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RESEARCH ARTICLE

The positive effects of Mediterranean-neutropenic diet on nutritional status of acute myeloid leukemia patients under chemotherapy

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INTRODUCTION: Cancer and chemotherapy-induced malnutrition increase death, reduce the response to treatment, and increase multiple kinds of side effects. The aim of this study was to investigate the effects of Mediterranean-neutropenic diet on the nutritional status of acute myeloid leukemia patients under chemotherapy.
MATERIALS AND METHODS: 50 patients were divided into two groups by a random allocation scheme: the Mediterranean-neutropenic diet (n = 25) and the neutropenic diet group (n = 25). The intervention was implemented during a one month period. The nutritional status was evaluated based on PG-SGA. Serum albumin levels and dietary intake were also measured.
RESULTS: After the intervention, the mean serum albumin level in the intervention group was significantly higher than the beginning of the study (p = 0.09) and in comparison with the control group (p = 0.01). Also, the mean serum albumin level in the control group significantly decreased at the end of the study compared to the beginning of the study (p = 0.03). After intervention, the nutritional status of the patients in the intervention group was significantly improved compared to the control group.
CONCLUSION: In general, based on the results of this study, the Mediterranean neutropenic diet improves nutritional status during chemotherapy by increasing food intake, preventing weight loss and increasing serum albumin levels

Keywords nutritional status, Mediterranean diet, neutropenic diet, AML, chemotherapy

Introduction

Malnutrition is a common side effect of chemotherapy among patients with cancer (Zarif Yeganeh et al., 2007; Turedi et al., 2010). Studies have suggested that 20% of deaths in these patients are due to malnutrition (Bauer et al., 2002; Khoshnevis et al., 2012). Quality of life may also detoriate due to various factors including appetite loss and weight loss. All of these may lead to impairments of the immune system responses resulting in an increase of the risk of infections (Oliva et al., 2011; Buckley et al., 2017; Tinsley et al., 2017). Prognosis in leukemia is directly related to the incidence and severity of weight loss. It is observed that a weight loss of 5% may increase side effects of cancer therapy, delay response to treatment, increase hospitalization duration, long last disease and higher mortality rate (Khoshnevis et al., 2012). Long duration of untreated weight loss may lead to cachexia which decreases the chance of survival and increases the mortality rate. About 2 million patients die as a result of cachexia every year. By running nutritional screening and nutritional assessments for patient when referring to health care centers and during treatment process, patients with malnutrition may be diagnosed and clinical symptoms, quality of life, medication efficacy and response to treatment will improve as a results of nutritional-interventional strategies which result in lower costs(Owens et al., 2013). Among standardized questionnaires for nutritional assessment, PG-SGA is the easiest to be completed by patients. It is also the most valid and specific tool for screening patients with cancer.

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As Mediterranean dietary pattern is based on olive oil, fruits and vegetables, whole grains, legume, fish and low fat diary consumption, high fiber and low glycemic index contents, it shows anti-inflammatory and antioxidant beneficial effects on cancer prevention (Martinez-Gonzalez et al., 2012; Agnoli et al., 2013; Richard et al., 2013; Filomeno et al., 2014; Rotelli et al., 2015; Ostan et al., 2015). This study was aimed to evaluate the effect of Mediterraneandiet on nutritional status in patients with AML undergoing chemotherapy.

Methods

Sampling

Participants were selected among patients who referred to oncology department of Shariati hospital in Tehran with AML diagnosis approved by hematologist. 50 Patients were assigned to two groups of 25 each by simple random method allocation. After completing informed consent form the intervention started to last for a month.

Dietary intake assessment

Calorie, carbohydrate, protein and fat intake was assessed by nutritionist interviewer using 3 days food record questionnaire for each patient, before and after intervention. Data from questionnaires were analyzed using Nutritionist 4 software.

Anthropometric assessment

Before and after intervention, patient's bodyweight was measured using scale with the precison of 1000 g with the lightest cloths and height was measured using meter with the precison of 0.5 cm without shoes. BMI was then calculated for each participant using formula (Rasool et al., 2015).

Nutritional assessment

For evaluating malnutrition and its severity, PG-SGA questionnaire was translated to Persian under nutritionist and oncologist supervision. The variables were weight loss, changes in dietary intake, nutrition related complaints, physical activity status and patient's clinical examinations. Weight loss within first or 6 past months was calculated according to the questionnaire manual. Nutritional complaints and adipose tissue examination scores were categorized as following: > 6 for severe problems, 3-6 for moderate and < 3 for mild problems. Weight loss was determined within the past month and in case of determining weight loss within the past 6 month, $> 20\%$, 10%-20%, 5%-10% and $< 5\%$ were the divisions. Required interventions were taken according to questionnaire manual which were defined in 3 levels, A (for appropriate nutrition), B (prone to malnutrition) and C (severe malnutrition) (Khoshnevis et al., 2012).

