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PART 2 OF TWO PARTS

Conference on Nutrition and Cancer Therapy

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Parenteral Nutrition Techniques in Cancer Patients[1]

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Summary

If a patient is expected to respond optimally to one or more forms of oncologic therapy, he should simultaneously be in the best possible nutritional and metabolic condition. When the alimentary tract cannot be used effectively for feeding cancer patients, parenteral nutrition can be lifesaving. Moreover, patients who are poor candidates or noncandidates for any antineoplastic therapy because of their debility or cachexia can be converted to reasonable candidates following a course of i.v. hyperalimentation. This i.v. hyperalimentation can significantly reduce the morbidity and mortality of cancer patients without stimulating tumor growth when applied conscientiously according to the established principles and techniques and when integrated with specific tumor therapy.

With the use of ambulatory or home hyperalimentation techniques, normal nutritional status can be restored or maintained during prolonged periods of antineoplastic therapy on a practical and relatively economical outpatient basis. It is anticipated that specific nutrient substrate formulas and parenteral therapy techniques will be developed to maintain optimal host nutrition while adversely affecting the neoplasm.

Introduction

Nutrient substrates are required by the human body in sufficient quantity and of adequate quality to supply basal metabolic needs and to support a state of nutritional equilibrium and positive nitrogen balance under a wide variety of conditions associated with catabolism. Moreover, requirements can be significantly accentuated by major trauma, burns, sepsis, metabolic disorders and, possibly, malignant diseases. For many years it has been postulated that metabolic demands are increased in patients with malignant neoplasms, but this has never been clearly documented. When the diagnosis of cancer is made initially, patients are usually adequately nourished. However, various forms of effective antineoplastic therapy often result in severe nutritional deficits and are associated with weight loss, protein malnutrition, and inanition. On the other hand, loss of body mass can be the initial clinical sign in patients with specific cancers such as leukemia, lymphoma, and oat cell carcinoma of the lung. In such patients, tumor bulk can achieve rather large proportions before symptoms become manifest, and weight loss may in part reflect the increased nutritional demands imposed upon the host by the progressive tumor burden. Conversely, breast cancer, malignant melanoma, most soft tissue sarcomas, and the majority of gastrointestinal cancers produce early signs and symptoms (such as bleeding or a palpable mass) while the tumor mass is relatively small, and any weight loss secondary to the demands of the neoplasm can be identified or appreciated. Some specific alimentary tract cancers, particularly those of the oropharynx and esophagus, induce weight loss because of reduced p.o. intake secondary to obstruction or dysphagia. Similarly, lymphoma of the small bowel and certain hormone-secreting tumors, such as carcinoma of the pancreatic islet cells, can result in malnutrition secondary to malabsorption. Nevertheless, the malnutrition seen in patients with cancer is usually iatrogenic as a result of oncological therapy, unless the patient has neglected his symptoms for several months and has become cachectic secondary to diminished p.o. intake and increased tumor mass.

During oncological treatment, malnutrition and inanition can be prevented, minimized, or corrected by the appropriate use of currently available i.v. and enteral nutrient regimens. Whenever possible, the gastrointestinal tract should be utilized for digestion, absorption, and assimilation of nutrients. The most natural and practical method of nutrient administration is p.o., and the next most feasible method of nutrient delivery is via nasogastric or nasoduodenal feeding tubes. However, operative insertion of a gastrostomy or jejunostomy tube may be necessary for long-term nutritional maintenance in some patients. Unfortunately, optimal nutritional rehabilitation via the alimentary tract can require an inordinate amount of time, and specific antineoplastic therapy cannot always be deferred until protein and energy stores have been replenished adequately by this route.

During the past decade, IVH[3] has become available to the oncologist as a safe, effective, and practical method of nutritional rehabilitation. The concept of concentrated i.v. nutrients to meet the high caloric and protein requirements of critically ill patients was originally tested in 1966 (6). In the initial experiment, beagle puppies fed exclusively by vein with a 30% nutrient solution consisting primarily of glucose and protein hydrolysates via the superior vena cava grew and developed normally for periods up to 9 months. Following this experience the technique of IVH was successfully adapted for use in pediatric and adult humans (7).

[1] Presented at the Conference on Nutrition and Cancer Therapy, November 29 to December 1, 1976, Key Biscayne, Fla.

Although many individual patients with malignant disorders had received nutritional support via parenteral hyperalimentation, extensive applications of this technique to the nutritional rehabilitation of cancer patients in a prospective clinical study were pioneered at the M. D. Anderson Hospital and Tumor Institute (4). Since the hyperalimentation team was established in 1972, more than 2000 patients in our series have received IVH as a means of nutritional maintenance or restoration prior to, during, and/or following treatment with chemotherapy, radiotherapy, or surgery. Because of IVH, the gastrointestinal tract can be bypassed and rested in a basal state while positive nitrogen balance and a state of anabolism can be attained within 7 to 10 days. This technique of total parenteral nutrition has proven to be safe and effective, and stimulation of tumor growth has not been observed as a consequence of the i.v. feeding.

