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Randomized Study of the Effect of Dietary Counseling During Adjuvant Chemotherapy on Chemotherapy Induced Nausea and Vomiting, and Quality of Life in Patients With Breast Cancer

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ABSTRACT

Patients with breast cancer (PsBC) usually face with chemotherapy induced nausea and vomiting (CINV). The aim of this study was to assess the impact of nutritional counseling on CINV and quality of life (QoL) of PsBC. 150 PsBC were randomly assigned for receiving a personalized diet, which contained 1.2–1.5 g/kg of protein, 30% of energy from fat and 55–60% of energy from carbohydrate, a face to face nutrition education, and a pamphlet which contained beneficial nutrition information to reduce the severity of CINV before each chemotherapy session for three times ($n = 75$) or regular care ($n = 75$). CINV, QoL, and dietary intake were evaluated after each chemotherapy session. Nausea rating index, overall nausea index, and visual analog scale ($P < 0.001$) were dramatically lower in the intervention group. Global health status/QoL as well as physical functioning, role functioning, emotional functioning, and cognitive functioning ($P < 0.001$) were significantly better in the intervention group. Patients in the control group experienced more fatigue, nausea and vomiting, pain, dyspnea, loss of appetite, constipation, and diarrhea ($P < 0.001$). Nutrition counseling during adjuvant chemotherapy among PsBC reduced the occurrence of CINV and led to significant improvements in the QoL.

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Introduction

Many types of treatments for cancer, such as surgery, chemotherapy, and radiotherapy have several chronic and acute side effects that might endanger the nutritional status of patients (1). Chemotherapy, which is one of the common therapies for cancers, causes many complications such as nausea, vomiting, diarrhea, constipation, appetite changes, anorexia, and food distress which all can lead to malnutrition (2). Furthermore, chemotherapy may affect the QoL of patients with breast cancer (PsBC), including functional dimensions such as physical, emotional and role functioning as well as fatigue, pain, dyspnea, and gastrointestinal symptoms including nausea, vomiting, diarrhea, or constipation (3,4).

Meanwhile, chemotherapy induced nausea and vomiting (CINV) might be associated with serious complications such as weakness, weight loss, electrolyte imbalance, esophageal rupture, dehydration, or anorexia (5). Further, CINV has found to have significant negative effects on QoL of patients undergoing chemotherapy, which could be a major barrier to the effective chemotherapy treatment (6,7). Indeed, patients with dehydration, disability, malnutrition, electrolyte imbalance, or those who have undergone surgery or radiotherapy might be more exposed to the serious complications of CINV (6,8). Moreover, other risk factors may increase the likelihood of CINV such as individuals under the age of 50 yr, female gender as well as a history of alcohol consumption, vomiting following a previous chemotherapy, motion sickness, vomiting, and nausea during pregnancy and anxiety (7,9).

Despite the dramatic improvements that have been made in cancer treatment over the past 30 yr as well as the administration of antinausea drugs during

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chemotherapy, vomiting and in particular nausea are still two of the most uncomfortable chemotherapy complications in cancer treatment. 30% of patients still experience CINV, thus, these two common side effects require more control and further investigations (5,8–10).

Detailed information on dietary changes and nutritional status of patients undergoing chemotherapy can help to modify the recommended guidelines during chemotherapy (11–13). Nutrition education for patients with cancer before the initiation of chemotherapy would increase their compatibility with new conditions and possible complications of treatment. Studies have shown that providing useful and effective information to patients with cancer would have positive consequences which can reduce the related symptoms such as anxiety, depression, pain, nausea, and vomiting or improve compliance and thus, create realistic expectations as well as promoting self-care (11,13). According to a study by Hartmuller, nearly half of patients with cancer had not received any nutritional counseling from the health care professionals (11). A recent study found that instructional DVDs for nutritional education after chemotherapy would increase the awareness and management skills for encountering the chemotherapy complications among patients (14–16).

However, there were no studies that have evaluated the effects of individual nutritional education for women with breast cancer during chemotherapy.

The aim of this study was to elucidate the impact of nutritional education during adjuvant chemotherapy in PsBC on CINV and QoL.

Materials and Method

Study Design and Subjects

The present study was a single-center, single blind, and randomized controlled clinical trial. Recruitment took place in Breast Cancer Research Center in Tehran, Iran, between January 2016 and January 2017. This study was conducted according to the guidelines laid down in the Declaration of Helsinki. The study protocol was approved by the Research Committee of Ethics in Breast Cancer Research Center, Tehran, Iran (IR.ACECR.IBCRC.REC.1394.41) and was registered at the Iranian Registry of Clinical Trials (IRCT) with the code number IRCT2016111823861N3 which is available at: http://irct.ir/user/trial/20288/view. All enrolled patients provided written informed consent.

