Effects of Total Parenteral Nutrition and Chemotherapy on the Metabolic Derangements in Small Cell Lung Cancer

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ABSTRACT

Changes in energy metabolism, substrate use, and hormone profiles were prospectively studied in 31 patients with small cell lung cancer receiving chemotherapy. Patients were randomized to receive either 4 weeks of total parenteral nutrition (n = 15) or to continue self-regulated p.o. diet (control group; n = 16). The initial actual resting energy expenditure measured by indirect calorimetry was 31% higher than the predicted resting energy expenditure determined by the Harris-Benedict formula. The p.o. calorie intake was inappropriately low for these hypermetabolic patients. Total parenteral nutrition resulted in a significant positive net energy balance, but in follow-up was associated with prolonged anorexia and a negative energy balance. Complete response to therapy reduced resting energy expenditure and increased calorie intake, whereas the contrary was true in nonresponders. Elevated plasma-free fatty acids (800 ± 62 µM; S.E.) and a low respiratory quotient (0.74 ± 0.02) indicate that the dominant energy source in patients with small cell lung cancer is fat, and that increased fat oxidation continues despite tumor response. Elevated fasting plasma catecholamines and insulin resistance may contribute to continued fat mobilization. Initially, there was a significant increase in blood lactate (1118 ± 95 µM) suggesting either increased tumor or tumor-mediated glycolytic activity. Response to therapy was associated with a fall in blood lactate levels. The most effective way of improving the metabolic derangements in patients with small cell lung cancer was to achieve tumor response to therapy.

INTRODUCTION

Significant weight loss is often the first manifestation of a malignant neoplasm. In SCLC, an apparently small tumor burden may be associated with significant weight loss (18) and a poor prognosis (13). In general terms, weight loss may result from a negative energy balance due to: (a) increased energy requirements; (b) reduced calorie intake; or (c) metabolic derangements that impair nutrient use. Isolated reports of metabolic abnormalities have been noted in a variety of cancers (2, 3, 5, 8, 11, 12, 14, 15, 20, 23). These may also result in a negative energy balance, and include: (a) increased resting energy expenditure (2, 19, 26); (b) reduced calorie intake due to anorexia (4); (c) impaired substrate use due to preferential mobilization of fat (10) and insulin resistance (16).

Despite such sporadic data, resting energy expenditure, calorie intake, substrate oxidation, and hormonal milieu have not been systematically examined in SCLC under controlled conditions of nutrient administration. This study was a randomized, controlled trial in which patients receiving total parenteral nutrition were compared with those eating a normal diet. Furthermore, we were able to study both the acute effects of chemotherapy and the effects of a complete response to therapy on these metabolic parameters.

MATERIALS AND METHODS

Experimental Design. The changes in energy metabolism (measurement of actual REE and determination of predicted REE and caloric intake) and substrate hormone profiles were prospectively studied in 31 patients with newly diagnosed SCLC. All patients in Toronto, Ontario, Canada, were part of a multinstitutional trial supported by the Nutrition Program of the Division of Cancer Treatment, the National Cancer Institute. The aim of the trial was to evaluate the efficacy of TPN as an adjunct to chemotherapy in measurable SCLC.

Upon entry to the study, all patients had standard nutritional assessment and tumor staging performed. Patients were stratified according to the extent of disease (limited versus extensive), the degree of weight loss over the 3 months preceding their study (less than 5% and greater than 5%), their performance status (Eastern Cooperative Oncology Group), and institution. After stratification, patients were randomized into 2 groups by a central randomization procedure at the National Cancer Institute: a TPN group which received in-hospital TPN for 4 weeks and a control group which continued to consume a self-regulated p.o. diet.

