical efficiency after adjustment for the individual resting energy expenditure (14).

Metabolic and ventilatory variables and heart rate

Metabolic and ventilatory variables were measured in expired air by using a breathing mask (Oxycon Beta; Jaeger, Wurzburg, Germany). The device was calibrated before each test. Simultaneously, heart rate was registered every minute by using a sport tester (PE 3000; Polar Electro Oy, Kempele, Finland).

Biochemical variables

A venous blood sample was taken to measure plasma lactate concentration. Blood was collected in a vacuum tube (Vacutainer; Becton Dickinson, Franklin Lakes, NJ). The blood samples were stored on ice (4 °C) and centrifuged for 5 min at 3120 × *g* (Sigma 2-15; Lameris, Breukelen, Netherlands). Plasma lactate concentration was determined by an enzymatic method with use of an automated system (Cobas Mira; Roche, Basel, Switzerland). Plasma lactate was measured at rest, every 2 min during exercise, and once during recovery (2 min after completion of the test). In part 2, a venous catheter was placed in the forearm to obtain venous blood samples. These venous blood samples were analyzed for glucose concentration to monitor gastric emptying and lactate concentration indirectly.

Statistics

The data were analyzed to evaluate the effects of the nutritional supplements on pulmonary function and to examine the endurance and the metabolic, cardiovascular, and subjective responses to exercise. The mean response of $\dot{V}O_2$, $\dot{V}CO_2$, RQ, minute ventilation (V_E), and heart rate was measured 30 min after the supplement was consumed and was calculated over 35–40, 40–50, and 50–60 min, the last 3 min while cycling at 50% of *W*max, and the last minute of the exercise test. Oxygen saturation was measured before and after the supplement was consumed and the mean saturation was calculated over 0–5, 5–10, 10–15, 15–30, 30–40, 40–50, and 50–60 min after the supplement, the last 3 min while cycling at 50% of *W*max, and the last minute of the exercise test. The difference in response to the 2 nutritional supplements was assessed at each time interval in every patient. For comparison between the different supplements, analysis of variance (ANOVA) was used with the postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor. If appropriate, the corresponding baseline value was used as a covariate (analysis of covariance). In part 1, if the results of treatment were significantly different, a post hoc Tukey test