PsBC scheduled to receive adjuvant chemotherapy consisting of doxorubicin, cyclophosphamide and docetaxel were eligible to participate. Patients received a standard regime with intravenous antiemetic during each cycle of chemotherapy on day 1 before the start (3 mg granisetron and 8 mg dexamethasone), 8 mg dexamethasone on days 1, 2, and 3 after chemotherapy.

The 18 to 60-yr-old female patients who met the following criteria were considered eligible for the study. 1) Patients with histopathologically confirmed breast cancer. 2) Patients who passed their breast surgery, including lumpectomy, mastectomy and etc. 3) Females whose breast cancer disease were at stage IA to IIIB but without distant organ metastasis. 4) Females who currently received at least one adjuvant chemotherapy. 5) Patients who were treated with 3-weekly cycles of chemotherapy. 6) Patients who had experienced vomiting during or after the previous sessions of chemotherapy. 7) Patients with normal biochemical functional tests including leukocyte and platelet counts more than 3,500/mm^3 and 100,000/mm^3, respectively, aspartate aminotransferase and alanine aminotransferase concentrations under the 2.5 times of the upper limit range, total bilirubin level under 1.8 mg/dl, and serum creatinine level below 1.3 mg/dl. 8) Individuals who were able to complete the study questionnaires.

Patients with mental disability and/or emesis-inducing diseases such as hypertension, liver, and renal failure as well as patients who received other antiemetic drugs or therapeutic methods except the routine antiemetic including aprepitant, dexamethasone, and granisetron, patients suffered from cancer cachexia, and patients who refused to continue their participation were excluded from the trial.

Since all subjects in this study have experienced nausea and vomiting during the previous chemotherapy period(s), our objects were to decrease nausea and vomiting trend and improve quality of life trend during the three chemotherapy courses in the intervention group compared with control.

Randomization and Allocation Concealment

The randomization assignment was performed using a computer-generated random numbers. Patients were randomly allocated into two groups, however, concealment was not possible. Patients and observers were not blind to the intervention, while the analyzer was blinded to the study procedures.

Nutritional Intervention

Individuals in the intervention group received a personalized diet by a trained dietitian before each chemotherapy session. The related daily diet was estimated individually based on each subject's age, current weight, and height before the subsequent session of chemotherapy and contained 1.2–1.5 g/kg of protein, 30% of energy from fat, which mainly consisted of mono- and poly-unsaturated fatty acids and 55–60% of energy from carbohydrate that consisted mainly of whole grain (1,2).

Moreover, a face to face nutrition education was performed by the trained dietitian among patients in the intervention group in 1 h prior to the beginning of each chemotherapy session, in order to reduce CINV.

Nutrition education included the following points: eating small meals frequently, consuming cold foods or foods that were kept at room temperature. Avoid having meals in any warm places, rinsing mouth before and after each meal, sitting up or lying back with their head raised for at least an hour after every meal, avoid eating spicy, very sweet, greasy, or fried foods. Consuming blended, soft and easy-to-digest foods in the scheduled times for chemotherapy treatment, having foods without any strong smell. Eating liquids with ice chips or frozen juice chips, drinking clear, and cold liquids such as ginger ale, apple juice, broth, and tea as well as sucking on hard candy with pleasant smells for example lemon drops or mints which help them to get rid of bad tastes. Having slow and deep breaths along with relaxation after every chemotherapy. If patients developed a dislike for red meat and meat broths during their treatments, they were advised to have other protein sources such as fish, chicken, beans, and nuts (3–5).

A pamphlet was also given to patients in the intervention group which contained beneficial nutritional information to reduce the severity of chemotherapy induced nausea and vomiting. The related specific dietary regimen and nutritional education were given to the intervention group for three periods.

Individuals in the control group followed a usual diet based on their food patterns, regular chemotherapy drug regimen without having any pamphlet, nutritional education and dietary intervention.

Nutrient intakes were derived using 3-day 24-h recall, including one weekend day and two weekdays and they were finally analyzed using Nutritionist IV software (First Databank, San Bruno, CA) modified for Iranian foods.

