

*Original articles***High fat, low carbohydrate, enteral feeding lowers PaCO<sub>2</sub> and reduces the period of ventilation in artificially ventilated patients**N.M. Al-Saady<sup>1</sup>, C.M. Blackmore<sup>2</sup> and E.D. Bennett<sup>1</sup><sup>1</sup>Department of Medicine and <sup>2</sup>Department of Dietetics, St. George's Hospital Medical School, London, UK

Received: 15 August 1988; accepted: 28 December 1988

**Abstract.** The objective of this study was to compare the effect of a high fat, low carbohydrate enteral feed with a standard isocaloric, isonitrogenous enteral feed on PaCO<sub>2</sub> and ventilation time in patients with acute respiratory failure requiring artificial ventilation. 20 clinically stable patients requiring enteral feeding were randomized to either feed in a double-blind fashion. Initial ventilator standard settings were adjusted according to clinical state. Measurements including minute volume and arterial blood gases were made twice daily. Weaning was carried out according to set criteria. During the feeding period, PaCO<sub>2</sub> just prior to weaning fell by 16% in the high fat group but increased by 4% in the standard feed group ( $p = 0.003$ ). The high fat group spent a mean of 62 h less time on the ventilator ( $p = 0.006$ ). A high fat, low carbohydrate enteral feed appears to be beneficial in patients undergoing artificial ventilation.

**Key words:** Artificial ventilation – Respiratory failure – Enteral nutrition

The nutritional status of patients with respiratory insufficiency is important [5, 9]. The incidence of malnutrition is high, both in patients with chronic respiratory disease and those hospitalized with acute respiratory failure [6, 7, 13, 14]. Little attention has, however, been given to the composition of the diet recommended for these patients. There is evidence that the metabolism of carbohydrate results in a marked increase in carbon dioxide (CO<sub>2</sub>) production [4, 15], in part due to an increase in respiratory quotient to a value which may exceed 1.0. Indeed, respiratory failure precipitated by a high carbohydrate diet has been reported [3, 8]. Furthermore it has been suggested that, in certain cases, such a diet may increase the time that patients

with respiratory failure require artificial ventilation [16].

Two studies [11, 12] have investigated the role of dietary composition on patients requiring artificial ventilation for acute respiratory failure, showing that a high fat, low carbohydrate enteral feed reduced the respiratory quotient (RQ) by 12–17% and decreased CO<sub>2</sub> production. Such results suggest that a high fat, low carbohydrate feed could decrease the time on a ventilator by reducing CO<sub>2</sub> production.

The present study was therefore undertaken to compare the effects of a high fat, low carbohydrate enteral feed with a standard isocaloric enteral feed on PaCO<sub>2</sub> and ventilation time in patients with acute respiratory failure undergoing artificial ventilation.

**Materials and methods**

Adult patients requiring artificial ventilation as a result of chronic obstructive airways disease, pneumonia, asthma, brain damage or surgery, who could be enterally fed, were entered into the study. Patients were considered eligible to remain in the study after they had been continuously fed at their optimal rate for a minimum of 48 h during ventilation.

Patients were excluded from the study if they had evidence of diabetes mellitus, nephrotic syndrome or hepatic failure.

The feeding regimen was only commenced after a stable ventilatory state had been achieved. Water was administered via a Ryles or fine bore polyurethane nasogastric tubes for 12 h before commencing the enteral feed. This was administered using a Flexiflo II enteral feeding pump. Patients were then allocated randomly in a double-blind fashion to receive either a high fat, low carbohydrate feed (Pulmocare, Abbott Laboratories, Maidenhead, England) or a standard enteral feed (Ensure Plus, Abbott Laboratories, Maidenhead, England).

Nutritional assessment was carried out to determine energy and protein requirements using the standard suggested by Fleisch [10] and modified to include the impact of disease [18]. These assessments were carried out prior to the commencement of the feed and subsequently on a daily basis. Thus the total caloric input prescribed each day for each patient was determined by the calculated resting energy requirements which took into account the patient's core temperature measured at the time of the daily assessment.

