



BioBacta



Journal of Medical and Life Science

www.jmals.journals.ekb.eg



Efficacy of l-carnitine and silymarin administration on the health-related quality of life in 120 patients with cancer undergoing anthracycline-based chemotherapy

Zeinab Alkasaby Zalat¹, Mohamed M. Abdel-Latif², Badriyah S. Alotaibi³,
Mohamed A. Alm El-Din⁴, Neveen A. Kohaf⁵, and Hosny A. Elewa⁶

¹Department of Clinical Pharmacy, Faculty of Pharmacy (Girfa), Al-Azhar University, Cairo, Egypt.
(zeinabalkasaby.pharmg@azhar.edu.eg)

²Department of Clinical Pharmacy, Faculty of Pharmacy, Assuit University, Assuit, Egypt.

³Department of Pharmaceutical science, Faculty of Pharmacy, Princess of Nourah bint Abdulrahman University, Riyadh, Saudi Arabia

⁴Department of Clinical Oncology, Faculty of Medicine, Tanta University, Tanta, Egypt.

⁵Master degree in pharmaceutical Sciences, Faculty of Pharmacy, Al-Azhar University, Cairo, Egypt.

⁶Department of Pharmacy Practice, Faculty of Pharmacy, Horus University, Dominate City, Egypt.

* Corresponding author: helewa@horus.edu.eg

Received May 19, 2020; Accepted June 18, 2020; Published June 21, 2020

DOI: 10.21608/jmals.2020.111233

Abstract

Objectives: To investigate changes after adding L-carnitine and silymarin compared to anthracycline chemotherapy alone on the health-related quality of life (HRQoL) of women with breast cancer receiving anthracycline-based chemotherapy. **Methods:** A prospective, randomized comparative, study that included 120 women with breast cancer who received anthracycline in their chemotherapeutic regimen. Patients were divided into three groups, anthracycline alone (control group), chemotherapy and l-carnitine (l-carnitine group), and chemotherapy plus silymarin (silymarin group). HRQoL was evaluated using the EORTC QLQ-C30 and EORTC QLQ-BR23 instruments 7 days before chemotherapy and after the third month of chemotherapy. **Results:** On the application of (EORTC QLQ-C30), there was a significant decrease in global health status/QoL score, functional scale scores from baseline to after three months ($P \leq 0.001$) within the control group and a significant increase in symptom scale scores from baseline to after three months. In l-carnitine and silymarin groups, there was a non-significant difference in the scale scores. On the application of (EORTC QLQ-BR23), there was a significant decrease in functional scale scores ($p \leq 0.001$) within the control group and a significant increase in symptom scale scores ($p \geq 0.05$). In the l-carnitine and silymarin groups, there was a non-significant difference in functional scale scores from baseline to after three months ($p \geq 0.05$). **Conclusions:** QOL was negatively affected by chemotherapy. For BC cases, HRQoL becomes typically worse during the third month of chemotherapy compared with the pretreatment duration. The addition of l-carnitine and silymarin to anthracycline-based chemotherapy showed improvement in the health-related quality of life of cancer patients.

Keywords: Anthracycline, silymarin, l-carnitine, health-related quality of life, breast cancer.

Introduction

The distribution of cancer is currently growing, and the number of new patients is set to grow from 14 million in 2012 to 22 million annually by 2030 [1]. The second most common disease in the world in new cases (1.7 million cases) is breast cancer (BC), and the fifth category is regarded as a cause of death. [2]. With survival rates rising during BC therapy, greater consideration is given to improving health-related quality of life (HRQoL) during and following cancer drugs. Although anthracycline chemotherapy is associated with positive benefits in decreasing the risk of BC recurrence [3], it also affects negatively the HRQoL of survivors [4]. Furthermore, the reality that BC is gradually identified in earlier stages as a result of screening initiatives further increases the number of people who have obtained curative-intent adjuvant chemotherapy. The symptomatology and adverse effects profile of anthracycline chemotherapy on HRQoL should be taken into consideration. For example, chemotherapy induces important effects in BC people, such as exhaustion, febrile neutropenia, depression, dyspnea, discomfort, nausea, and vomiting. [5]. In addition, emotional distress, such as confusion or concern of recurrence and posttraumatic stress, pain, and work strain can include carcinogenic sequelae [6].

In the framework of culture and value systems, the idea of the quality of life (QoL) can be described as a sense of identity in its place in life and in relation to its objectives, desires, values, and concerns [7]. When this term is just linked to health expectations, the expression is titled HRQoL. This expression is a multi-domain term, representing the patient's general perception of the impact of illness and treatment on other aspects of life. [8]. The expression HRQoL is therefore used to include those elements that are usually not addressed in health contexts (such as income independence and environmental quality). Focusing on the development

of HRQoL thus requires analyzing nearly all health-related aspects of life [9].

In order to improve HRQoL and maintain emotional, social, and physical wellness, it is thus essential to understand the requirements of patients, besides the control of clear signs and symptoms throughout the therapy. Therefore, it is important to search for new strategies to improve HRQoL in cancer patients, such as adding l-carnitine and silymarin to patient's treatment protocols.

L-carnitine is important for the synthesis of long-chain free fatty acids into acylcarnitines and their subsequent transfer to the mitochondrial matrix where they are beta-oxidized in the production of cellular resources. L-carnitine's exogenous supplemental therapies seem to support anorexia, chronic fatigue, cardiovascular disease, diphtheria, hypoglycemia, male infertility, and muscular illness [10].