Outcome Measures

The Measurement of Nausea and Vomiting

To assess the levels of nausea and vomiting, patients were asked to fill out the McGill Questionnaires (6), after each of the three sessions of chemotherapy. The questionnaire consists of three indexes of nausea including two quantitative and one qualitative parameters. The quantitative components measure the intensity of nausea by a numeric-verbal rating, the overall nausea index (ONI) and a visual analog scale (VAS). The qualitative parameter, which is known as the nausea rating index (NRI), includes sets of verbal affective descriptors of nausea and the rank of each set increases with the severity. Every patient was asked to choose the word from each set that best described the severity of her nausea. The NRI score was also obtained by summing the rank values of the selected words bysubjects. The length of the line used in VAS was also measured in centimeters. Higher scores in ONI, VAS, and NRI parameters indicated that nausea and vomiting occurred in patients frequently and they suffered more from nausea and vomiting.

QoL Measurement

QoL was assessed by the European Organization for Research and Treatment for Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30).

The QLQ-C30 consists of nine multi-item scales, including a global health status/QoL scale, 5-functional scales and 9-symptom scales. The scales range from 0 to 100 and final scores are computed according to EORTC instructions (8). Higher scores of the global health and functional scales reflect better QoL in contrast to the symptom scales, in which the higher scores reflect worse QoL. EORTC QLQ-C30 questionnaires were given to the subjects after the first, second, and third session of chemotherapy.

The necessary education was provided to patients by the trained nutritionist in order to complete the McGill and QoL questionnaires. These questionnaires were filled up by patients at home and collected by the same trained nutritionist at the next chemotherapy session.

Anthropometric Measurement

Anthropometric measurements were done by the trained dietitian. Body weight was measured to the nearest 0.1 kg (Seca700) without heavy clothing. Height was evaluated to the nearest 0.5 cm in a standing position without shoes using a portable stadiometer (Seca700) and body mass index (BMI) was

calculated by dividing body weight (kg) by the squared of height (m^2).

Demographic data were collected by self-report, and medical data were abstracted from records.

Sample Size

The primary endpoints were any changes in CINV and the secondary endpoints were alterations in QoL dimensions.

The sample size calculation was determined based on a previous study (9), in which nausea and vomiting score of Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) was used as the key variable. A sample size of 124 subjects (62 in each group) was chosen to provide 80% power with alpha level of 0.05 to detect a mean difference of 0.7 (minimal importance change difference in nausea and vomiting) between the intervention and control groups. We predicted a probable loss to follow up about 20%, therefore, we considered 150subjects, which was 75 for each group.

Statistical Analyses

Kolmogorov-Smirnov test was used to assess the normality of distribution, all data were not normally distributed, except VAS and EF after the first session of chemotherapy and EF ($P = 0.1$) after the second session of chemotherapy and thus, non-parametric tests were used to compare the median values of variables. The quantitative variables are presented as median with in quartile range (IQR). The independent *t*-test was used to compare quantitative variables in two independent groups. We used Mann-Whitney, chi-square, Friedman's repeated, and repeated measure tests for analyzing the changes of outcomes during the three measurements in within group comparisons. Between-group differences were evaluated by Friedman's repeated test, repeated measure and generalized estimation equation (GEE). The difference in the mean distribution of age and BMI was assessed using Mann-Whitney test and the difference in the mean distribution of education, marital status and occupation was determined using chi-square test. Frequency distribution of baseline characteristics in between-group comparisons were measured with Mann-Whitney test, we also assessed the differences of macro- and micro-nutrient intakes of subjects between the two groups using repeated measures test. Changes in the QoL dimensions in the three measurements were assessed. Finally, *P*-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS, version 22.0.

Results

In this randomized clinical trial that was conducted between January 2015 and January 2016, one hundred fifty PsBC were randomized to either the dietary intervention group ($n = 75$) who received a specific dietary regimen, nutrition education and related pamphlet, or control group ($n = 75$) who followed a usual diet based on their food patterns, regular chemotherapy drug regimen without having any pamphlet, nutritional education, and dietary intervention.

Thirteen individuals dropped out before completing the intervention. The questionnaires could not be obtained completely from six subjects in the control group and four patients in the intervention group. Three individuals were also excluded due to their changed chemotherapy regimen and thus, 137 patients, including 70 patients in the intervention group and 67 patients in the control group were included in the final analysis (Fig. 1).

The characteristics of 137 subjects who completed the intervention are presented in Table 1.

The analysis of general characteristics showed no significant differences between the two groups. The majority of subjects were married in both groups (87% in the control vs. 91% in the intervention group, respectively). 61% and 80% of subjects in the control and intervention group were housewives, respectively.

