METABOLIC EFFECTS OF NUTRITIONAL SUPPORT TO CANCER PATIENTS

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(Received 22 April 1985)

An adequate understanding of the utilization of administered nitrogen and energy sources as well as the regulation of whole body energy expenditure are important factors for maintaining body weight and body composition. The efficacy and metabolic consequences of adjunct nutritional support to cachectic cancer patients has recently been investigated in a number of studies. This review examines some recent investigations in this area. Depleted cancer patients seem to have a slightly higher resting energy expenditure but a normal metabolic and energetic response to administration of energy substrates. Studies of protein metabolism suggest that depleted cancer patients have a disturbed metabolic response of protein anabolism compared with depleted controls. This could be due to differences in peripheral versus visceral tissues. Adjunct nutritional support plays an important role in restoring the depleted cancer patients although clear correlation to functional parameters is still lacking.

Key words: Cancer, Nutrition, Metabolism, Humans.

INTRODUCTION

Positive energy and nitrogen balance are fundamental prerequisites for maintenance of body weight and body composition. Cachetic cancer patients are characterized by a combined protein and caloric undernutrition (PCU) resulting in loss of weight, contraction of lean body mass, depletion of fat mass and hypoproteinemia. The clinical significance of the problem with protein-calorie undernutrition was demonstrated by De Wys and co-workers who documented the association between undernutrition and decreased survival in a variety of cancer patients. The recognition of this has encouraged physicians to overcome the malnutrition by intensive use of enteral and parental nutrition. However, results of prospective clinical trials using nutritional support as an adjuvant to intensive antineoplastic therapy have been disappointing when effects on morbidity and survival have been examined. A drawback in a number of these studies has been the necessity to rely on traditional nutritional indicators, which are only affected over longer time periods and do not adequately mirror the metabolic events that precede the repletion of the patients.

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Recent efforts have therefore been made, firstly to further the understanding of the metabolic abnormalities that continuously aggravate cancer cachexia, secondly, we have tried to assess our ability to reverse or at least alleviate these metabolic derangements by the delivery of exogenous nitrogen and energy substrates. We have recently reviewed most of these studies elsewhere.

One of the major controversies in the repletion of cancer patients has been the ability of tumour influenced tissue to respond to nutrition in a similar fashion to depleted tissues influenced by a non malignant stress such as trauma, infection or injury. This review will discuss the impact of nutritional support to cancer patients with special reference to body composition, protein metabolism and energy metabolism. Whenever possible, a comparison will be made with the response to nutrition in depleted non cancer patients.

BODY COMPOSITION

It has been demonstrated that total parenteral nutrition (TPN) is capable of increasing body weight in patients with malignancy. This change can be attributed to increased lean muscle mass, body fat stores, and total body water or combinations of these components. It is the exact nature of the
weight gain achieved by TPN that is controversial. Nixon et al. concluded from elemental balance studies that positive nitrogen balance and weight gain in cancer patients with advanced disease undergoing hyperalimentation does not represent increased synthesis of lean tissue. These authors suggested that tumor induced abnormalities in liver and muscle protein metabolism could explain the differences observed between the depleted cancer group as compared to the depleted non cancer groups. A contributing factor to the altered mineral balance between cancer and non cancer patients during nutrition could hypothetically be the fact that the tumor per se has a different composition from the host.

Most reports have agreed that a weight gain is accompanied by an increase in body fat during nutritional support. This seems quantitatively to be in line with observations made in depleted non cancer patients. The increase in body weight has also been associated with a positive nitrogen balance and an elevation in total body potassium, the latter generally being accepted as an indicator of lean body mass. This was recently challenged by Shike and coworkers who measured total body potassium and total body nitrogen in depleted patients with small-cell lung cancer receiving TPN during a 4-week period. They reported a 5% gain in body weight during the 4 weeks of nutritional support and showed that this could be ascribed to an accumulation of body fat and body potassium and not to the accretion of protein since body nitrogen levels remained unaltered. Therefore, these authors claimed that measurements of whole body potassium are invalid indicators of nitrogen status.

It can be questioned whether increased nitrogen retention is indeed the aim of the treatment in these patients, since studies on anorexia nervosa patients have demonstrated a significant improvement of muscle function concomitant with a small improvement in nitrogen (9%) and a more pronounced increase in fat (44%) and potassium (21%) during refeeding.

In conclusion, nutritional support will restore body fat, retain whole body potassium and bring the patient into a positive nitrogen balance. It is questionable whether this corresponds to a true deposition of protein. It is suggested that further body composition studies should be associated with functional studies.

PROTEIN METABOLISM

Protein metabolism is extensively altered in cancer patients. As the tumour enlarges the host muscle mass is depleted; this is in contrast to the sparing of liver, kidneys, adrenal glands, and spleen which may even enlarge. In early stages of cancer cachexia the total body nitrogen pool may be unchanged, although nitrogen is redistributed from muscle to the tumour and the liver. Later, concomitant with an increased anorexia, the total body protein pool declines.

It has recently been demonstrated that depleted cancer patients have an increased whole body protein turnover compared to depleted non cancer patients and starved healthy subjects. No study has yet compared the effect of nutritional support on whole body protein metabolism in depleted cancer patients with depleted non cancer patients. Burt et al. reported an enhanced whole body protein flux in patients with oesophageal carcinoma receiving nutritional support for 14 days. A tendency to an enhanced whole body protein synthesis and a simultaneously decreased degradation was also seen. These observations may seem to be at variance with the above mentioned unaltered protein deposition. One explanation may be that the kinetic observations are related to changes in the pool of liver proteins with rapid turnover whereas the determinations of whole body nitrogen reflected changes in the muscle compartment which is of quantitatively larger importance.

Protein metabolism in peripheral tissues of cachectic patients is characterized by a decreased protein synthesis. These patients improve their protein synthesizing capacity in skeletal muscles after 14 days of TPN, as reflected by an increased muscle RNA content in muscle tissue and an improved leucine incorporation into proteins in vitro.

We have documented a similar trend in vivo by assessing the net balance of total amino acids over peripheral tissue (the leg) before and after 14 days of enteral nutrition. However, in this respect the cancer group responded less efficiently than the controls (see Fig. 1). Moreover, peripheral tissue remained in negative nitrogen balance. This implies that nutritional support preferentially enhances protein synthesis in the visceral compartment in cancer patients. These observations support the above difficulties in restoring the protein compartment during cancer cachexia from a quantitative point of view, since retention of amino acids in muscle tissue was increased to only a minor extent.

ENERGY AND OXIDATIVE METABOLISM

The energy ingested by individuals which varies in