

Evaluation of parenteral nutrition therapy in patients undergoing HSCT

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Abstract

Background and Aims: Parenteral nutrition (PN) therapy remains an essential part of patients' care during HSCT. There are many studies that focused on nutrition therapy in this population study, but there is not any consensus statement about nutrition therapy in patients who are hospitalized for bone marrow transplantation. The aim of the present study was to assess PN status and related complications in the patients during the course of HSCT in the HSCT wards of a referral teaching hospital. This study was conducted in the three HSCT wards of shariati Hospital, Tehran, Iran.

Methods: During a prospective study, data related to PN therapy were collected by clinical pharmacist during six-month period. PN therapy information including PN initiation, PN content, PN duration, and total daily calories intake in comparison with standard calories intake was recorded for each patient. An internal protocol for PN therapy was designed based on reliable guideline. The data related to patients' nutrition therapy were compared with this protocol. The nutrition therapy was considered appropriate if it was compatible with the protocol regarding time of PN initiation, PN content, rout of PN administration, PN duration, and total kilocalories received.

Result: The average of duration of hospital stay and PN therapy were 27.17 ± 9.16 and 15 ± 6.1 days respectively. One hundred and fifty-seven of medication errors were detected during the study period in the patients. Overall rate of PN therapy errors was 2.3 numbers per patient during hospitalization. Errors in the rate of errors in the content of PN administration (100%) and incorrect total daily calories intake (55.9%), incorrect PN initiation (54%) and incorrect PN duration (25.6%) were the most common types of PN therapy.

Conclusion: Our result showed that inappropriate PN therapy occurred commonly in the patients undergoing HSCT. Improvement in knowledge and attention of health-care workers about nutrition support for preventing of malnutrition in aspect of nutrition therapy.

Key Words: Parenteral nutrition, HSCT, Nutrition therapy

Received: 8, Apr, 2012

Accepted: 15, May, 2012

Introduction

Parenteral Nutrition (PN) therapy remains an essential part of patients' care during Hematopoietic Stem Cell Transplantation (HSCT). In these Patients, several factors including increased energy requirement, fluid restrictions and hepatotoxicity of PN, make it difficult to provide adequate nutrition consistently. (1)

In one hand, inappropriate nutritional and metabolic support has increased the risk of malnutrition; and on the other hand,

malnourished patients have higher complications, longer hospitalizations, increased healthcare costs, and higher morbidity and mortality rates. (2-5)

Although PN is a well supportive care and aids to maintain the nutritional status and body weights of patients after HSCT (6) especially in patients with graft-versus-host disease (GVHD) or malnourished status (7-9), there is not any consensus statement about use of PN as supportive care routinely. Fear of complications and limitations of PN such as hepatic

dysfunction, catheter-related sepsis, delayed platelet engraftment, hyperglycemia and fluid overload strongly associated with inappropriate PN therapy in general medicine. (10-12)

To ensure the nutritional status of patients during HSCT is optimal, it is important that nutritional status be monitored accurately and individual energy requirements be provided. Therefore, this study was designed to evaluate appropriateness of PN therapy in HSCT patients and related complications in these patients' population.

Methods

During a prospective study, data were collected by clinical pharmacist from June 2011 to 2012 in patients with malignant and nonmalignant diseases who underwent allogeneic or autologous HSCT in the Hematology-Oncology and Bone Marrow Transplantation Research Center at Shariati Hospital, Tehran, Iran.

Demographic, clinical and laboratory information of the patients who received PN therapy during the course of hospitalization were collected from their medical records. The collected data included sex, age, type of transplant (autologous or allogeneic), weight, body mass index (BMI), blood sugar, nutritional status according to the subjective global assessment rating (SGA), nitrogen

balance (NB), and laboratory data (such as albumin, pre-albumin and total protein), serum electrolytes, and liver function tests (AST, ALT, Bil). Also, the patients' PN therapy information including, PN initiation, PN content, route of PN administration, PN duration, and total daily calories intake in comparison with standard calories intake and PN-related complications such as hyperglycemia, hepatic dysfunction, and catheter infection were evaluated.

An internal protocol for PN therapy was prepared under the guidance of the A.S.P.E.N. Board of Directors by the clinical pharmacists (Table 1).

This protocol was approved by the local expert panel including four clinical pharmacists.