Table 2 illustrates the amounts of energy intakes and nutrients. As it is shown, based on the 3-day food records, it was found that there were significant changes in the measures of protein ($P < 0.001$), fat ($P < 0.001$), SFA ($P = 0.005$), MUFA ($P < 0.001$), phosphor ($P < 0.001$), tryptophan ($P = 0.001$), and sodium ($P < 0.001$) in the intervention group during the three sessions of nutritional education. Further, between groups comparisons also showed significant differences for the previously mentioned nutrients.

The measures of NRI ($P < 0.001$), ONI ($P < 0.001$), and VAS ($P < 0.001$) were improved significantly during the three sessions of chemotherapy in the intervention group. Table 3 also illustrates that the measures of global health status/QoL ($\beta = 18.29$), NRI ($\beta = -2.15$), ONI ($\beta = -1.70$), and VAS ($\beta = -3.69$) were significantly improved in the intervention group compared to the control group ($P < 0.001$). Moreover, it was observed that the status of QoL, NRI, ONI, and VAS was much better among patients in the

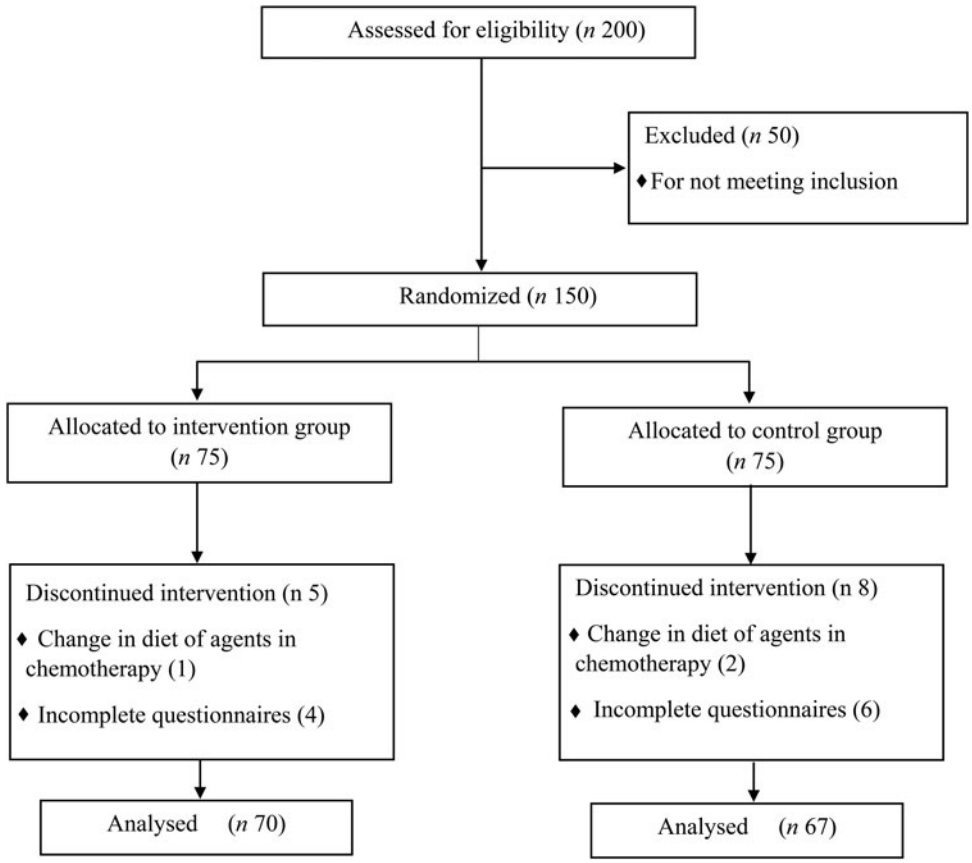

Figure 1. Flow diagram of the study.

Table 1. General characteristics of the subjects (*n* 137) (mean values and SDs).

	Control ($n=67$)		Intervention ($n=70$)		
	Mean	SD	Mean	SD	*P**
Age (yr)	46.0	8.8	46.9	12.4	0.98
Height (cm)	159.7	6.1	161.2	6.1	0.10
Weight (kg)	71.8	10.9	72.6	14.1	0.91
BMI (kg/m^2)	28.2	4.5	27.6	5	0.35

BMI, body mass index.
*Mean values were not significantly different between the groups for any of these variables (Mann-Whitney test)

intervention group in comparison to the control group, after each session of chemotherapy ($P<0.001$).

