Nutritional Support in Pediatric Patients Undergoing Bone Marrow Transplantation

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Abstract

Background : Children undergoing bone marrow transplantation (BMT) are prone to develop severe gastrointestinal (GI) complications and metabolic imbalance which consequently impair their nutritional status. Nutritional support is an important adjunctive treatment during BMT.

Objective : To assess GI complications, metabolic complications and nutritional outcome of children undergoing BMT with nutritional support intervention.

Method : Retrospective study of 20 children (median age 6.8 years, 11 males) undergoing BMT at Ramathibodi Hospital from March 1995 to July 2000 was conducted. Their medical records were reviewed.

Results : The patients underwent autologous (n = 9) and allogenic BMT (n = 11). Median z-scores of weight for age, height for age and weight for height were 0.06 ± 1.93, -0.55 ± 1.18 and 0.48 ± 1.94, respectively. Nineteen patients had vomiting for 9.8 ± 5.5 days. Eighteen patients developed diarrhea for 9.6 ± 7.2 days. The durations of vomiting and diarrhea, as a percentage of total hospital days, were 33.5 ± 16.3 per cent and 30.4 ± 17.0 per cent, respectively. There were no differences between the patients with autologous and allogenic BMT regarding these durations. All patients needed enteral and/or parenteral nutrition support for 21.0 ± 7.7 days except for one patient who could take adequate oral intake. The duration of enteral nutrition support was not significantly different between the groups but the duration of parenteral nutrition support was significantly longer in the allogenic group. Metabolic complications were hypokalemia, hypophosphatemia and one case of arrhythmia secondary to hypomagnesemia. All patients developed febrile neutropenia but none developed catheter-related sepsis. The length of hospital stay was 30.5 ± 10.2 days. The median z-score of weight for height on the day of discharge was 1.08 ± 2.03.

Conclusion : Children undergoing BMT usually have GI symptoms of vomiting, diarrhea and mucositis as well as metabolic imbalances such as hypokalemia, hypophosphatemia and hypomagnesemia. Despite these complications, their nutritional status could be restored by proper nutritional support.

Key word : Nutritional Support, Bone Marrow Transplantation

ISARIYAVUTH V, SUTHUTVORAVUT U, CHATVUTTINUN S, et al
J Med Assoc Thai 2002; 85 (Suppl 4): S1191-S1198

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Bone marrow transplantation (BMT) is a procedure which requires high dose chemotherapy and may also include total body irradiation. As a consequence, this results in immune suppression[1] followed by infection, graft *versus* host disease, pulmonary complications, venoocclusive disease and gastrointestinal (GI) complications[2,3] such as anorexia, dysgeusia, vomiting, diarrhea, mucositis and pancreatitis[4]. Many patients develop metabolic complications[5] including hypokalemia, hypophosphatemia, hypomagnesemia and syndrome of inappropriate antidiuretic hormone secretion[6]. All conditions consequently have negative effects on nutritional status and increase the mortality rate especially in pediatric patients.

Previous studies showed that nutritional support could restore nutritional status and improve the long-term survival rate of patients receiving BMT[7,8]. Enteral nutrition (EN) support is cheaper, easier to provide, resulting in better nutritional response and fewer complications than parenteral nutrition (PN) but its tolerance and effectiveness may be compromised in severely ill patients[1,8-11]. PN is particularly advantageous in this group but high cost, high risk of infection and metabolic complications should be considered[1,11,12]. Recent studies showed that an existing combined EN and PN regimen with close monitoring could be used for better outcome[10,11,13].

The present study determined gastrointestinal, metabolic and nutritional outcomes of children undergoing BMT with coexisting nutritional support intervention.

PATIENTS AND METHOD

Medical records of pediatric patients under the age of 15 years who underwent BMT in the Pediatric Hematology-Oncology Unit, Department of Pediatrics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University from March 1995 to July 2000 were reviewed.