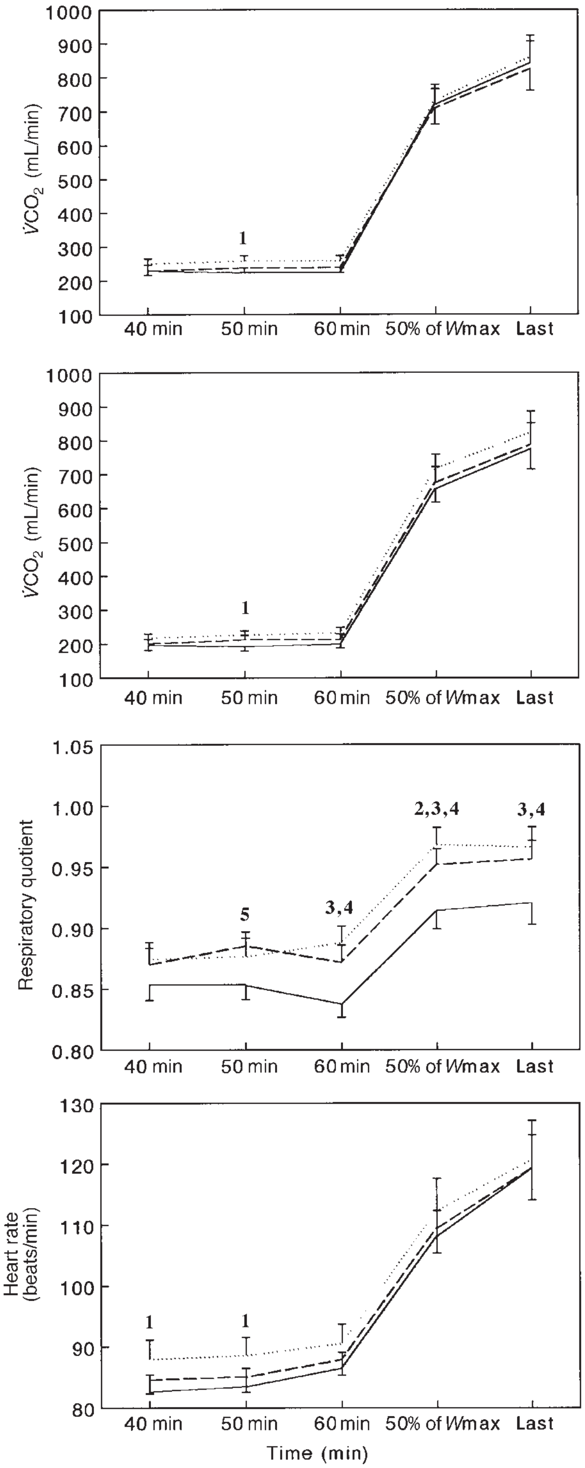

FIGURE 2. Mean (±SEM) response of oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), respiratory quotient, and heart rate postprandially and during exercise after consumption of placebo (solid line), a 1046-kJ supplement (dashed line), and a 2092-kJ supplement (dotted line). Last, the last measurement during the exercise test. $n = 14$. ^{1,3}2092-kJ supplement significantly different from placebo: $^1P < 0.05$, $^3P < 0.01$; ^{2}1046-kJ supplement significantly different from 2092-kJ supplement, $P < 0.05$; ^{4,5} 1046-kJ supplement significantly different from placebo: $^4P < 0.01$, $^5P < 0.05$ (ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor; the Tukey test was performed post hoc.)

was performed. For comparison of the baseline characteristics of the subjects before each test an independent Student's *t* test was used. A *P* value < 0.05 was considered significant. All measured variables are expressed as means ± SDs, except when means ± SEMs are used in the figures.

RESULTS

Part 1

Comparison of lung function before and after supplement ingestion showed no negative effects on pulmonary function (data not shown). The time course of $\dot{V}O_2$ and of $\dot{V}CO_2$ after the different supplements were ingested is shown in **Figure 2**. During the measurement period at rest, $\dot{V}O_2$ tended to be higher after the 2092-kJ than after the 1046-kJ supplement or placebo. However, $\dot{V}O_2$ after the 2092-kJ supplement was significantly higher than after the placebo only 50 min after the supplement was consumed. During exercise, $\dot{V}O_2$ was not different among the 3 supplements. The value of $\dot{V}CO_2$ was also significantly higher 50 min after consumption the 2092-kJ supplement than after the placebo. During exercise, the effects of the supplements on $\dot{V}CO_2$ did not differ significantly.

There was a clear effect of the different energy loads on RQ. At rest at 60 min postingestion, RQ was significantly higher after the 1046-kJ and 2092-kJ supplements than after the placebo (0.87 ± 0.05, 0.89 ± 0.05, and 0.84 ± 0.04, respectively). During exercise, RQ remained significantly elevated after the 1046-kJ and 2092-kJ supplements compared with the placebo. At 50% of *W*max, RQ after the 2092-kJ supplement was significantly higher than the RQ after the 1046-kJ supplement, as shown in Figure 2.

The effect on V_E was less apparent, but after 50 min, V_E was significantly elevated after the 2092-kJ supplement compared with the placebo (14.1 ± 2.1 and 12.7 ± 2.4 L/min, respectively; $P = 0.01$). During exercise, however, there was no difference in V_E among the 3 supplements. The heart rate after the 2092-kJ supplement was significantly different from that after the placebo at 40 and 50 min postingestion, as shown in Figure 2. There were no significant differences during the exercise test.

The changes in oxygen saturation were small, but significant, at 10 and 30 min after ingestion of the 1046-kJ (93.8 ± 1.9% and 94.1 ± 1.6%; $P < 0.05$) and 2092-kJ (93.6 ± 1.6%; $P < 0.01$; 94.2 ± 1.4%; $P < 0.05$) supplements, respectively, compared with placebo. There were no differences in lactate concentrations during the experiment among the 3 supplements. Also, the relative increase in lactate was not significantly different among the placebo, and 1046-kJ and 2092-kJ supplements (107 ± 73%, 104 ± 89%, and 108 ± 95%, respectively).