The percentage energy profiles of the two feeds were as follows: Pulmocare: protein 16.7 (62.6 g/l), fat 55.2 (92.1 g/l), carbohydrate 28.1 (105.7 g/l); Ensure Plus: protein 16.7 (62.6 g/l), fat 30 (50 g/l), carbohydrate 53.3 (200 g/l).

Any additional carbohydrate load in the form of intravenous dextrose or syrup for oral drugs was avoided.

Full strength feed was initially administered continuously for 6 h at a rate of 20 ml/h and if tolerated was increased every 6 h by 20 ml/h until the required rate was achieved. Any additional fluid requirement was given as sterile water added to the feed.

All feeds were given continuously though gastric contents were aspirated 4 hourly for the first 72 h. If the aspirated volume exceeded that of the feed given in the previous 2 h, the aspirate was returned to the stomach, feeding discontinued for 2 h and then recommenced at the previous rate. Feeding was also discontinued for 30 min before and after chest physiotherapy. Enteral feeding was continued for 24–48 h after weaning.

Normal clinical criteria were used to determine the initial settings of tidal volume (9–12 ml/kg) and frequency of ventilation (12–16 breaths/min). An inspired oxygen concentration (FIO<sub>2</sub>) of between 30% and 50% was used. The ventilator settings and FIO<sub>2</sub> were then adjusted as required to maintain PaCO<sub>2</sub> at 5–6 kPa and PaO<sub>2</sub> at 10–12 kPa.

Prior to ventilation blood gas measurements were made. Baseline measurements (see below) were taken at the start of intermittent positive pressure ventilation and subsequently recorded at 12-h intervals. After enrolment in the study measurements were carried out within one hour of the start of feeding, every 12 h thereafter and immediately prior to weaning. PaCO<sub>2</sub>, PaO<sub>2</sub> and respiratory rate measurements were made between 1 and 24 h post-weaning.

Tidal volume (VT), frequency of respiration (F), minute volume (V), and peak inspiratory pressure (PIP) were obtained from the digital display of the ventilator (Veolar, Hamilton). These measurements have been validated using an external electronic respirometer (Kontron respirometer 3111), the accuracy of which has been previously tested [1].

Inspired oxygen concentration (FIO<sub>2</sub>) was adjusted according to the clinical state of the patient. It was measured using a Beckman paramagnetic oxygen analyzer which was calibrated with the following gases: 100% N<sub>2</sub>, air and 100% O<sub>2</sub>. Inspired air was sampled downstream from the humidifier.

Arterial blood was collected in heparinised plastic syringes from an indwelling arterial catheter. The time from collection to blood gas analysis was always less than 10 min and was carried out using a Model 1312 (Instrumentation Laboratory Warrington, England). Each sample was measured twice, the mean value being calculated.

The following criteria had to be met before initiation of the weaning process:

1. Minute ventilation < 12 l/min
2. Frequency of ventilation < 20 /min
3. PaO<sub>2</sub> at FIO<sub>2</sub> 40% > 8 kPa
4. PaCO<sub>2</sub> 5–6 kPa
5. pH ≥ 7.3

Each patient was assessed daily and the weaning process implemented if the above criteria were met. With the patients remaining intubated but breathing spontaneously through a T-piece circuit, weaning was considered to have been successful if the following conditions were maintained for more than 24 h:

1. Stable clinical state
2. Adequate circulation
3. Minute ventilation < 10 l/min
4. Spontaneous respiratory rate < 30 /min
5. PaO<sub>2</sub> at FIO<sub>2</sub> 0.4 > 8 kPa
6. PaCO<sub>2</sub> 5–6 kPa
7. pH ≥ 7.3

If the patient was unable to maintain these criteria artificial ventilation was recommenced and the weaning process deemed to have failed.

Statistical analysis was performed using paired and unpaired Student's *t*-tests. *P*-values of < 0.05 were regarded as significant. All results are expressed as mean ± 1 SD.

## Results

A total of 40 patients were recruited into the study, 20 of whom did not fulfil the entry criteria for the following reasons:

Four patients required changing to high frequency jet ventilation, 3 of whom were in the standard feed group, early death occurred in 3 of each group; surgical intervention was necessary in 4 patients, 3 of whom were in the high fat feed group; 3 in each treatment group were successfully weaned from artificial ventilation within 48 h from the start of feeding.

