Medical Nutritional Therapy in Hematopoietic Stem Cell Transplantation (HSCT)

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ABSTRACT

Hematopoietic Stem Cell Transplantation (HSCT) is a method used for the treatment of patients with severe aplastic anemia, leukaemia and some other malignancies. As it causes many adverse sequelae (anorexia, nausea, vomiting, diarrhea, and mucositis), adequate oral diet is usually unachievable and artificial nutrition support is required. In order to reduce the risk of infections, the protective benefit of “low-microbial / neutropenic diets” is suggested to use in immunosuppressed patients. Traditionally, total parenteral nutrition (TPN) has been the chosen method for the nutritional support of patients undergoing HSCT. Secondly enteral nutrition (especially with enteral tube feeding - ETF) is an alternative method for nutritional support. It is important that dietary guidance for HSCT patients to minimize the risk of microbial exposure, optimize nutrient consumption and energy intake is very important.

Keywords: Hematopoietic Stem Cell Transplantation, Nutrition, Neutropenic diet, Nutritional support

ÖZET

Hematopoietik Kök Hücre Transplantasyonu (HKHT)’nda Tıbbi Beslenme Tedavisi

Hematopoietik Kök Hücre Transplantasyonu (HKHT) ağır aplastik anemi, lösemi ve diğer bazı maligniteleri olan hastaların tedavisi için kullanılan bir yöntemdir. Hastalıktan birçok yan etkileşimi (işthahsızlık, bulantı, kusma, ishal ve mukozit) neden olduğundan, çoğunlukla yeterli oral beslenme sağlanamamakta ve beslenme desteği gerekmektedir. Bağışıklığı baskılanmış hastalarda enfeksiyonlar riskini azaltmak için “düşük-mikrobiyal / nötropenik diyetler” koruyucu yarar sağlanması nedeniyle önerilmektedir. Geleneksel olarak, HKHT uygulanan hastalarda total parenteral beslenme (TPN), beslenme desteği için seçilen yöntem olmuştur. İkinci bir yöntem olan enteral beslenme uygulaması (özellikle enteral tüp ile beslenme - ETB), beslenme desteği için alternatif bir yöntemdir. HKHT hastalarına yönelik oluşturulan diyet rehberlerinde, enfeksiyona maruz kalma riskini en aza indirgemek amacıyla optimal besin tüketimi ve enerji alımı çok önemlidir.

Anahtar Kelimeler: Hematopoietik kök hücre transplantasyonu, Beslenme, Nötropenik diyet, Nutrisyonel destek
INTRODUCTION

Hematopoietic Stem Cell Transplantation (HSCT) is the infusion of stem cells collected from the bone marrow, peripheral blood, or placental cord blood to treat blood and other cancers, bone-marrow-related diseases, and a variety of immunologic and genetic disorders. Depending on who the donor is, there are two types of transplantation: allogeneic and autologous. In allogeneic transplantation, stem cells from a histocompatible donor, who may or may not be a relative, are infused into the patient; in autologous transplantation, the patient’s own hematopoietic cells are used. The advantages of autologous transplantation over allogeneic procedures are the greater availability of hematopoietic stem cells and the prevention of graft-versus-host disease (GVHD), which in turn leads to less morbidity, less mortality, and a lower economic cost. The greatest disadvantage is potential graft contamination with tumor cells, with a higher risk of recurrence of neoplasia. Different chemotherapies and radiotherapies have an effect not only on tumor cells but also on non-tumor cells, especially on rapidly replicating cells. Enterocytes, colonic epithelial cells, and lymphocytes belong to this group. The effects produced on such cells bring about important functional changes in the gastrointestinal tract and the immune system. The conditioning regimen thus induces very aggressive changes, causing in turn important metabolic and nutritional alterations. The kind of the diseases treated by HSCT is shown in Table 1.

