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Nutrition for the Patient with Respiratory Failure:

Glucose vs. Fat

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High glucose intakes given during administration of total parenteral nutrition (TPN) have been demonstrated to increase CO_2 production. The workload imposed by the high CO_2 production may precipitate respiratory distress in patients with compromised pulmonary function.

Changes in CO_2 production and O_2 consumption induced by TPN using either glucose as the entire source of non-protein calories, or fat emulsions as 50 per cent of the non-protein calories, have been analyzed either in patients with chronic nutritional depletion or in acutely ill patients secondary to injury and infection. In patients with chronic nutritional depletion, shifting from the lipid to the glucose system caused a 20 per cent ($P < 0.025$) increase in CO_2 production which resulted in a 26 per cent increase in minute ventilation ($P < 0.01$). In the acutely ill patients receiving the glucose system, CO_2 production was significantly higher than in those receiving the lipid system (179 *vs.* 147 $ml \cdot min^{-1} \cdot m^{-2}$; $P < 0.01$).

Fat emulsions can serve as a source of non-protein calories and are associated with lesser degrees of CO_2 production than isocaloric amounts of glucose. (Key words: Carbon dioxide: elimination; production. Lung: respiratory failure. Oxygen: consumption. Metabolism: fat emulsions; glucose; oxygen consumption; parenteral nutrition; respiratory quotient.)

THE NON-PROTEIN ENERGY of total parenteral nutrition (TPN) is usually supplied in the United States as glucose, which is oxidized with a Respiratory Quotient (RQ) of 1.0.[1,2] Patients receiving 5 per cent dextrose only as nutritional support normally must oxidize endogenous fats in order to meet their energy requirements. With nutritional depletion, the major energy source shifts from endogenous fat (RQ = 0.7) to administered glucose, and there is a rise in CO_2 production concurrent with the increase in RQ. Furthermore, the characteristic response of a normal subject to a glucose load above energy needs is to convert the excess glucose to fat. Conversion of carbohydrate to fat is associated with an RQ of approximately 8, and results in a large increase in CO_2 production[3]. There is only a small energy expenditure associated with fat synthesis and, therefore, O_2 consumption increases only minimally.

Nutritionally depleted patients seem to have a relatively normal response to glucose loads above energy expenditure. They show a small increase in oxygen consumption $\dot{V}_{O_2}$, with an RQ greater than 1.0.[4,5] In hypermetabolic patients, a glucose load is associated with a greater increase in O_2 consumption, an increased urinary norepinephrine excretion, while RQ increases only minimally.[4,5] In either case, there is a marked increase in CO_2 production which can precipitate respiratory distress.[4,6]

In addition, patients who require TPN, often have some impairment of the ratio of dead space (V_D) to tidal volume (V_T)[7] associated with increased resting levels of minute ventilation ($\dot{V}_E$). The workload imposed by the high CO_2 production associated with large glucose loads, can precipitate respiratory failure in this group of patients. Weaning from mechanical ventilatory support may be especially difficult during administration of TPN. Fat emulsions which are oxidized with an RQ of 0.7 could prove useful as a calorie source under the circumstances.

This study indicates that intravenous fat emulsions may minimize CO_2 production in patients receiving total parenteral nutrition and may be particularly useful energy sources for patients with compromised respiratory function.

Changes in CO_2 production and O_2 consumption induced by TPN using either glucose as the entire source of non-protein calories, or fat emulsions as 50 per cent of the non-protein calories, have been analyzed either in patients with chronic nutritional depletion or in acutely ill patients secondary to injury and infection.

Methods

Two groups were studied, patients with chronic nutritional depletion and patients who were acutely ill secondary to injury or infection.

Group I: The nutritionally depleted patients were five patients who had undergone prior pathologic

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TABLE 1. The Resting Energy Expenditure for Each Patient Receiving 5 Per cent Dextrose

Nutritionally Depleted Patients

	BSA (m^2)	Age (Yr)	Sex	Diagnosis	Weight Loss (Per Cent)	REE (kcal/day)	
						Predicted	Measured
Patient 1	1.34	52	F	S/P resection of stomach for carcinoma	33	1238	1028
Patient 2*	1.66	52	M	Malnutrition S/P esophago-gastrectomy for stomach carcinoma	60	1643	1303
Patient 3	1.41	44	F	Crohn's disease	31	1340	950
Patient 4	1.74	48	M	S/P Sulfuric acid ingestion, esophageal, stricture	14	1900	1768
Patient 5†	1.53	79	M	Small bowel obstruction	37	1425	1056
Average	1.54	55			35	1509	1221

