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Evaluation the Nutritional Status of Leukemia Patients Before and After Bone Marrow Transplantation

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Abstract: Bone marrow transplantation (BMT) and related complications can cause gastrointestinal (GI) side effects that can lead to poor nutrition, which has been associated with several morbidity and mortality issues. Therefore, the present study was carried out to evaluate the nutritional statues of leukemia patient before and after bone marrow transplantation. Among 49 leukemia patients enrolled in Nasser Institute hospital at Cairo, Egypt, 9 (18.37%) patients were not analyzed because of unavailability of consent for study or inadequate data. The remaining enrolled 40 patients aged 31.17 to 53.43 years with a mean age of 45.60+11.56 years. They were 29 (72.50%) males and 11 (27.50) females. Data of analysis indicated that leukemia patients were suffered from malnutrition. This is confirmed by the depletion in food intake of different macro and micronutrients. All of these data are going in concomitant with the decreasing of some hematological parameters related to the nutrition status. So, the challenge of addressing the problem (malnutrition in leukemia patients) therefore remains an urgent imperative for health development and need further studies in the future.

Keywords: leukemia, Dietary intake, BMI, vitamins, iron, ferritin

Introduction

Leukemia is a group of cancers that usually begin in the bone marrow and result in high numbers of abnormal white blood cells (Manisha, 2012). These white blood cells are not fully developed and are called *blasts* or *leukemia cells* (NCI, 2013). Global deaths due to leukemia in 2010 were about 281,500 (Lozano *et al.,* 2012). In 2000, leukemia accounted for about 3% of the seven million deaths due to cancer and about 0.35% of all deaths from any cause around the world (Mathers *et al.,* 2002). There is a racial divide in the prevalence of

leukemia; white American children are almost twice more likely to develop leukemia than black American children and boys are more likely to be affected than girls. Hispanics under 20 years of age are at the highest risk for leukemia, while whites, Native Americans, Asians, and Alaska Natives are at higher risk than blacks. Around 30 percent more men than women are diagnosed with leukemia and die from the disease (Siegel *et al.,* 2013). But more than 90% of all leukemias are diagnosed in adults with the peak incidence between 40 and 60 years (Vardiman *et al.,* 2002). Symptoms may include bleeding and bruising problems, feeling tired, fever, and an increased risk of infections (NCI, 2013). These symptoms occur due to a lack of normal blood cells Diagnosis is typically made by blood tests or bone marrow biopsy (NCI, 2013).

Treatment may involve some combination of chemotherapy, radiation therapy, targeted therapy, and bone marrow transplant, in addition to supportive care and palliative care as needed (WCR, 2014). Bone marrow is the spongy tissue found inside the bones. Bone marrow makes stem cells, which grow and divide and become red blood cells (which carry oxygen to body tissues), white blood cells (which help fight off infection), and platelets (which aid in blood clotting) (Hardy, 1989). Stem cells are found in the blood stream, normally at low concentrations. However, the number of stem cells in the peripheral blood can be increased by giving a donor a "growth factor." In a bone marrow transplant, some marrow (about 5 percent) is “harvested” from the donor’s hip bone in a surgical procedure that lasts about an hour and requires general anesthesia. These cells are pooled, processed and transfused into the patient. Peripheral stem cells, on the other hand, can be taken from the blood circulating in the body after the donor is injected with a growth factor called Granulocyte Colony Stimulating Factor (G-CSF). This medication stimulates the donor's bone marrow to produce excess quantities of stem cells which are released into the circulating blood. The donor's blood is drawn and a special blood processing system concentrates the stem cells. These cells are transfused into the patient. The donor experiences no surgical pain. Peripheral blood stem cell transplant generally provides more stem cells and results in a more rapid recovery of white blood cells and platelets. However, it may be associated with a higher risk of chronic graft vs. host disease (Bechard *et al.,* 2010).

One reason BMT and peripheral blood stem cell transplantation (PBSCT) are used in cancer treatment is to make it possible for patients to receive very high doses of chemotherapy and/or radiation therapy (Hardy, 1989). To understand more about why BMT and PBSCT are used, it is helpful to understand how chemotherapy and radiation therapy work. Chemotherapy and radiation therapy generally affect cells that divide rapidly. They are used to treat cancer because cancer cells divide more often than most healthy cells. However, because bone marrow cells also divide frequently, high-dose treatments can severely damage or destroy the patient's bone marrow. Without healthy bone marrow, the patient is no longer able to make the blood cells needed to carry oxygen, fight infection, and prevent bleeding. BMT and PBSCT replace stem cells destroyed by treatment. The healthy, transplanted stem cells can restore the bone marrow's ability to produce the blood cells the patient needs. In some types of leukemia, the graft-versus-tumor (GVT) effect that occurs after allogeneic BMT and PBSCT is crucial to the effectiveness of the treatment. GVT occurs when white blood cells from the donor (the graft) identify the cancer cells that remain in the patient's body after the chemotherapy and/or radiation therapy (the tumor) as foreign and attack them (French *et al.*, 2011).

