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ORIGINAL ARTICLE

Impact of clinical pharmacist-based parenteral nutrition service for bone marrow transplantation patients: a randomized clinical trial

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Abstract
Purpose Parenteral nutrition (PN) is a well-documented supportive care which maintains the nutritional status of patients. Clinical pharmacists are often involved in providing PN services; however, few studies have investigated the effect of a clinical pharmacy-based PN service in resource-limited settings.
Methods We designed a randomized clinical trial to compare the clinical pharmacist-based PN service (intervention group) with the conventional method (control group) for adult patients undergoing hematopoietic stem cell transplantation in Shariati Hospital, Tehran, Iran (2011–2012). In the intervention group, the clinical pharmacists implemented standard guidelines of nutrition support. The conventional method was a routine nutrition support protocol which was pursued for all patients in the bone marrow transplantation wards. Main study outcomes included nutritional status (weight, albumin, total protein, prealbumin, and nitrogen balance), length of hospital stay, time to engraftment, rate of graft versus host disease, and mortality rate. Patients were followed for 3 months.
Results Fifty-nine patients were randomly allocated to a study group. The overall intake (oral and parenteral) in the control group was significantly lower than standard daily needed calories ($P<0.01$). Patients in the intervention group received fewer days of PN (10.7±4.2 vs. 18.4±5.5 days, $P<0.01$). All nutritional outcomes were either preserved or improved in the intervention group while the nutritional status in the control group was deteriorated (P values<0.01). Length of hospital stay was significantly shorter in the intervention group ($P<0.01$). Regarding PN complications, hyperglycemia was observed more frequently in the intervention group (34.5 %, $P=0.01$). Two patients in the control group expired due to graft versus host disease at the 3-month follow-up.
Conclusion A clinical pharmacist-based nutrition support service significantly improved nutritional status and clinical

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outcomes in comparison with the suboptimal conventional method. Future studies should assess the cost effectiveness of clinical pharmacists' PN services.

Keywords Parenteral nutrition · Clinical pharmacist · Bone marrow transplantation · Nutrition status · Clinical outcome · Randomized clinical trial · Iran

Introduction

Malnutrition has been identified as a major challenge in hematopoietic stem cell transplantation (HSCT) patients [1]. Different etiologic factors including adverse effects of high-dose chemotherapy (conditioning regimen), comorbidities, and HSCT complications can increase the rate of malnutrition during patients' hospital stay [2]. In HSCT patients, nutritional inadequacy usually occurs as a consequence of gastrointestinal dysfunctions including mucositis, vomiting, anorexia, and diarrhea [3, 4].

Malnutrition can cause considerable adverse effects on the body composition, functional or clinical outcomes, and the impairment of immune system functions [5–7]. Studies have shown that altered nutritional status might lead to higher rates of complications including infections and graft versus host disease (GVHD), longer hospitalizations, and increased healthcare costs [8–10]. Impaired nutritional status and electrolytes imbalance have also been associated with delayed engraftment time [11, 12]. Therefore, proper nutrition support therapy has been suggested to improve treatment outcomes, patients' quality of life, and their sense of well-being [13, 14].

Parenteral nutrition (PN) is a well-documented supportive care which maintains the nutritional status of patients after HSCT especially in patients with GVHD and malnourishment [4, 15]. However, there is conflicting evidence to support the incorporation of PN into routine clinical practice [15, 16]. Clinicians often argue against employing PN therapy owing to its complications such as hyperglycemia, delayed platelet engraftment, catheter-related sepsis, hepatic dysfunction, and fluid overload [16–20]. Moreover, lack of PN therapy stewardship for implementing international PN guidelines [13, 21] is also an imperative barrier for providing standard care and managing complications in resource-limited clinical settings.

Several clinical pharmacy services have been developed and implemented in recent decades particularly in developed countries [22, 23]. Literature on clinical pharmacist interventions has revealed major improvement of patient outcomes and significant cost savings [24]. However, few studies have investigated the efficacy of a clinical pharmacy service for providing parenteral nutrition support [25, 26].

Therefore, we designed a randomized clinical trial to evaluate the effect of a clinical pharmacist-based PN service on nutritional status, clinical outcomes, and PN therapy complications after HSCT in adult patients.