From the symptoms assessed by visual analogue scale, the change in satiety after the supplements was significantly different for the 2092-kJ supplement than after the placebo, as shown in **Figure 3**. The symptoms shortness of breath, fatigue, and pain in the legs did not change during the experiment.

The differences in the mean duration of the exercise test after the 3 supplements were small and insignificant. There were insignificant differences in mechanical efficiency after the 3 supplements.

There were 3 patients who were not able to cycle 5 min at 50% of *W*max after the 2092-kJ supplement. The endurance time was dramatically lower in these outliers than in the other 11 patients, as shown in **Figure 4**. A low body mass index (18.9 ± 1.7), low fat-free-mass index (fat-free mass divided by height^2: 14.7 ± 0.5),

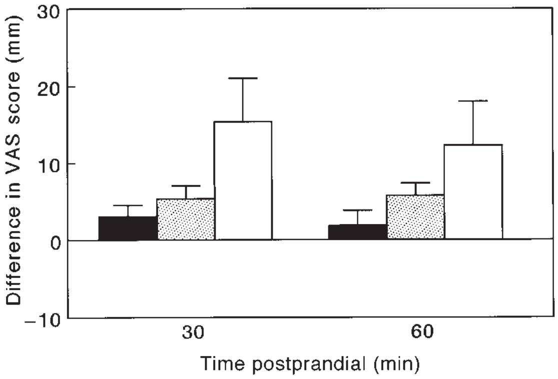

FIGURE 3. Difference between the mean (±SEM) post- and preprandial satiety score on a visual analogue scale (VAS) 30 and 60 min after consumption of placebo (■), a 1046-kJ supplement (▩), and a 2092-kJ supplement (□). $n = 14$. 2092-kJ supplement significantly different from placebo at 30 min, $P < 0.05$ (ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor; the Tukey test was performed post hoc.)

low maximal exercise performance (49 ± 3 W), and low mechanical efficiency characterized these patients.

Part 2

Pulmonary function before and after ingestion of the supplements is shown in **Table 3**. Comparable with part 1, there were no negative effects of the supplements on pulmonary function. Peak expiratory flow increased significantly after the carbohydrate-rich supplement compared with baseline and compared with after the fat-rich supplement.

The courses of $\dot{V}O_2$ and $\dot{V}CO_2$ are shown in **Figure 5**. There were no significant differences in response to the 2 supplements. After the carbohydrate-rich supplement there was a slightly lower $\dot{V}O_2$ during the whole experiment than after the fat-rich supplement. The RQ was significantly higher after the carbohydrate-rich supplement than after the fat-rich supplement during the whole experiment except at the last minute of the exercise trial. The higher RQ suggests a relatively higher $\dot{V}CO_2$ after the carbohydrate-rich supplement. Although $\dot{V}CO_2$ and V_E are highly correlated (last minute of exercise after the carbohydrate-rich and fat-rich supplement, respectively: $r = 0.87$, $P = 0.01$; $r = 0.96$, $P < 0.001$), V_E was not significantly different after the ingestion of the fat-rich or carbohydrate-rich supplement.

There were no significant differences in heart rate after the carbohydrate-rich and fat-rich supplements. Blood saturation seemed slightly lower after the carbohydrate-rich supplement, and was significantly so 10 and 15 min after ingestion ($P < 0.05$). However, on average, the slightly lower saturation after the carbohydrate-rich supplement was not clinically significant (ie, a drop in oxygen saturation >4%).

Lactate concentration was significantly different at the start of the exercise test between patients consuming the carbohydrate-rich and fat-rich supplements: 1.7 ± 0.3 and 1.3 ± 0.2 mmol/L, respectively ($P < 0.05$). The relative increase in lactate was not significantly different after the 2 supplements.

Blood glucose concentration was measured during the whole experiment. At rest, blood glucose increased significantly after ingestion of the carbohydrate-rich supplement. The highest blood glucose value was at 30 min after ingestion (△ glucose: 2.6 mmol/L, range: −0.2 to 5.5 mmol/L). At the start of the exercise test, blood glucose was not significantly different between subjects who consumed the carbohydrate-rich and the fat-rich supplement (5.7 ± 1.3 and 5.3 ± 0.7 mmol/L, respectively). During the exercise test, blood glucose concentration was not significantly different for the 2 supplements.