Bone marrow transplantation (BMT) and related complications can cause gastrointestinal (GI) side effects that can lead to poor nutrition, which has been associated with several morbidity and mortality issues (Cheryl and Teresa, 2008). They also reported that adolescents require adequate nutrition not only to maintain health but to advance with normal growth and development. This article synthesizes the bone marrow transplant (BMT) literature regarding adolescents' nutritional needs, etiologies of altered oral intake, GI symptoms, nutritional assessments, nutritional interventions, and quality of life associated with poor nutrition. In addition, gaps in knowledge in the literature are identified. To provide effective and thorough care to patients during their BMT recovery, the knowledge base of nutritional and eating issues after transplant needs to become more comprehensive (Sheean, 2005). Nurses play an important role in gathering and reporting clinical information. By anticipating potential risk factors, assessing and identifying symptoms, and initiating appropriate interventions promptly, patients can experience a more positive BMT experience (Cheryl and Teresa, 2008).

Good nutrition is a very important part of BMT patients' recovery. It helps their body resist infection and repair tissue damage caused by chemotherapy and/or radiation therapy. Losing interest in food after a long illness is to be expected. Some of the side effects patients might have experienced while in the hospital may continue even after patients go home. These side effects may include nausea, vomiting, loss of appetite, taste changes, and a sore or dry mouth. With these symptoms, it may be difficult for you to imagine eating high-calorie, nutrient-rich meals (Grant and Kravits, 2010). Although all of these studies with others explained the BMT and related complications, further studies are recommended for the nutritional ones. Therefore, present study was carried out to evaluate the nutritional statues of leukemia patient before and after bone marrow transplantation.

Patients and Methods

Patients

The study protocol was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients were approved in advance by the Ethical Committee of Faculty of Home Economics, Minoufiya University, Shebin El-Kom, Egypt. Verbal informed consent was obtained from all patients, witnessed and formally recorded. Survey was conducted from February 2015 to Jaunary 2016, in Nasser Institute hospital at Cairo, Egypt. This Institute serve a lot of leukemia patients from the all Egyptian Governorates. A total of 49 patients with leukima enrolled, 9 (18.37%) patients were not analyzed because of unavailability of consent for study or inadequate data. The remaining enrolled 40 patients aged 31.17 to 53.43 years with a mean age of 45.60+11.56 years. They were 29 (72.50%) males and 11 (27.50) females.

A field pretested interviewing questionnaire was used for anthropometric measurements and body mass index was calculated according to Geoffrey, (1995). Nutritional history was obtained during visits including the dietary recall and the record was used for patients who were asked for all foods and fluids consumed while she was at home and hospital before and after the BMT. Daily food intake of each patient was calculated using the "Diet Analysis Program, 1995" (Lifestyles

Technologies, Inc., Northbridge Point, Valencia, California) and was then compared with the Recommended Dietary Allowances (RDA, 1989).

Hematological analysis

Blood samples were withdrawn from the antecubital vein into glass centrifuge tubes and used for hematological analysis. CBC parameters include HB, WBC's and lymphoblasts as well as serum glucose were determined such as mentioned in Stroev and Makarova, 1989). Serum iron (Fe) content samples were determined by the adaptation the method mentioned by Singh *et al.,* (1991). One hundred µl of plasma sample were transferred into a digested glass tube and 2 ml of tri-acids mixture (containing nitric acid: perchloric acid: sulfuric acid in the ratio of 20: 4: 1 v/v respectively) were added to each tube. The tubes content were digested gradually as follow, 30 min at 70 ^{0}C; 30 min at 180 ^{0}C and 30 min at 220 ^{0}C. After digestion, the mixture was cooled, dissolved in MilliQ water, and the volume was increased to 10 ml in volumetric beaker. After filtration in ashless filter paper, aliquots were analyzed for Fe and Se content using of atomic absorption spectrophotometer, type Perkin - Elmer, Model 2380.