A rational approach to nutritional rehabilitation is to replenish the cancer patient rapidly, using IVH until the alimentary tract can be used effectively. The patient can be maintained with a chemically defined diet or other acceptable formulation until ingestion, digestion, absorption, and assimilation of adequate quantities of normal foodstuffs are possible enterally.

The purpose of this paper is to describe and discuss the composition and preparation of IVH solutions; the technique of central venous catheter insertion and long-term catheter maintenance; the principles of IVH administration and patient monitoring; the prevention, recognition, and management of complications during IVH therapy; the institution of an IVH team; and the application of ambulatory or home hyperalimentation.

Composition and Preparation of the Nutrient Solution

IVH solutions prepared in our institutions are quite hypertonic, having an osmolarity of 1800 to 2400 mOsmoles/liter. They are admixed in the pharmacy under laminar-flow, filtered-air hoods, either by mixing 500 ml of 50% dextrose with 500 ml of an 8.5% crystalline amino acid solution or by mixing 350 ml of 50% dextrose with 750 ml of 5 to 10% protein hydrolysate in 5% dextrose. Such solutions provide approximately 1000 Cal per liter and between 5.25 and 10.0 g of nitrogen per liter. Electrolytes and vitamins must be added to these base solutions in appropriate dosages to satisfy daily requirements. Although the protein hydrolysate solutions (casein or fibrin based) contain various electrolytes and trace elements as contaminants of their processing and storage in glass containers, the major electrolytes must be added to these solutions prior to infusion. The usual electrolyte additives to the hypertonic nutrient mixtures derived from the protein hydrolysate solutions include approximately 40 to 50 mEq sodium chloride, 20 to 40 mEq potassium chloride, 10 to 15 mEq magnesium sulfate and 15 to 20 mEq potassium acid phosphate per liter. Although the casein hydrolysates that are prepared by the enzymatic hydrolysis of the phosphoprotein casein contain large amounts of phosphorus (20 to 40 mmoles/liter), the phosphorus content varies considerably among preparations. Indeed, the 1st reported occurrence of hypophosphatemia during hyperalimentation was in a patient receiving casein hydrolysate as the nitrogen source. Fibrin hydrolysate, prepared by the acid hydrolysis of bovine or porcine fibrin, contains no significant amounts of phosphorus, and additions of this crucial intracellular element must be made to solutions of this nitrogen source.

The amino acids in the i.v. crystalline amino acid products currently commercially available in this country are present as the acetate and chloride or hydrochloride salts. These preparations are acidic and the addition of inordinate amounts of sodium and/or potassium chloride can result in hyperchloremic metabolic acidosis in some patients, particularly those in pediatric and geriatric age groups. Therefore, sodium and potassium should be added to the base solution as the acetate, bicarbonate, chloride, lactate, or acid phosphate salt as dictated by the patient's acid-base status and serum electrolyte concentrations. Despite the fact that phosphorus has been added to some of the more recent commercially available amino acid solutions in moderate amounts, our experience indicates that an additional 15 to 20 mEq of phosphate, as the potassium acid phosphate salt, must be added to each liter of solution to maintain normal serum phosphate concentrations, especially during the 1st week of therapy.

Hypomagnesemia will often occur within 10 days of initiating IVH if sufficient quantities of magnesium have not been added to the solutions. Similarly, hypocalcemia will result if adequate quantities of calcium are not provided, usually in dosages of 4 to 9 mEq calcium gluconate per day. Both the fat- and water-soluble vitamins must be added to 1 liter of IVH solution per day, and folic acid, vitamin K, and vitamin B_{12} are usually administered i.m. or i.v. once a week. In patients with bone marrow depression following chemotherapy or radiotherapy, addition of these vitamins to the IVH solutions is preferable to i.m. injection in order to avoid hematoma formation secondary to impaired coagulation mechanisms. Serum albumin concentrations below 3 g/100 ml should be corrected to levels of at least 3.5 g/100 ml by the daily administration of 12.5 to 50 g of salt-poor human albumin, which can be added directly to the bottles or bags of IVH solution. Colloid osmotic pressure thereby can be restored promptly, and protein nutrition will be supplemented. In most patients, albumin synthesis in the liver will be restored to normal within 7 to 10 days of IVH administration, and exogenous serum albumin will no longer be required. The formulation of representative IVH solutions for infusion into adult patients with normal concentrations of serum electrolytes, magnesium, phosphorus, and calcium is given in Table 1. The formulation of IVH solutions for use in infants is outlined in Table 2.

The minimum daily energy requirement necessary to maintain an adult patient in the basal metabolic state is approximately 1500 cal/day. In the absence of adequate exogenous calories, energy is generated primarily by lipolysis and the conversion of tissue protein into glucose via gluconeogenesis. The work of Cuthbertson (5) on the catabolic response following trauma in humans demonstrated

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