After approval of the protocol, data related to patients' PN therapy were compared to that. PN therapy was considered appropriate if it was compatible with the protocol regarding PN initiation, PN content, route of PN administration, PN duration, route of PN administration and total daily calories intake. Any mistake in the time of initiation, content, duration, route of PN administration and total daily calories intake in comparison with standard calories intake, was considered as PN therapy error. The definitions for each type of errors have been shown in Table 2.

Table 1- Protocol of PN therapy

Name:	Room:	Date:	Age-year:	Sex:	Diagnosis:
Weight-Kg:	Height-meter:		BMI-Kg/m2:	Type of transplant:	
SGA grade : A <input type="checkbox"/> B <input type="checkbox"/> C <input type="checkbox"/>					
Cause of TPN indication : Oral intake <50% (1-Sever malnourished <input type="checkbox"/> 2-weight depleting <input type="checkbox"/> 3-diaheara <input type="checkbox"/> 4Nausea/vomiting <input type="checkbox"/> 5-Mucositis <input type="checkbox"/> 6-Anorexia <input type="checkbox"/> 7-GVHD <input type="checkbox"/> 8-Albumin <2.5 g/dl <input type="checkbox"/>) Number of Days with Oral intake <50% : 3-5 d <input type="checkbox"/> 5-7d <input type="checkbox"/> >7d <input type="checkbox"/> Time of PN initiation:					
Calorie needs(25Kcal/Kg): Osmolality ≤900: PERIPHERAL LINE Osmolality >900: CENTRAL LINE			PN assessment: Nitrogen Balance ≥0 <input type="checkbox"/> <0 <input type="checkbox"/> Prealbumin ≥17 <input type="checkbox"/> <17 <input type="checkbox"/>		Cause of PN stop: Oral intake >50% Time of PN stop:

Table 2- Definition of PN therapy errors

Type of error	Definition
Incorrect PN initiation	PN was started before decrease of oral intake until 50% or PN was started lately
Incorrect PN content	PN was prepared incompletely(without vitamins, trace elements, phosphate)
Incorrect total daily calories intake	Total calories received was less than standard calories intake
Incorrect route of PN administration	PN was administrated from peripheral line while osmolarity of PN content was higher than 900 mOsm/L
Incorrect PN duration	PN was continued while patient was able to consume ≥50% of their daily requirements orally

According to ASPEN guideline, parenteral nutrition was initiated if patient was expected not to eat sufficiently for 3-5 days in severe malnutrition, 5-7 days in mild or moderate malnutrition, and 7-10 days in well-nourished patients.

Patients were classified as either well-nourished (grade A), moderately malnourished (grade B), or severely malnourished (grade C), based on the history and physical examination, and a process which we now refer to as Subjective Global Assessment (SGA). (13) If the actual body weight is greater than 30% of the calculated ideal body weight (IBW), adjusted body weight was used for calculating nutrient needs of obese patients. The following formula was used for adjusted body weight: $AjBW = IBW + 0.4(ABW - IBW)$.

A normal diet provides individuals with an adequate mix of carbohydrates, fats and proteins for energy and tissue development. PN therapy must provide patients with these dietary components, with protein in the form of amino acid, carbohydrate in the form of dextrose and fat as a lipid emulsion. In addition, PN should provide other dietary components, including water, electrolytes (Mg, Ca, P, Na, k), vitamins (B, C) and trace elements (Zn, Mn, Mo, Cd, Cr, Cu and Se). (14)

Total calorie needs were considered as 25-35 kcal/kg/day plus 1.4 g protein/kg/day. Vitamins and trace elements should be added daily in recommended amounts. Electrolytes should be adjusted daily based on serum chemistries. The duration of PN depended on the recovery of gastrointestinal function and discontinued when patients could be able to consume $\geq 50\%$ of their daily requirements orally. (14)

Assessment of PN therapy in this study was considered by nitrogen balance (NB), prealbumin and serum albumin.

The Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) version 20 was used for data analysis. Data were analyzed by basic descriptive tests. The qualitative variables are presented by their frequency of distribution. The quantitative variables are summarized as means with standard deviation. Descriptive statistics (cross-tabs) followed by the selection of chi-square and risk were used for the evaluation of correlations and calculation of odds ratio and confidence interval.