Table 1. Diseases treated by hematopoietic stem cell transplantation

<table>
<thead>
<tr>
<th>Hematologic Malignancies</th>
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<tbody>
<tr>
<td>Acute leukemias, myelogenous and lymphoblastic</td>
<td>Chronic myelogenous leukemia</td>
</tr>
<tr>
<td>Lymphomas, non-Hodgkin and Hodgkin</td>
<td>Myelodysplastic and myeloproliferative disorders</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Solid Tumors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer (metastatic or high-risk primary disease)</td>
<td>Neuroblastoma</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>Sarcoma</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>Small-cell lung cancer</td>
</tr>
<tr>
<td>Brain tumors</td>
<td>Renal carcinoma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genetic Disorders</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassemia</td>
<td>Sickle cell disease</td>
</tr>
<tr>
<td>Immunodeficiency disorders (severe combined immunodeficiency disorder, combined immunodeficiency, Wiskott-Aldrich syndrome)</td>
<td>Fanconi’s anemia</td>
</tr>
<tr>
<td>Osteopetrosis</td>
<td>Enzyme deficiency disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other non-malignant diseases</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe aplastic anemia</td>
<td>Paroxysmal nocturnal hemoglobinuria</td>
</tr>
<tr>
<td>Acquired immunodeficiency disease</td>
<td>Autoimmune disorders (multiple sclerosis, systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis)</td>
</tr>
</tbody>
</table>

Figure 1. Overview of phases of transplantation

<table>
<thead>
<tr>
<th>PHASE</th>
<th>Preparation</th>
<th>Cytoreduction</th>
<th>Neutropenia</th>
<th>Engraftment/Early</th>
<th>Long-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAYS</td>
<td>60</td>
<td>10</td>
<td>0</td>
<td>20</td>
<td>70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Starting of disease</th>
<th>Fluid and electrolyte imbalances</th>
<th>Bacterial, fungal infections</th>
<th>Acute GVHD (skin, GI, liver)</th>
<th>Chronic GVHD (multisystem)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor selection</td>
<td>Acute nausea, vomiting</td>
<td>Kidney, lung, heart</td>
<td>Viral, fungal infections</td>
<td>Pulmonary fibrosis</td>
</tr>
<tr>
<td>Treatment plan</td>
<td>Tumor lysis</td>
<td>Organ toxicities</td>
<td>Acute GVHD (oral, GI, VOD,</td>
<td>Infertility, ovarian failure</td>
</tr>
<tr>
<td>Stem cell mobilization</td>
<td>Acute nausea, vomiting</td>
<td>Hyperacute GVHD</td>
<td>Chronic GVHD</td>
<td>Delayed growth</td>
</tr>
<tr>
<td>and collection</td>
<td></td>
<td></td>
<td></td>
<td>Relapse</td>
</tr>
<tr>
<td>(autologous patients)</td>
<td></td>
<td></td>
<td></td>
<td>Secondary tumors</td>
</tr>
</tbody>
</table>

The day of transplant is referred to as day 0.

GI: Gastrointestinal; GVHD: Graft- Versus –Host- Disease; VOD: Venoocclusive Disease
Establishment of an accurate diagnosis, stating of tumor for cancer diagnoses, and identification of the donor and the histo-compatibility between patient and donor are critical before HSCT to ensure patients receive optimal treatment to eradicate the cancer and create marrow space for the new graft. HSCT can be characterized by events that occur in five general phases or time periods (Figure 1).5

All patients undergoing HSCT are at an increased risk for malnutrition in the phase before transplantation and afterward. Regarding body weight on admission, both obesity (BMI ≥ 30 kg/m²) and undernourishment (BMI < 18.5 kg/m²) have been considered as risk factors for complications and increased relapse/nonrelapse mortality in HSCT patients.6-8

1. THE ROLE OF NUTRITION INTERVENTION

1.1 Pretransplantation Nutrition Assessment

The most of the patients undergoing HSCT may be considered at nutritional risk because of the anticipated toxicities that affect ability to sustain adequate oral intake for a minimum of 3 to 4 weeks. The patient's baseline nutritional status is highly important and the alteration of the pretransplantation nutritional status is a negative prognostic factor for the evolution of these patients. In fact, well-nourished patients require less time, in general, for the graft to prove effective.9

Causes of poor nutritional state during transplantation:
1. Mucositis
2. Nausea and vomiting caused by chemotherapy/radiotherapy
3. Acute or chronic gastrointestinal GVHD
4. Poor absorption of food following total body irradiation
5. Dental health problems
6. Infection of gastrointestinal tract
7. Altered taste and dry mouth
8. Dislike of food offered and lack of availability of favorite foods
9. Anxiety or distress.10

Some special considerations of pretransplant nutrition assessment are discussed below:

1.1.1. Anthropometric Status

Weight history, including preillness weight, is important in determining ideal body weight because of the fluctuations that may occur with previous treatment and often over an extended period of time. Splenomegaly can add weight, and some attempt should be made to estimate the weight of the spleen and correct for its effect on ideal body weight. For chemotherapy that is dosed by body weight, doses may be downward for obese patients. Adjusted body weight is often used, which accounts for the increased lean tissue needed to support excess fat stores. Patients, who recently took corticosteroid therapy may weigh more because of fluid retention or fat deposition without gaining any lean body mass. The dietician can bring these aspects nutrition assessment to the attention of the medical term. Arm anthropometry (skinfold measurements) and other techniques that estimate muscle mass and function, such as bioelectric impedance or hand dynamometry, are also useful in establishing baseline values and monitoring serial changes, especially in allogeneic grafts that have a higher risk of long-term complications and cumulative muscle protein losses.5,10-13

1.1.2. Biochemical and Medical Evaluation

Major renal or hepatic dysfunction is almost always a contraindication to transplantation. The pretransplant serum creatinine value serves as a benchmark for evaluating posttransplant renal insufficiency. In the multivariate model, transplant type (relative risk: 4.2), FEV1 (relative risk: 4.5), performance status (relative risk: 3.7), serum creatinine (relative risk: 3.8), and serum bilirubin (relative risk: 3.7) were found to be independent predictors of early toxic mortality.15 Bone marrow transplant recipient acquires hepatic mucormycosis from ingestion of a naturopathic medicine containing Mucor. Metabolic problems such as diabetes and hyperlipidemia can influence nutrition support strategies.15

1.1.3 Diet History

During the pretransplant patient interview, any active problems that interfere with the ability to meet nutrient needs and sustain weight should be evaluated and a care plan instituted. Some patients
may follow diets that limit food variety such as very low fat or other special diets, fitting these individuals’ diet preferences into posttransplant care plans can be a special challenge. High dose vitamin supplementation and use of herbals are common practices, some of which may have risks, such as fungal or bacterial contamination or organ toxicity, and it may be prudent to restrict consumption. A careful proactive assessment to identify, treat, and, hopefully, prevent adverse events is essential to a successful transplant.16-18

1.2. Cytoreduction and Neutropenia

1.2.1. Dietary Energy

Nutritional requirements in patients undergoing transplantation are increased due to the intense catabolism.19 Duro et al.20 observed significant reduction in resting energy expenditure (REE) during a 4-week period in children undergoing HSCT. Although the amount of energy expended by a patient with HSCT may vary according to whether it is autologous or allogeneic, there is agreement as to the energy requirements of the transplant recipient, which may increase up to 130-150% of the estimated basal energy expenditure, which corresponds to 30-50 kcal/kg of body weight per day. No data with children have been reported, but 1.6 times basal energy needs is a safe starting point.21,22

Taveroff et al.23 reported that energy intake of 25 kcal/kg in adults (as compared with 35 kcal/kg) resulted in less pronounced dearangements in serum sodium, potassium, and albumin without adverse effects on nitrogen balance. On the contrary, underfeeding allogenic graft patients during the early posttransplant period may result in significant weight loss before onset of acute and chronic GVHD when metabolic needs appear higher and may be more difficult to achieve.

1.2.2. Dietary Protein

In adult patients undergoing allogenic HSCT, nitrogen losses are high, especially during the first month after transplantation. Based on this data, protein needs are estimated at twice normal requirements, probably for all age groups, although nitrogen balance studies have not included children younger than 12 years. Protein requirements are also high and are generally met with the addition of 1.5-2 g/kg of body weight per day of a standard amino acid solution.24

1.2.3. Fluid and Electrolytes

Fluid needs during cytoreduction are based on individual drug regimens and may range from 1.0 to 2.0 times maintenance needs. Maintenance fluid needs are calculated as:

- 100 ml/kg up to 10 kg
- 1000 ml+50 ml/kg for 10-20 kg
- 1500 ml+ 20 ml/kg for 20-40 kg
- 1500 ml per square meter of body surface area for weights greater than 40 kg in which body surface area is calculated by the square root of [height (cm) x eight (kg)] divided by 60.3

Patients with signs and symptoms of pulmonary edema, heart failure, ascites, or other serious consequences of fluid overload require restriction of fluid and usually of sodium.