Silymarin is a nontoxic natural polyphenolic flavonoid extracted from the seeds of the plant milk thistle (*Silybum marianum*), which is an ancient medicinal plant for the treatment of various liver diseases [11]. Due to its strong antioxidant and tissue regenerative properties, silymarin is being studied as a hepatic, neural, renal, and cardiac protective ingredient. [12]. Silymarin could be helpful in patients with oncology, particularly, for reducing the side effects of cancer chemotherapy [10]. In common cancers such as lung prostatic, stomach, breast, bladder, and hepatocellular carcinoma, even, silymarin has an anti-cancer effect [13].

This research aimed to measure QOL in BC patients and compare the algorithms before and after chemotherapy and determine the impact of l-carnitine and silymarin on HRQoL.

Method

A prospective study to assess HRQoL in 120 Egyptian BC patients who performed the first oncological consultation at the Oncology Department, Tanta University Hospital, Egypt. Women ≥ 18 years of age, histologically documented BC, which has an intervention with breast surgery, and which depends on adjuvant or neoadjuvant chemotherapy as anthracycline, are included.

Patients were divided into three groups: control group (anthracycline- based regimen alone, n=40), l-carnitine group (anthracycline-based regimen + l-carnitine 1 g daily, n=40) and silymarin group (anthracycline- based regimen + silymarin 140 mg daily, n=40)

The evaluation of the patient's HRQoL was evaluated using the EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire) and EORTC QLQ-BR23 (EORTC BC-specific Quality of Life Questionnaire). The patients performed questionnaires in two stages (i. e., one week before the beginning of the chemotherapy (baseline) and in the third month of therapy, roughly in the 4th period (3-month follow-up), all of these instruments are checked, converted into Arabic, formal, and self-administrative information from medical records such as sociodemographic details (educational level and marital condition), menopause status, family history of cancers, and data were obtained from the Eastern Cooperative Oncology Group scale, measured no more than two weeks before research enrollment. The questionnaire was evaluated according to the systematic approach proposed by the EORTC Group. The research was formulated and performed in compliance with the ethical values of the Standards for Good Clinical Practice and the Helsinki Declaration. The methodology of research was accepted by the

National Research Ethics Committee at Tanta University with acceptance number (32551/09/2018), and written informed consent of all patients was received.

Drugs:

L-carnitine® 500 mg capsules obtained from (MEPACO)

Silymarin (Legalon ® 140 mg capsule obtained from (MEDA).

One-way analysis of variance test (one-way ANOVA) followed by LSD post hoc test was used to assess any significant differences among the three groups. A paired t-test was used to assess any significant differences within each group at baseline and after chemotherapy. All probability values presented were two-tailed, and $p \leq 0.05$ was considered statistically significant.

Results

1- Study population

Results concerning sociodemographic and clinical characteristics from the 120 patients included in the study are described in Tables 1, 2, and 3.

There were no significant differences in age, marital status, education level, and menopausal state between the studied groups (p -value ≥ 0.05) as shown in Table 1.

In Tables 2 and 3, there were also non-significant differences regarding family history of cancer (Eastern Co-Operative Oncology Group) ECOG performance, a model of breast cancer detection, and stage of breast cancer between the studied groups (p -value ≥ 0.05)

Table (1): Demographic data of the studied groups

Variable	Groups			P-value
	Control Group N=40	l-carnitine group N=40	Silymarin group N=40	
Age (years) Mean \pmSD	44.455 \pm 9.47	45.64 \pm 9.941	44.68 \pm 12.44	0.61
Marital status				0.775
Married	43(71.6%)	18(72%)	19(76%)	
Single	17(28.3%)	7(28%)	6(24%)	
Education level				0.726
Elementary or middle school	55(91.6%)	21(84%)	22(88%)	
High school	3(5%)	3(12%)	2(8%)	
College	2(3.33%)	1(4%)	1(4%)	
Menopausal state				0.700
Premenopausal	10(16.6%)	3(12%)	4(16%)	
Perimenopausal	33(55%)	18(72%)	17(68%)	
Postmenopausal	17(28.3%)	4(16%)	4(16%)	

Age represented in mean \pm standard deviation

Data are represented as number and percentage. $p \leq 0.05$ value considered significant

Table (2): Demographic data of the studied groups

Variable	Groups			P value
	Control Group N=40	l-carnitine group N=40	Silymarin group N=40	
Family history of cancer				0.815
No	25(41.6%)	10(40%)	11(44%)	
Yes (breast)	20(33.3%)	5(20%)	6(24%)	
Yes (breast and other)	5(8.3%)	6(24%)	5(20%)	
Yes (other)	10(16.6%)	4(16%)	3(12%)	
ECOG performance status				0.850
0	55(91.6%)	23(92%)	22(88%)	
1	5(8.33%)	2(8%)	3(12%)	
Model of breast cancer detection				0.674
Screen detected	30(50%)	16(64%)	15(60%)	
Symptomatic	20(33.3%)	5(20%)	6(24%)	
Unknown	10(16.6%)	4(16%)	4(16%)	

ECOG: Eastern Cooperative Oncology Group

Table (3): Distribution of patients regarding pathology and stage in the studied groups

Variable	Groups						P-Value
	Control		L- Carnitine		Silymarin		
	N	%	N	%	N	%	
Stage:							
Breast adjuvant	27	(67.5%)	33	(82.5%)	31	(77.5%)	0.742
Breast neoadjuvant	4	(10%)	2	(5%)	6	(15%)	
Breast metastatic	4	(10%)	1	(2.5%)	2	(5%)	
	5	(12.5%)	4	(10%)	1	(2.5%)	

Data are represented as number and percentage. $p \leq 0.05$ value considered significant

Age represented in mean \pm standard deviation

$p \leq 0.05$ value considered significant

2-HRQoL scores

Application of (EORTC QLQ-C30). There was a significant decrease in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months ($p \leq 0.001$) within the control group. There was a significant increase in symptoms scale include fatigue, nausea and vomiting, dyspnea, insomnia, appetite loss, constipation, and diarrhea scores from baseline to after three months. Table (4) and figures 1-3

In the l-carnitine group, there was a non-significant difference in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months ($p \geq 0.05$). There was also a non-significant change in symptoms scale include pain, insomnia, appetite loss, and constipation scores from baseline to after three months. Table (4) and figures 1-3

In the silymarin group, there was a non-significant difference in global health status/QoL score, physical functioning, role functioning, emotional functioning, and social functioning scores from baseline to after three months ($p \geq 0.05$) and there was also a non-significant change in symptom scale include fatigue, pain, insomnia, appetite loss, and constipation scores from baseline to after three months. Table (4) and figures 1-3

Application of (EORTC QLQ-BR23).