Table 4 shows the data for all functional and symptom scales of QoL assessment after the first, second and third session of chemotherapy in the two groups. As it is obvious, patients in the nutrition education group had better physical function ($\beta=16.68$, $P<0.001$), role function ($\beta=15.17$, $P<0.001$), emotional function ($\beta=16.72$, $P<0.001$), and cognitive function ($\beta=14.05$, $P<0.001$) than patients without nutritional education. Furthermore, patients in the intervention group experienced less fatigue ($\beta=-19.68$, $P<0.001$), nausea and vomiting ($\beta=-20.90$, $P<0.001$), pain ($\beta=-24.36$, $P<0.001$), dyspnea ($\beta=-12.86$, $P<0.001$), sleep loss ($\beta=-15.06$, $P<0.001$), appetite loss ($\beta=-21.11$, $P<0.001$), constipation ($\beta=-16.67$, $P<0.001$), and diarrhea ($\beta=-9.87$, $P<0.001$) than the control group.

Discussion

This randomized controlled trial demonstrated that individual nutritional counseling could reduce the severity of nausea which led to better Global health status/QoL and functional measures of QoL including physical, emotional, mental, social, and role play.

One of the major complications of chemotherapy is its possible negative impact on QoL among patients with various types of cancers (10,11) such as breast cancer (12,13). Similar to our findings related to QoL, Leinert et al. (12) reported that global health status was notably reduced in 4 wk after the chemotherapy initiation in PsBC.

CINV was reported to have a negative impact on QoL (14–16) and conducting new non-pharmacological and nutritional interventions have found to be important in the management of CINV (11). Regarding that, the present study showed that nutrition education could reduce CINV, which

Table 2. Dietary intakes of subjects throughout the study (mean values and SDs).

		Chemotherapy sessions							
		C1		C2		C3			
	Groups	Mean	SD	Mean	SD	Mean	SD	P^a	P^b
Energy (kcal/day)	Control	994.6	195	1001.2	238	1020.5	220	0.49	0.08
	Intervention	1051.0	185	993.5	132	1010.5	200	0.06	
Carbohydrate (g/day)	Control	124.1	28	127.2	36	129.9	35	0.35	0.68
	Intervention	126.3	32	131.9	22	129.5	27	0.46	
Protein (g/day)	Control	36.7	8	36.7	10	37.3	11	0.85	0.002
	Intervention	40.5	11	34.3	8	37.2	9	<0.001	
Fat (g/day)	Control	41.2	11	40.4	11	41.2	10	0.75	0.01
	Intervention	44.6	8	38.2	9	41.4	12	<0.001	
SFA (g/day)	Control	10.4	3	10.3	4	11.0	4	0.43	0.03
	Intervention	12.2	3	9.9	5	10.8	6	0.005	
MUFA (g/day)	Control	16.3	4	16.4	5	16.3	4	0.96	0.004
	Intervention	17.6	3	14.9	3	16.5	5	<0.001	
PUFA (g/day)	Control	10.8	2	10.7	3	10.6	2	0.77	0.26
	Intervention	11.4	2	10.5	2	11.2	2	0.11	
Cholesterol (mg/day)	Control	114.2	71	112.8	71	131.6	76	0.11	0.34
	Intervention	129.0	62	112.4	61	127.1	71	0.17	
Dietary fiber (g/day)	Control	8.8	2	8.6	2	9.0	3	0.54	0.61
	Intervention	9.8	9	8.5	2	9.7	7	0.44	
K (mg/d)	Control	1346.0	354	1286.1	369	1380.1	402	0.11	0.23
	Intervention	1423.6	436	1308.0	328	1338.2	352	0.08	
P (mg/day)	Control	526.3	151	539.5	177	539.6	179	0.75	0.001
	Intervention	603.3	160	508.0	148	537.8	159	<0.001	
Pyridoxine (mg/day)	Control	0.8	0.3	0.7	0.3	0.8	0.4	0.13	0.81
	Intervention	0.8	0.3	0.8	0.3	0.8	0.3	0.11	
Tryptophan (mg/day)	Control	341.1	107	331.2	115	337.9	116	0.78	0.04
	Intervention	385.5	147	323.1	101	355.6	111	0.001	
Na (mg/d)	Control	557.6	244	484.2	272	557.5	266	0.07	0.01
	Intervention	583.9	223	459.1	221	453.8	224	<0.001	
Mg (mg/day)	Control	124.5	33	125.9	42	123.9	44	0.90	0.21
	Intervention	137.0	63	122.0	37	131.5	57	0.19	
Zn (mg/day)	Control	4.1	1	4.2	1	4.4	1	0.11	0.34
	Intervention	5.1	2	3.9	1	6.1	12	0.26	