Nutritional status, gastrointestinal and metabolic complications of the patients were determined. Nutritional status was assessed anthropometrically by weight for age, height for age and weight for height, expressed as standard deviation scores (z-scores) based on the United States NCHS reference. GI complications were determined by clinical signs and symptoms of diarrhea, vomiting and mucositis. Metabolic complications were assessed by baseline (day before conditioning regimen of chemotherapy) and serial (every 5 days after graft infusion) serum electrolytes, phosphorus, magnesium and albumin which were determined until engraftment and/or the patients were stable.

Nutritional support protocol

Central venous catheterization *via* subclavian vein, using Hickman® catheter or subcutaneous port, was performed in all patients before chemotherapy.

The patients initially received regular clean diet and nutrient-caloric count was performed every day until they could not eat well or refused food. Then, EN support was started by using oral liquid medical food (lactose-free or medium-chain triglyceride formula).

If EN provided less than two-thirds of the patient's total energy requirement, or there was intolerance or any contraindications of EN, PN would be started *via* a central line. PN was discontinued when the patient's daily energy intake *via* the enteral route was more than 80 per cent of the daily requirement.

Statistical analysis

Data are presented as mean ± SD, median and range. Unpaired Student's *t*-test and Fisher's exact test were used for comparison between the groups. P-value of less than 0.05 was considered significant.

RESULTS

Twenty patients (11 males and 9 females) were enrolled in the study. Eighteen patients received BMT from 1997 to 2000 while 2 patients received BMT from 1995 to 1996. Their median age was 6.8 years (range 1.3-14.7). Indications for BMT were hematologic malignancy, soft tissue malignancy and thalassemia disease in 11, 4 and 5 cases, respectively. Nine patients underwent autologous and 11 underwent allogenic BMT. Their baseline median z-scores of weight for age, height for age and weight for height were 0.03, -0.79 and 0.0, respectively, as shown in

Table 1. Clinical characteristics of patients at baseline.

	Autologous BMT (n=9)	Allogenic BMT (n=11)	Total (n=20)
Age* (year)	6.6 (1.3-14.5)	7.0 (2.2-14.7)	6.8 (1.3-14.7)
Male : Female	6 : 3	5 : 6	11 : 9
Indications of BMT			
Hematologic malignancy	6	5	11
Soft tissue malignancy	3	1	4
Thalassemia disease	0	5	5
Types of graft			
Bone marrow	4	6	10
Peripheral blood stem cells	5	3	8
Cord blood	0	2	2
Nutritional status*			
Z-score of weight for age	0.39 (-1.72 to 5.42)	-0.89 (-2.58 to 1.93)	0.03 (-2.58 to 5.42)
Z-score of height for age	-0.76 (-1.51 to 1.12)	-0.82 (-2.13 to 2.96)	-0.79 (-2.13 to 2.96)
Z-score of weight for height	1.07 (-0.90 to 5.34)	-0.46 (-2.34 to 1.41)	0.0 (-2.34 to 5.34)

* Data are presented as median and range.

Table 2. Gastrointestinal (GI) complications.

GI complications	Occurrence	Duration (day)	Duration (% of hospital days)
Vomiting			
Autologous (n=9)	8	9.1 ± 5.1	36.7 ± 20.4
Allogenic (n=11)	11	10.4 ± 6.0	30.9 ± 12.6
Diarrhea			
Autologous (n=9)	8	7.7 ± 4.1	30.6 ± 18.6
Allogenic (n=11)	10	11.5 ± 9.3	30.2 ± 16.5
Mucositis			
Autologous (n=9)	1	NA	NA
Allogenic (n=11)	4	NA	NA