Methods

Study design and clinical setting

This study was a single blind, randomized, controlled trial which was conducted at the Hematology-Oncology and Bone Marrow Transplantation Research Center, Shariati Hospital, Tehran, Iran (2011–2012). The study protocol was approved by the institutional ethics committee. Shariati Hospital is the first clinical center in Iran which has established a special facility, where PN solution is prepared based on patient's individual requirements by clinical pharmacists under a standard aseptic condition [27]. On the contrary, the conventional method of PN at the Bone Marrow Transplantation wards of the hospital consisted of a routine nutrition support protocol administered by the staff nurses.

Patients

Patients who were over 18 years old and were admitted to one of the three participating BMT wards for an initial autologous or allogeneic HSCT were included in the study (May 2011–April 2012). Individuals who had a history of respiratory, hepatic, renal, or cardiac dysfunction were excluded. A total sample size of 60 patients was calculated based on similar studies comparing nutritional supportive services [20, 28]. The patients were assigned in a 1:1 ratio to clinical pharmacist-based PN service (intervention group) or conventional PN service (control group) using block randomization technique. Patients' diagnostic categories and conditioning regimens are summarized in Table 1.

Study procedures

All patients received conditioning regimens prior to transplantation (Table 1). In addition, prophylaxis against GVHD was given to allogeneic patients (cyclosporine and low-dose methotrexate). Fever and neutropenia were managed based on the guideline of the Infectious Diseases Society of America [29]. Patients were classified as either well nourished (level A), moderately malnourished (level B), or severely malnourished (level C) based on clinical history, physical examination, and Subjective Global Assessment (SGA) tool [30]. All patients were encouraged to maintain oral intake as far as possible to preserve gastrointestinal function. The amounts of patients' oral intake were calculated according to the food nutrition charts provided by the nutrition department of the hospital.

Table 1 Diagnostic categories and conditioning regimens

	Intervention group (n=29)	Control group (n=30)	P value
Diagnostic category [n (%)]			0.1
Acute myelogenous leukemia/acute lymphocytic leukemia	8 (27.5)	15 (50.0)	
Hodgkin's disease/Non-Hodgkin's disease	10 (34.5)	7 (23.4)	
Multiple myeloma	6 (20.7)	5 (16.7)	
Aplastic anemia	2 (6.9)	2 (6.6)	
Other malignancies	3 (10.2)	1 (3.3)	
Conditioning regimen [n (%)]			0.56
Busulphan/cyclophosphamide	10 (34.5)	15 (50.0)	
Melphalan/fludarabine	6 (20.7)	5 (16.7)	
Lomustine/etoposide/melphalan	10 (34.5)	7 (23.4)	
Etoposide/cyclophosphamide/carboplatin	1 (3.4)	1 (3.3)	
Cyclophosphamide/anti-thymocyte globulin	2 (6.9)	2 (6.6)	

In the control group, patients received intravenous 5 % glucose solution (2,000 mL) and 10 % amino acid (Aminoven®, Fresenius Kabi; 500 mL) daily, and 10 % fat emulsion (Intralipid®, Fresenius Kabi; 500 mL) twice a week. The patients received several vitamins via parenteral route daily (vitamin B_1 10 mg, vitamin B_2 4 mg, vitamin B_3 40 mg, vitamin B_5 6 mg, vitamin B_6 6 mg, vitamin B_9 2 mg, and vitamin C 500 mg). Vitamin B_{12} injection (1,000 mcg) was administered twice a week. They also received electrolytes (potassium, sodium, and magnesium) based on corresponding serum levels. The patients did not receive phosphate or any trace elements. The aforementioned nutrition support protocol was employed routinely for HSCT patients. PN was started on the first day after transplantation regardless of oral feeding and was maintained until the catheter was removed at discharge. The staff nurses, who were all trained for practice on HSCT wards, administered the PN in the control group.