C1: after the first session of chemotherapy. C2: after the second session of chemotherapy. C3: after the third session of chemotherapy.
SFA, saturated fatty acids. MUFA, monounsaturated fatty acids. PUFA, polyunsaturated fatty acids. K, potassium. Ca, calcium. P, phosphor. Na, sodium. Mg, magnesium. Zn, zinc.
[a]Within group effect (repeated measures test).
[b]Between groups effect (repeated measures test).

Table 3. Effect of nutrition education during the chemotherapy on global health status, NRI, ONI and VAS in patients with breast cancer (median (Q1, Q3), βs and their standard errors).

		Chemotherapy sessions						
	Groups	C1 Median (Q1, Q3)	C2 Median (Q1, Q3)	C3 Median (Q1, Q3)	P^a	β^b	SE^b	P^b
QoL	Control[c]	50 (41.6, 58.3)	50 (33.3, 58.3)	50 (33.3, 58.3)	0.11	18.29	3.00	<0.001
	Intervention	66.6 (50, 83.3)	66.6 (41.6, 83.3)	66.6 (47.9, 83.3)	0.17			
Mcgill index								
NRI	Control[c]	3 (1, 6)	3 (2, 6)	4 (2, 6)	0.60	−2.15	0.30	<0.001
	Intervention	2 (1, 4.7)	1 (0.2, 2.7)	1 (0, 2)	<0.001			
ONI	Control[c]	3 (2, 4)	3 (2, 4)	3 (2, 4)	0.78	−1.70	0.10	<0.001
	Intervention	2 (1, 2)	1 (1, 2)	1 (0, 1)	<0.001			
VAS	Control[c]	6 (4.5, 8.5)	6.5 (4, 8.5)	6.5 (4.5, 9)	0.15	−3.69	0.30	<0.001
	Intervention	3.7 (2, 5)	2 (1, 3.3)	1 (0, 2.5)	<0.001			

C1= after the first session of chemotherapy. C2 = after the second session of chemotherapy. C3 = after the third session of chemotherapy.
QL, global health status/QoL. NRI, nausea rating index. ONI, overall nausea index. VAS, visual analog scale.
[a]Obtained from Friedman test.
[b]Obtained from GEE model.
[c]For QL (intervention $n = 70$, control $n = 67$) for Mcgill (intervention $n = 60$, control $n = 67$).

consequently led to advantageous impacts on QoL among PsBC. Moreover, Ravasco et al. (17,18) proved the role of nutrition as a key factor in the status of QoL in patients with cancer. They have reported that although the stage of cancer would be one of the main determinants of QoL, the effect of nutrition on QoL among these patients was much more important.

Table 4. EORTC QLQ-C30 mean scores after nutrition education during chemotherapy in patients with breast cancer using GEE model (median (Q1, Q3), βs and their standard errors).

