Gastro-Intestinal Graft-Versus-Host Disease: A Guide for Recent Dietary Therapy: Review

Gastro-İntestinal Graft-Versus-Host Hastalığı: Güncel Diyet Tedavisi İçin Rehber

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ABSTRACT Graft versus host disease (GVHD) is a common complication of allogeneic hematopoietic stem cell transplantation which has high morbidity and mortality ratios. Acute GVHD (aGVHD) which usually develops in the first three months after transplantation is a clinic-pathological syndrome mainly involving skin, liver, and gut. Immunosuppressive therapy is started before transplantation to prevent development of GVHD. A special stage and grading system developed for aGVHD is used to propose treatment. High dose corticosteroid is the first line treatment. Supportive therapy improves quality of life and may affect response to treatment positively. Chronic GVHD (cGVHD) usually appears after 3 months post-transplant. cGVHD which is the most important cause of mortality after stem cell transplantation (SCT) except late relapses, needs multidisciplinary approach for treatment. Infection is the most common cause of mortality in patients with cGVHD. Thus, antimicrobial drugs should be prescribed during immunosuppressive treatment. In recent years, different prevention and treatment methods had been developed in the light of new data on both acute and chronic GVHD pathogenesis. As survival rates have improved, there has been an increased focus on supportive care. Nutrition is a supportive-care modality that has been associated with improved tolerance to chemo/radio therapy, improved survival, increased quality of life, and decreased risk of infection in patients undergoing GVHD therapy. The gastrointestinal (GI) tract is one of the major organs affected by GVHD. The GI GVHD diet is a four-phase progressive diet, which aims to maximize oral intake and minimize stooling. An appropriate diet level for the GVHD patient is determined by his/her gut function.

Key Words: Graft vs host disease; hematopoietic stem cell transplantation; diet therapy

ÖZET Graft-versus-host hastalığı (GVHD), allojenik hematopoetik kök hücre transplantasyonlarından sonra gelişen morbidite ve mortalitesi yüksek, yaygın bir komplikasyon tablosudur. Nakil sonrası ilk üç ay içinde ortaya çıkabilen akut GVHD esas olarak deri, karaciğer ve bağırsakları tutar. Oluşumunu önlemek amacıyla hastalara nakilden önce immünsüpresif tedavi başlanır. Tedavinin planlanmasında akut GVHD (aGVHD) için geliştirilmiş evre ve derecelendirme sistemi kullanılır. Yüksek doz kortikosteroid aGVHD tedavisinde ilk basamaktır. Destekleyici tedavi hastaların yaşam kalitesini iyileştirir ve tedaviye cevabı olumlu yönde etkileyebilir. Kronik GVHD genel olarak nakil sonrası 3. aydan sonra görülmeye başlanır. Allojenik kök hücre naklini takiben geç dönem relaps haricinde mortalitenin en önemli nedeni olan kronik GVHD, multidisipliner bir tedavi yaklaşımı gerektirir. Enfeksiyon, kronik GVHD'li hastaların en sık ölüm nedenidir. Bu nedenle; bu hastalara immünsüpresif tedavi sırasında profilaktik antimikrobiyal ilaçlar verilmesi gereklidir. Son yıllarda hem akut hem de kronik GVHD'nin patogenezinde ortaya çıkarılan bulgular doğrultusunda farklı koruyucu ve tedavi edici yöntemler geliştirilmiştir. Sağkalım oranlarının artması, destekleyici bakım hizmetlerine olan ilgiyi artırmıştır. GVHD tedavisi gören hastalarda, destekleyici bir bakım yöntemi olan beslenme, artan kemo/radyoterapi toleransı, yaşam kalitesi, sağkalım süresi ile enfeksiyon riskinin azalması ile ilişkilidir. Gastro intestinal system (Gİ) GVHD'den etkilenen en önemli organlardan biridir. Gİ GVHD diyeti, oral alımın artması ve dışkılamayı en az indirgemek üzere planlanmış dört aşamalı ilerleyen bir diyettir. GVHD hastası için en uygun diyet şekli, hastanın bağırsak fonksiyonlarına göre belirlenmektedir.