There were no significant differences in the mean duration of the exercise test after the carbohydrate-rich and fat-rich supplements (12.6 ± 7.2 and 13.1 ± 7.1 min, respectively). Also, the mechanical efficiency after the 2 supplements was not significantly different (20.0 ± 5.8% and 19.8 ± 5.9%, respectively).

The symptoms satiety, fatigue, and pain in the legs did not change significantly during the experiment after ingestion of the supplement. Only the symptom shortness of breath changed: there was a significantly greater increase in dyspnea after ingestion of the fat-rich supplement than after the carbohydrate-rich supplement, as shown in **Figure 6**.

DISCUSSION

Nutritional supplements are needed in some COPD patients to reverse weight loss or to improve nutritional status. In contrast with a long-held belief, the present investigation did not show significant adverse effects of the studied nutritional supplements on the ventilatory system. Remarkably, there were even positive effects of

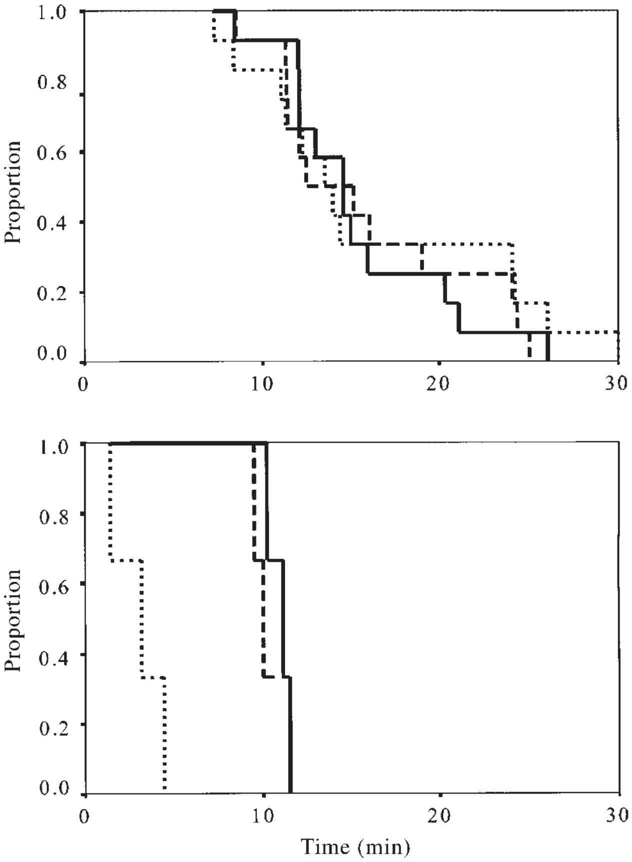

FIGURE 4. Kaplan-Meier plot of endurance time during submaximal cycle ergometry after consumption of placebo (solid line), a 1046-kJ supplement (dashed line), and a 2092-kJ supplement (dotted line). Upper panel: total group − outliers ($n = 11$); lower panel: outliers ($n = 3$).

TABLE 3
Pulmonary function before and after consumption of the supplements in part 2 of the study[1]

	Carbohydrate rich		Fat rich	
	Before	After	Before	After
FVC (L)	3.1 ± 0.7	3.5 ± 1.3	3.0 ± 0.6	3.0 ± 0.7
FEV_1 (L)	1.1 ± 0.3	1.1 ± 0.4	1.0 ± 0.4	1.0 ± 0.4
PEF (L/s)	3.1 ± 1.0	3.3 ± 1.2[2]	3.1 ± 0.9	3.1 ± 0.9

[1] x ± SD; n = 11. FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; PEF, peak expiratory flow.

[2] Significantly different from before carbohydrate-rich supplement and after fat-rich supplement, $P < 0.05$ (ANCOVA with postprandial value as dependent variable, with treatment and period as fixed factors, and patient as a random factor; baseline value was a covariate).

a carbohydrate-rich supplement relative to those of a fat-rich one at a relatively low energy content, as will be discussed below.