Twenty patients completed the study. Eleven received the standard feed (8 male, 3 female, median age 58 y, range 19–75 y). Nine patients received the high fat feed (5 male, 4 female, median age 59 y, range 29–68 y).

Tables 1 and 2 show the pre-ventilation baseline information for age, sex, weight, estimated energy requirements and blood gas analyses. There were no significant differences in any of the variables, both groups showing evidence of moderately severe respiratory failure. In the 11 patients of the standard feed group 3 had postoperative respiratory failure (one with evidence of chronic obstructive airways disease and another developing bacterial pneumonia); 3 patients had bacterial pneumonia (1 having co-existent chronic obstructive airways disease); 1 patient had toxic shock syndrome; 1 patient had an empyema; 1 patient suffered encephalomyelitis and 2 patients had thoracic injuries following road traffic accidents.

In the 9 patients of the high fat feed group 2 had postoperative respiratory failure (1 with co-existing chronic obstructive airways disease, the other developing a subsequent pneumonia); 4 patients had pneumonia (1 viral, 1 aspiration and 2 bacterial with co-existing chronic obstructive airways disease); 1 admitted with acute on chronic obstructive airways disease and 2 patients with adult respiratory distress syndrome.

The average daily doses of sedative agents are shown in Fig. 1. There were no significant differences between the two treatment groups. Three patients in the standard feed and four in the high fat feed had muscle relaxing agents added to their regimens.

Both groups of patients spent a similar length of time on ventilation prior to commencement of feeding. The standard feed group spent a mean of 64.3 ± 37.7 h (range 20–130 h) and the high fat feed

**Table 1.** Pre-ventilation baseline measurements in standard feed group

Pts.	Age (y)	Sex	Wt. (kg)	EER <sup>a</sup> (Kcal/d)	pH	PaCO <sub>2</sub> (kPa)	PaO <sub>2</sub> (kPa)	FIO <sub>2</sub> (%)	Diagnosis
1	66	M	78	1550	7.295	7.14	10.9	40	Ruptured aortic aneurysm. Postoperative respiratory failure, pneumonia
4	26	M	80	2433	6.98	11.76	7.4		Traffic accident-fractured ribs, bilateral haemopneumothoraces
5	66	F	60	1600	6.98	13.2	11.9	50	Chronic obstructive airways disease. Perforated duodenal ulcer. Cardiorespiratory arrest. Subsequent surgery
7	19	M	76	2500					Encephalomyelitis
11	58	M	62	1933	7.271	9.14	7.4	35	Chronic obstructive airways disease, pneumonia
12	48	F	67	1924	7.235	6.72	7.8	50	Pneumonia
13	27	F	82	3120					Toxic shock syndrome
14	63	M	57.2	1718	7.272	6.37	5.75	28	Empyema, aortic valve disease, pseudomembranous colitis, renal failure
17	72	M	79.5	1544	7.441	6.39	11.9	54	Pneumonia
19	44	M	76	2650	7.34	4.74	10.9	60	Road traffic accident, left haemothorax, mediastinal haematoma, thoracotomy
20	75	M	57.3	1800	7.075	10.2	5.4		Gastrointestinal bleeding, post-operative respiratory failure
Mean			70.5	2070.2	7.21	8.4	8.8	45.3	
±SD			9.8	525.4	0.2	2.8	2.6	11.3	

<sup>a</sup> Estimated energy requirements

group a mean of  $69.6 \pm 47$  h (range 20–130 h) before starting enteral feeding.

Table 3 shows the results obtained prior to commencement of feeding (Pre-feed), within 1 h after the start of feeding (Day 1) and immediately prior to weaning (Pre-wean). The changes in the values from the start of feeding to pre-weaning in the two treatment groups are shown in Table 4. In the high fat feed group reductions in PaCO<sub>2</sub>,  $\dot{V}$ , VT and PIP were noted which differed significantly from the standard feed group where these variables actually increased.

Figure 2 shows that the time spent on artificial ventilation from the commencement of feeding to successful weaning was 42% less in the high fat feed group ( $86.1 \pm 17.8$  h) compared to the standard feed group ( $148.7 \pm 36.7$  h) [ $p < 0.001$ ].