Anahtar Kelimeler: Graft vs host hastalığı; hematopoetik kök hücre transplantasyonu; diyet tedavisi

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Hematopoietic stem cell transplantation (HSCT), which is being used widely day by day; is a treatment method for management of mainly lympho-hematopoietic diseases and also immunological and metabolic disorders. Graft-versus-host disease (GVHD) is a complicated clinical syndrome involving a severe immune reaction mediated by immunologically competent cells, mainly T lymphocytes resulting in organ dysfunction. It is accepted as the most important cause of mortality and morbidity after stem-cell transplantation (SCT). Although improvements have been made in the prevention of GVHD, which is usually classified as acute and chronic according to time of appearance, these advances have not resulted in a concomitant improvement in the treatment of this condition.[1,2]

Acute GVHD (aGVHD) which usually develops in the first three months after transplantation is a clinicopathological syndrome mainly involving skin, liver, and gut. Immunosuppressive therapy is initiated before transplantation to prevent development of GVHD. Acute GVHD damages the skin, gut, and liver. Nausea, vomiting, abdominal pain, diarrhea, bloody stool, and jaundice may occur.[1]

Chronic GVHD (cGVHD) which is the most important cause of mortality after SCT except late relapses, needs multidisciplinary approach for treatment Progress in the field of cGVHD has been slow and based primarily on advances in aGVHD. Recently, paradigms have shifted and the International Transplant Community has focused more on cGVHD. Steroid and cyclosporine are the gold standards of treatment.[3,4]

GVHD and its treatment with corticosteroids cause profound immunodeficiency, predisposing the patient to fatal infection. Most survivors of transplantation are active and healthy, but some delayed complications, particularly cGVHD, can be serious. The risk increases with recipient and donor age and is increased for peripheral-blood grafts or grafts from unrelated donors. Chronic GVHD occurs 100 days or more after the transplant procedure and may take the form of various oral manifestations.[5,6]

In this review, the new approaches in the dietary treatment of gastrointestinal (GI) GVHD will be summarized.

DIETARY MANAGEMENT OF GASTROINTESTINAL GVHD (GI GVHD)

Gut involvement due to GVHD particularly impairs the host nutritional status and quality of life (QOL) due to long-lasting diarrhea and anorexia.[7] Hence, effective supportive care of patients suffering from GVHD should include attention to intense nutritional support and bone mineral retention, since many receive steroid therapy.[8,9] With the development of gut GVHD, patients are often recommended to withhold oral intake (NPO, ''bowel rest'') to avoid further damage to the GI mucosa. However, this raises a serious concern since NPO care can induce atrophic deficit of the GI mucosa and resultant dysfunction of the GI system. Moreover, it has recently been reported that enteral nutrition (EN) was more effective than parenteral nutrition (PN) for the nutritional support of patients with an injured intestine due to trauma or an invasive operation.[10] Taken together, these findings suggest that the current patient management procedure that includes the interruption of oral feeding to enforce ''bowel rest'' in SCT patients suffering from GVHD should be critically reevaluated. Furthermore, EN, if tolerable, may be a preferred route for maintaining digestive and absorptive function as intact as possible. In those suffering from GI involvement of GVHD, such evaluation becomes more complex since diarrhea is very often multifactorial and includes secretory dysfunction, osmotic factors, and rapid passage. Hence, the establishment of a standard care procedure remains very difficult.[11]

DIARRHEA IN GVHD

Generally in cancer patients, the most common cause of diarrhea is the cancer treatment itself (chemotherapy, radiotherapy, bone marrow transplantation, and/or surgery). In patients undergoing bone marrow or SCT, diarrhea may be secondary to the conditioning regimen or GVHD due to infections related to immunosuppressive therapy.[12]

In general, diarrhea related to the conditioning regimens resolves by the third week after treatment.[13] Mucosal injury results in net fluid secretion by the intestine, i.e., secretory diarrhea, and resolves with mucosal restitution. After 20 days, aGVHD is the most common cause of diarrhea in these patients. Therefore, persistent diarrhea should raise the suspicion of aGVHD and/or infectious etiologies, although the latter occur less frequently in this population. In patients with persistent diarrhea, colorectal mucosal biopsy can be performed to assess for mucosal regeneration and to evaluate for GVHD.[14,15]

Treatment of Diarrhea

Diarrhea is treated by identifying and treating the problems causing diarrhea. For example, diarrhea may be caused by stool impaction and medications to prevent constipation. Dietary manipulation that may help to decrease diarrhea include eating small frequent meals and avoiding some of the following foods:

- Milk and dairy products
- Spicy foods
- Alcohol
- Caffeinated foods and drinks
- Some fruit juices
- Gas-forming foods and drinks
- High- fiber foods
- High-fat foods

For mild diarrhea, a diet of bananas, rice, apples, and toast (the BRAT diet) may decrease the frequency of stools. Patients should be encouraged to drink up to 3 quarts of clear fluids per day including water, sports drinks, weak decaffeinated tea, caffeine-free soft drinks, clear juices, and gelatin. For severe diarrhea, the patient may need intravenous fluids or other forms of total PN (TPN).

CORTICOSTEROID THERAPY IN GVHD

Corticosteroid therapy is used commonly for prophylaxis and treatment of GVHD.[16] Table 1 lists nutritional implications of steroid therapy and suggested interventions.

MUCOSITIS IN GVHD

Mucositis is a frequent complication of high-dose chemo-radiotherapy regimens commonly used as conditioning therapy before allogeneic HSCT. Oral mucositis occurs as a result of chemotherapy- and radiotherapy-induced mucosal epithelial injury, submucosal endothelial injury, and connective tissue injury in an immunocompromised host.[17,18] Severe oral mucositis occurs in up to 75% of myeloablative allogeneic HSCT recipients, often occurs within the first week after conditioning therapy, and usually resolves only when normal hematopoiesis resumes.[19]

Oral mucositis is a significant problem for most HSCT recipients and has been reported to be the most debilitating side effect of transplantation.[20] Mucositis has immediate detrimental effects

TABLE 1: Nutritional implications of steroid therapy.

Nutrition Implication	Suggested Intervention
Sodium and fluid retention	Restrict sodium intake to 2-4 g/day.
Hyperphagia and weight gain	Educate patient on healthy and energy-reduced food choices. Encourage intake of fruits and vegeta bles, high-fiber foods, and whole grains. Monitor portion sizes.
Gastric irritation	Avoid acidic foods, caffeine, pepper, and other gastric irritants.
Decreased insulin sensitivity and hyperglycemia or steroid-induced	Institute a no-concentrated-carbohydrates diet
Skeletal muscle catabolism and	Include a protein-rich food at each meal and snack (e.g., lean diabetes meats, dairy products, peanut butter, nuts, soy).
Osteoporosis (with long-term,> 3 months, steroid use)	Increase intake muscle atrophy of foods containing calcium and vitamin D and/or supplements. Perform weight-bearing exercise as tolerated.

on patient quality of life by causing oral and oropharyngeal pain and by impairing communication and swallowing. As a result of pain related to mucositis, narcotic analgesia and PN are commonly required in the recovery period after HSCT.[21] In addition, oral mucositis is associated with adverse economic and clinical outcomes after HSCT, including an increased length of hospital stay and decreased survival at 100 days.[22] Although several attempts to prevent, minimize, and treat mucositis after allogeneic stem cell transplantation have been made, no single therapy has been shown to be effective in randomized clinical trials, and the current standard therapy for mucositis is supportive care alone.[23]

Esophageal involvement by GVHD is uncommon in patients with cGVHD.[24,25] Affected patients have desquamation of the esophageal mucosa and may also develop submucosal fibrosis and structure formation. Patients usually complain of dysphagia but may also have retrosternal discomfort and reflux-related symptoms due to reduced esophageal peristalsis. Salivary gland destruction secondary to GVHD also impairs swallowing and reduces acid neutralization and clearance. Treatment of cGVHD at its early stages may prevent esophageal involvement.[26,27]

GASTROINTESTINAL GRAFT-VERSUS HOST DISEASE (GI GVDH)

The gastrointestinal (GI) tract is one of the major organs affected by GVHD. Symptoms of GI GVHD include nausea, vomiting, abdominal cramping, and diarrhea. In severe disease, high-volume diarrhea (more than 2 L/day) and intestinal bleeding may occur. Alterations in oral diet can have a direct effect on stooling volume in GI GVHD and other conditions characterized by high-volume stooling.[28]

OBJECTIVES OF DIET MANAGEMENT IN GI GVHD

- Provide adequate nutritional support.
- Minimize diarrhea and abdominal cramping.
- Heal intestinal lumen with necessary nutrients.
- Satisfy patient preferences, when possible.