There was a significant decrease in functional scale include body image score and a significant decrease in sexual functioning, sexual enjoyment scores from baseline to after three months ($p \leq 0.001$) within the control group, and there was a significant increase in symptoms scale include systemic therapy side effects and breast symptom scores from baseline to after three months ($p \geq 0.05$). Table (5) and figures 4,5

In the l-carnitine group, there was a non-significant difference in functional scale include body image

score, sexual functioning, and sexual enjoyment scores from baseline to after three months ($p \geq 0.05$). Table (5) and figures 4,5

In the silymarin group, there was a non-significant difference in functional scale include body image score, sexual functioning, sexual enjoyment, and arm symptom scores from baseline to after three months. Table (5) and figures 4,5

Table 4. Comparison of HRQoL between the study segments (EORTC QLQ-C30).

Variable	Groups					
	Control Group N=40		l-carnitine Group N=40		Silymarin Group N=40	
	At base line	After 3 months	At base line	After 3 months	At base line	After 3 months
Global health status/ QoL						
Global health status/ QoL	77.6 ± 16.02	55.18±15.3	76.7 ± 15.6	71.2 ± 13.2	78.7±13.5	77.4±14.6
P-value	0.001*		0.1847		0.745	
functional scales						
Physical functioning	89.73 ± 4.51	67.5±10.33	90.1± 4.88	88.3± 4.093	88.6± 2.89	87.8±11.3
P-value	0.001*		0.1641		0.7331	
Role functioning	80.78±19.6	52.3 ±18.3	79.3±15.4	73.1±14.6	80.4 ±16.8	79.6 ±14.5
P-value	0.001*		0.1506		0.8577	
Emotional functioning	72.3±19.3	48.32±20.5	70.8 ±17.5	58.3 ±25.6	71.6 ±18.7	68.4 ± 23.4
P-value	0.001*		0.0495*		0.595	
Cognitive functioning	83.4±20.2	75.6±19.8	85.1±21.3	83.6±16.8	80.6±17.5	80.3±20.6
P-value	0.1744		0.783		0.956	
Social functioning	87.3±15.4	59.6±20.14	88.6±19.5	89.3±18.6	86.7±17.5	88.4±21.4
P-value	0.001		0.897		0.759	
Symptom scales						
Fatigue	14.8±2.3	58.7±14.3	13.6±5.3	18.6±1.3	15.3±2.2	16.4±1.3
P-value	0.001		0.001		0.0346	
Nausea and vomiting	1.02±0.02	12.6±1.5	1.5±1.1	5.6±2.1	1.8±1.2	4.7±3.2
P-value	0.001		0.001		0.001	

Variable	Groups					
	Control Group N=40		l-carnitine Group N=40		Silymarin Group N=40	
	At base line	After 3 months	At base line	After 3 months	At base line	After 3 months
Pain	28.3±23.2	36.3±24.2	27.3±12.5	30.5±21.2	29.1±15.6	31.2±18.3
P-value	0.239		0.518		0.664	
Dyspnoea	7.6±4.3	18.2± 5.7	7.9±2.6	15.2±1.8	7.5±2.8	10.6±3.5
P-value	0.001		0.001		0.0011	
Insomnia	28.3±19.3	52.6±23.2	29.2±12.5	33.5±18.6	28.7±21.2	32.4±18.7
P-value	0.001		0.001		0.452	
Appetite loss	7.4±3.2	22.3±14.3	6.5±2.8	8.6±5.2	7.6±1.5	6.6±12.5
P-value	0.001		0.0818		0.0928	
Constipation	18.6±14.5	33.5±17.6	17.5±12.2	20.3±14.8	19.3±14.3	17.2±12.3
P-value	0.002		0.469		0.5803	
Diarrhoea	1.02±2.2	9.3±4.9	1.3±2.1	6.2±5.3	1.5±2.1	3.5±2.5
P-value	0.001		0.001		0.0036	
Financial difficulties	27.3±26.3	31.2±21.3	26.3±19.8	30.2±27.3	25.6±21.3	32.1±28.3
P-value	0.567		0.568		0.363	

Table 5. Comparison of HRQoL between study segments. Specific questionnaire for BC (EORTC QLQ-BR23).