Injury/Infection Patients

	BSA (m^2)	Age (Yr)	Sex	Diagnosis	REE (kcal/day)	
					Predicted	Measured
Glucose System						
Patient 1	2.03	30	M	Stab wounds, lung, L ventricle, cardiac arrest	2116	2000
Patient 2	1.49	59	M	Abdominal sepsis following resection colon carcinoma	1377	1300
Patient 3‡	1.66	51	F	S/P A-V splenic shunt repair, partial pancreatectomy with development abdominal abcess	1534	1455
Patient 4	2.07	29	M	Multiple fractures; pelvis, femur, tibia, tibula	2159	2244
Patient 5	1.83	66	M	Pancreatic abcess, sepsis	1783	1900
Patient 6	1.60	46	M	Necrotizing pancreatitis following cholecystectomy	1626	1850
Average	1.78	47			1766	1792

	BSA (m^2)	Age (Yr)	Sex	Diagnosis	REE (kcal/day)	
					Predicted	Measured
Lipid System						
Patient 1	2.01	40	M	Stab wounds, chest and abdomen	2043	1950
Patient 2	1.74	55	F	S/P esophagogastrectomy	1608	1300
Patient 3	1.91	18	M	Gunshot wound of abdomen; development of abdominal sepsis	2067	2110
Patient 4	1.69	45	M	Multiple stab and gunshot wounds, S/P cystectomy	1762	1825
Patient 5	1.92	21	M	Auto accident, blunt trauma, pancreatitis	2000	2100
Patient 6	1.93	21	M	Motorcycle accident, abdominal trauma	2012	2600
Average	1.87	33			1915	1980

* Three 2-week studies performed.
† Two 2-week studies performed.
‡ Studied on both diets.

weight loss and who required total parenteral nutrition (TPN). Patients in this group had no evidence of sepsis and, if surgical patients, were at least three weeks post-surgery.

Group II: The acutely ill patient group consisted of twelve patients. Six patients were febrile (temperature > 38.6°C) with positive blood culture and/or evidence of localized intra-abdominal infection. Six patients were acutely ill secondary to injury. In the case of the septic patients, many had been nutritionally depleted prior to the development of sepsis. In the injured patients, it was anticipated that a return to normal oral intake would be unlikely for seven or more days, therefore, parenteral nutrition was started on day 2 following injury. All studies were carried out within the first week post-injury.

For the first day of the study, patients were maintained on intravenous 5 per cent dextrose. Resting energy expenditure (REE)‡‡ for each patient was calculated from O_2 consumption, CO_2 production, and nitrogen excretion. These procedures have been previously described[8–10] and are briefly summarized here. Energy contents of diets were calculated from published values.[11] Urine, feces and other body excretions (drainage) were collected and analyzed for total nitrogen. In addition, urea was determined in urine and drainage, creatinine was determined in urine, and glucose was determined in those urine samples in

‡‡ Resting energy expenditure consists of an average of energy expenditure measured throughout the day at rest. Basal energy expenditure is measured upon awakening, at rest and is generally 10 per cent lower than REE.

TABLE 2. Mean Caloric Intakes (kcal/day)

	Glucose System				Lipid System			
	Protein	Carbohydrate	Fat	Total	Protein	Carbohydrate	Fat	Total
Nutritionally depleted patients	500	1548	——	1948	503	774	803	2080
Injury/infection patients	530	1993	——	2523	535	998	1089	2622

which qualitative tests (Ketodiastix,® Ames Co., Elkhart, Inc.) were positive. A manual micro-Kjeldahl procedure was used for digesting samples for total nitrogen determination. Subsequent stages in nitrogen determination and analyses of urea and creatinine were carried out with single channel automated analyzers according to the manufacturer's procedures (Auto Analyzer®, Technicon Company, Tarrytown, New York). Blood urea nitrogen (BUN) was measured by an automated enzymatic procedure (BUN Analyzer®, Beckman Instruments, Inc., Fullerton, California).

Oxygen consumption and CO_2 production were measured with the patients lying at rest, using a rigid lucite head canopy developed in this laboratory.[8,9] This permits frequent measurements, each of relatively long duration—three to five periods per day of 40–60 min each—evenly spaced throughout the 24-hour period, with minimal discomfort to the patient. Resting energy expenditure, total RQ, and non-protein RQ were calculated.