Blood hemoglobin (Hb) concentration was determined using cyanmethemoglobin method according to Villanova (1994). Anemia was diagnosed when Hb concentrations below the values adjusted for age groups (Wonke *et al.,* 2007). The plasma ferritin concentrations and hematocrit value were assayed using specific Kits (Al-Gomhoria Company for Drugs, Chemicals and Medical Instruments, Cairo, Egypt) according to the methods mentioned in Tietz, (1999). The complete blood count was done using Coulter 1660 to determine the erythrocyte indices (mean corpuscular volume [MCV], mean corpuscular Hb [MCH], MCH concentration, and red cell diameter width.

Statistical analysis

Data obtained from the study were coded, entered and statistical analyzed using the software MINITAB 12 computer program (Minitab Inc., State College, PA).

Results and Discussion

Anthropometric and nutritional status of patients before and after bone marrow transplantation

In the present study, among 49 patients enrolled, 9 (18.37%) patients were not analyzed because of unavailability of consent for study or inadequate data. The remaining enrolled 40 patients aged 31.17 to 53.43 years with a mean age of 45.60+11.56 years. They were 29 (72.50%) males and 11 (27.50) females. The anthropometric and nutritional status data are shown in Table (1). From such data it could be noticed that the mean of BMI (kg/m^2) and nutritional status score (%) were 19.07±3.45 and 80.96±3.17 in leukemia patients which significantly increased to 22.98±2.98 and 96.53±2.26 for the same patients after BMT. It is mean that treatment of leukemia patients by BMT leads to increase the BMI and nutritional status score by the rates of 20.50 and 19.23%, respectively.

Table 1. Anthropometric and nutritional Status data of leukemia patients before and after bone marrow transplantation, PMT (n=40, data expressed as mean ± SD)

Parameter	Leukemia patients before BMT	Leukemia patients after BMT	Compare before to after (%)	Ref. Range
Weight (kg)	51.30±3.76 [b]	61.80±2.66[a]	20.47	---
Height (cm)	1.64±2.09 [a]	1.64±2.09 [a]	0.00	---
BMI (kg/m^2)	19.07±3.45 [b]	22.98±2.98 [a]	20.50	15-24.9
Nutritional status score (%)	80.96±3.17 [b]	96.53±2.26 [a]	19.23	90-100

* Mean values in the same raw bearing different superscript letters are significantly different at $P<0.05$.

Food intake of leukemia patients before and after bone marrow transplantation

Data of the food intake among leukemia patients before and after BMT are shown in Table (2). From such data it could be noticed that the mean of protein (g/d), fat (g/d), carbohydrate (g/d) and total energy (kcal/day) were 56.7±1.32, 37.8±10.65, 330.75±23.43 and 1890±145.43 which cover 71.77, 80.43, 96.15 and 89.32% of the RDI in leukemia

patients which significantly increased to 76.875±2.34, 45.55±6.35, 333.125±10.43 and 2050±102.43 which cover 97.30, 96.92, 96.84 and 96.88% of the RDI for the same patients after BMT, respectively. It is mean that treatment of leukemia patients by BMT leads to increase the RDI of protein, fat, carbohydrate and total energy by the rates of 35.57, 20.50, 0.72 and 8.46%, respectively. The same trend was observed for some vitamins (A, C and E) and mineral (Se). Such investigation, the increasing of such vitamins and minerals as the result of BMT, represents an important notice because of their roles as biological antioxidant.

Table 2. Food intake of leukemia patients before and after bone marrow transplantation, PMT (n=40, data expressed as mean ± SD)

Parameter	Leukemia patients before BMT			Leukemia patients after BMT		% of change
	RDI	Mean ± SD	RDI %	Mean ±SD	RDI %	
Total Protein (g/d)	79	56.7±1.32 [b]	71.77	76.87±2.34 [a]	97.30	35.57
Total Fat (g/d)	47	37.8±10.65 [b]	80.43	45.55±6.35 [a]	96.92	20.50
Carbohydrate (g/d)	344	330.75±23.4 [a]	96.15	333.13±10.43	96.84	0.72
Total energy kcal/day)	2116	1890±145.43 [b]	89.32	2050±102.43 [a]	96.88	8.46
Vit. A (µg/day)	900	657±77.56 [b]	73.00	738±49.92 [a]	82.00	13.89
Vit. C (mg/d)	90	72±10.45 [a]	80.00	76.5±3.59 [a]	85.00	6.25
Vit. E (mg/d)	15	9.75±2.10 [b]	65.00	11.85±0.98 [a]	79.00	21.54
Selenium (µg/day)	55	31.35±7.34 [b]	57.00	39.05±3.11 [a]	71.00	24.56

* Mean values in the same raw bearing different superscript letters are significantly different at $P<0.05$.