In the intervention group, patients were considered for PN therapy if any of the following conditions were satisfied (1) oral intake <50 % due to nausea, vomiting, diarrhea, anorexia, severe mucositis, or GVHD which was maintained for 3–5 days in level C, 5–7 days in level B, and 7–10 days in level A; (2) inability to use enteral feeding based on the clinician judgment; (3) serum albumin level <3. Patients received 25 kcal/kg/day plus 1.4 g protein/kg/day [31]. Adjusted body weight was used for calculating nutrient needs of overweight and obese patients (body mass index (BMI)>27) [32]. The PN solution (2,500–3,500 mL) was prepared using 10 % glucose solution, 10 % amino acids (Aminoven®, Fresenius Kabi; 500 mL), 10 % fat emulsion (Intralipid®, Fresenius Kabi; 500 mL), electrolytes (Mg, Ca, P, Na, and K), vitamins (B and C), and trace minerals (Mn, Zn, Mo, I, Fe, Cu, and Cr). Vitamins and trace elements were added daily in their recommended amounts [33]. The electrolytes were adjusted daily based on serum chemistries [32]. Hyperglycemia associated with PN was managed based on the safe practice guideline [33]. The volume of PN was adjusted according to patients' oral intake to make up the deficit in nutritional requirements not met by oral intake. PN therapy in the intervention group was entirely carried out by the three pharmacists of the clinical pharmacy team who were trained for IV admixture and PN services. They carried out all the procedures of PN (order, preparation, monitoring, and discontinuation). The service was delivered on a daily basis. The staff nurses administered the PN solution under their supervision. The duration of PN in the intervention group depended on the recovery of gastrointestinal function and it was discontinued when patients were able to consume ≥50 % of their daily requirements orally.

PN therapy characteristics including PN initiation time, duration, and total daily calories intake (oral plus PN) were recorded. Discharge criteria for both groups included absolute neutrophil count (ANC)>=500, and being afebrile, off antibiotics, and able to tolerate>=50 % of nutrient needs via oral intake.

Study outcomes

Baseline demographic and clinical characteristics of the patients such as sex, age, type of HSCT (autologous or allogeneic), BMI, diagnostic category, and conditioning regimen were recorded. Three categories of outcomes were evaluated in the study of which nutritional status, length of hospital stay, and rate of GVHD were considered as the primary outcomes. The categories included:

1. Nutritional status: subjective global assessment level, anthropometric measurements, nitrogen balance, alteration in body weight, mid-arm muscle circumference, and laboratory data (albumin, pre-albumin, and total protein levels). Weight, albumin, and total protein data were collected on

the day +1 after HSCT and discharge day. Nitrogen balance and pre-albumin levels were measured on PN initiation and discontinuation days in each group.

2. Clinical outcomes: length of hospital stay, time to engraftment, days on antibiotics, fever duration, laboratory data (total bilirubin and liver function tests), and electrolyte disturbances.
3. Safety outcomes: complications such as hyperglycemia (mean fasting blood glucose level >150 mg/dL), hepatic dysfunction (alteration in ALT/AST), and rate of probable catheter infection (defined as redness and inflammation around catheter plus uncontrolled fever). Rates of readmission for any reason, acute GVHD, and mortality at 3-month follow-up were also recorded.

Statistical analysis

Means, medians, standard deviations, and ranges were used to examine and describe the distribution of data. Student *t* test, Mann–Whitney *U* test, and Pearson Chi-squared test were used to compare demographic characteristics or study outcomes between groups whenever each test was appropriate. Multivariate general linear model was employed to assess the effect of any confounding factors. For all tests, a two-sided *P* value of less than 0.05 was considered as the statistical significance threshold.

Results

Patients' characteristics

Fifty-nine patients who had the inclusion criteria were enrolled in the study (30 patients in the control group and 29 patients in the intervention group). Patients' characteristics did not differ significantly between the study groups except for gender (P=0.04). No patients had pre-existing diabetes mellitus. Patients' baseline characteristics are summarized in Table 2.

Parenteral nutrition therapy characteristics

The initiation day of PN therapy for the intervention group was significantly later in the post-transplant period (+4.03±2.5 versus +1.00±0.0 days, P<0.01). In addition, the duration of PN therapy in the intervention group was significantly shorter than the control group (10.6±4.2 versus 18.5±5.5 days, P<0.01). The overall nutrient intake (oral and parenteral) in the control group was significantly lower than standard daily needed calories (751.0±267 Kcal intake versus 1,764.0±333 Kcal needed, P<0.01). In contrast, the intervention group received a sufficient amount of calories per day (1,763.0±216 Kcal intake versus 1,662.0±263 Kcal needed, P=0.19).