The resting energy expenditure calculated for each patient while receiving 5 per cent dextrose is shown in table 1 and was used as a basis for calculating dietary intake. During total parenteral nutrition, energy intake was set at 1.5 times the REE as measured on 5 per cent dextrose to achieve positive nitrogen balance. The mean nutritional intake for each patient group during TPN is shown in table 2. Measurements were repeated after 4–7 days on the assigned nutritional regimens.

In the group of nutritionally depleted patients, the canopy system was coupled to a spirometry-computer system previously described.[9] The spirometer connected to the canopy provided a breath-by-breath record of lung volume changes. Spirometry and gas exchange data were acquired and processed by a digital computer. Air flow to the canopy was controlled to provide a stable spirometer baseline position. Algorithms, for quantifying each breath and determining tidal volume (V_T), frequency (f), inspiratory time (T_I), expiratory time (T_E), inspiratory flow and minute ventilation ($\dot{V}_E$) at evenly spaced points in time, were executed by the computer for V_T measurements. An accuracy of ± 10 ml is achieved at breathing frequencies of 5–40 breaths/min. The program excludes

TABLE 3. Gas Exchange and Breathing Patterns in the Nutritionally Depleted Patients

	$\dot{V}_{O_2}$ (ml/min)	$\dot{V}_{CO_2}$ (ml/min)	RQ	V_T (ml)	f (CPM)	$\dot{V}_E$ (l/min)	T_I (s)	Inspiratory Flow (ml/s)
				Lipid System				
Patient 1	147	131	.89	172	14.9	2.56	2.20	78
Patient 2*	148	126	.85	256	21.5	5.42	0.96	246
Patient 3	222	195	.88	344	16.5	5.76	0.84	410
Patient 4	271	236	.87	333	23.7	7.82	1.11	300
Patient 5†	203	177	.87	343	17.8	6.00	1.57	219
MEAN	198	173	.87	290	18.9	5.51	1.34	251
± SD	52	46	.02	75	3.6	1.90	.56	121
				Glucose System				
Patient 1	155	154	.99	205	15.7	3.29	1.59	129
Patient 2	150	144	.96	296	24.7	7.31	1.02	296
Patient 3	224	227	1.01	351	24.2	8.49	1.80	439
Patient 4	287	299	1.04	478	21.9	10.50	1.26	379
Patient 5	217	220	1.01	354	22.0	7.79	1.18	300
Mean	206	208	1.00	379	21.7	7.48	1.17	309
± SD	56	63	.03	99	3.6	2.60	2.90	117
Per cent Change	5	20	15	30	15	26	−13	29
P	NS	<0.025	<0.001	NS	NS	<0.01	NS	<0.01

* Average of three 2-week studies.

† Average of two 2-week studies.

TABLE 4. Alterations in Gas Exchange in the Acutely Ill Patients (Mean ± SD)

	5 Per Cent Dextrose Solution			TPN		
	$\dot{V}_{O_2}$ (ml·min^{-1}·m^{-2})	$\dot{V}_{CO_2}$ (ml·min^{-1}·m^{-2})	RQ	$\dot{V}_{O_2}$ (ml·min^{-1}·m^{-2})	$\dot{V}_{CO_2}$ (ml·min^{-1}·m^{-2})	RQ
Lipid System	157 ± 11	114 ± 13	.73	172 ± 15	147 ± 12	.85
Glucose System	141 ± 8	112 ± 11	.79	190 ± 12	179 ± 12	.94

all $V_T < 50$ ml. This system was used to obtain data on changes in $\dot{V}_E$, V_T, f, as well as inspiratory time during the different nutritional intakes.

Zinc, copper and iodine were given orally. Apart from trace elements and water *ad libitum*, there was no other oral intake. Amino acids were given as 10 per cent Aminosyn.®§§ Nitrogen intake was 10 g/day.

The details of the experiments, including risks, were explained to each patient, usually in the presence of members of his or her family, and written consent was obtained. The protocol for this study was approved by the Columbia University Institutional Review Board.