Data are presented as mean ± SD
NA = Not available

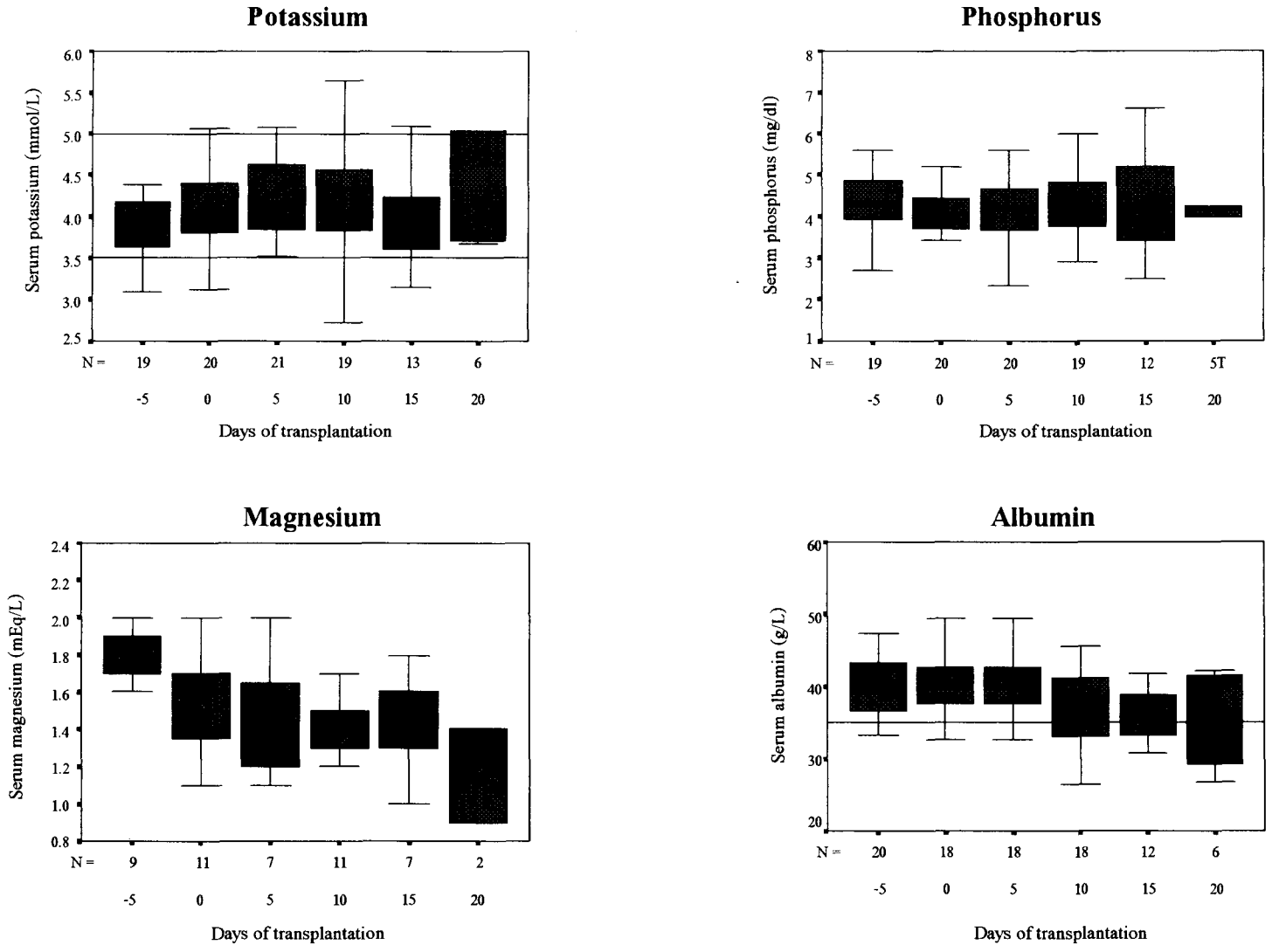

Fig. 1. Serum levels of electrolytes and albumin during transplantation.

Table 3. Duration of nutritional support.

	Duration (days)		P-value
	Autologous BMT (n = 9)	Allogenic BMT (n = 10)	
EN	3.6 ± 6.1	1.9 ± 3.4	0.453
EN and PN	2.9 ± 3.7	4.4 ± 6.1	0.531
PN	8.8 ± 9.1	17.6 ± 9.1	0.046
Total	15.2 ± 7.9	23.8 ± 7.8	0.025

Data are presented as mean ± SD
EN = enteral nutrition, PN = parenteral nutrition

Table 1. Mean duration of engraftment was 11.1 ± 1.9 days in autologous and 17.5 ± 11.1 days in the allogenic groups. Mean lengths of hospital stay were 26.1 ± 6.6 days in the autologous group and 34.1 ± 11.5 days in the allogenic group.