Table 2 Patients' baseline characteristics

Characteristic	Intervention group (n=29)	Control group (n=30)	P value
Male [n (%)]	13 (44.8)	23 (74.2)	0.04
Age (year)	38.0±12.2[a]	35±11.24	0.70
Weight (kg)	67.0±10.7 [a]	74.5±20.7	0.08
BMI[b] [n (%)]			0.18
<18.5	0	2 (6.7)	
18.5–25	18 (62.1)	13 (3.3)	
≥25	11 (37.9)	15 (50.0)	
SGA[c] level [n (%)]			0.44
A	27 (93.1)	26 (86.7)	
B	2 (6.9)	4 (13.3)	
C	0	0	
Type of transplant [n (%)]			0.07
Allogeneic	15 (51.7)	22 (74.2)	
Autologous	14 (48.3)	8 (25.8)	

[a] Numbers are reported as mean ± SD

[b] Body mass index

[c] Subjective global assessment

Nutritional status

Most patients were well-nourished at admission. Overall, 43.3 % of transplant recipients were overweight and only two patients were classified as underweight according to the BMI classification of National Heart, Lung, and Blood Institute guideline [34]. There was a significant difference between groups regarding baseline weight (P=0.02); and the difference between baseline nitrogen balance levels was marginally significant (P=0.07). Thus, we calculated and analyzed the difference between pre/post values for each nutritional outcome (Table 3). All nutritional outcomes were either preserved or improved in the intervention group while the nutritional status in the control was deteriorated. Moreover, there was a significant reduction in mid-arm muscle circumference (−1.1 cm, P<0.01) in the control group.

Clinical outcomes

Length of hospital stay was significantly shorter in the intervention group (P<0.01). Days to engraftment did not differ significantly between study groups (P=0.78). More patients received antibiotics during hospitalization in the control (P=0.02). Febrile duration and antibiotic therapy duration were longer in the control group (P=0.01 and 0.03, respectively). Electrolyte disorders including alterations in serum levels of potassium, sodium, phosphorus, and magnesium were observed more frequently in the control group (P<0.01). The summary of clinical outcomes is presented in Table 4.

Table 3 Nutritional status

	Baseline levels[a]		Difference in groups[b]		
	Intervention group (n=29)	Control group (n=30)	Intervention group (n=29)	Control group (n=30)	P value[d] (t test)
Weight (kg)	65.57±10.44[c]	76.22±20.65	1.37±2.04	−4.03±2.50	<0.001
Body mass index (kg/m^2)	23.53±3.28	26.07±5.91	0.50±0.75	−1.36±0.86	<0.001
Albumin (mg/dl)	3.82±0.40	3.81±0.38	−0.24±0.46	−0.55±0.46	0.01
Total protein (mg/dl)	6.05±0.57	6.21±0.82	−0.40±0.68	−1.07±0.84	0.001
Pre-albumin (mg/dl)	20.02±7.02	22.71±7.21	3.77±8.76	−3.93±7.81	0.002
Nitrogen balance	3.20±4.36	5.30±4.25	4.98±5.28	−9.49±5.17	<0.001

[a] Baseline data were collected on day +1 for weight, albumin, and total proteins and on TPN initiation day for pre-albumin and nitrogen balance

[b] Discharge day value minus day +1 value for weight, albumin, and total protein and TPN discontinuation day value minus initiation day value for pre-albumin and nitrogen balance

[c] Numbers are reported as mean ± SD

[d] All corresponding p values in multivariate analysis were less than 0.01

Safety outcomes

Hyperglycemia was observed more frequently in the intervention group (P=0.01). Patients required a median of 51 IU of insulin per day to reach the target blood glucose level. A mean blood glucose level of 145±39 per deciliter was achieved. In the control group, a median of 9 IU of insulin per day was required to reach a mean blood glucose level of 118±25 mg per deciliter. Total bilirubin and liver function tests were evaluated at admission and biweekly. Both groups showed transient changes in total bilirubin and liver function tests (three times increase in ALT/AST baseline levels for less than 24 h) especially during the post-transplantation period (Table 5). None of the patients in the intervention group had probable catheter infection; but seven patients in the control group developed this complication (P=0.04). In the control group, severe GVHD was observed in six patients (27.3 % of at risk patients) and two of them died at 3-month follow-up. Only one patient in the intervention group had severe GVHD (6.6 % of at risk patients). Four patients in the intervention group and ten patients in the control group were readmitted during the follow-up period (4 vs. 27 readmissions, respectively; P=0.02).