In the high fat feed group, the majority of patients showed a reduction in both PaCO<sub>2</sub> and minute volume in contrast to the standard feed groups where

none of these changes were shown (Fig. 3 and Table 3).

In the immediate 24 h following weaning, the PaCO<sub>2</sub> and respiratory rate in the high fat feed group were maintained at a significantly lower level compared to patients in the standard feed group (Table 5).

Only 1 patient experienced delay in gastric emptying. This occurred on the second day but following 2 h discontinuation the feed was resumed at the previous rate with no further problems.

Three patients in each group developed diarrhoea, but all of these patients were receiving broad spectrum antibiotics and in each case the diarrhoea ceased despite continuation of the feed.

## Discussion

These data show that patients fed on a high fat, low carbohydrate feed spent on average 62 h less on arti-

**Table 2.** Pre-ventilation baseline measurements in high fat feed group

Pts.	Age (y)	Sex	Wt. (kg)	EER <sup>a</sup> (Kcal/d)	pH	PaCO <sub>2</sub> (kPa)	PaO <sub>2</sub> (kPa)	FIO <sub>2</sub> (%)	Diagnosis
2	67	M	78	1550	7.29	7.1	10.8	40	Postoperative respiratory failure, pneumonia, renal failure
3	68	F	47	1350	7.401	6.77	9.7		Acute on chronic obstructive airway disease
6	66	F	60	1600	6.98	12.84	11.9	50	Chronic obstructive airways disease, gastrointestinal bleeding, postoperative respiratory failure
8	56	F	62	1765	7.161		5.8	50	Septicaemia, adult respiratory distress syndrome, mitral stenosis
9	29	M	66	2285					Varicella pneumonia
10	59	M	63	1933	7.14	10.71	10.3	50	Chronic obstructive airways disease, pneumonia
15	37	F	59	1612	7.31	6.12	11.1	30	Septicaemia, adult respiratory distress syndrome
16	38	M	86.4	2542	7.204	6.7	8.7	36	Aspiration pneumonia, septicaemia, cardiac arrest
18	63	M	63	2450	7.314	6.5	7.2	56	Chronic obstructive airways disease, pneumonia
Mean			64.9	1898.6	7.225	8.1	9.2	44.6	
±SD			±11.4	±430.1	0.1	2.6	2.2	9.4	

<sup>a</sup> Estimated energy requirements

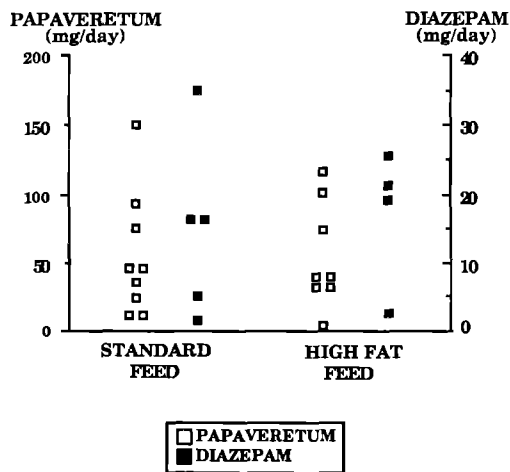


Fig. 1. The average daily dose of sedatives used in each patient

cial ventilation following commencement of feeding compared with those on a standard feed. In addition,  $\text{PaCO}_2$  and minute volume in the high fat feed group showed significant reductions prior to weaning from the ventilator when compared to the standard feed group.

There are several factors which might have affected these findings. The amount of sedative and muscle relaxing agents may have influenced the ease with which patients were weaned from the ventilator; no significant differences in the administration of these agents to the treatment groups were, however, seen. The clinical diagnosis and underlying lung pathology could affect the duration of ventilation though both groups were on mechanical ventilation for a similar time before starting enteral nutrition. Although there were some differences in the aetiology of the respiratory failure between the two groups we do not feel these were sufficient to account for the results obtained.