GI complications are shown in Table 2. Nineteen of twenty patients developed vomiting and 18 patients had diarrhea. Five patients developed mucositis. Mean durations of vomiting and diarrhea were longer in the allogenic group but not statistically significantly different. The duration of vomiting, as percentage of hospital days, were 36.7 ± 20.4 and 30.9 ± 12.6 per cent in the autologous and allo-genic groups, respectively. The duration of diarrhea, as percentage of hospital days, were 30.6 ± 18.6 per cent and 30.2 ± 16.5 per cent in the autologous and allogenic groups, respectively. The durations of GI complications were not significantly different between both groups. The mucositis was more severe in the allogenic group. No patients developed pancreatitis.

Eight and 9 patients had hypokalemia and hypophosphatemia, respectively. Serum potassium and phosphorus levels were restored during the transplantation period (Fig. 1). One patient in the allogenic group had severe hypomagnesemia (0.78 mEq/L) on the 18th day after graft infusion. He developed premature ventricular contraction with stable vital signs which was corrected to sinus rhythm within 12 hours by parenteral magnesium infusion.

Nutritional support and outcome

Nineteen of 20 patients needed nutritional support. Eleven cases needed only EN. Seven patients initially received EN, followed by PN. One patient in the allogenic group received PN since the start of nutritional support because of severe vomiting and diarrhea. One patient with thalassemia did not need nutritional support during allogenic BMT because of adequate oral intake and the absence of serious GI side effects. The mean duration of nutritional support of nineteen patients who needed EN and/or PN was 21.0 ± 7.7 days. The duration of EN was not significantly different between both groups but duration of PN was significantly longer in the allogenic group as shown in Table 3.

Mean serum albumin dropped slightly from 42.4 ± 5.9 g/L to 37.3 ± 5.4 g/L on the tenth day after graft infusion but no clinical signs of hypoalbuminemia were seen (Fig. 1).

Mean z-scores of weight for height before BMT and the day of discharge were 0.48 ± 1.94 and 1.08 ± 2.03, respectively, which were not significantly different. However, 19 of 20 patients had increased z-scores of weight for height.

DISCUSSION

The present study demonstrated that vomiting and diarrhea were common following BMT. Mucositis was also observed but pancreatitis, a rare complication, was not seen in the presented patients.

Multiple factors may contribute to hypokalemia during BMT, such as GI loss[13] as well as side effects of drugs such as amphotericin B, furosemide and prednisolone. Serum potassium levels were slightly decreased in the presented patients but remained within normal ranges throughout BMT which may be due to potassium supplementation.

Hypomagnesemia and hypophosphatemia were also common because of malnutrition and other factors such as treatment with amphotericin B. The means of serum magnesium concentrations were

within normal ranges in the present study. One patient in the allogenic group who developed premature ventricular contraction due to clinical signs of hypomagnesemia had multiple contributing factors including high dose amphotericin B, cyclophosphamide, furosemide and severe diarrhea. His arrhythmia was converted to sinus rhythm by parenteral magnesium.

Hypoalbuminemia may result from increased metabolism, decreased protein synthesis, volume redistribution, protein loss from gut in graft *versus* host disease[13-15] and rotavirus or cytomegalovirus infection during BMT.

A previous study has shown that nutritional status deteriorates during chemotherapy if no nutritional support is provided[16]. Malnutrition has impacts on disease outcome[17,18]. Some clinicians have, therefore, recommended that nutritional support be a routine part of treatment of childhood cancer. The goals of nutritional support are to maintain lean body mass and provide nutrients for recovery of hematopoietic and the immune system[13]. Enteral nutrition support, when tolerated, is cheaper and safer than parenteral nutrition[19]. PN is associated with gut atrophy and a higher infection rate. The present study showed that nutritional status can be restored by using multiple modalities of nutritional support depending on the patient's GI functions.