P-values less than 0.05 were considered as significant

RESULTS

Total of 68 patients in 3 adult HSCT wards who underwent HSCT were enrolled. The patients' mean age was 38.5 ± 12.4 (range, 18–65) years. Most patients were well nourished at admission. Overall, 35.3% of transplant recipients were overweight (BMI >25 kg/m²), and only three patients were classified as underweight (BMI <18.5 kg/m²) according to BMI classifications from the Centers for Disease Control and Prevention. (15) The patients' characteristics are summarized in table 3.

Table 3- Characteristics of patients

Subjects	
38 (55.9%)	Male sex - n (%)
38.5±12.4	Age - yr (mean ± SD)
71.2±17.6	weight - kg (mean ± SD)
25.2±6.5	BMI (kg/m ²) categories, n (%)
3(4.4)	<18.5
38(55.9)	18.5< BMI <25
24(35.3)	≥ 25
	SGA rating, n (%)
59 (86.8)	A
8(11.8)	B
1(1.5)	C
	Type of Transplant
38(55.9)	Allogeneic
30(44.1)	Autologous
	Diagnosis
16(23.5)	AML
8(11.8)	ALL
17(25)	HD
12(17.6)	MM
5(7.4)	AA
10(14.7)	OTHER

The average of duration of hospital stay and TPN therapy were 27.17 ± 9.16 and 15 ± 6.1 days respectively.

Our results showed anorexia (94.1%), nausea/vomiting(73.5%), diarrhea(63.2%), mucositis (51.5%), weight depleting (48.5%), albumin <3 mg/dl(23.5%) and GVHD(20.6%)

were the most common reasons that increased energy requirements respectively in these patients.

Energy intake was 978.0 ± 567 Kcal/ day, notably different with standard calories 1697 ± 303 Kcal/ day ($P < 0.01$).

Despite of nutrition support, their body weights and visceral protein showed worsening. As a result, the NB and prealbumin levels also dropped after transplantation. These changes in body weight, energy intake and NB during the six-month study period were also significant ($P < 0.01$, $P < 0.003$ and $P < 0.01$, respectively).

Patients' body weight, the ratio of energy intake/energy requirements, prealbumin and nitrogen balance during the study are shown in Table 4.

In considering PN related-complication assessment, there was no patient with hepatic dysfunction that needed the intervention or interruption of PN. However, there was a transit changes in total bilirubin and liver function tests (ALT,AST) but the difference was not clinically impressive. Ten patients with probable catheter infection were found.

No patients had preexisting diabetes mellitus but hyperglycemia occurred in 20.6% of patients that required a median of 29.8 IU of

insulin for a mean blood glucose level of 133 ± 33.8 mg per deciliter.

Evaluation of patients' electrolyte status demonstrated average rate of 5.6 electrolyte disorder per patient, with hypophosphatemia (47.1%) as the most electrolyte disorder (Table 5).

According to this center, the PN was started on the first day after transplantation regardless of oral feeding and was maintained until the catheter was removed at discharge. Patients received intravenous 5% glucose solution daily, amino acid 10% daily, and intralipid 10% twice a week. Patients also received parenteral minerals (potassium, sodium, and magnesium), and vitamins (B, C). But they did not receive phosphate or trace elements. On the basis of protocol which was approved in this trial, one hundred and fifty-seven PN therapy errors were detected during the study period with an average rate of 2.3 PN therapy errors per patient. Following the analysis of the data, errors in the content of PN administration (100%) and incorrect total daily calories intake (55.9%), incorrect PN initiation (54%) and incorrect PN duration (25.6%) were the most common types of PN therapy respectively (Table 6). We don't have any errors regarding the route of PN administration.

Table 4-Body weight, energy intake, prealbumin and nitrogen balance of patients in different stages of the study (n=68)

	Body weight (Kg) Mean±S.D	Energy intake/ energy needs Mean±S.D	Nitrogen balance Mean±S.D	Pre-albumin (gr/dl) Mean±S.D
At the start of PN therapy	69.6±17.6	1.43±0.35	2.37±7.6	21.08±7.3
At the end of PN therapy	68.6±16.8	0.7±0.15	-0.84±6.67	17.8±7.6

Table 5- PN related complications

	Number (%)
Hypophosphatemia	32 (47.1)
Hyperglycemia	14 (20.6)
Hypertriglyceridemi	10 (14.7)
Catheter infection	10 (14.7)
LFT increase	8 (11.8)

Table 6- Types of the detected errors

Type of error	Number of errors (%)
Incorrect PN initiation	36(52.9)
Incorrect PN content	68(100)
Incorrect total calories received	38(55.9)
Incorrect route of PN administration	0
Incorrect PN discontinuation	18(26.4)

Discussion

To the best of our knowledge, this is the first study that has evaluated PN therapy errors in

adult patients undergoing HSCT in hospital setting.