TABLE 2: Gastrointestinal Graft-Versus-Host Disease Diet.

Phase	Type of the diet
Phase 0	Bowel rest: No oral diet
Phase 1	Liquids
Phase 2	Introduction of solids
Phase 3	Diet expansion
Phase 4	Continued diet expansion

*Each diet phase includes all foods from earlier phases plus additional foods as listed.

The GI GVHD diet is a "four-phase progressive diet", which aims to maximize oral intake and minimize stooling. An appropriate diet level is determined by gut function. Phases 0 through II-I of this diet are not nutritionally adequate unless TPN is provided. Phases IV and V can be nutritionally adequate, but the patient may still require TPN because of continued lack of appetite and lingering GI side effects. Table 2 presents a summary of the GI GVHD diet used at MD Anderson Cancer Center.[29]

PRINCIPLES OF GI GVHD DIETS

At the MD Anderson Cancer Institute, The GVHD diet is used to be indicated for patients having moderate to severe diarrhea.[29] It is particularly geared towards patients undergone HSCT. The GVHD diet can be classified in four steps as "GVHD-I", "GVHD-II", "GVHD-III", and "GVHD-IV".[28] The beginning stages of the diet are inadequate in many nutrients. Therefore, the first two stages are intended only brief periods depending on patient tolerance. It may be necessary to supplement with clear liquid or elemental nutritional supplements, or in some cases, TPN may be required until tolerance to adequate EN is achieved.[30]

GVHD-Step I Diet

The first stage of the GVHD Diet is similar to a "clear liquid" diet. All foods are liquid at room temperature and absorbed with minimum digestive activity. Milk with milk derivatives and caffeine should be avoided. The GVHD-I diet is used to provide fluids and nutrients while minimizing the

TABLE 3: The GVHD-step I diet.

Food groups	Foods
Soups	Fat-free clear broth, consommé, bouillon
Fruits	All strained fruit juices especially apple juice (except prune and orange juice, and pear nectar)
Vegetables	None
Desserts	Gelatine (without milk or fruit), popsicle
Beverages	Decaffeinated coffee or tea (without milk), decaf feinated beverages, clear fruit flavored beverages
Supplements	Elemental or clear liquid oral supplements

amount of fecal material in the colon. It is used as the initial feeding after episodes of, or in the presence of severe diarrhea caused by gastrointestinal GVHD. The diet is inadequate in all nutrients. It is composed mainly of water and carbohydrate and should be used for only a brief period of time. If it is used for such an extended period, an elemental formula and/or clear liquid oral supplement is recommended (Table 3).

GVHD-Step II Diet

In the second stage of the diet, a few solid foods are added slowly, starting with complex carbohydrates. The diet allows all foods from GVHD-I and aims to provide foods that are low in fat, fiber and lactose. The GVHD-II diet is indicated to test patients' tolerance to solid foods in the presence of disturbances of fat digestion and absorption, or diarrhea from gastrointestinal GVHD.

The diet is inadequate in most of the nutrients; including protein, fat-soluble and other vitamins. The GVHD-II diet is intended for a brief step towards a more nutritionally adequate diet. If it is used for such an extended period, an elemental formula and/or clear liquid oral supplement is recommended (Table 4).

GVHD-Step III Diet

In the third stage of the GVHD diet, fat and fiber are permitted in little amounts. Servings from food groups that are main sources of fat or fiber in the diet are controlled. This diet is also low in lactose. Highly seasoned foods that can cause irritation of the gastro-intestinal mucosa are omitted. The GVHD-III diet is indicated to help control diarrhea, disturbances of fat absorption and digestion, and to prevent malabsorption of fat-soluble vitamins and certain vitamins, such as calcium and magnesium. The GVHD-III diet, if carefully planned, decreases fat, fiber and lactose intake while providing adequate intake of most nutrients (Table 5).

GVHD-Step IV Diet

The fourth stage of the GVHD diet aims to offer a fairly wide variety of foods while limiting the number of servings allowed from different food groups which supply fat and fiber to the diet. Moderate amounts of lactose are allowed. As some people may have difficulty digesting lactose in milk products, it may be necessary to have low-lactose milk or take lactase pills before consuming lactose-containing

TABLE 4: The GVHD-step II diet.