Variable	Groups					
	Control Group N=40		l-carnitine Group N=40		Silymarin Group N=40	
	At base line	After 3 months	At base line	After 3 months	At base line	After 3 months
Functional scales						
Body image	90.66 ± 8.51	65.5±12.33	90.1± 8.88	88.3± 8.093	87.6± 7.89	88.8±18.3
P-value	0.001*		0.4575		0.7647	
Sexual functioning	52.78±19.6	16.3 ±15.3	52.3±16.4	44.1±15.6	51.3 ±14.8	48.3 ±19.5
P-value	0.001*		0.0763		0.542	
Sexual enjoyment #	69.3±19.7	28.32±21.5	70.7 ±17.5	33.3 ±25.6	71.7 ±15.7	66.4 ± 13.4
P-value	0.001*		0.001*		0.02054	

Variable	Groups					
	Control Group N=40		l-carnitine Group N=40		Silymarin Group N=40	
	At base line	After 3 months	At base line	After 3 months	At base line	After 3 months
Future perspective	33.4±20.2	39.6±19.8	34.1±21.3	35.2±16.8	32.6±17.5	33.3±20.6
P-value	0.278		0.8402		0.8975	
Symptom scales						
Systemic therapy side effects	8.8±9.3	58.7±18.3	7.6±6.3	48.6±16.3	8.3±7.2	36.4±20.3
P-value	0.001		0.001		0.001	
Breast symptoms	32.3±23.2	18.6±21.5	33.5±21.1	17.6±22.1	32.8±21.2	19.3±23.2
P-value	0.035		0.0123		0.0406	
Arm symptoms	34.3±23.2	20.3±24.2	35.3±12.5	22.5±21.2	33.1±15.6	25.2±18.3
P-value	0.0421		0.0123		0.107	
Upset by hair loss [#]	NA	68.2± 35.7	NA	65.2±31.8	NA	62.6±35.5
P-value						

*Statistically significant p-value from the Wilcoxon test.

NA, not applicable; there was no valid information available. # According to the EORTC Scoring Manual [14], the variation in the number of responses in EORTC QLQ-BR23 is predicted since the fields ‘sexual enjoyment’ and ‘upset by hair loss’ do not apply when the responses related to these scales are ‘no’.

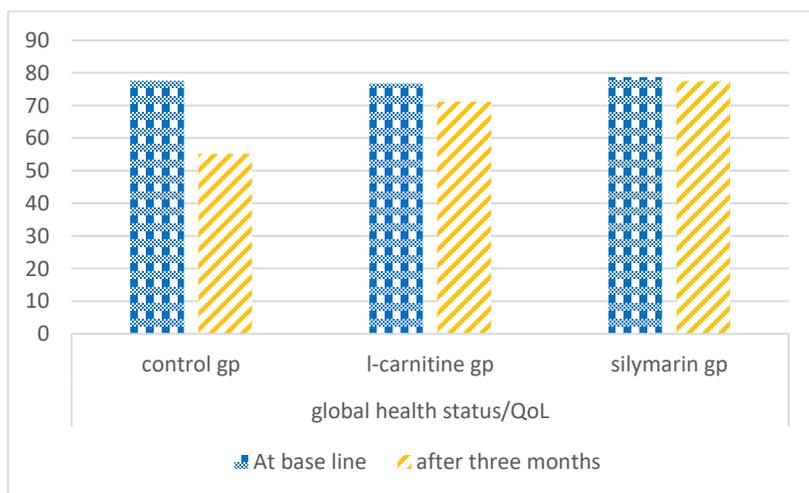


Figure (1): Comparison between studied groups regarding global health status (EORTC QLQ-C30)