According to these results, the decreasing in antioxidant vitamins in plasma could be attributed to their consumption in scavenge, quench and/or trap ROS resulted from leukemia injury. Vitamins include A, E and C, the non-enzymatic antioxidants that prevent or retards the oxidation of sensitive molecules found in the body. Vitamin E is considered as primarily intracellular antioxidants associated with cell membranes (krinskey, 1992). It is a potent peroxyl radical scavenger (Burton *et al*., 1986) and can protect polyunsaturated fatty acids (PUFA) within phospholipids of biological membranes and in plasma lipoproteins (Jialal *et al*., 1995). β-carotene i.e. precursor of vitamin A and other carotenoids belong to the large family of conjugated polyenes. It has antioxidant activity through its property as singlet oxygen ($1 O_2$) quenchers and their

ability to trap peroxyl radicals (Truscott, 1990; Stahl and Sies 1993). It is also able to inhibit free radical reactions (Palozza and Krinsky, (1992). Vitamin C is an important antioxidant. Its water solubility allows it to be widely available in both the extracellular and intracellular spaces in most biological systems (Halliwell and Gutteridge 1990). Antioxidant roles of ascorbic acid can be' summarized in the following*:* scavenges the different free radicals, inhibits lipid peroxidation and reduces nitroxide radicals (Anderson *et al*.,1988; Hialliwell and Qutteridge 1990; Frei, 1991). Also, Se is an essential trace element. It is importance for human and animal metabolism has become apparent more recently, spurred by the discovery of a Se-dependent enzyme, glutathione peroxidase (widely distributed in tissues), and suggestive evidence that selenium plays a role in the prevention of certain forms of cancer (Linder, 1991 and Packer *et al.*, 1999). Such data proved that BMT not only play an important role in dietary food intake but also participate in improve the body immune system through raising the antioxidant activities.

CBC and Glucose level of leukemia patients before and after bone marrow transplantation

Data of the CBC and glucose levels among leukemia patients before and after BMT are shown in Table (3). From such data it could be noticed that the mean Hb (g/dL), WBCs (10^3cell/ml), lymphoblasts (%) and glucose (mg/dL) levels were 7.5±2.23, 1.76±2.08, 1.7±0.2 and 86±1.78 in leukemia patients which significantly increased to 10.43±1.87, 8.8±1.22, 5.1±0.96 and 108±1.90 for the same patients after BMT, respectively. It is mean that treatment of leukemia patients by BMT leads to increase the activities of Hb, WBCs, Lymphoblasts and glucose in by the rates of 39.07, 400, 200 and 25.58%, respectively.

Table 3. CBC and Glucose level of leukemia patients before and after bone marrow transplantation, PMT (n=40, data expressed as mean± SD)

Parameter	Leukemia patients before BMT	Leukemia patients after BMT	Compare before to after (%)	Ref. Range
Hb (g/dL)	7.5±2.23 [b]	10.43±1.87 [a]	39.07	11.0-13.3
WBCs (10^3cell/ml)	1.76±2.08 [b]	8.8±1.22 [a]	400	4.5-10.5
Lymphoblasts	1700±2.82 [b]	5100±2.51 [a]	200	6000-9000
Lymphoblasts %	1.7±0.2 [b]	5.1±0.96 [a]	200	6-9
Glucose (mg/dL)	86±1.78 [b]	108±1.90 [a]	25.58	70-110

* Mean values in the same raw bearing different superscript letters are significantly different at P<0.05.

Such as mentioned by Ann *et al.*, (2002) measurement of Hgb, the concentration of oxygen carrying protein, is a more sensitive and direct test for many diseases including leukemia. Treatment of leukemia patients by BMT leads to increase Hb that carry oxygen and other materials to all tissues of the body. Also, Manisha (2012) reported that leukemia is a neoplastic proliferation of one particular cell type (granulocytes, monocytes, lymphocytes or infrequently RBCs). The defect originates in hematopoietic stem cell, the myeloid, or lymphoid cells.leukocytosis refers to an increased level of leukocytes in circulation. Treatment of leukemia patients by BMT leads to increase in WBCs (leukocytes), cells that help make up the body' defense mechanism. Also, the present data reported that treatment of leukemia patients by BMT leads to increase the level of serum glucose but in the normal range (70-110 mg/dL).