Discussion

In the present study, a clinical pharmacist-based PN service brought substantial improvements in nutritional status and clinical outcomes for HSCT patients in comparison with the conventional PN method. One of the principal findings of the present study was that the conventional PN method did not provide optimal nutrition care for HSCT patients. This method was routinely employed in the bone marrow transplantation wards in our institution for years. Such a major flaw could be attributed to lack of stewardship for post-transplant nutrition support service and should be considered as a confounder in our study which overestimates the effect of clinical pharmacist-based PN service. Although evidence shows that utilizing a multidisciplinary team to provide PN services could be an effective approach [35], such a pragmatic trial reveals the real impact of designing and implementing clinical pharmacy services particularly in resource-limited clinical settings of developing countries.

The clinical pharmacist-based PN therapy was delivered later in the course of patients' hospital stay and was also continued

Table 4 Clinical outcomes

Outcome[a]	Intervention group (n=29)	Control group (n=30)	P value (t test)	P value (multivariate model)
Time to engraftment	13.06±4.9[c]	13.66±4.6	0.63	0.18
Antibiotics duration	11.3±5.7	14.66±5.7	0.03	0.02
Febrile duration	2.7±2.5	4.4±2.3	0.01	0.01
Electrolyte disorder[b]	2.7±2.09	6.9±4.06	0.01	<0.01
Number of antibiotics	2.5±1.2	3.2±1.3	0.02	0.05
Length of hospital stay (LOS)	24.7±6.2	29.5±8	0.01	0.04

[a] All outcomes except for the number of antibiotics and electrolyte disorder are measured as days

[b] Incidence rate of electrolyte disorders is reported

[c] Numbers are reported as mean ± SD

Table 5 Frequency of parenteral nutrition complications

Complication	Intervention group (n=29)	Control group (n=30)	P value
Hypertriglyceridemia[a]	3 (10.3 %)[b]	5 (16.6 %)	0.7
Hyperglycemia[c]	10 (34.5 %)	2 (6.0 %)	0.01
Increase in LFT[d]	3 (10.3 %)	5 (16.6 %)	0.7

[a] Serum triglyceride concentration of 400 to 500 mg/dL

[b] Numbers in parentheses are reported as percent

[c] Mean fasting blood glucose level >150 mg/dL

[d] A three times increase in ALT/AST baseline level (liver function test)

for a shorter period of time. Our findings also showed that patients in the intervention group, who were generally more dependent on oral intake in comparison with the control group, had a lower rate of GVHD. Mattson et al. reported that poor oral intake early after transplantation may be associated with higher rates of GVHD in HSCT patients [36]. Lower rate of GVHD in our study may be associated with higher dependence on oral intake; however, the issue of causality could not be assured. The lower rate of GVHD could also be attributed to the higher percentage of autologous HSCT patients in the intervention group versus the control group.

We evaluated patients' nutritional status using multiple indicators. However, BMI and pre-albumin have been identified as the most valuable and easily measureable indices for nutritional assessment in HSCT patients [37, 38]. In the intervention group, patients' BMI and pre-albumin level were maintained while patients' nutritional status in the control group significantly deteriorated during the post-transplant period. Such improvements in the nutritional status of patients might have led to superior clinical outcomes in our study.

We observed substantial improvements in the clinical outcomes of the intervention group. Length of hospital stay was significantly shorter in this group. Literature on HSCT has reported different lengths of hospital stay based on underlying diseases and types of transplant [15, 16]. It has also been suggested that PN therapy might be associated with longer hospitalization in HSCT patients [19]. Roberts et al. compared total PN with oral nutrition in HSCT patients [28]. They reported a mean of 25.4 days of hospitalization for the oral nutrition group versus 28.7 days for the total PN group. Our findings showed that the intervention group had 24.7 days of hospitalization while the corresponding figure in the control group was 29.5 days. Several factors may have contributed to shorter length of hospital stay in the intervention group. The patients in the intervention group endured a shorter period of fever and required fewer numbers of antibiotics. On the same line, the antimicrobial therapy period was significantly shorter than the control group (11.3 versus 14.6 days). Our findings were superior to Roberts et al. study who reported 20.8 days of antibiotic therapy in the total PN group while patients in their control group received antimicrobials for 17.7 days [28].