		Chemotherapy sessions						
		C1 Median (Q1, Q3)	C2 Median (Q1, Q3)	C3 Median (Q1, Q3)	P^a	β^b	SE^b	P^b
QoL[c]	Control	50 (41.6, 58.3)	50 (33.3, 58.3)	50 (33.3, 58.3)	0.11	18.2	3.0	<0.001
	Intervention	66.6 (50, 83.3)	66.6 (41.6, 83.3)	66.6 (48, 83.3)	0.17			
Functioning scales								
PF[c]	Control	66.6 (53.3, 86.6)	73.3 (53.3, 80)	60 (46.6, 73.3)	0.006	16.6	2.3	<0.001
	Intervention	86.6 (73.3, 100)	80 (66.6, 93.3)	83.3 (73.3, 93.3)	0.10			
RF[c]	Control	66.6 (33.3, 83.3)	66.6 (50, 83.3)	66.6 (33.3, 66.6)	0.13	15.1	3.0	<0.001
	Intervention	83.3 (66.6, 100)	83.3 (66.6, 100)	75 (66.6, 100)	0.35			
EF[c]	Control	58.3 (33.3, 75)	58.3 (41.6, 75)	58.3 (41.6, 66.6)	0.48	16.7	3.1	<0.001
	Intervention	75 (58.3, 100)	66.6 (56.2, 83.3)	66.6 (50, 83.3)	0.08			
CF[c]	Control	83.3 (66.6, 100)	83.3 (66.6, 100)	66.6 (66.6, 83.3)	<0.001	14.0	2.5	<0.001
	Intervention	100 (83.3, 100)	100 (83.3, 100)	100 (83.3, 100)	0.04			
Symptom scales								
FA[d]	Control	44.4 (33.3, 66.6)	55.5 (33.3, 66.6)	55.5 (33.3, 77.7)	0.11	−19.6	2.8	<0.001
	Intervention	33.3 (22.2, 44.4)	33.3 (22.2, 55.5)	33.3 (22.2, 44.4)	0.08			
NV[d]	Control	33.3 (16.6, 50)	33.3 (16.6, 50)	33.3 (16.6, 50)	0.20	−20.9	2.4	<0.001
	Intervention	0 (0, 16.6)	0 (0, 16.6)	0 (0, 16.6)	0.9			
PA[d]	Control	33.3 (16.6, 50)	33.3 (33.3, 50)	50 (33.3, 66.6)	0.01	−24.3	2.8	<0.001
	Intervention	16.6 (0, 33.3)	33.3 (0, 33.3)	33.3 (0, 33.3)	0.93			
DY[d]	Control	0 (0, 3.3)	33.3 (0, 33.3)	33.3 (0, 33.3)	0.05	−12.8	2.6	<0.001
	Intervention	0 (0, 33.3)	0 (0, 33.3)	0 (0, 0)	0.25			
SL[d]	Control	33.3 (0, 66.6)	33.3 (33.3, 66.6)	33.3 (33.3, 66.6)	0.47	−15.0	3.5	<0.001
	Intervention	33.3 (0, 33.3)	33.3 (0, 66.6)	33.3 (0, 33.3)	0.12			
AP[d]	Control	33.3 (0, 66.6)	33.3 (33.3, 66.6)	33.3 (33.3, 66.6)	0.17	−21.1	3.7	<0.001
	Intervention	33.3 (0, 33.3)	33.3 (0, 33.3)	33.3 (0, 33.3)	0.95			
CO[d]	Control	33.3 (0, 33.3)	33.3 (0, 33.3)	33.3 (0, 33.3)	0.85	−16.6	2.9	<0.001
	Intervention	0 (0, 33.3)	0 (0, 33.3)	0 (0, 33.3)	0.67			
DI[d]	Control	0 (0, 33.3)	0 (0, 33.3)	0 (0, 33.3)	0.77	−9.8	2.9	<0.001
	Intervention	0 (0, 33.3)	0 (0, 33.3)	0 (0, 8.3)	0.04			

C1 = after the first session of chemotherapy. C2 = after the second session of chemotherapy. C3 = after the third session of chemotherapy.
EORTC, European Organization for Research and Treatment of Cancer; QL, global health status/QoL; PF, physical functioning; RF, role functioning; EF, emotional functioning; CF, cognitive functioning; FA, fatigue; NV, nausea and vomiting; PA, pain; DY, dyspnea; SL, insomnia; AP, appetite loss; CO, constipation; DI, diarrhea.
[a]Obtained from Friedman Test.
[b]Obtained from GEE model.
[c]The scores range from 0 to 100, where a higher score represents a higher functional level.
[d]The scores range from 0 to 100, where a higher score represents a greater degree of symptoms.

On the other hand, Ovesen et al. (19) performed a nutritional counseling intervention among patients with lung, ovary and breast cancer undergoing chemotherapy and revealed that nutrition education did not have a significant positive impact on improving the QoL amongsubjects, as the QoL index was significantly increased in both intervention and control groups. One might argue that, the difference in the types of intervention and chemotherapy regimen as well as the different types of cancers among subjects and different questionnaires related to QoL could cause these conflicting outcomes.

A study by Poulsen et al. (20) showed that intensive and individual dietary counseling among patients with gastro-esophageal, gastric, and gynecological cancers, who were under chemotherapy or radiotherapy treatment, led to better weight maintenance compared to the control group. However, contrary to the findings of our study, Poulsen et al. (20) found that intensive, individual dietary counseling could not improve the QoL among patients with cancer. A possible reason for this controversy is that we performed the investigations among PsBC with chemotherapy treatment, contrary to the mentioned study that monitored patients with different types of cancers undergoing either radiotherapy or chemotherapy or both.