During the 4 weeks of TPN, p.o. intake was restricted to noncaloric fluids. In nondepleted patients (<5% body weight loss in the 3 months prior to diagnosis), the TPN provided between 1 and 1.25 g/kg body weight/day of crystalline amino acids (Travasol; Baxter-Travenol Laboratories of Canada) and a nonprotein calorie intake of between 32 and 40 kcal/kg body weight/day given as an equicaloric mixture of dextrose and lipid (Nutralipid; Pharmaclia, Canada). Depleted patients (>5% body weight loss in the 3 months prior to diagnosis) received an amino acid intake of between 1.50 and 2.0 g/kg body weight/day and a nonprotein calorie intake of 48 to 64 kcal/kg body weight/day. Both the protein and calorie intake were reassessed each week, and minor adjustments were made depending on clinical assessment of the nutritional status. All patients received electrolytes, vitamins, and trace elements in similar amounts (21). Chemotherapy started in the control group after completion of the initial nutritional evaluation, and in the TPN group after 7 days of parenteral nutrition. All patients received CAV consisting of high-dose cyclophosphamide (1200 mg/sq m), doxorubicin (Adriamycin, 70 mg/sq m; Adria Laboratories of Canada, Ltd.), and vincristine (2 mg) for 2 cycles 3 weeks apart, provided that it was well-tolerated, that there was no...
bleeding or infection, and that there were adequate granulocyte and platelet counts. All patients were given prophylactic trimethoprim-sulfa- methoxazole, 2 tablets twice daily, from Days 8 to 18 during each cycle of CAV. At 6 weeks, all patients were reevaluated and classified as responders (partial or complete response) or nonresponders (stable disease or progression). Responders then received 2 cycles of moderately-dose CAV (called CAV2): cyclophosphamide (1000 mg/sq m), doxorubicin (50 mg/sq m), and vincristine (2 mg) and prophylactic cranial irradiation after the second cycle of CAV (2000 rads in 5 fractions over 1 week). Partial responders with limited disease were also given locoregional radiotherapy (2500 rads in 10 fractions over 2 weeks). At this point, responders were switched to VP-16-213 (Etoposide; 100 mg/sq m daily for 3 days), methotrexate (50 mg/sq m), and p.o. folinic acid (10 mg every 6 hr for 6 doses, beginning at 36 hr after methotrexate) for 5 cycles at 3 weekly intervals, after which they crossed back to CAV. This was continued until they reached a total cumulative dose of doxorubicin of 450 mg/sq m. They then received VP-16-213, Methotrexate, and folinic acid for 5 further cycles to complete 1 year of therapy.

Nonresponders at 6 weeks received VP-16-213 (100 mg/sq m daily for 3 days), Methotrexate (50 mg/sq m), and folinic acid (10 mg every 6 hr for 6 doses beginning at 36 hr after Methotrexate) every 3 weeks until progression. Complete response was defined as complete disappearance of all tumor lesions, assessed clinically and by chest radiography and liver and bone scans. Partial response was defined as a decrease of >50% in the product of the cross-sectional diameter of the primary lung lesion without progression of metastases.

Patients. All patients had histologically or cytologically documented tumor, and none had been previously treated with either chemotherapy or radiotherapy. All patients had evaluable or measurable disease and a life expectancy of greater than 8 weeks. On entry to the study, all patients had adequate bone marrow, hepatic and renal function (WBC, >3000 cu mm; platelets, >100,000 cu mm; bilirubin, <2 mg/dl; serum creatinine, <2 mg/dl; and blood urea nitrogen, <30 mg/dl). The protocol was approved by the Human Experimentation Committee of the University of Toronto, and written consent was obtained from all patients. Patients were excluded from the study according to the following criteria: (e) recent myocardial infarction (<3 months from the date of diagnosis), congestive cardiac failure, or cardiac arrhythmias; (b) documented central nervous system metastases; (c) superior vena cava obstruction precluding central venous catheterization for TPN; (d) inappropriate anti-diuretic hormone syndrome; (e) other comorbid disease which rendered treatment inappropriate; (f) performance status of 4 on the Eastern Cooperative Oncology Group scale.

There were 16 patients in the control group and 15 in the TPN group. There were 10 females and 21 males with a mean age of 55.8 years (range, 30 to 75 years). There were 9 males in the TPN group and 12 in the control group. Twenty-one patients had limited disease, and 10 patients had extensive disease (5 patients in each group with extensive disease). Fifteen patients had lost more than 5% of body weight in the 3 months prior to diagnosis (9 in the TPN group and 6 in the control group).