Differences in the clinical state at initiation of feeding could have influenced the duration of ventila-

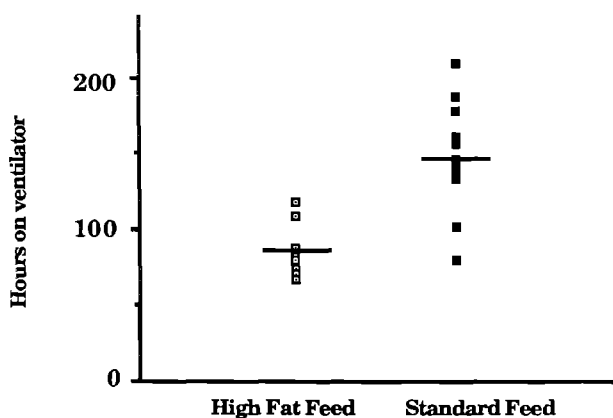


Fig. 2. Hours spent on ventilator following commencement of feeds

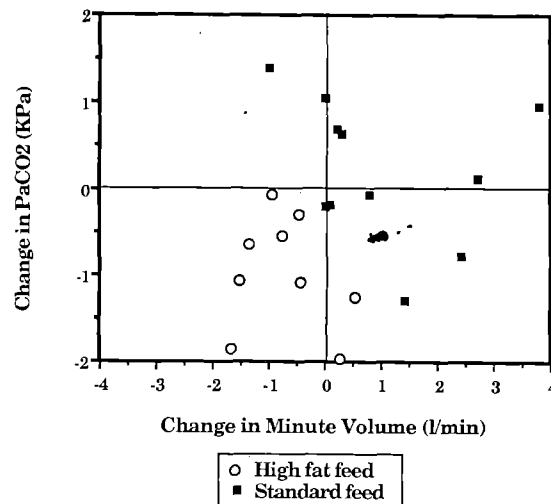


Fig. 3. Changes in minute volume and  $\text{PaCO}_2$  for both groups during feeding

tion. These include  $\text{CO}_2$  production and dead space ventilation which were not measured.  $\text{PaCO}_2$  and minute volume at the start of feeding were not different in the two groups and, if similar  $\text{CO}_2$  productions are assumed, the physiological dead space would also

Table 3. Mean values ( $\pm$ SD) of variables taken. Pre-feed, Day-1 and Pre-wean for each treatment group

	Pre-feed	Day-1	Pre-wean
$\text{PaCO}_2$ (Kpa)			
Standard feed	$5.86 \pm 1.1$	$5.8 \pm 1.1$	$5.98 \pm 0.9$
High fat feed	$6.09 \pm 0.8$	$6.09 \pm 0.8$	$5.13 \pm 0.4$
$\text{FIO}_2$ (%)			
Standard feed	$41.6 \pm 11.0$	$41.5 \pm 8.5$	$36.6 \pm 9.5$
High fat feed	$42.8 \pm 11.9$	$42.0 \pm 11.2$	$36.0 \pm 8.6$
$\text{PaO}_2$ (Kpa)			
Standard feed	$12.0 \pm 2.3$	$11.8 \pm 3.0$	$12.3 \pm 4.6$
High fat feed	$12.5 \pm 3.7$	$11.4 \pm 3.2$	$12.0 \pm 2.5$
Frequency (b/m)			
Standard feed	$15.7 \pm 2.9$	$15.3 \pm 2.8$	$15.1 \pm 2.9$
High fat feed	$14.6 \pm 1.7$	$13.9 \pm 2.4$	$13.8 \pm 2.3$
Minute volume (l/m)			
Standard feed	$10.2 \pm 0.8$	$9.9 \pm 0.8$	$10.9 \pm 1.7$
High fat feed	$10.5 \pm 2.9$	$10.5 \pm 3.0$	$9.7 \pm 2.7$
Peak inspiratory pressure (l/m)			
Standard feed	$30.9 \pm 10.0$	$29.9 \pm 8.2$	$31.8 \pm 9.6$
High fat feed	$34.7 \pm 5.1$	$33.3 \pm 5.1$	$29.1 \pm 5.7$