Regarding the functional aspects of QoL, severe nausea and vomiting have found to have significant negative effects on the physical function of patients with chemotherapy treatment (11). Similar to our study, Ravasco et al. (21) revealed that nutritional counseling led to improvements in all functional scales of QoL in subjects with colorectal cancer who had radiotherapy.

In another study of Ravasco (17) in order to determine the impact of cancer treatment and nutrition-related factors on QoL, this study reported that energy and protein intakes had positive relation with general health, physical function, emotional function, and negative relationship with fatigue, pain, nausea and vomiting.

Furthermore, it was found that according to SF-36 questionnaire, the status of physical function and role function were significantly less among PsBC under chemotherapy treatment than those who did not receive chemotherapy (22).

In a cohort study by Leinert et al. (12) physical activity status was reduced during chemotherapy. In addition, De MattaTeizi et al. (22) and Heidi et al. (23) found that after chemotherapy treatment among patients with acute myeloid leukemia, the status of physical function decreased significantly. In accordance with these findings, our study found that patients in the control group had a significant reduction in the status of physical function and those who received nutrition counseling had a significantly better physical performance. Therefore, nutritional interventions during and after the chemotherapy treatment are of particular importance to maintain the status of physical functioning.

Previous studies have shown that chemotherapy could disrupt the cognitive function of patients with cancer (24,25). in consistent with these results, the present study showed that although cognitive function decreased in both intervention and control groups, this reduction was significantly lower in the intervention group which could be due to the appropriate dietary status including consumption of foods that were rich in antioxidant (26) or lower consumption of fats (27,28).

The present study reported that the score of nausea and vomiting, which was assessed based on QoL-C30 questionnaire among patients, was reduced after the nutrition education. In accordance with this finding, Thompson et al. (29) found that an educational video containing nutritional side effects during chemotherapy treatment increased the knowledge and skills of patients with cancer in order to manage any nutritional complications during chemotherapy. Further, similar to the present study, Baqai et al. (9) observed that providing educational package to reduce the complications of chemotherapy in patients with cancer, led to significant reduction in the symptom scales of QoL such as nausea and vomiting.

Other studies reported that nutritional interventions in patients with different types of cancer who were under chemo- or radio-therapies resulted in better gastrointestinal signs of QoL (17,21).

According to the McGill questionnaire in our study, patients who received nutrition counseling were significantly less likely to have nausea and felt less discomfort compared to those who did not receive any nutrition counseling.

We also reported that the intervention group significantly suffered less from constipation and diarrhea and significantly had less feeling of fatigue during chemotherapy compared to the control group. In line with these results, Zick et al. (30) assessed the effect of dietary regimen in breast cancer survivors and showed that consuming a diet containing whole grains, vegetables, vitamin C, fish, and omega-3-containing nuts could reduce the feeling of fatigue and improve the sleep status.

Additionally, the current study pointed out that sleep disturbances during chemotherapy were significantly lower in the intervention group. Likewise, Liu et al. (31) assessed the sleep disorders before and after chemotherapy in PsBC and concluded that the quality of sleep in these patients were reduced during chemotherapy. Improper physical functioning might be associated with sleep disturbance and the increased status of the sleep disturbance could be associated with lower QoL. Indeed, one possible reason for the improvement of quality of sleep in the intervention group was higher intake of tryptophan through eating nuts, lamb, beef, chicken, turkey, fish, and eggs, as tryptophan led to more production of serotonin which could improve the sleep status, sleep cognition, and emotion (32,33).

The present study had some strengths. It was the first study that assessed the impact of individual nutritional counseling on the rate of nausea and vomiting and QoL status in PsBC during chemotherapy using a large sample size. Moreover, in addition to the nutrition education, a personalized diet was performed based on the caloric requirement of every subject in the intervention group, which led to additional improvements on the status of nausea, and vomiting. We should mention some of the limitations of the present study. We did not follow patients up to the end of their treatments and as our study has been conducted in a population of women with breast cancer, the results cannot be extended to men or even women with other types of cancers.

Conclusion

Nutritional education during adjuvant chemotherapy in PsBC reduced the severity of CINV and improved the status of QoL.

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Disclosure Statement

The authors have no conflict of interest to declare.

Author Contributions

S. Najafi and M. Zarrati carried out the study design, recruitment of patients and data collection. M. Raji Lahiji, E. Razmpoosh,and R. Abdollahi were involved in laboratory testing and analysis, statistical analysis, and manuscript writing. Sh. Haghighat and M. Chamari carried out data analysis, and data interpretation. M. Asgari critically revised the manuscript for important scientific content. All authors read and approved the final version of the manuscript.

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