Energy Metabolism. The actual REE was determined by indirect calorimetry. After an overnight fast, and while at complete rest, the patient’s expired air was collected in a Douglas bag through a mouthpiece over a period of 5 to 10 min. Collection of air started only after a period of adaptation to the mouthpiece. The volume of the expired gas was measured with a Wright spirometer (Ohio Medical Products, Madison, WI). The spirometer was calibrated regularly and was also compared with a Tissot spirometer. Oxygen concentration in expired air was measured with a polarographic O2 analyzer (Beckman OM-11; Beckman Instruments, Inc., Fullerton, CA). The carbon dioxide content of the expired air was measured with an IR CO2 analyzer (Beckman LB-2). After correction of expired gas volumes to standard temperature pressure dry conditions, the energy expenditure was calculated directly from oxygen consumption (liters of oxygen consumed in 24 hr, VO2), CO2 production (liters of carbon dioxide produced in 24 hr, VCO2), and total urinary nitrogen in 24 hr (UN) measured from a 24-hr urine collection by the micro-Kjeldahl method, according to the formula of Weir (24):

\[ \text{REE} = 3.94 \times \frac{\text{VO}_2}{\text{VCO}_2} + 1.106 \times \frac{\text{CO}_2}{\text{UN}} - 2.17 \times U_n \]

The predicted REE was calculated by the Harris-Benedict formula (7). The nonprotein RQ was also calculated using the oxygen consumption, carbon dioxide production, and total urinary nitrogen.

The actual REE, predicted REE, and RQ were determined in 20 normal subjects and in the 31 patients with SCLC on admission and at 1, 2, 3, 4 (TPN group only), 7, 10, and 26 weeks.

Calorie Intake. The calorie intake for patients taking a p.o. diet was determined from 3-day diaries prepared by the patients at home. The caloric equivalent of foodstuffs was obtained from tables of the Department of Agriculture (1). The daily calorie intakes were recorded at the same intervals as the REE, so that net energy intake above resting requirements could be calculated. For patients receiving TPN, the calorie intake was precisely defined by the amount infused.

Substrates-Hormones. Blood for determination of substrate-hormone profiles was drawn, after an overnight fast, following the collection of expired air. Plasma cortisol was determined by radioimmunoassay (25) and plasma catecholamines by a radioenzymatic technique (22). Blood glucose, lactate, ß-hydroxybutyrate, plasma FFAs, immunoreactive insulin, and immunoreactive glucagon were determined by methods described elsewhere (10).

Statistical Analysis. Results of measurements are reported as mean ± S.E. Standard t tests, paired and unpaired as appropriate, were used to examine the significance of differences between means.

RESULTS

Energy Metabolism

In the 20 normal subjects (10 male and 10 female; mean age, 32.8 years; range, 21 to 59 years), who were hospital employees without any clinical abnormalities, the mean actual REE measured after an overnight fast by indirect calorimetry was 1513 ± 52 kcal/day, not significantly different from the predicted REE of 1501 ± 33 kcal/day, calculated by the Harris-Benedict formula. In this group, the RQ was 0.79 ± 0.011. In 4 additional patients with a mean age of 68 years, admitted for elective surgery and asymptomatic at the time of study, the mean RQ was 0.79 ± 0.026, and the measured and predicted REE were 1235 ± 102 and 1414 ± 102, respectively. In contrast, in the 31 patients with SCLC, studied under the same conditions as the patients in elective hospital admissions, the mean base-line actual REE was 1804 ± 86 kcal/day, significantly higher than the mean predicted REE of 1374 ± 27 kcal/day (p < 0.001). This demonstrates that patients with SCLC are hypermetabolic, with a 31% increase in REE above the predicted normal even when compared with controls in the same age range. The percentage increase in patients with metastatic disease (39.5 ± 7.9%) was not statistically different (p < 0.30) from those with limited disease (25.7 ± 6.2%).

Table 1 outlines the calorie intake and REE in the control and TPN patients at base line, during the period of TPN (Weeks 1 to 4) and during follow-up (Weeks 7 to 26). The base-line calorie intake, REE, and net energy intake above resting requirements were not significantly different between the 2 groups. However, the net positive energy intakes above resting requirements were well below the normal required for the energy expenditure of daily activity. The calorie intake was clearly inappropriately low in these patients who are hypermetabolic.

