The Role of Parenteral Nutrition in Acute Leukemia

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Patients with acute leukemia who undergo hematopoietic stem cell transplantation (HSCT) are susceptible to malnutrition caused by several factors including intensive cytotoxic therapy. This paper discusses the significance of malnutrition in these patients and provides an overview of nutrition therapy by the oral, enteral, and parenteral routes. The goal is to investigate whether the use of parenteral nutrition (PN) produces improved clinical outcomes in patients with acute leukemia and to identify criteria for the selection of patients most likely to benefit from this therapy. Although PN may be appropriate for patients suffering from complications such as graft-versus-host disease (GVHD) and mucositis, the data available at this time do not support PN as first-line therapy for all recipients of HSCT.

Introduction

Approximately 200,000 people in the United States are living with leukemia [1]. Of the new cases of blood cancers in 2005, 30% of those will be leukemia. Acute myelogenous leukemia (AML) and acute lymphocytic leukemia (ALL) account for 11% more cases than chronic leukemia. The survival rate of these patients has improved over the years thanks to advances in supportive care and new variations in hematopoietic stem cell therapy (HSCT). The relative survival rate (compared with a person without leukemia) has increased dramatically over the past several decades. In the early 1960s the 5-year relative survival rate was only 14%. It jumped to 34% in the mid 1970s and was 48% between 1995 and 2001 [1].

Malnutrition in acute leukemia is a product of metabolic alterations and inflammatory responses inherent in the disease process, coupled with the intensive treatment regimens. The overall incidence of malnutrition during the course of cancer ranges from 30% to 90%, depending on the type of cancer and the treatment regimen [2]. Malnutrition has also been demonstrated in immunosuppressed populations. Body mass index (BMI), triceps skinfold, and mid–upper arm muscle circumference were all shown to be significantly decreased in patients with lower CD4+ cell counts and undetectable IgA proteins [3].

Malnutrition in Acute Leukemia

Pathogenesis

Malnutrition in patients with acute leukemia is multifactorial. All treatments associated with this disease—including chemotherapy, radiation, steroids, and immunosuppression—are hazardous to nutritional status. Chemotherapy and radiation may induce stomatitis, esophagitis, nausea, vomiting, diarrhea, colitis, enteritis, and neutropenia, and all of these conditions potentially contribute to altered taste perception, loss of appetite, decreased oral intake, impaired absorption, altered metabolism, reduced metabolic waste excretion, and a significant nutrient deficiency state.

Patients undergoing intensive treatment for acute leukemia are also predisposed to viral, bacterial, and fungal infections of the gastrointestinal (GI) tract. Infection may play a significant role in the development of malnutrition, with at least 50% of patients reportedly severe enteritis after HSCT [4,5]. Recurrent infections induce an acute-phase metabolic reaction resulting in negative nitrogen balance and decreased lean body mass [6]. The extensive catabolism cannot be reversed until the underlying infection has resolved. Anorexia, decreased oral intake, increased energy expenditure, and increased intestinal losses can further compound the infected patient’s risk of protein-calorie malnutrition [6,7].

Graft-versus-host disease

Graft-versus-host disease (GVHD) is a common complication of HSCT that contributes to malnutrition. GVHD occurs when engrafted donor cells attack the patient’s organs and tissues. It can affect the skin, liver, or GI tract. Manifestations tend to be more severe in patients receiving
mismatched transplants from family members or unrelated donors [8]. GVHD can be classified as acute, occurring before 100 days post-transplantation, or chronic, developing or persisting after 100 days. The risk of severe acute GVHD varies from 20% to 50% depending on the age of the patient and donor compatibility [9].

Malnutrition of acute GVHD manifests through decreased oral intake, nausea, vomiting, abdominal pain with cramping, large-volume secretory diarrhea, and nutrient malabsorption. Hypermetabolism required for tissue regeneration contributes as well. This process can also induce protein-losing enteropathy, in which the catabolic stress of conditioning regimens and loss of protein across the intestinal mucosa lead to a negative nitrogen balance. Parenteral nutrition (PN) is the accepted form of feeding during this acute phase [8].

Malnutrition in chronic GI GVHD is different from malnutrition in the acute form, in that lower intestinal involvement is rare, whereas dysphagia and reflux of the upper GI tract are common [10]. At the University of Washington’s Fred Hutchinson Cancer Center, 60% to 70% of HSCT patients develop some form of GVHD, and 20% of these patients develop stage 1 GI GVHD without skin involvement, defined as anorexia, nausea, vomiting, or diarrhea for more than 20 days following HSCT [11].

Mucositis

Mucositis is another complication of HSCT that contributes to malnutrition and is associated with negative outcomes in transplant patients [12,13]. Oral mucositis—erythema, ulceration, atrophy, and edema of the oral mucosa—can adversely affect the swallowing of food, fluid, and medications [14]. The inability to consume enough nutrients, the increased risk of infection, and the resulting malnutrition may increase morbidity and reduce the length of survival in HSCT populations [13].

Oral and gastrointestinal mucositis cause pain and may be dose-limiting for cancer treatments. Mild oral mucositis has been reported in 99% of transplant patients and severe mucositis may occur in as many as 70% [14]. PN is often started in patients with severe mucositis to preserve nutritional status while oral intake is substantially decreased. Damage to oral mucosa greatly increases the risk of perforation and excessive bleeding during feeding tube insertion in the thrombocytopenic patient.

Medications

Medications used in the treatment of patients with acute leukemia can also have adverse effects on the metabolism of micronutrients and macronutrients (Table 1). Corticosteroids can induce hyperglycemia, increase BUN and urinary nitrogen losses, cause metabolic alkalosis, and lead to peripheral muscle wasting. Cyclosporine can cause hypertriglyceridemia, hyperkalemia, and hypomagnesemia. These electrolyte disturbances usually begin 1 to 3 days after initiation of the offending drug. Amphotericin B tends to induce hypernatremia, hypokalemia, hypomagnesemia, and metabolic acidosis [15,16].

Diagnosing malnutrition

Diagnosing the type and degree of malnutrition in patients with acute leukemia is made difficult by the lack of a “gold standard” for defining nutritional status and the influence on nutritional parameters of nonnutritional factors. Biochemical markers used to measure visceral protein stores include albumin, prealbumin, and transferrin (all of which are influenced by fluid status), inflammation, chemotherapy, radiation, sepsis, GVHD, and liver function.

Albumin is synthesized in the liver and has a long half-life of 21 days. Hypoalbuminemia is associated with morbidity and mortality in hospitalized patients, but many nonnutritional factors can alter the predictive capacity of these levels (Table 2). Exogenous albumin administration, whole blood transfusion, and dehydration can falsely elevate albumin levels. Liver disease, ascites or edema, and large wounds or burns can decrease levels.

Transferrin is also synthesized in the liver and may be more sensitive to protein depletion than albumin because of its shorter half-life of 7 to 8 days. Whole blood transfusion, dehydration, and iron deficiency anemia may elevate serum transferrin levels, whereas liver disease, ascites or edema, stress, trauma, or sepsis may decrease levels.

Prealbumin is a carrier protein that transports thyroxine. Its half-life is only 2 to 3 days, making it more effective for nutritional evaluation than albumin or transferrin. Because prealbumin is metabolized in the