Serum iron and ferritin levels of leukemia patients before and after bone marrow transplantation

Data of the iron and ferritin levels among leukemia patients before and after BMT are shown in Table (4). From such data it could be noticed that the mean of iron (µg/dL) and ferritin (%) levels were 51.33±12.28 and 42.78±9.58 in leukemia patients which significantly increased to 97.51±46.76 and and 42.78±9.58 for the same patients after BMT, respectively. It is mean that treatment of leukemia patients by BMT leads to increase the levels of serum iron and ferritin by the rates of 89.97 and 197.41%, respectively.

Table (4): Iron and ferritin levels of leukemia patients before and after bone marrow transplantation, PMT (n=40, data expressed as mean ± SD)

Parameter	Leukemia patients before BMT	Leukemia patients after BMT	Compare before to after (%)	Ref. Range
Serum iron (µg/dL)	51.33±12.28 [b]	97.51±36.76 [a]	89.97	65 to 176
Serum ferritin (µg/L)	22.78±9.58 [b]	87.23±31.90 [a]	282.92	30–300

* Mean values in the same raw bearing different superscript letters are significantly different at P<0.05

Such as mentioned by Fairbanks (1991) serum iron concentration can be measured directly and generally decreases as iron stores are depleted. However, serum iron may not reflect iron stores accurately

because it is influenced by several additional factors, including iron absorption from meals, infection, inflammation, and diurnal variation (Oski, 1993). On the other side, ferritin is a storage compound for iron, and serum ferritin levels normally correlate with total iron stores. As iron stores are depleted, serum ferritin levels decline and are the earliest marker of iron deficiency (Ann *et al.,* 2002). Serum ferritin has high specificity for iron deficiency, especially when combined with other markers such as Hb. In addition, serum ferritin is an acute-phase reactant that can become elevated in the setting of inflammation, chronic infection, or other diseases (Fairbanks, 1991 and Oski, 1993).

Conclusion

It could be concluded that the leukemia patients are suffered from malnutrition. This is confirmed by the results of this study, which showed that leukemia injury causes' depletion in food intake of different macro and micronutrients. All of these data are going in concomitant with the decreasing of some hematological parameters related to the nutrition status. The challenge of addressing the problem therefore remains an urgent imperative for development and need further studies.

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تقييم الحالة الغذائية لمرضى اللوكيميا قبل وبعد زراعة نخاع العظام

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الملخص العربى:

تسبب عمليات زراعة نخاع العظام وما يتعلق بها من مضاعفات فى العديد من التأثيرات الجانبية بالقناة الهضمية والتى تؤدى الى سوء التغذية وما يرتبط به من مشكلات تتعلق بالإعتلال الصحى والوفيات. لذلك أجريت الدراسة الحالية بهدف تقييم الحالة الغذائية لمرضى اللوكيميا قبل وبعد زراعة نخاع العظام. حيث تم إعداد عينة فوامه ٤٩ مريضا باللوكيميا من مستشفى معهد ناصر بالقاهرة- مصر ، واصل فى الدراسة ٤٠ مريضا منهم وبالباقى ٩ حالات تم إستبعادهم لعدم إنتظامهم فى الدراسة وعدم إكتمال البيانات والنتائج المتعلقة بهم. تراوحت أعما الحالات المرضية (٣١,١٧-٥٣,٤٣ عاما) ومتوسط عمر ٤٥,٦٠ عاما، كما مثلت نسبة الذكور بالعينة ٢٩ حالة (نسبة ٧٢,٥٠%) والإناث ١١ حالة (٢٧,٥٠%). ولقد أوضحت النتائج أن جميع مرضى اللوكيميا بالعينة الواقعة تحت الدراسة يعانون من سوء التغذية والتى تأكد من خلال نقص الداخل من الغذاء من كافة المغذيات الكبرى والصغرى. ولقد تلازم مع هذا الأمر حدوث نقص فى بعض مقاييس الدم التى لها علاقة وثيقة بالحالة الغذائية. وبالتالي فإن التحدي المتمثل في معالجة تلك المشكلة (سوء التغذية لمرضى اللوكيميا) يبقى ضرورة ملحة للتنمية الصحية والتى تحتاج الى دراسات عديدة فى المستقبل.

الكلمات المفتاحية: اللوكيميا- الداخل من الغذاء- معدل كتلة الجسم - الفيتامينات- الحديد- الفريتين.