Metabolic Derangements in SCLC
Effect of Chemotherapy. There were no significant short-term effects of chemotherapy (base line compared with Weeks 1 to 3) on either calorie intake or REE in the control patients (Table 1).

Effect of TPN. The 4 weeks of TPN resulted in a significant increase in calorie intake compared with the base-line p.o. calorie intake (p < 0.001), and a significant positive net energy intake above resting requirements (p < 0.001) (Table 1). After 1 week of TPN and before the first course of chemotherapy, the mean actual REE increased by 8.5% from 17873 ± 167 kcal/day to 1933 ± 132 kcal/day (p < 0.05). This increase represents the specific dynamic action of TPN (comparable to the specific dynamic actions of p.o. feeding), since the REE measurements were performed while the TPN solutions were being infused. In the follow-up period (Weeks 7 to 26), there were no significant changes in the metabolic parameters compared with the base line in the control patients, while the TPN patients showed a significantly lower calorie intake (p < 0.001) and a negative net energy intake above resting requirements. During this follow-up period, the mean daily p.o. calorie intake after cessation of TPN was not significantly different in the patients who obtained a complete clinical response (1520 ± 228 kcal/day; n = 4) compared with the non-responders (1556 ± 101 kcal/day; n = 11).

Effect of Response to Therapy. Twelve patients had a complete clinical response to therapy between 10 and 26 weeks after induction chemotherapy. On the initial assessment of these 12 patients, 7 had limited disease and 5 had extensive disease, while 8 patients were in the control group and 4 in the TPN group. At base line in these 12 patients, there was a 27.6 ± 4.5% increase in the actual REE above predicted while, following a complete clinical response to therapy, there was a significant reduction in the REE to only 7.5 ± 4.5% above predicted (p < 0.01). In the partial responders and the nonresponders, there was no significant change in the REE.

Table 2 compares these changes in energy metabolism in the patients who obtained a complete clinical response to therapy compared with nonresponders. The significant reduction in REE in the responders (p < 0.01) and maintenance of calorie intake resulted in a positive net energy balance (+451 ± 137 kcal). In contrast, the nonresponders had a significant reduction in calorie intake (p < 0.05) and no reduction in REE such that they went into a negative net energy balance (−93 ± 144 kcal). Clearly, the energy balance was significantly higher in patients at the time of complete response to therapy compared with the energy balance in the nonresponders (p < 0.02).

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Calorie intake (kcal)</th>
<th>Resting energy expenditure (kcal)</th>
<th>Net energy intake above resting requirements (kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control patients (n = 16)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base line</td>
<td>1971 ± 140</td>
<td>1832 ± 79</td>
<td>+136 ± 135</td>
</tr>
<tr>
<td>Wk 1-3</td>
<td>1996 ± 104</td>
<td>1727 ± 56</td>
<td>+268 ± 91</td>
</tr>
<tr>
<td>Wk 7-26</td>
<td>1918 ± 88</td>
<td>1677 ± 52</td>
<td>+241 ± 79</td>
</tr>
<tr>
<td><strong>TPN patients (n = 15)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base line</td>
<td>2020 ± 174</td>
<td>1783 ± 167</td>
<td>+236 ± 201</td>
</tr>
<tr>
<td>Wk 1-4 (TPN)</td>
<td>2281 ± 103</td>
<td>1848 ± 69</td>
<td>+973 ± 87</td>
</tr>
<tr>
<td>Wk 7-26</td>
<td>1524 ± 104</td>
<td>1534 ± 50</td>
<td>−9 ± 116</td>
</tr>
</tbody>
</table>

*Mean ± S.E.

Effect of Response to Therapy. Table 5 and 6 compare the substrate-hormone profiles in responders compared with non-responders. In the responders, there was a significant increase in fasting catecholamines (norepinephrine, epinephrine, and dopamine; p < 0.01), whereas base-line plasma insulin, glucagon, and cortisol were normal. While the FFA were raised in the fasting state as compared with controls, there was no hyperglycemia. There was a significant increase in fasting blood lactate compared with normal (p < 0.01), suggesting increased tumor or tumor-mediated production of lactic acid. There was evidence of increased oxidation of fat and ketone body production with increased fasting plasma FFAs (p < 0.01) and β-hydroxybutyrate (p < 0.05). Preferential fat oxidation was noted by a low mean nonprotein RQ, 0.73 ± 0.03, compared with 0.79 ± 0.01 in both young and elderly controls (p, not significant).