Serum albumin measurement

Blood samples were taken before and after intervention to measure serum albumin level after centrifuge and serum separation in −80°C. Serum albumin level was measured using coloring method with Zellbio Germany company kit with the precison of 0.3 gr/dl.

Diet

Patients were under nutritionist's supervision in Shariati hospital oncology department. For intervention group, Mediterranean diet with 47% carbohydrate, 15% protein and 38% fat (24% MUFAs especially olive oil) was administered (Lopez-Moreno et al., 2016). Patients in intervention group consumed 30 ml olive oil daily for four weeks. Patients in control group received neutropenic diet which is the common dietary pattern in cancer, including cooked foods and vegetables, raw fruits like banana and orange, boiled water, pasteurized and packed dairy products and well cooked meat and egg. The calorie intake in control group was similar to intervention group (Lassiter et al., 2015; Sonbol eet al., 2015). Required calorie for weight maintenance was calculated using Mifflin formula with appropriate physical activity and stress factor.

Data analysis

Date was processed by SPSS software. Quantitive and qualitive variables were reported as means and standard deviation, number and percent, respectively. To determine the effect of intervention according to variables, *t*-test and paired *t*-test or chi-square were used.

Ethical issues

The study protocol was approved by Nutrition Research Institute ethical committee.

Results

The average participant's age in intervention group was 41.2 ± 14.2 and in control group was 40.8 ± 12.7 years. Participant's basic information is shown in Table 1. There was no significant difference between age, bodyweight, height, BMI and gender within the both groups.

The average of serum albumin level before and after the intervention is demonstrated in Table 2. There was no significant difference in serum albumin level at the beginning of the study. After intervention, serum albumin level increased significantly in intervention group in comparison to control group (p-value = 0.01). The serum albumin level decreased significantly in control group at the end of study (p-value = 0.03).

Table 3 shows the average of participant's calorie and

Table 1 participant's basic information in intervention and control group before and after intervention

Variables*	Mediterian-neutropenic group	Control group	p value$^{€\#}$
Number	25	25	
Male	15 (60%)	14 (56)	0/7
Female	10 (40%)	11(44%)	
Age (yrs)	41±14/3	40±12/8	0/9
Height (cm)	167/3±0/8	169/6±8/95	0/35
Weight (kg)	69/41±11/3	74/78±11/94	0/1
BMI (kg/m^2)	24/74±3/63	26/21±5	0/23

* data are shown as average±SD
# t-test
€ p-value⩽0.05 is significant

Table 2 serum albumin level before and after intervention

variable*	Intervention group	Control group	p value$^{\#€}$
Albumin (gr/dlit)			
Before intervention	3/28±0/6	3/51±0/79	0/25
After intervention	3/55±0/79	3/09±0/5	0/01
p value^{β}	0/09	0/03	

* data are shown as average±SD
# t-test
β paired t-test
€ p-value⩽0.05 is significant

Table 3 participant's calorie and macronutrients intake

variable*	Intervention group	Control group	p value$^{\#€}$
Energy (kcal)			
Before intervention	1090/6±402/79	1174/95±410/88	0/46
After intervention	1430/6±488/8	1270/22±319/49	0/17
p value^{β}	$>$0/001	0/33	
Protein (gr)			
Before intervention	56/95±19/71	56/29±19/14	0/9
After intervention	72/2±24/12	64/82±21/56	0/26
P value	0/001	0/2	
Carbohydrate (gr)			
Before intervention	169/54±75/06	179/19±68/27	0/63
After intervention	198/77±69/22	176/86±58/72	0/22
P value	0/04	0/91	
Total fat (gr)			
Before intervention	30/49±15/27	30/26±11/15	0/95
After intervention	42/8±9/86	33/46±9/7	$>$0/001
p value	$>$0/001	0/39	

* data are shown as average±SD
# t-test
β paired t-test
€ p-value⩽0.05 is significant

macronutrients intake. There was no significant difference between diet components intake in the two groups at the beginning of the study, although there was a significant difference in total fat intake within groups at the end. Moreover, there was a significant difference in total calorie, carbohydrate, protein and fat intake in control group at the beginning and the end of study.

The anthropometric data and nutritional status at the beginning and the end of the study are shown in Table 4 and Table 5, respectively. There was no significant difference in BMI and nutritional status between the groups at first but there was a significant improvement in mentioned factors in intervention group after the intervention was finished.