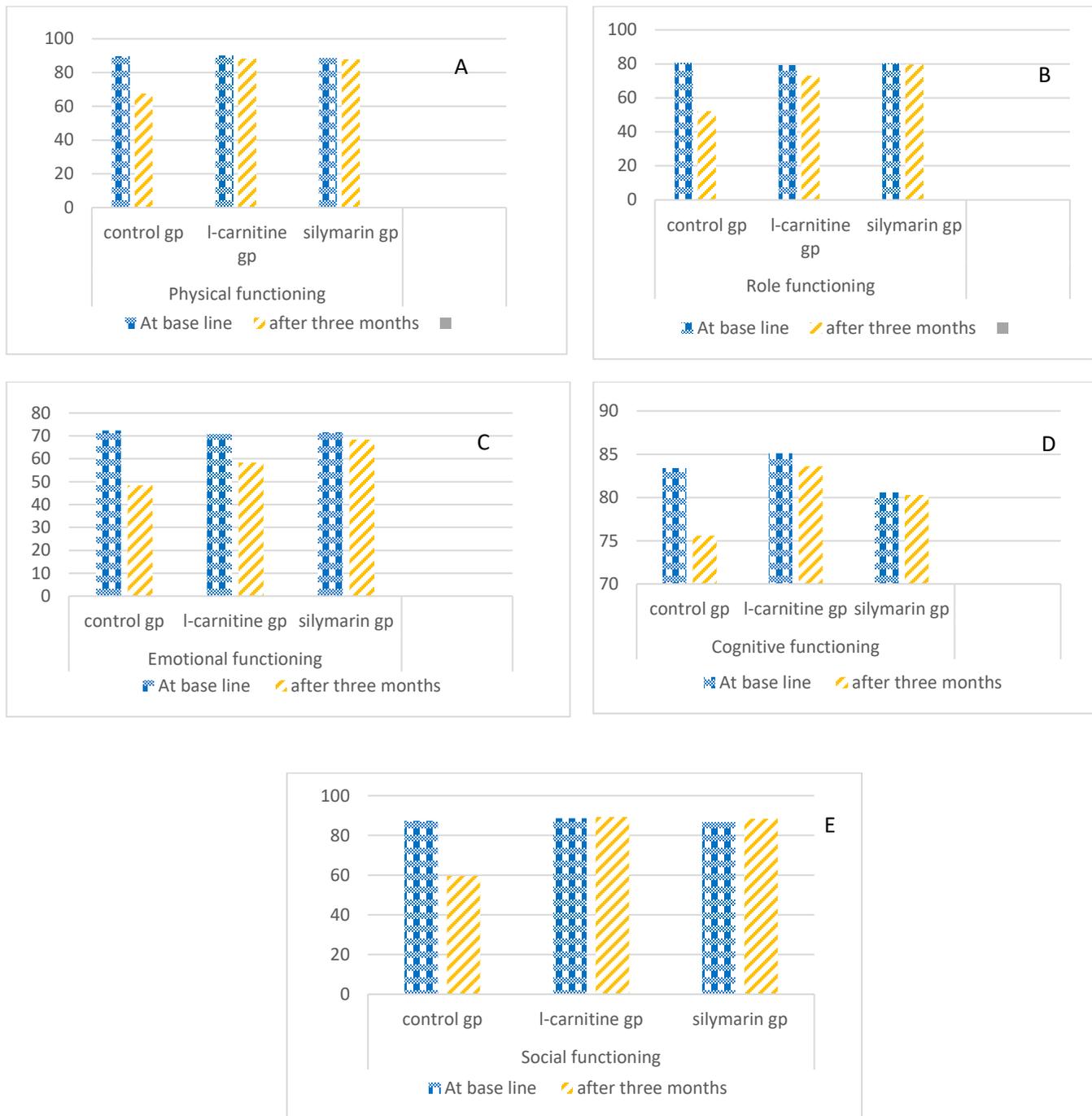
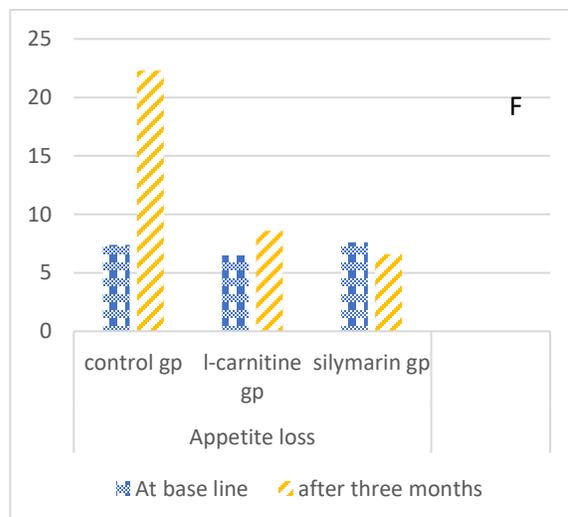
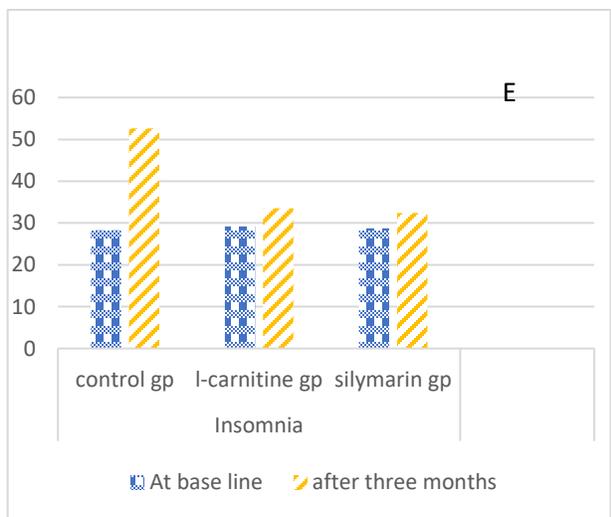
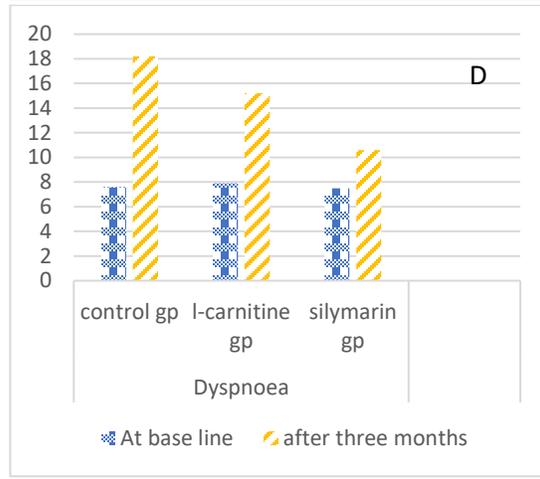
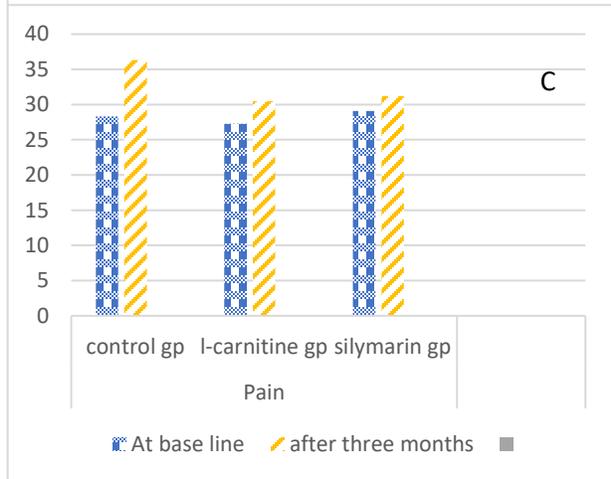
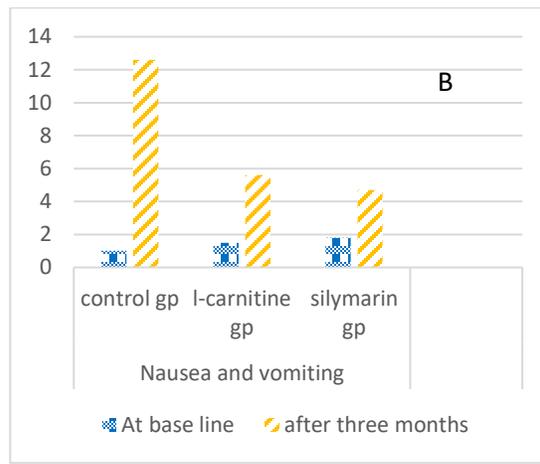
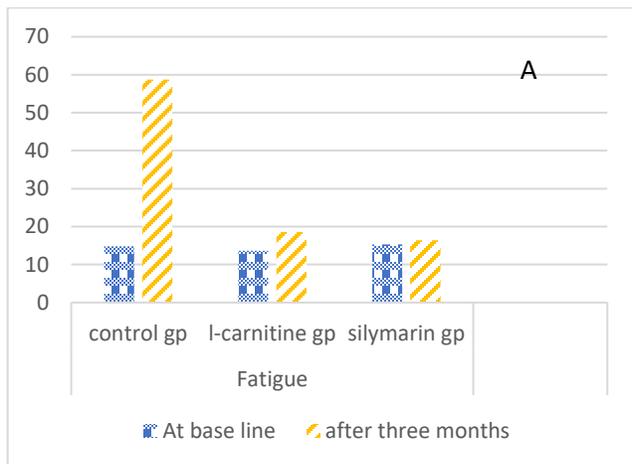