Effect of Chemotherapy. There were no significant acute effects of chemotherapy on the substrate-hormone profile in the 2 weeks following induction chemotherapy in the control patients. Fasting blood lactate remained elevated (984 ± 63 μM) and fasting plasma FFAs and blood β-hydroxybutyrate were also elevated (691 ± 30 and 127 ± 46 μM, respectively). Fat oxidation continued as evidenced by a low RQ of 0.72 ± 0.02.

Effect of TPN. Table 4 outlines the effect of 1 week of TPN on the substrate-hormone profile prior to chemotherapy. There was almost complete suppression of the blood β-hydroxybutyrate, which fell from 90.7 ± 26.4 to 13.3 ± 2.7 μM (p < 0.02), while there was a marked increase in plasma immunoreactive insulin from 0.54 ± 0.05 to 5.07 ± 1.67 ng/ml (p < 0.01). However, the plasma FFA level continued to be elevated (880 ± 127 μM) despite this marked increase in plasma insulin, and the RQ remained low at 0.76 ± 0.16 even after 4 weeks of TPN in which at least 50% of calories were given as glucose. The RQ was not significantly higher than in the control patients with SCLC (0.70 ± 0.09; p, not significant), who were not receiving additional nutritional support.

Effect of Response to Therapy. Tables 5 and 6 compare the substrate-hormone profiles in responders compared with non-responders. In the responders, there was a significant increase in fasting blood lactate from 1059 ± 10 to 595 ± 82 μM (p < 0.001). Response to therapy was not associated with a significant change in substrate use, since FFA remained elevated in both responders (824 ± 105 μM) and nonresponders (678 ± 70 μM) and RQ low in both responders (0.76 ± 0.03) and nonresponders (0.76 ± 0.03). Preferential fat oxidation appears obligatory despite a complete clinical response to therapy.
DISCUSSION

Energy Metabolism. The results of this study showed that patients with SCLC were hypermetabolic. In addition, prior to any therapy, their mean calorie intake exceeded mean resting requirements by only 138 and 236 kcal/day in controls and TPN patients, respectively. This excess of calorie intake over resting requirements is clearly insufficient to meet the energy needs of day-to-day activity, and it is, therefore, not surprising that 15 patients had lost more than 5% body weight on admission. Hence, weight loss in these patients represents a combination of hypermetabolism and a relative anorexia.

The administration of TPN for 4 weeks placed these patients in a markedly positive energy balance compared with controls who continued to eat as before. We have already reported that this increase in calorie intake was associated with a rise in body weight, total body potassium, and body fat. The interesting finding is that this gain in body weight was followed by profound anorexia in TPN patients compared with controls at the same stage of their disease. In consequence, after 4 weeks of TPN, the observed calorie intake over a 19-week period was below the resting metabolic requirements. The characteristics of this anorexia were that it was not transient, but lasted several months after TPN was discontinued, and that it was not due to disease progression, since both responders and nonresponders had a similar reduction in p.o. intake following cessation of TPN. Hence, we are left with the interesting conclusion that changes in body composition and weight gain were associated with appetite suppression. In other words, appetite control was set to maintain subnormal weight. The reduced p.o. calorie intake following TPN resulted in a sharp decline in body weight, total body potassium, and total body nitrogen such that, after 32 weeks, there were no significant differences in body weight and body composition between the TPN and control patients.

It is of interest that chemotherapy had little overall effect on calorie intake or metabolic expenditure, whereas response to therapy reduced energy expenditure and improved intake. The contrary was true in nonresponders. The reduced intake in responders is unlikely to be due to prior TPN, as it was observed 6 weeks after TPN had been discontinued. These findings indicate the dominant nature of tumor activity in controlling appetite and hypermetabolism. The mechanisms involved need further study.