Table 4 bodyweight, BMI before and after intervention

variable*	Intervention group	Control group	*p* value#€
Weight(*Mean*±*SD*)			
Before intervention	69/41±11/3	74/78±11/94	0/1
After intervention	70/3±11/74	71/38±12/64	0/75
p valueβ	0/049	0/13	
BMI			
Before intervention	24/74±3/63	26/21±5	0/23
After intervention	25/09±4/02	24/69±4/76	0/89
p value	0/03	0/12	

*, data are shown as average±SD
#, *t*-test
β, paired *t*-test
€, *p*-value⩽0.05 is significant

Table 5 nutritional status before and after intervention

variable*	Intervention group	Control group	*p* value μ€
Nutritional status			0/6
Before intervention			
appropriate	8(32%)	5(20%)	
Prone to malnutrition	8(32%)	10(40%)	
severe	9(36%)	10(40%)	
After intervention			0/001 <
appropriate	(76%)19	1(4%)	
Prone to malnutrition	5(20%)	6(24%)	
sever	1(4%)	18(72%)	

*, data are shown as number and percent
μ, Chi-square test
€, *p*-value⩽0.05 is significant

Discussion

This study was the first study to evaluate the effect of Mediterranean-neutropenic diet on nutritional status in patients with AML undergoing chemotherapy. There are lack of sufficient studies in Iran on nutritional status of AML patient's undergoing chemotherapy hence there are no data the prevalence of malnutrition and nutritional status (Zarif Yeganeh et al., 2007; Khoshnevis et al., 2012; Esfahani eet al., 2014). Mediterranean diet components include antioxidants, unsaturated fatty acids, fiber and vitamin C which have beneficial effects in cancer prevention and protection (Benetou et al., 2008; Grosso et al., 2013; D'Alessandro et al., 2016). The objectives of this study were to evaluate 1) nutritional status and 2) the effect of Mediterranean-neutropenic diet on nutritional status in patients with AML undergoing chemotherapy. Our results have suggested that Mediterranean-neutropenic diet may improve anthropometric indices, nutritional status and dietary intake in patients with AML. Turedi et al. (2010) have suggested that malnutrition prevalence is high in patients with leukemia and takes a growing trend after chemotherapy. Sarvarian's et al. study in Tehran has indicated that the prevalence of malnutrition is high in patients with cancer and treated by chemotherapy and Mediterranean diet improved nutritional status in these patients significantly (Sarvarian et al., 2013).

There was a significant difference in total fat intake between two groups at the end of our study. Also, the results have suggested significant difference between calorie, carbohydrate, protein and fat intake in the intervention group at the beginning and the end of intervention. The intake of calorie and other macronutrients increased in control group, but was not significant. The increase in calorie and fat intake in intervention group may be due to olive oil consumption, but is seems that olive oil was did not just increase calorie intake, but also increased intake of other macronutrients which may be a result of appetite improvement.

Chemotherapy independently, and combined with radiotherapy and surgery, is an effective treatment for cancer (Beer and Bubalo, 2004; Held-Warmkessel, 2011). Chemotherapy may leads to mouth sores, xeserostoma, nausea, vomiting and appetite loss which can increase the risk of malnutrition. Chemotherapy and malnutrition can decrease the level of serum albumin level (Khoshnevis et al., 2012; Fazeli et al., 2013). Esfahani et.al, have evaluated the nutritional status of patients with leukemia undergoing chemotherapy and have suggested that serum albumin level was less than 3.5 in

42.5% of patients. Moreover, albumin level was below 3.5 in 62.6% of patients after chemotherapy. Sanchez et.al have assessed the biochemical and immunological profile of patients with AML concluding that serum albumin level was significantly lower in comparison to healthy subjects (Sanches et al., 2015). In this study, the serum albumin level has significantly increased after intervention, although there was a significant decrease in control group. Decrease in albumin serum level needs nutritional interventions. The improvement of serum albumin level in intervention group showed the efficacy of Mediterranean diet.

The results from this study have indicated that patient's bodyweight in intervention group has increased significantly which was not compatible to results from other studies and may be due to participant's variation, as participants from other studies were obese or with diabetes or metabolic syndrome but our participants were patients with AML (Esposito et al., 2011).

In conclusion, malnutrition has a high prevalence in patients who receive only neutropenic diet. Serum albumin level decreases during chemotherapy. Mediterranean-neutropenic diet may improve nutritional status during chemotherapy by increasing food intake, prevention of weight loss and increasing serum albumin level. Further studies are needed to approve this fact.

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