Figure (2): Comparison between studied groups regarding functional scale: A: physical functioning, B: role functioning, C: emotional functioning, D: cognitive functioning, E: social functioning (EORTC QLQ-C30)



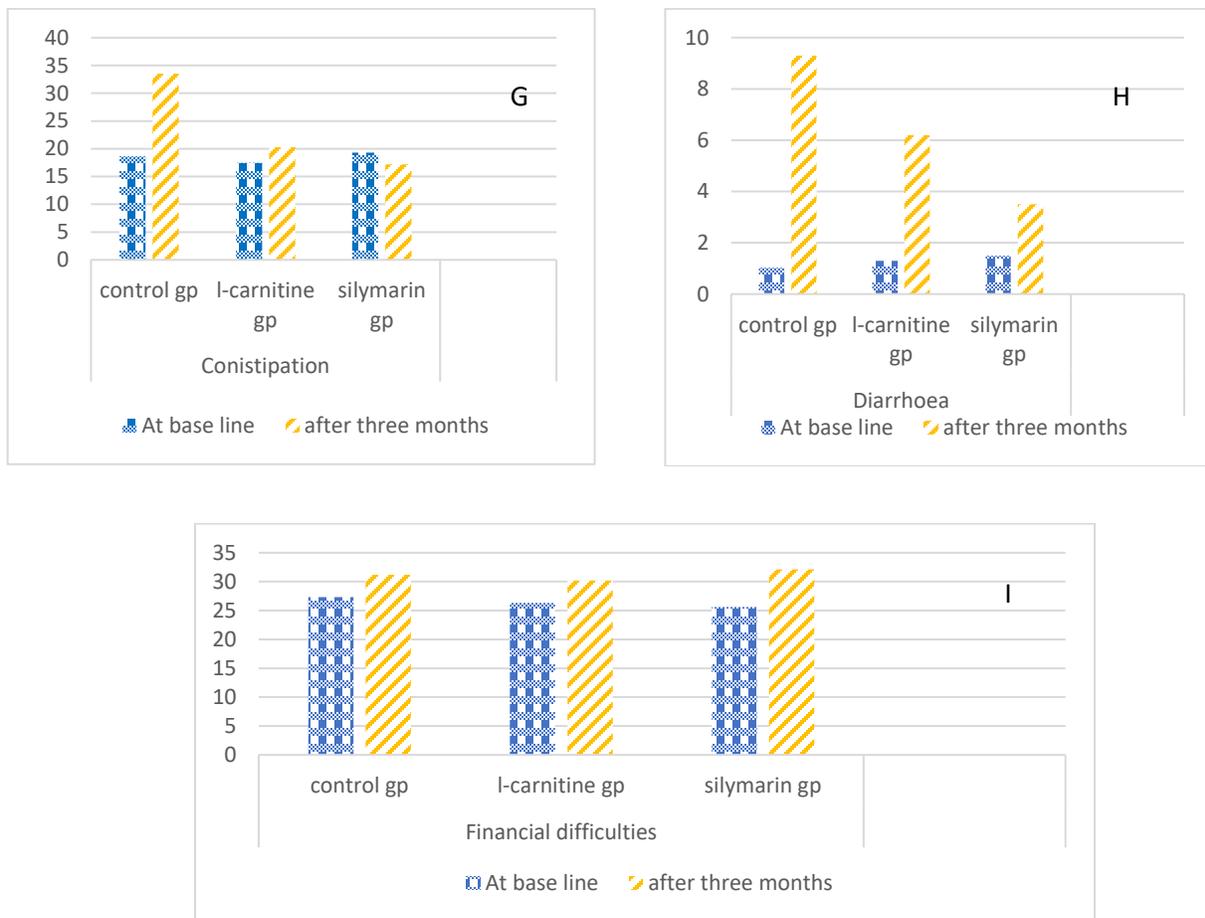


Figure (3): Comparison between studied groups regarding symptom scales- A: fatigue, B: nausea and vomiting, C: pain, D: dyspnoea, E: insomnia, F: appetite loss, G: constipation, H: diarrhoea,I: Financial difficulties (EORTC QLQ-C30)