Electrolytes may be provided in total parenteral nutrition (TPN) or hydration solution, as separate or combination infusions.5

1.2.4. Vitamins and Minerals

The data on vitamin and mineral requirements are negligible; intervention related to complications is largely driven by clinical judgement. Patients with HSCT present depletion of certain nutrients with antioxidant properties, such as vitamin E and ß-carotene. Administering antioxidants (vitamins C and E) may be beneficial to these patients because of their effect on oxidative stress and tumor cell apoptosis. For all patients, not receiving TPN, it is prudent to provide an oral multivitamin and mineral supplement because of the restricted intake of a normal diet, often for an extended period. The nutritional requirements of HSCT patients are indicated in Table 2.25

1.3. Oral Dietary Management

Care plans for nutrition management is associated with the common gastrointestinal (GI) toxicities. Nausea and vomiting are most acute during administration of cytoreduction therapy, but mild symp-
toms persist for 3 to 6 weeks. Mucositis peaks at 10 to 14 days posttransplant, and the associated pain and swelling are the principal deterrents to eating during the neutropenic phase. Crampy abdominal pain and diarrhea secondary to mucosal crypt aberrations, epithelial flattening, cell degeneration, and increased bowel permeability peak 1 to 2 weeks after the start of conditioning and return to normal by 3 to 4 weeks after the transplant.26 Oral mucositis occurs in up to 75% of recipients of high-dose chemoradiotherapy conditioning regimens used for allogeneic HSCT. As a result of mucositis, narcotic analgesia and total parenteral nutrition (TPN) are commonly required after HSCT.27 Glutamine can behave as an essential amino acid in clinical settings where there is marked metabolic stress, such as occurs after HSCT. This amino acid plays a relevant role in the immune system, given its condition as a metabolic synthesis substrate in multiple pathways. It is also known for its role as an essential nutrient for some cell types, such as enterocytes and lymphocytes. In the case of patients with HSCT, one of the main roles of glutamine is to function as an energy substrate for rapidly replicating cells, such as those lining the intestinal mucosa. Administering glutamine would help to minimize the intestinal mucosal atrophy associated with TPN and the damage caused by chemotherapy or radiotherapy.26 Rzepecki et al.26 indicate that it would be worthwhile conducting a larger trial to see whether or not giving glutamine reduces the 100-day allogeneic transplant-related complications. Crowther et al.31 also indicated that there was no effect of oral or i.v. glutamine on overall transplant-related mortality at day +100. In another study, compared parenteral nutrition (PN) and glutamine versus standard PN showed that the certain benefits of PN with added glutamine compared to standard PN for reducing hospital stay are no longer definite.32 In conclusion, there may be beneficial effects of glutamine in HSCT but larger, well-designed studies are required to confirm the beneficial effects and investigate possible adverse effects.

1.3.1. “Low-Microbial” / “Clean” / “Neutropenic” Diets

In order to reduce the risk of infection, the profoundly immunosuppressed patient has traditionally been protected from the external environment by means of a plastic tent or laminar air-flow room, given high doses of antibiotics to make the gastrointestinal tract sterile, and only given steril
foods. The protective benefit of low-microbial diets against infection has never been established. Low–micro-organism diets are indicated to prevent sepsis in transplant recipients. Nonetheless, such diets are often fed to patients with neutropenia to minimize acquisition of organisms from food sources and food handlers.

Table 3 describes one set of diet restrictions for HSCT patients undergoing treatment both in the hospital and at home. Autologous graft recipients are advised to follow the diet for 3 months after chemotherapy and allogeneic graft patients until 1 year after transplant, or longer if they are still taking immunosuppressants for GVHD.

Generally foods which pose the greatest risk to immunosuppressed patients include:

- Raw or undercooked animal foods such as eggs or unpasteurized milk or dairy products, raw vegetables and salads,
- Meat, especially if inappropriately thawed or undercooked, or if raw meat juices contaminate other foods during food storage or preparation,
- Shellfish,
- Foods in opened containers or used communally (e.g. large cartons of ice-cream, the domestic butter dish or tubs of fat spread, jars of jam or marmalade, bottled sauces),
- Foods which are stale or near their “use by” date.

1.3.2. Safe Cooking Methods

Conventional gas and electric ovens: The oven should always be preheated to ensure that the food cooks rapidly. The cooking time should be sufficient to achieve a core temperature of 70°C in the food. If necessary this can be checked using a thermometer with a probe on a dublicate food sample; the probe must not be used on food to be eaten by the patient.