In different stages of PN therapy, including time of initiation, content, total daily calories

intake and duration, at least one error was detected. Errors in the content of PN administration, incorrect total daily calories intake, incorrect PN initiation and incorrect PN duration were the most common types of errors, respectively.

Hyper metabolic state in HSCT is requiring a high level of energy (16) whereas, 44.1% of HSCT patients in our study intake adequate amounts of energy as PN therapy to maintain or improve nutritional status.

Trace elements are metabolic cofactors essential for the proper functioning of several enzyme systems. They are also constituents of proteins and hormones. Some of them (Cu, Zn, Mn, and Se) acts as antioxidants. (17) Although a certain amount of trace elements are supplied with plasma infusions, but malabsorption and an increased need for bone marrow reconstitution may induce trace element deficiency in some patients. In order to prevent trace element deficiency, additional trace mineral supplementation may be required in these patients.(18)

Our result showed that daily intake for parenteral trace minerals is not provided in PN therapy, therefor multi-elements solutions which are convenient and easy to use were suggested .(17)

Micronutrient requirements such as electrolytes in a PN order must be individualized for each patient. Electrolyte management is one of the most difficult aspects of PN therapy. (19)

Often electrolytes are outside of the normal range based on an underlying cause rather than directly related to the PN solution so incremental dose adjustments are made concurrent with treatment of the underlying cause of electrolyte abnormality. Like similar other studies, hypophosphatemia was the most common electrolyte disturbance in our patients who were receiving PN therapy. (20-21)

Although the incidence of this condition is only 0.5 to 3% in general hospital population, it is as high as 31% in patients receiving nutritional support. (21) Hypophosphatemia occurs as a result of new tissue synthesis and a shift of phosphate from the extracellular to the intracellular compartments.

On the basis of our result, other electrolytes including sodium, potassium, magnesium, and calcium except phosphorus were administered

during startup of PN therapy. Phosphate supplementation during PN therapy is essential to prevent hypophosphatemia. (22) An additional example of PN therapy error in this study was initiation time of PN therapy. 86.8% patients in our study were well-nourished, hence, accordance with the guideline (14), PN therapy should have been started within 7-14 days after 50% reduction of oral intake, but this study reported 54% early PN therapy at first day after transplantation. A multi-center trial of Fuji and et al. on the survey of nutritional support after hematopoietic stem cell transplantation revealed early PN therapy is a common practice in all institutes. (23) In fact, PN was started before patients developed malnutrition. This information clearly revealed lack of firmly established recommendations for the nutritional support in the field of HSCT. Absence of a PN consultant could be a limitation to discourage physicians from pursuing appropriate PN therapy. (24) A reason could be limitation of human resources in field of nutrition support. (25) A.S.P.E.N. publishes discipline-based (e.g., physician, dietitian, nurse, pharmacist) standards that should be provided to assure safe and efficacious nutrition care. (26)

A majority of studies have demonstrated the positive influence on clinical outcomes, once clinical pharmacist's service is added to the care of inpatients in general. (27-29) Involvement of clinical pharmacist as core in nutrition support team due to skillfully and capability of PN implementation and discontinuance at appropriate time can reduce the errors and also increase the clinical outcomes.

Conclusion

Findings of this study showed high rate of PN therapy errors in the bone marrow transplantation wards. Preparing local PN therapy protocol and establishment of educational programs are recommended for the HSCT patients. It also must be kept in mind that PN therapy should be considered an invasive procedure that require patients' close monitoring. Improvement in knowledge and attention of health-care workers about nutrition support is necessary for preventing malnutrition in aspect of nutrition therapy.

Ultimately, intervention of PN therapy as a supplement by multi-disciplinary nutritional support team could be an effective way for detecting and correcting PN related errors, which might also be a topic of future clinical trials after HSCT.

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