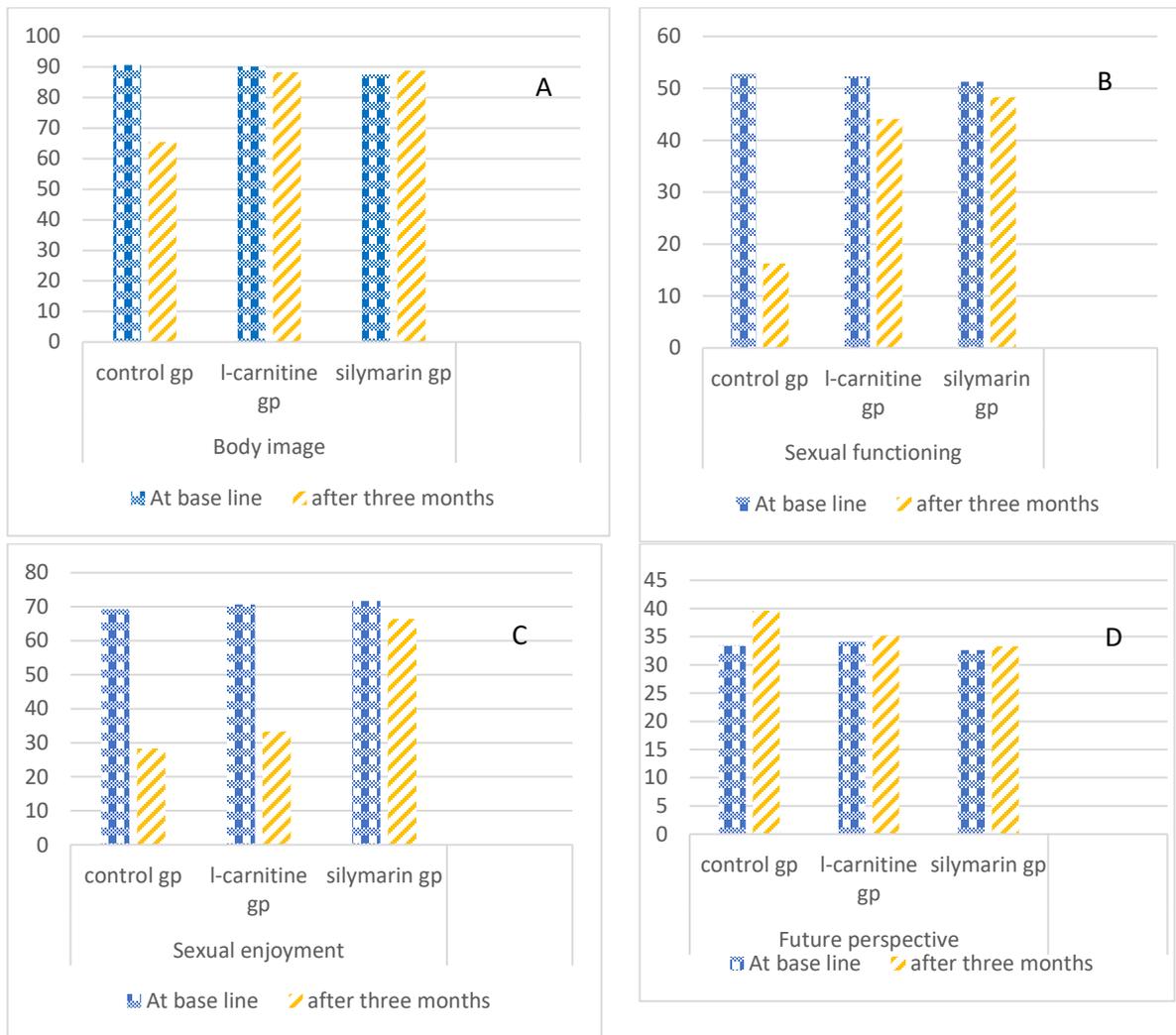


Figure (4): Comparison between studied groups regarding functional scales -A: body image, B: sexual functioning, C: sexual enjoyment, D: future perspective, (EORTC QLQ-BR23)