Substrate Use and Hormone Profile. In patients with SCLC, the dominant fuel used for energy is fat. Fasting plasma FFA levels were high (880 ± 127 μM). This could be due to the tumor, or the relative insulin resistance of age. However, in other patients with nonmalignant conditions studied by Nordenstrom et al. (19) using a comparable TPN regimen, the FFA levels were not similarly raised, being 397 ± 17 and 373 ± 35 μM in acutely ill and depleted patients, respectively. By comparison, their healthy controls had a mean FFA level of 543 ± 165 μM, results comparable to our own controls. Furthermore, in our patients, even during TPN, the high FFA levels were unsuppressed despite a high circulating level of insulin (5.07 ± 1.66 ng/ml or 126.79 ± 41.5 μunits/ml). This finding was in contrast to Nordenstrom's

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observation in patients on a comparable regimen of TPN where the FFA levels were only 373 ± 35 μmol/liter with much lower levels of insulin (8 ± 3 μunits/ml) (19). In previous studies, we had similarly observed comparably low FFA and insulin levels in patients without cancer on a comparable regimen of TPN containing lipid (9).

These findings indicated that there was continuing fat mobilization unsuppressed by insulin in patients with SCLC, not seen in other patients on a comparable lipid regimen of TPN. Furthermore, associated with fat mobilization, the RQ was low, indicating that fat was oxidized in preference to carbohydrate. Data calculated from MacFie et al. (17) indicated that the mean starting RQ in 7 patients without cancer on TPN using a lipid system was 0.79 ± 0.05, but rose to over 0.92 on TPN using a comparable glucose-lipid regimen. In contrast, the RQ of our patients remained at 0.76 ± 0.168. Thus, the higher fatty acid levels and lower RQ observed are not due to lipid infusions, since they were not observed in several different studies in patients receiving equivalent or higher glucose-fat ratios in TPN. Increased fat oxidation seemed to continue despite tumor response. In contrast, the increased blood lactate levels fell in the responders. These findings suggest that fatty acid mobilization is likely to be an indirect effect of the tumor. In contrast, since the lactate production fell when the tumor responded, it is likely to be the result of tumor-mediated glycolytic activity. Such an effect could be due to the action of tumor-specific lactic acid dehydrogenase. In part, the continued fatty acid mobilization is due to insulin resistance and elevated catecholamines, as evidenced by the fact that the marked increase in insulin levels during TPN failed to reduce circulating FFAs. The only increase in counterregulatory hormones was in the catecholamine levels, but other causes also possible.

Finally, the administration of TPN, a forced intake of excess calories, resulted in net fat synthesis and weight gain, but with concurrent hypercatabolism and fat mobilization.

In conclusion, patients with SCLC are hypermetabolic, preferentially use fat stores, and are also relatively anorexic. A forced increase in calorie intake reduced neither hypercatabolism nor fat mobilization. Weight gain imposed by artificial means in the absence of tumor may have an indirect effect of the tumor. In contrast, since the lactate production fell when the tumor responded, it is likely to be the result of tumor-mediated glycolytic activity. Such an effect could be due to the action of tumor-specific lactic acid dehydrogenase. In part, the continued fatty acid mobilization is due to insulin resistance and elevated catecholamines, as evidenced by the fact that the marked increase in insulin levels during TPN failed to reduce circulating FFAs. The only increase in counterregulatory hormones was in the catecholamine levels, but other causes also possible.

Finally, the administration of TPN, a forced intake of excess calories, resulted in net fat synthesis and weight gain, but with concurrent hypercatabolism and fat mobilization.

In conclusion, patients with SCLC are hypermetabolic, preferentially use fat stores, and are also relatively anorexic. A forced increase in calorie intake reduced neither hypercatabolism nor fat mobilization. Weight gain imposed by artificial means increased anorexia, so that weight loss was even more rapid than usual when nutritional support was discontinued. The single most effective way of improving the balance between intake and catabolism is to achieve tumor response to therapy.
ACKNOWLEDGMENTS

We would like to thank nurses Mame Clark, Linda Millband, Betty Mullis, Sandra Stewart, and Diane Taylor for all of their hard work on the study; and nutritionists Karen Paul and Sandra Mitchell for preparing diet diaries. Special thanks go to Jocelyn Whitwell and Dr. A. Bruce-Robertson for their help in preparing the manuscript.

REFERENCES

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