The present study has a limitation since it is retrospective. Furthermore, the assessment of nutritional status by weight for height may be interfered by other conditions such as fluid retention.

In conclusion, BMT in children can cause many GI side effects and metabolic complications which adversely affect nutritional status and survival rate. Proper nutritional support could restore the nutritional status of these children.

(Received for publication on September 23, 2002)

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โภชนบำบัดในผู้ป่วยเด็กที่เข้ารับการปลูกถ่ายไขกระดูก

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ผู้ป่วยเด็กที่เข้ารับการรักษาโดยวิธีปลูกถ่ายไขกระดูกมักมีปัญหาในระบบทางเดินอาหารและระบบเมตาบอลิสม ซึ่งมีผลกระทบในด้านลบต่อภาวะโภชนาการของผู้ป่วย ปัจจุบันการให้โภชนบำบัดเป็นส่วนหนึ่งในการปลูกถ่ายไขกระดูก

การวิจัยนี้จึงมุ่งศึกษาผลกระทบต่อระบบทางเดินอาหารและเมตาบอลิสมในผู้ป่วยเด็กที่เข้ารับการปลูกถ่ายไขกระดูก พร้อมกับได้รับโภชนบำบัด โดยการศึกษาย้อนหลังในผู้ป่วย 20 ราย ที่เข้ารับการปลูกถ่ายไขกระดูกในภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี ตั้งแต่เดือนมีนาคม 2538 ถึง เดือนกรกฎาคม 2543 เป็นการปลูกถ่ายไขกระดูกแบบ autologous 9 ราย และ allogenic 11 ราย ค่ามัธยฐานของ z-score ของน้ำหนักตามอายุ ส่วนสูงตามอายุและน้ำหนักตามส่วนสูงเป็น 0.06 $\pm$ 1.93, -0.55 $\pm$ 1.18 และ 0.48 $\pm$ 1.94 ตามลำดับ ผู้ป่วย 19 รายมีอาการอาเจียนเป็นเวลาเฉลี่ย 9.8 $\pm$ 5.5 วัน และ 18 ราย อุจจาระร่วงเป็นเวลาเฉลี่ย 9.6 $\pm$ 7.2 วัน และไม่พบความแตกต่างระหว่างกลุ่ม autologous และ allogenic ผู้ป่วยทุกรายได้รับโภชนบำบัดโดยการให้อาหารทางหลอดเลือดดำและ/หรือการให้อาหารทางการแพทย์ทางปาก เป็นเวลาเฉลี่ย 21 $\pm$ 7.7 วัน ยกเว้นผู้ป่วย 1 ราย สามารถรับประทานอาหารและดื่มน้ำได้เพียงพอ ระยะเวลาที่ผู้ป่วยทั้งสองกลุ่มได้รับโภชนบำบัดด้วยอาหารทางการแพทย์ไม่ต่างกัน แต่กลุ่ม allogenic ได้รับอาหารทางหลอดเลือดดำนานกว่า

พบภาวะผิดปกติทางเมตาบอลิสมคือโปแตสเซียมและฟอสเฟตในเลือดลดลง และผู้ป่วย 1 ราย มีภาวะหัวใจเต้นผิดปกติจากภาวะแมกนีเซียมในเลือดต่ำ ระยะเวลาเฉลี่ยในการอยู่โรงพยาบาลนาน 30.5 $\pm$ 10.2 วัน ค่ามัธยฐานของ z-score ของน้ำหนักตามความสูงในวันที่ออกจากโรงพยาบาลเป็น 1.08 $\pm$ 2.03

ผลการศึกษาครั้งนี้พบว่าผู้ป่วยที่เข้ารับการปลูกถ่ายไขกระดูกได้รับผลกระทบต่อระบบทางเดินอาหารและระบบเมตาบอลิสมของร่างกาย การให้โภชนบำบัดจะสามารถช่วยเหลือผู้ป่วยเหล่านี้ได้

คำสำคัญ : โภชนบำบัด, การปลูกถ่ายไขกระดูก

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จดหมายเหตุทางแพทย์ ฯ 2545; 85 (ฉบับพิเศษ 4): S1191-S1198

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