**Table 4.** Changes in variables between Day-1 and Pre-wean for each treatment group

Variable	Standard feed	High fat feed		<i>p</i> -value
	(%)	(%)	(%)	
Tidal volume (ml)	+46.1 ± 75.6 (+7)	-40.3 ± 50.5 (-4)		0.009
Frequency (b/m)	-0.2 ± 2.4 (-1)	-0.1 ± 0.6 (-0.8)		n.s.
Minute vol (l/m)	+0.9 ± 1.4 (+9)	-0.7 ± 0.8 (-7)		0.007
Peak. insp. pr. (cmH <sub>2</sub> O)	+1.9 ± 7.8 (+6)	-4.2 ± 3.9 (-13)		0.046
PaCO <sub>2</sub> (kPa)	+0.2 ± 0.8 (+4)	-1.0 ± 0.7 (-16)		0.003
PaO <sub>2</sub> (kPa)	+0.5 ± 3.8 (+4)	+0.6 ± 2.1 (+5)		n.s.
FIO <sub>2</sub> (%)	-4.8 ± 10.5 (-7)	-6.0 ± 6.5 (-15)		n.s.

be similar. If other clinical factors did not differ in the two groups, then changes in the dead space to tidal volume ratio (VD/VT) or CO<sub>2</sub> production could account for our findings. Other clinical parameters that could have affected the duration of mechanical ventilation were not different in the two groups during the weaning period. These included temperature, oxygen exchange, lung mechanics and amount of sedation. Another study using feeds identical to ours in patients with acute respiratory failure showed that CO<sub>2</sub> production was 24% lower on the high fat feed [11]. This change in CO<sub>2</sub> production could account for all of the differences we observed. Because PaCO<sub>2</sub> is linearly related to both alveolar ventilation and CO<sub>2</sub> production [17], a 24% decrease in CO<sub>2</sub> production would result in the combination of the 16% fall in PaCO<sub>2</sub> and the 8% fall in minute ventilation that we observed. No other changes, including changes in dead space ventilation, need have occurred.

Our findings can therefore be best explained by considering the differences in CO<sub>2</sub> production resulting from the metabolism of carbohydrate, fat and protein. It is well established that the combustion of one calorie of each of these nutrients produces 0.2, 0.15 and 0.19 l of CO<sub>2</sub> respectively. The combustion of 1000 calories of the high fat feed used in this study would result in the production of 173.6 l of CO<sub>2</sub>. This

contrasts with the 186 l of CO<sub>2</sub> produced from 1000 calories of the standard feed.

Respiratory failure can be precipitated in patients with COAD when they are fed with a high carbohydrate diet [3, 8]. Reductions in CO<sub>2</sub> production (20%), RQ (7%), and PaCO<sub>2</sub> (4%) have been seen when patients with stable chronic obstructive airways disease were switched from a standard enteral feed to one high in fat content similar to the two feeds used in our study [2].

A more marked effect was seen when critically ill patients requiring artificial ventilation are studied [12]. In these patients changing from standard enteral feed to one high in fat and low in carbohydrate resulted in a reduction in RQ (17%). They were, however, unable to demonstrate a significant reduction in ventilation time.

The results of both these studies and our study suggest that critically ill patients show a greater responsiveness to manipulation of the dietary composition than less ill patients. It is also interesting to note that in the post-weaning period the high fat feed group, continued to show a lower PaCO<sub>2</sub> and respiratory rate compared to the standard feed group.

More attention should therefore be paid to the dietary composition of the nutritional support given to patients requiring artificial ventilation for acute respiratory failure. A nutritional regimen with a high fat content may reduce ventilatory requirements and therefore reduce the duration of mechanical ventilation. This would significantly reduce morbidity and mortality related to complication of mechanical ventilation. Further studies are now required to understand the mechanisms of these effects and confirm these findings in a broader cross-section of acutely ill patients.

**Acknowledgements.** We wish to thank the Intensive Therapy Unit staff for their help and Abbott Laboratories Ltd. for financial support in supplying feeds and equipment.

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**Table 5.** Mean values (±SD) of PaCO<sub>2</sub>, PaO<sub>2</sub> and respiratory rate for each treatment group in the post-weaning period

	PaCO <sub>2</sub> (kPa)	PaO <sub>2</sub> (kPa)	Respiratory rate (breaths/min)
Standard feed	5.78 ± 0.7	12.8 ± 3.0	27.0 ± 3.8
High fat feed	4.88 ± 0.5	12.2 ± 3.1	20.6 ± 5.6
<i>p</i> -value	0.004	n.s.	0.02

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