Food groups	Foods
Cereals	White bread, plain white bagel, English muffin, steamed white rice, melba toast, breakfast cereals (rice crispies, corn flakes, froot loops, honeycombs, frosted flakes) (with low lactose-skim milk)
Fruits	All strained fruit juices (except prune and orange juice, and pear nectar), canned peaches in light syrup (limit 2 halves/day), starined "baby-food" fruits
Vegetables	None
Desserts	Gelatine, popsicle, pretzels, crackers, hard candy (no peppermint)
Beverages	Coffee or tea, low-lactose skim milk, carbonated beverages, clear fruit flavored beverages
Supplements	Elemental or clear liquid oral supplements
Miscellaneous	Clear broth, consommé, bouillon, sugar, salt, honey, jelly, maple syrup

TABLE 5: The GVHD- step III diet.

Food groups	Foods
Milk and milk products	Low-fat, low-lactose skim milk (i.e. lactaid milk), non-fat plain or fruit flavored yoghurt
Meat and protein (limit 3 servings/day)	Chicken or turkey breast (without the skin), fish (packed in water if canned), egg (1 yolk per day), lean ham
Cereals	White bread, plain white bagel, English muffin, white rice, oatmeal, cream of wheat, grits, cream of rice, melba toast, breakfast cereals (rice crispies, corn flakes, froot loops, honeycombs, frosted flakes) (with low lactose-skim milk)
Fruits	All fruit juices (except prune), canned peaches, apricots, fruit cocktail
Vegetables (limit 2 ½ servings/day)	Asparagus tips, carrots, green pepper, mushrooms, potato (bakes, boiled or mashed), tomatoes (canned or sauce), summer squash, yams
Desserts	Gelatine, popsicle, cakes, pretzels, crackers, hard candy (no peppermint)
Beverages	Coffee or tea, low-lactose skim milk, carbonated beverages, clear fruit flavored beverages
Fats (limit to 2 servings/day)	1 teasponn (tsp)/serving: butter or margarine, mayonnaise, low fat/fat free margarine 1 tablespoon (tbsp)/servings: low fat/fat free mayonnaise, fat free cream cheese
Supplements	Boost, elemental or clear liquid oral supplements
Miscellaneous	Marshmallows, mustard, ketchup, sugar, salt, honey, jelly, syrup,

foods. The GVHD-IV diet is indicated to help control diarrhea, disturbances of fat absorption and digestion, and to prevent malabsorption of fat-soluble vitamins and certain minerals, such as calcium and magnesium. The GVHD-IV diet, if carefully planned, decreased fat and fiber intake while providing adequate intake of most nutrients (Table 6).

NUTRITIONAL SUPPORT THERAPY (NTS) IN GVHD

Specialized nutrition support (enteral or parenteral nutrition) is intended to nutritionally support SCT recipient through periods of inadequate oral intake. The use of EN should be ruled out before PN is initiated. The patient should be evaluated by the dietitian in consultation with the medical team for appropriateness of route of nutrition support as well as adequacy of nutrients provided.[31]

Nutrition support therapy (NST) is appropriate in malnourished patients undergoing hematopoietic cell transplantation (HCT) who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time. The American Society for Parenteral and Enteral Nutrition recommends the following in regard to nutrition support in the SCT and/or oncology population:[32]

NUTRITIONAL SUPPORT THERAPY (NST) IN HEMATOPOETC CELL TRANSPLANTATION (HCT)

1. All patients undergoing HCT with myeloablative conditioning regimens are at nutritional risk and should undergo nutritional screening to identify those who require formal nutrition assessment with development of a nutritional care plan.

2. NST is appropriate in malnourished patients undergoing hematopoietic cell transplantation who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time. When PN is used, it should be discontinued as soon as toxicities have resolved after stem cell engraftment.

3. Enteral nutrition should be used in patients with a functioning gastrointestinal tract in whom oral intake is inadequate to meet nutritional requirements.

4. Pharmacological doses of parenteral glutamine may benefit patients undergoing hematopoietic cell transplantation.

5. Patients should receive dietary counseling regarding foods which may pose infectious risks and safe food handling during the period of neutropenia.

TABLE 6: The GVHD-step IV diet.