In the first part of the study, we evaluated the most optimal energy load to be given as a supplement between regular meals. As expected, relative to the 1046-kJ supplement, the metabolic and ventilatory response at rest was significantly higher after the 2092-kJ supplement. During exercise, this difference was eliminated. For the total group, there were no differences in exercise endurance capacity. Satiety, however, was clearly greater after the 2092-kJ supplement, which might interfere with a normal meal pattern. Another remarkable observation was the strikingly reduced endurance capacity of 3 patients after the 2092-kJ supplement, whereas no difference was seen between the placebo and the 1046-kJ supplement. Although this phenomenon was observed in only a few patients, these results are important to consider because this subgroup was characterized by a low body mass index and fat-free-mass index, low maximal exercise capacity, and low mechanical efficiency. One potential cause could be an increased oxygen cost of breathing because Mannix et al (15) recently reported a significant inverse relation between body mass index and the oxygen cost of breathing in COPD. Furthermore, we showed in a previous study a significantly elevated ratio of V_E to $\dot{V}O_2$ in COPD patients with a decreased mechanical efficiency (5).

Suggested positive effects of a carbohydrate-rich compared with a fat-rich 1046-kJ supplement are based on the following observations. A significant increase in peak expiratory flow was shown relative to baseline and relative to the fat-rich supplement. In contrast with the forced expiratory flow in 1 s, the peak expiratory flow is dependent of respiratory muscle strength. Blood glucose is a rapidly available substrate, as was indirectly observed in the insignificantly lower increase in lactate during exercise after the carbohydrate-rich supplement. Specifically, for COPD patients, this may be clinically relevant because a reduced oxidative capacity has been observed, as reflected in low muscle concentrations of oxidative enzymes such as citrate (si)-synthase and β-hydroxyacyl dehydrogenase (alone or combined with increased concentrations of the regulating glycolytic enzyme phosphofructokinase) (16). One study even showed a decreased ATP-ADP ratio in resting muscle associated with an increased inosine monophosphate concentration as marker of an imbalance between ATP synthesis and production (17). Positive effects of a carbohydrate load on muscle have been described and are being used in sports medicine. The amount of carbohydrate given in this study is comparable with the recommended dose.

The RQ was indeed higher after the carbohydrate-rich supplement, but this was not due to an increased $\dot{V}CO_2$ but to a lower $\dot{V}O_2$. This could reflect more efficient metabolism and could be related to a lower gastric-emptying time for the carbohydrate-rich supplement, when given in a fixed period, as was observed previously by Akrabawi et al (18) after a moderate-fat compared with a high-fat supplement. There are clinical ramifications to delayed gastric emptying, especially in patients with COPD. Because of the disease process itself, such patients already have hyperinflation, a flattened diaphragm, and a reduction in abdominal volume, which results in feelings of bloating, abdominal discomfort, and early satiety. A significant delay in gastric emptying may lead to an extended period of abdominal distention, affecting diaphragmatic mobility and thoracic expansion.