We also observed a significant reduction in the frequency of electrolyte disorders in the intervention group. Our previous study had revealed a negative correlation between serum electrolyte levels, particularly phosphate, and time to engraftment [11]. In the present study, patients in the intervention group had a lower rate of electrolyte disorders but their time to engraftment period was not shorter than the control group (13.06 and 13.66 days). This inconsistency may suggest a "safe range" of serum electrolyte levels for the engraftment process despite the fact that a significant decline in serum electrolyte levels takes place during the engraftment period. This hypothesis requires further investigation.

Parenteral nutrition complications have been a major concern for HSCT patients. Sheean et al. reported hyperglycemia as the main consequence of total PN exposure during HSCT [19, 39, 40]. They have also reported that total PN and hyperglycemia were associated with significant delay in engraftment time and higher rate of infections. Although the intervention group of our study experienced a higher incidence of hyperglycemia (34.5 %), the patients' engraftment time was not significantly different in comparison with the control group (6.0 % hyperglycemic patients). In addition, patients in the intervention group had fewer numbers of antibiotics plus shorter fever and antimicrobial therapy period. However, in our study, we pursued the suggestion of Sheean et al. to maintain the blood glucose level lower than 150 mg/dl in the intervention group [19].

Strengths and limitations

We used a single blind, randomized controlled trial design to evaluate the impact of a clinical pharmacist-based PN service. A block randomization method was employed to balance the number of patients between the study groups. However, an imbalance in type of HSCT method was observed between study groups (allogeneic transplant, 51.7 % in the intervention group and 74.2 % in the control group) which may have led to an overestimation of the observed effects in the intervention group. Hence, we performed a multivariate general linear model analysis to assess the effect of "type of transplant" and "gender" on nutritional status and clinical outcomes. The supplementary analysis did not alter any of the results for the aforementioned outcomes. Thus, it could be inferred that type of transplantation and gender have not been confounding factors in our study. Another limitation to our study could be the short-term follow-up (3 months). Few studies on PN for HSCT patients have assessed the patients' survival for periods longer than 6 months [41, 42]; nevertheless, future studies on clinical pharmacist-based PN service should address the long-term survival of HSCT patients.

Conclusion

Parenteral nutrition serves as an important means of supportive care for malnourished HSCT patients. A clinical pharmacist-based PN service assures careful initiation, monitoring, and discontinuation of PN in a resource-limited setting. This service provides significant improvements in nutritional status and clinical outcomes. Nevertheless, a multidisciplinary team approach may be required to maximize the impact of nutrition support service.

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Conflicts of interest We have no conflicts of interest to declare. The study was carried out as part of the doctoral thesis of the first author. We have full control of all primary data and we agree to allow the journal to review the data if requested.