Food groups	Foods
Milk and milk products	Milk containing 2% fat or less (low lactose may be indicated), yoghurt (low-fat), ice milk, and frozen yoghurt
Cheese (limit 2 servings/day)	Reduced-fat cheese or cheddar, mozzarella (part skim), Provolone, Swiss
Meat and protein (limit 3 servings/day)	Beef (lean cuts only), Chicken or turkey breast (without the skin), fish(packed in water if canned), egg whites, whole egg (limit 1 per day), ham (93-97% fat-free), luncheon meats: turkey breast, turkey pastrami, turkey ham, reduced fat roast beef, chicken breast, reduced fat ham, turkey sausage
Cereals	White bread, plain white bagel, English muffin, white rice, oatmeal, cream of wheat, grits, cream of rice, melba toast, breakfast cereals (rice crispies, corn flakes, froot loops, honeycombs, frosted flakes) (with low lactose-skim milk)
Fruits	Apricots (canned), cherries, grapefruit (without membranes), juices (all except prune), mango, orange, mandarin, peach, pear (canned only), pineapple
Vegetables	Asparagus tips, celery, green pepper, mushroom, onions, pickles, potato (bakes, boiled or mashed without skin), pumpkin, tomatoes (canned or whole), summer squash, zucchini, carrots, green beans, spinach, peas
Desserts	Gelatine, gingersnaps, food cake, crackers, popsicle, red licorice, hard candy (no peppermint)
Beverages	Coffee or tea, carbonated beverages, clear fruit flavored beverages
Fats (limit to 2 servings/day)	1 tsp/serving: butter or margarine, mayonnaise, vegetable oils tbsp/servings: cream cheese, gravy, low fat salad dressing, non-dairy creamer, non-dairy whipped topping, sour cream, peanut butter, low fat margarine
Supplements	Boost, Enlive (use as tolerated)
Miscellaneous	Bouillon (fat-free broth), marshmallows, mustard, ketchup, sugar, salt, honey, jelly, syrup

6. NST is appropriate for patients undergoing hematopoietic cell transplantation who develop moderate to severe graft-vs-host disease accompanied by poor oral intake and/or significant malabsorption.[32,33]

Traditionally, PN has been given as the first option of nutrition support to bone marrow transplantation (BMT) patients. This is in preference to EN which is the delivery of oral or tube feeding via any route connected to the gastrointestinal tract. The advantages of either of these types of nutritional support in BMT patients are not clear but PN is associated with more complications e.g. increased line infections and reduction in gut mucosal integrity which may lead to longer hospitalization. In the event that patients nutritional intake is inadequate because of an inadequate oral intake, oral mucositis or because they are unable to tolerate tube feeding and are given PN with added glutamine they are likely to have less infections but may not necessarily discharge from hospital earlier.[34,35]

PARENTERAL NUTRITION

PN allows the practitioner to deliver adequate energy and protein to a patient who is otherwise unable to consume an adequate oral diet. PN should be reserved for patients who have failed EN trials because of a nonfunctioning GI tract or severe GI side effects that cannot be controlled through nutritional or pharmacological interventions and that deteriorate with enteral feeding.[36,37]

ENTERAL NUTRITION

EN can be a challenging therapy in SCT recipients because of the high incidence of GI complications. Also, pancytopenia can make placement of feeding tubes difficult. Therefore, EN may be better utilized in patients experiencing continued weight loss and poor oral intake after engraftment and recovery from some of the acute side effects of SCT. However, an attempt should be made to provide enteral nutrition before initiating PN unless an obvious contraindication to enteral nutrition exists.[36]

Parenteral nutrition does not seem to decrease the incidence of GVHD in individuals undergoing HCT. In fact, high dextrose (100% nonprotein energy) PN has been associated with an increased incidence of GVHD. Incidence of GVHD appears to decrease with increased protein intake in patients consuming standart oral diet or EN. Once GVHD occurs, oral nutrition can become increasingly challenging. Although there are no data on the impact of NST on the resolution of GVHD, it seems logical that NST should be used to maintain/improve nutritional status during prolonged nutrition compromise resulting from GVHD.[37-40]

CONCLUSION

Nutritional status has an important effect on quality of life and sense of well-being in GVHD patients. Nutritional support therapy is appropriate in malnourished patients receiving active anticancer treatment who are malnourished and who are anticipated to be unable to ingest and/or absorb adequate nutrients for a prolonged period of time.

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