Boiling: Food should be put into rapidly boiling water and bought back to boiling point as soon as possible.

Pressure cooking and steaming: Either a domestic-sized pressure cooker or large-scale catering steamer may be used.

1.3.3. Special Food Service Needs and Food Preparation

Traditional hospital food service with set meal-times, limited food choices, and advance menu selection may fail to meet the dietary needs of the majority of HSCT patients. Key points include sufficient trained stuff to help meal selection, a satellite kitchen on the HSCT or oncology unit, availability of foods and beverages typically requested and a way of accurately assessing daily oral intake.

For patients in hospital, food preparation and service should be carried out in a kitchen within the unit where patients are treated. This has several advantages:

- Food preparation is more easily controlled and there is less risk of food contamination.
- Food can be provided as needed rather than at fixed meal times, thus encouraging more frequent consumption of foods and liquids and hence better nutrient intake.
- Food intake is more easily monitored.

In the hospital setting, cutlery and plates should be preferably disposable. Reusable plastic cutlery and crockery should be kept in Milton solution and designated for the sole use of a particular patient Table 4 shows the food safety guidelines for immunosuppressed patients.

Following discharge from hospital, patients will need to observe “clean” food measures for 3-6 months, or until the white cell count is at a level which provides sufficient immunocompetence. When “clean” food measures are no longer necessary, it is usually advisable for patients to avoid high-risk foods such as unpasteurized milk and milk products, soft cheeses, live yoghurts, shellfish for a further month after discontinuing the diet. Opportunistic infections, including food-borne illnesses, may occur during periods of immunosuppression. Food-handling behaviors and practices to control food-borne illnesses were presented to focus groups and during interviews with cancer and transplant patients and health care providers.
Table 3. Diet for immunosuppressed patients

<table>
<thead>
<tr>
<th>Food groups</th>
<th>Allowed</th>
<th>Not allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dairy</strong></td>
<td>All pasteurized milk and milk products, and yoghurt, commercially packaged cheese and cheese products made with pasteurized milk, pasteurized ice cream, commercial nutritional supplements and baby formulas</td>
<td>Unpasteurized or raw milk, cheese and yoghurt and other milk products, soft cheeses, cheeses from delicatessens; cheeses containing chili peppers or other uncooked vegetables; cheeses with molds</td>
</tr>
<tr>
<td><strong>Meat and meat products</strong></td>
<td>All well-cooked or canned meats, well-cooked eggs (boiled for 10 minutes), (white cooked firm with thickened yolk is acceptable); pasteurized egg substitutes, commercially packaged salami, bologna, and other luncheon meats, shellfish</td>
<td>Raw or uncooked meat, tofu, precooked cold meats, hard cured salami in natural wrap, pickled fish, tempeh, products containing raw egg</td>
</tr>
<tr>
<td><strong>Bread and cereal products</strong></td>
<td>All wrapped breads, bagels, rolls, muffins, pancakes, sweet rolls, waffles, potato chips, corn chips, pretzels, popcorn, cooked pasta, rice, and other grains (all must either be used 24 hours, or frozen and used as required)</td>
<td>Raw grain products, unwrapped bread and rolls, cakes, pastries, cakes with cream, dried fruits, nuts or coconut</td>
</tr>
<tr>
<td><strong>Entrees, soups</strong></td>
<td>Freshly prepared all cooked entrees, soups</td>
<td>All miso products, reheated canned or home-made soup</td>
</tr>
<tr>
<td><strong>Fruits and nuts</strong></td>
<td>Canned and frozen fruit (except for berry fruits), fruit juices; well-washed and peeled fresh fruit*; canned or bottled roasted nuts, commercially packaged peanut butter</td>
<td>Unwashed and unpeeled raw fruits, damaged fruit, berry fruits (strawberries, raspberries, blackberries), grapes (unless peeled), unroasted raw nuts, roasted nuts in the shell, unpasteurized fruit juice dried fruits, roasted fruits, thicken by yolk is acceptable)</td>
</tr>
<tr>
<td><strong>Vegetables</strong></td>
<td>All cooked, frozen, canned, or fresh vegetables and potatoes, well washed raw vegetables*, dried herbs and spices (packaged) (if added before; not after cooking)</td>
<td>Unwashed raw vegetables or herbs, salad from delicatessens; commercial salsas stored in refrigerated case, dried pulses (e.g. beans, chick peas and lentils), herbs and spices should not be sprinkled on food after cooking</td>
</tr>
<tr>
<td><strong>Beverages</strong></td>
<td>Tap water, cooled boiled water, commercial bottled distilled, spring, and natural water; all canned, bottled, powdered beverages, instant and brewed coffee, tea; brewed herbal teas using commercially packaged</td>
<td>Well water (unless tested yearly and found safe), cold-brewed tea made with warm or cold water; unpasteurized fruit and vegetable juices,</td>
</tr>
<tr>
<td><strong>Desserts</strong></td>
<td>Refrigerated commercial and homemade cakes, pies, pastries, cookies, and pudding</td>
<td>Unrefrigerated, cream-filled pastry products (not shelf stable)</td>
</tr>
<tr>
<td><strong>Fats</strong></td>
<td>Oil, shortening; refrigerated lard, margarine, butter; commercial shelf-stable mayonnaise and salad dressings (including cheese based salad dressings; refrigerated after opening); cooked gavy and sauces</td>
<td>Unwrapped or communally used butter, margarine, spreads or ghee, fresh salad dressings containing aged cheese or raw eggs, stored in refrigerated case</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Salt (packaged), granulated sugar, brown sugar, jam, jelly, syrups (refrigerated after opening); pasteurized honey (commercially packaged), catsup, mustard, pickles, olives (refrigerated after opening), candy, gum (in the hospital setting, individual portions of sugar; jam, marmalade, or honey) (pepper: in the hospital setting this should be irradiated)</td>
<td>Raw or unpasteurized honey; herbal and nontraditional nutrient supplements, brewers’s yeast if eaten uncooked,</td>
</tr>
</tbody>
</table>