Results

The measured resting energy expenditure (REE) in the nutritionally depleted patients was 1221 kcal/day as compared to a predicted value of 1509 (table 1). The average weight loss was 35 per cent. The decrease in energy expenditure from predicted reflects the effect of semi-starvation. In the group of hypermetabolic septic and traumatized patients, the average measured energy expenditure was not significantly different than predicted. In this group, there were a number of patients who had a measured REE which was below predicted. These patients were nutritionally depleted prior to the development of the sepsis. In these patients the reduction in energy expenditure due to nutritional depletion exceeded the increase due to sepsis. Therefore, the REE was below predicted. Table 2 shows the mean caloric intakes in the two groups of patients with both feeding regimens. Table 3 shows alterations in gas exchange in the patients with chronic nutritional depletion. In shifting from the lipid to the glucose system, there was a 20 per cent increase in CO_2 production which resulted in a 26 per cent increase in $\dot{V}_E$. An increase in V_T was the major mechanism for the increase in $\dot{V}_E$. The RQ rose from 0.87 to 1.0. Tidal volume increased primarily through an increase in inspiratory flow. Alterations in gas exchange in the acutely ill patients are shown in table 4. The patients receiving the glucose system had a higher CO_2 production than those receiving the lipid system (179 *vs.* 147 ml·min^{-1}·m^{-2}; $P < 0.01$).

Discussion

The caloric requirements for total parenteral nutrition are usually given primarily as carbohydrates. This practice evolved due to past difficulty in obtaining a safe, FDA approved fat emulsion, and has been supported by studies of nitrogen balance. This study illustrates that other factors must be considered in determining the optimum, effective nutritional regimen.

Use of 5 per cent dextrose as nutritional support normally supplies only 300–400 kcal/day. Patients receiving 5 per cent dextrose utilize endogenous fat which is oxidized with a respiratory quotient of 0.7 to meet energy requirements. Nutritionally depleted patients receiving TPN utilize glucose (RQ = 1.0) as the primary source of energy. We have recently reported a case in which the increase in CO_2 production secondary to a high glucose intake precipitated respiratory distress in a septic patient.[4]

The response of the septic/injured patient to a high glucose intake seems to differ from the response of a nutritionally depleted patient.[5] The depleted patient has a "normal" response to excess glucose intake in that an intake of glucose above energy requirements results in synthesis of fat from carbohydrate. Gas exchange under these circumstances results in an RQ above 1.0 with a minimal rise in resting energy expenditure.[4–6] The minimal rise in energy expenditure presumably reflects the low energy cost of lipogenesis. In contrast, when the hypermetabolic patient is given large infusions of glucose, there is a minimal reduction in net lipolysis,[12] an increase in norepinephrine excretion and resting energy expenditure,[5,13] and continuing fat oxidation.[5] The result of these processes is a large increase in CO_2 production and oxygen consumption while the total and non-protein RQ remains below 1.0. The increased CO_2 production can be accurately predicted in the nutritionally depleted patient by the increase in RQ, while in the hypermetabolic patient, the RQ rise may not accurately reflect changes in CO_2 production.

In the acutely ill patients receiving TPN with fat partially replacing glucose, there was essentially no increase in O_2 consumption. Carbon dioxide production did increase, but not nearly to the extent seen in patients receiving glucose alone. Nitrogen balance was unaffected by the source of non-protein calories¶¶

§§ Abbott Laboratories, North Chicago, Illinois.

¶¶ Unpublished data.

agreeing with the previous results from this laboratory[14] and others,[15] while contradicting Long *et al.*[16] The differences in these studies may, however, be due to differences in the proportion of lipid used and the pathophysiologic state of the patients.

The relationship of minute ventilation to CO_2 production is relatively unchanged during the different nutritional intakes. This implies that there is no change in pulmonary efficiency[17] and that the respiratory changes are secondary to the increased CO_2 production. An increased tidal volume accounts for most of the increase in minute ventilation. The increased tidal volume is secondary to an increased inspiratory flow, while T_I remains fixed.

It should be noted that the difference in CO_2 production in the nutritionally depleted patients was significant even though the glucose intakes in the absence of lipids averaged only 1548 kcal/day. Large glucose intakes would result in an even higher RQ and greater levels of CO_2 production. We have measured an RQ of 1.2 in a patient receiving 4000 kcal/day of glucose.[4] Thus, with higher caloric intakes one would expect a greater effect of diet on CO_2 production.

In both nutritionally depleted patients and acutely ill patients, use of fat emulsions in moderate quantities results in a significant reduction in CO_2 production and hence in ventilatory requirements. Additionally, in the acutely ill patients, the increased O_2 consumption caused by high carbohydrate intakes can be significantly minimized by the use of fat emulsions. Clinically, the increase in CO_2 production caused by administration of a large carbohydrate load could be a critical factor in the patient with marginal pulmonary reserve. Fat emulsions which are oxidized with an RQ of 0.7 could prove useful in providing nutritional support without undue respiratory stress.

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