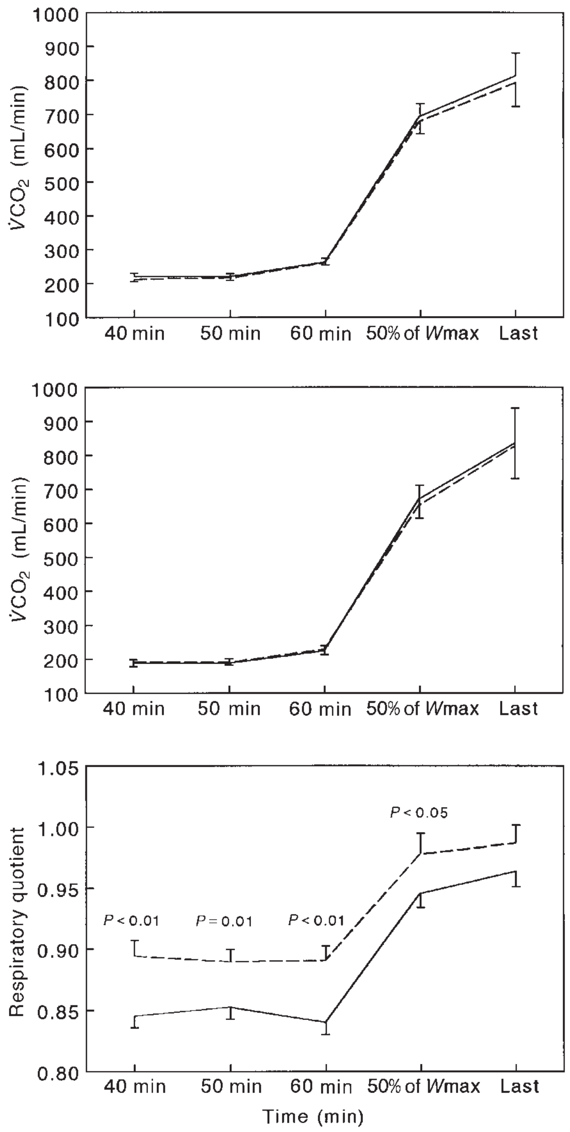

FIGURE 5. Mean (±SEM) response of oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and respiratory quotient postprandially and during exercise after a fat-rich (solid line) and a carbohydrate-rich (dashed line) 1046-kJ supplement. n = 11. ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor.

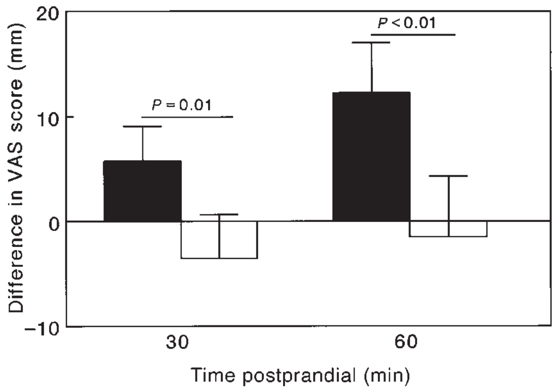

FIGURE 6. Difference between mean (±SEM) post- and preprandial shortness of breath score on a visual analogue scale (VAS) 30 and 60 min after consumption of a fat-rich (■) and a carbohydrate-rich (□) supplement. $n = 11$. ANOVA with postprandial value as the dependent variable, with treatment and period as fixed factors, and with patient as a random factor.

The protein content of the supplements was high on the basis of available data showing that, in healthy subjects and in those with stable disease, protein synthesis is optimally stimulated during administration of 1.5 g protein $\cdot$ kg$^{-1}\cdot$d^{-1} (19). The effects of wasting disease on protein metabolism are characterized by net protein catabolism, owing to differences between protein synthesis and breakdown rates. This is seen as a negative nitrogen balance. The pathophysiologic mechanisms of this catabolic reaction are related to disease severity. In many chronic wasting disorders, a negative nitrogen balance is associated mainly with a reduced protein synthesis rate, whereas protein breakdown is hardly affected. Morrison et al (20) found a reduced protein synthesis rate in underweight patients with emphysema. In weight-stable COPD patients in stable clinical condition, we recently found an increased protein turnover rate in the fasting state (21). Moreover, voluntary protein intake is important during acute exacerbations of COPD; we previously reported in hospitalized COPD patients a temporarily decreased protein intake that recovered slowly to 1.3 g/kg at discharge from the hospital (7).

The absence of adverse effects of nutritional supplements was also indirectly confirmed in previous studies that showed positive effects of 2–3 nutritional supplements (≈1046 kJ) as an integrated part of pulmonary rehabilitation on weight, fat-free mass, muscle function, and exercise capacity. Future studies using nuclear magnetic resonance or muscle biopsies might investigate the suggested specific effects of carbohydrates alone or combined with specific bioactive nutrients on oxidative muscle metabolism.

In conclusion, a liquid oral nutritional supplement with an energy content of 1046 kJ is preferable to an energy load of 2092 kJ because after the smaller load there was a better metabolic and ventilatory response and less satiety. Also, the carbohydrate-rich supplement was preferable to the fat-rich supplement because lung function increased and there was less shortness of breath.

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