* If neutrophil count is <1500/mm³: consumption of raw vegetables is not allowed.

** Shelf-stable refers to unopened canned, bottled, or packaged food products that can be stored before opening at room temperature; container may require refrigeration after opening.
1.4. Enteral and Parenteral Nutrition

Patients typically have little or no oral intake during the first weeks postransplant; therefore alternate routes of nutrition support, including enteral or parenteral nutrition support, are usually considered and have become a standardized component of care.\textsuperscript{39,40} Artificial nutrition, total parenteral nutrition in particular, is provided to patients undergoing HSCT to help minimize nutritional consequences of both conditioning regimens (mucositis, malabsorption, etc.) as well as complications resulting from the procedure (graft versus host disease, venoocclusive disease of the liver).\textsuperscript{25,41} The use of nutrition support has become standard practice in blood and marrow transplantation, but what remains unclear is whether patients receive adequate nutrition supplementation during this time.\textsuperscript{42} Enteral nutrition has a trophic role in the intestinal mucosa and contributes to its integrity also stimulates gallbladder function, which can reduce cholestatic complications during HSCT. Clinicians have to determine when to intervene with nutrition support and with what strategies. Several reports have attempted to determine if safe enteral access could be established via endoscopically placed gastrostomy tubes several weeks prior to transplant or nasal jejuna (NJ) tubes placed immediately prior to high-dose conditioning therapy and the onset of mucositis.\textsuperscript{24} Roberts and Miller\textsuperscript{43} report the successful use of gastrostomy tubes for long-term nutritional support in marrow transplant patients. The risk of infection after a gastrostomy limits this approach to those patients with good neutrophil counts and for whom a potential delay in transplant would not be medically contraindicated, or in the case of an unrelated donor, logistically difficult.

Because the function of GI is compromised, TPN is often used as a standard nutritional therapy. The following indications for TPN are now generally accepted: severe malnutrition at admission (BMI<18.5) or weight loss>10% during treatment or impossibility of oral feeding or failing to meet 60-70% of the requirements over 3 days.\textsuperscript{44} Evidence suggests that among allogeneic patients implementation of TPN during cytoreduction improves long-term survival and reduces relapse rates. Similar results have not been demonstrated for autologous patients with hematologic malignancies. Generally, HSCT patients are not good candidates for complete enteral alimentation by feeding tube mainly because nausea, vomiting, and oro-esophageal mucositis prevent the insertion and subsequent tolerability of nasogastric tubes. Gastropareasis, a known complication of HSCT, was a major problem in achieving full nasogastric feedings. Moreover, all patients undergoing HSCT have a central venous catheter in situ through which TPN can be easily administered. Finally, parenteral nutrition probably allows better modulation of fluid, electrolytes, and nutrient administration which can be of critical importance when complications such as GVHD or veno-occlusive disease (VOD) arise. Experimental alterations in nutritional support formulation and adjunctive therapy may ultimately improve the ability to nourish HSCT patients safely and effectively. Specialized nutritional support may contain:

- Glutamine
- Immunomodulatory formulas
- Arginine
- n-3 polyunsaturated fatty acids
- Purine/pyrimidines (RNA).\textsuperscript{10}

1.5. Engraftment and Early Recovery

Delayed toxicities from cytoreduction present challenges for patients trying to resume adequate dietary intake. Xerostomia and blunted taste may be pronounced in the first few months after transplant. Abdominal pain and nausea on food consumption are common and may be associated with biliary stasis and gallbladder sludge. Some clinicians advocate lactose restriction for up to a year after transplant, but no data conclusively demonstrate lactose intolerance in these patients. In the absence of diarrhea, milk product can be attempted. TPN has been associated with delayed resumption of adequate oral energy intake after hospital discharge. Unless a clinical condition, such as malnutrition, malabsorption, or significant GI toxicity, warrants otherwise, TPN can be safely discontinued in patients whose oral intake is as little as 20% to 35% of total needs.\textsuperscript{5,10}
CONCLUSION

HSCT is an intense and often prolonged medical therapy that presents a wide range of nutritional challenges. One of the major adverse side effects during hematopoietic stem cell transplantation (HSCT) is malnutrition. Due to severe neutropenia, the recommended diet for HSCT patients should carry a low bacterial content to prevent the transmission of infectious agents. While TPN is often given to patients to maintain their nutritional status during the peritransplant period, there is conflicting evidence to support its routine use. TPN is a treatment potentially associated with significant limitations including a fluid overload state and hepatic dysfunction. It can increase the number of subclavian vein thromboses, delay platelet engraftment, increase catheter-related/associated infections, and suppress normal appetite. Where possible use of intravenous fluids and oral diet should be considered as a preference to parenteral nutrition. It is important that dietary guidance to minimize the risk of microbial exposure takes account of individual preferences in terms of palatability, food texture and food choice in order to optimize nutrient and energy intake.

REFERENCES


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<table>
<thead>
<tr>
<th>Table 4. Food safety guidelines for immunosuppressed patients</th>
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<tbody>
<tr>
<td><strong>Buying Food:</strong> Always check “use by” dates. Avoid buying food near its “use by” date and never consume it after this date. Do not buy foods in damaged packaging, e.g. dented cans or torn/crushed packets</td>
</tr>
<tr>
<td><strong>Storing Food:</strong> Store raw and cooked food separately. Keep raw meat, fish and eggs in containers at the bottom of the fridge. Check fridge and freezer are at the correct temperature. The fridge should be below 5oC, the freezer below 18oC.</td>
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<td><strong>Preparing and Cooking Food:</strong> Wash hands thoroughly in hot, soapy water before and after handling food. It is also important to wash hands between handling raw food and cooked food. Keep kitchen surfaces and equipment scrupulously clean. Make sure that any item which comes into contact with food (knives, spoons, chopping boards, etc.) is as clean as possible and free from cracks or food encrustation. Metal spoons and ceramic chopping boards are preferable to wooden ones. Ensure that canned food is clean. Wash cans before opening and also wash the can opener in hot, soapy water before use. Ring-pull cans are suitable but do not use cans which have to be opened with a key. Do not use a microwave oven for cooking food. It can be used for heating food or defrosting frozen food. Keep cold foods cold and hot foods hot. Cold foods should be kept in a fridge until needed. Hot foods should be served as soon as they are cooked. Never reheat food which has already been heated. Never refreeze thawed frozen food. Avoid using food used communally, e.g. tubs of butter or spread, large cartons of ice-cram, or jams of jam or marmalade. Keep small supplies separately for your own use.</td>
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<td><strong>Eating Out:</strong> It is safer to avoid eating and drinking outside the home while on a “clean” food diet, as there is always a risk that strict food hygiene measures may not have been observed. If eating out is unavoidable ensure that you: never eat foods listed as unsuitable, e.g. salads, shellfish. Note that some types of fast foods, e.g. burger buns with seeds, are not suitable. Only consume foods from reputable restaurants or outlets, not street traders. Never eat barbecued food.</td>
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