References

1. Rzepecki P, Barzal J, Oborska S (2010) Blood and marrow transplantation and nutritional support. Support Care Cancer 18(2 Supplement):57–65. doi:10.1007/s00520-009-0730-3
2. Thompson JL, Duffy J (2008) Nutrition support challenges in hematopoietic stem cell transplant patients. Nutr Clin Pract 23(5):533–546. doi:10.1177/0884533608323423
3. Muscaritoli M, Grieco G, Capria S, Iori AP, Rossi Fanelli F (2002) Nutritional and metabolic support in patients undergoing bone marrow transplantation. Am J Clin Nutr 75(2):183–190
4. Lenssen P, Bruemmer B, Aker SN, McDonald GB (2001) Nutrient support in hematopoietic cell transplantation. JPEN J Parenter Enter Nutr 25(4):219–228
5. McDiarmid S (2002) Nutritional support of the patient receiving high-dose therapy with hematopoietic stem cell support. Can Oncol Nurs J 12(2):102–115
6. Schulte C, Reinhardt W, Beelen D, Mann K, Schaefer U (1998) Low T3-syndrome and nutritional status as prognostic factors in patients undergoing bone marrow transplantation. Bone Marrow Transplant 22(12):1171–1178. doi:10.1038/sj.bmt.1701502
7. McWhirter JP, Pennington CR (1994) Incidence and recognition of malnutrition in hospital. BMJ 308(6934):945–948
8. Correia MI, Waitzberg DL (2003) The impact of malnutrition on morbidity, mortality, length of hospital stay and costs evaluated through a multivariate model analysis. Clin Nutr 22(3):235–239
9. Horsley P, Bauer J, Gallagher B (2005) Poor nutritional status prior to peripheral blood stem cell transplantation is associated with increased length of hospital stay. Bone Marrow Transplant 35(11):1113–1116. doi:10.1038/sj.bmt.1704963
10. Pichard C, Kyle UG, Morabia A, Perrier A, Vermeulen B, Unger P (2004) Nutritional assessment: lean body mass depletion at hospital admission is associated with an increased length of stay. Am J Clin Nutr 79(4):613–618
11. Faghihi T, Iravani M, Shamshiri AR, Hadjibabaie M, Mousavi SA, Alimoghaddam K, Ghavamzadeh A (2009) Serum electrolyte changes at engraftment time in patients undergoing allogeneic hematopoietic stem cell transplantation. Ann Transplant 14(3):51–57
12. Hadjibabaie M, Tabeefar H, Alimoghaddam K, Iravani M, Eslami K, Honarmand H, Javadi MR, Khatami F, Ashouri A, Ghavamzadeh A (2012) The relationship between body mass index and outcomes in leukemic patients undergoing allogeneic hematopoietic stem cell transplantation. Clin Transplant 26(1):149–155. doi:10.1111/j.1399-0012.2011.01445.x
13. August DA, Huhmann MB (2009) A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. JPEN J Parenter Enter Nutr 33(5):472–500. doi:10.1177/0148607109341804
14. Marin Caro MM, Laviano A, Pichard C (2007) Impact of nutrition on quality of life during cancer. Curr Opin Clin Nutr Metab Care 10(4):480–487. doi:10.1097/MCO.0b013e3281e2c983
15. Murray SM, Pindoria S (2009) Nutrition support for bone marrow transplant patients. Cochrane Database Syst Rev (1):CD002920. doi:10.1002/14651858.CD002920.pub3
16. Arfons LM, Lazarus HM (2005) Total parenteral nutrition and hematopoietic stem cell transplantation: an expensive placebo? Bone Marrow Transplant 36(4):281–288. doi:10.1038/sj.bmt.1705039
17. Btaiche I, Khalidi N (2004) Metabolic complications of parenteral nutrition in adults, part 1. Am J Health Syst Pharm 61(18):1938–1949
18. Btaiche I, Khalidi N (2004) Metabolic complications of parenteral nutrition in adults, Part 2. Am J Health Syst Pharm 61(19):2050–2057
19. Sheean PM, Freels SA, Helton WS, Braunschweig CA (2006) Adverse clinical consequences of hyperglycemia from total parenteral nutrition exposure during hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 12(6):656–664. doi:10.1016/j.bbmt.2006.01.010
20. Cetin T, Arpaci F, Dere Y, Turan M, Ozturk B, Komurcu S, Ozet A, Beyzadeoglu M, Kaptan K, Beyan C, Yalcin A (2002) Total parenteral nutrition delays platelet engraftment in patients who undergo autologous hematopoietic stem cell transplantation. Nutrition 18(7–8):599–603
21. Standards for nutrition support pharmacists. American Society for Parenteral and Enteral Nutrition (1993). Nutr Clin Pract 8 (3):124–127
22. O'Dell KM, Kucukarslan SN (2005) Impact of the clinical pharmacist on readmission in patients with acute coronary syndrome. Ann Pharmacother 39(9):1423–1427. doi:10.1345/aph.1E640
23. Bond CA, Raehl CL, Patry R (2004) Evidence-based core clinical pharmacy services in United States hospitals in 2020: services and staffing. Pharmacotherapy 24(4):427–440
24. Kaboli PJ, Hoth AB, McClimon BJ, Schnipper JL (2006) Clinical pharmacists and inpatient medical care: a systematic review. Arch Intern Med 166(9):955–964. doi:10.1001/archinte.166.9.955
25. Hagiwara S, Mori T, Tuchiya H, Sato S, Higa M, Watahiki M, Hoshina M, Mochizuki T, Chiba T, Miwa A, Kawachi S (2011) Multidisciplinary nutritional support for autologous hematopoietic stem cell transplantation: a cost-benefit analysis. Nutrition 27(11–12):1112–1117. doi:10.1016/j.nut.2010.11.010
26. Llop-Talaveron J, Gracia-Garcia B, Machi-Ribes JJ, Perayre-Badia M, Badia-Tahull MB, Jodar-Masanes R (2008) Pharmaceutical interventions in metabolic and nutritional follow-up of surgical patients receiving parenteral nutrition. Farm Hosp 32(4):216–225
27. ASHP guidelines on quality assurance for pharmacy-prepared sterile products. American Society of Health System Pharmacists (2000). Am J Health Syst Pharm 57 (12):1150–1169
28. Roberts S, Miller J, Pineiro L, Jennings L (2003) Total parenteral nutrition vs oral diet in autologous hematopoietic cell transplant recipients. Bone Marrow Transplant 32(7):715–721. doi:10.1038/sj.bmt.1704204
29. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Raad II, Rolston KV, Young JA, Wingard JR, Infectious Diseases Society of A (2011) Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis 52(4):e56–e93

30. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, Jeejeebhoy KN (1987) What is subjective global assessment of nutritional status? JPEN J Parenter Enter Nutr 11(1):8–13
31. Raynard B, Nitenberg G, Gory-Delabaere G, Bourhis JH, Bachmann P, Bensadoun RJ, Desport JC, Kere D, Schneider S, Senesse P, Bordigoni P, Dieu L (2003) Summary of the standards, options and recommendations for nutritional support in patients undergoing bone marrow transplantation (2002). Br J Cancer 89(Suppl 1):S101–S106. doi:10.1038/sj.bjc.6601091
32. Koda-Kimble MA, Young LY, Kradjan WA, Guglielmo BJ, Alldredge BK, Corelli RL, Williams BR (2008) Applied therapeutics: the clinical use of drugs. In. Lippincott Williams & Wilkins, New York
33. Mirtallo J, Canada T, Johnson D, Kumpf V, Petersen C, Sacks G, Seres D, Guenter P (2004) Safe practices for parenteral nutrition. JPEN J Parenter Enter Nutr 28(6):S39–S70
34. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults (1998). The National Heart, Lung, and Blood Institute. Available at: www.nhlbi.nih.gov/guidelines/obesity/prctgd_c.pdf
35. Naylor C, Griffiths R, Fernandez R (2004) Does a multidisciplinary total parenteral nutrition team improve patient outcomes? A systematic review. J Parenter Enter Nutr 28(4):251–258. doi:10.1177/014860710402800425 1
36. Mattsson J, Westin S, Edlund S, Remberger M (2006) Poor oral nutrition after allogeneic stem cell transplantation correlates significantly with severe graft-versus-host disease. Bone Marrow Transplant 38(9):629–633. doi:10.1038/sj.bmt.1705493
37. Sucak GT, Suyani E, Baysal NA, Altindal S, Cakar MK, Aki SZ, Yegin ZA, Sanlier N (2012) The role of body mass index and other body composition parameters in early post-transplant complications in patients undergoing allogeneic stem cell transplantation with busulfan-cyclophosphamide conditioning. Int J Hematol 95(1):95–101. doi:10.1007/s12185-011-0980-y
38. Rzepecki P, Barzal J, Sarosiek T, Szczylik C (2007) Biochemical indices for the assessment of nutritional status during hematopoietic stem cell transplantation: are they worth using? A single center experience. Bone Marrow Transplant 40(6):567–572. doi:10.1038/sj.bmt.1705767
39. Sheean PM, Braunschweig CA (2007) Exploring the clinical characteristics of parenteral nutrition recipients admitted for initial hematopoietic stem cell transplantation. J Am Diet Assoc 107(8):1398–1403. doi:10.1016/j.jada.2007.05.007
40. Sheean PM, Braunschweig C, Rich E (2004) The incidence of hyperglycemia in hematopoietic stem cell transplant recipients receiving total parenteral nutrition: a pilot study. J Am Diet Assoc 104(9):1352–1360. doi:10.1016/j.jada.2004.06.024
41. Weisdorf SA, Lysne J, Wind D, Haake RJ, Sharp HL, Goldman A, Schissel K, McGlave PB, Ramsay NK, Kersey JH (1987) Positive effect of prophylactic total parenteral nutrition on long-term outcome of bone marrow transplantation. Transplantation 43(6):833–838
42. Charuhas PM, Fosberg KL, Bruemmer B, Aker SN, Leisenring W, Seidel K, Sullivan KM (1997) A double-blind randomized trial comparing outpatient parenteral nutrition with intravenous hydration: effect on resumption of oral intake after marrow transplantation. JPEN J Parenter Enter Nutr 21(3):157–161