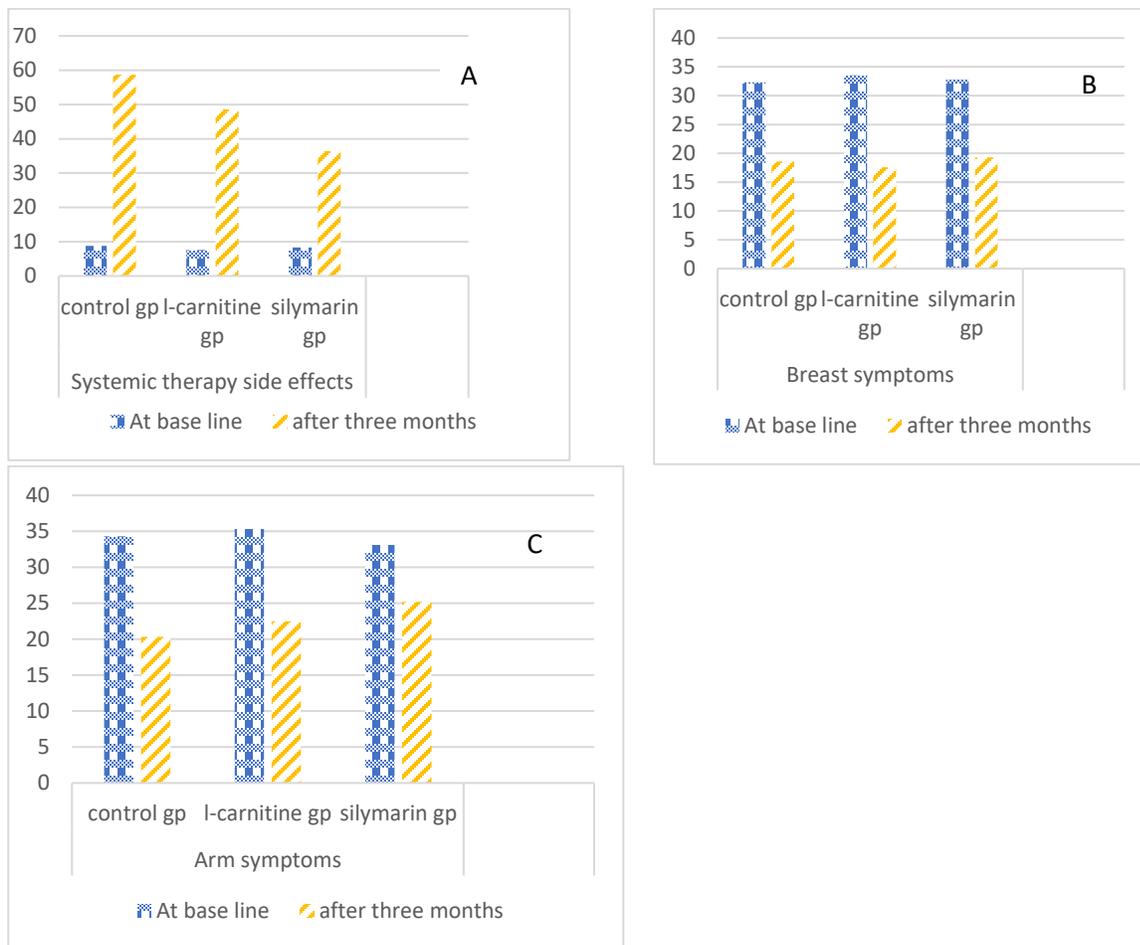


Figure (5): Comparison between studied groups regarding symptom scales – A: systemic therapy side effects, B: breast symptoms, C: arm symptoms (EORTC QLQ-BR23)

Discussion

The measurement of HRQoL is a valuable feature to determining the impact of medical care on diseases, psychological problems, lifetime happiness, and the well-being of patients. [15]. BC patients are at an increased risk for general HRQoL therapies (e.g., exhaustion, sleep problems, and pain) and psychological disorders (depression, anxiety, apprehension of recurrence, issues related to sex and body image) as well and general HRQoL. [16,17]. Chemotherapy often affects the patient's HRQoL expectations, as symptoms escalate and the functioning level declines. [18–20]. It is necessary to add a new strategy to deal

with chemotherapy's undesirable effects on patients' quality of life.

Our research is the first to examine the impact of silymarin and l-carnitine on the wellbeing of cancer patients undergoing anthracycline-based protocols and could also help oncologists assess classic symptoms that chemotherapy activates as well as the influence of chemotherapy, has psychosocial characteristics.

Our results showed that anthracycline has a negative effect on HRQoL, represented by a decline in global health status score, functional scales, and symptoms scale. This influence may be clarified by chemotherapy, which indicates that the

health status of women with BC is worsened during therapy. Binnoto et al. stated that global health worsened also with the rising complications of chronic medication during chemotherapy therapy [21]. In fact, BC patients have a high risk of developing behavioral changes that adversely affect HRQoL. [22]. According to previous studies [23, 24], the levels of psychological activity and body image during chemotherapy are substantially decreased, and modified body image is known to be a critical psychosocial issue for women with BC. [25]. This can be understood because the body image is influenced by the context of what others think and thus affects the trust of the individual. Psychological factors were strongly linked to global HRQoL and decreased social and emotional functioning in BC patients [26]. On comparing the results of the baseline scores and after 3 months, there was also a significant decline between the periods in cognitive functioning, pain, dyspnoea, and constipation between the two evaluations in the control group. These measures deal with physical effort, health, and support with basic needs and the ability to work or do daily work. This result is growing in patients with BC because of physical disabilities linked to illness and medication. The literature records similar results [18, 27]. As the physical performance of the target is consistently better earlier than the end of the procedure, if exhaustion progresses [19]. Regarding the hair loss scale disturbance, segments cannot be contrasted. In line with the EORTC Rating Manual [14], a variance in the EORTC QLQ-BR23 answers is expected as measures disrupted by hair loss and sexual pleasure are not valid where the responses correlated with this measure are 'no.' However, a high score on this examination suggests that the disorder adversely affected HRQoL.[14]. Alopecia is therefore life-altering and patients perceive these side effects as distressing [21]. This modification

may create discomfort as to how others see it or evaluate it, causing social interaction to disappear because it feels uncomfortable in public places. [18]. The social isolation of BC patients is associated with a number of reasons. Social stigmatization of the disease can affect BC woman's interactions with other people. Our research has affected the social functioning of chemotherapy, indicating that a patient's physical condition and treatment interferes with family relations and social activities [21]. Similar results were reported in other studies [18], demonstrating the effect of chemotherapy on social relationships. On the other hand, larger social networks are linked to greater HRQoL when patients get better social support from family and friends after a BC diagnosis. [28]. It is known that attraction can be affected by shifts in hormone levels and changes in body image after a cancer diagnosis. [29]. Our findings are in agreement with the study of Hall *et al* [30]. which revealed that, in the short and long term, the majority of systemic effects of chemotherapy tend to affect women's sexuality. The findings of elevated systemic adverse effects (systemic medication side effects, exhaustion, nausea and vomiting, depression, loss of appetite, and diarrhea) in patients treated with chemotherapy are compatible with the expected results of toxicity for the drug. Chemotherapy may also worsen toxicity at low levels [31] such as diarrhea, which may be enough to worsen patients' HRQoL. In cancer patients, insomnia is also a common problem. Chemotherapy's concomitant effect on insomnia symptoms is mediated by various oncological symptoms, such as urinary symptoms, nausea, and night and digestive symptoms. [32]. Smell and taste alterations also take place as a side effect of chemotherapy. These changes affect food behavior, reduce food consumption, or limit food intake [33].

As illustrated in our results, the addition of l-carnitine to anthracycline-based chemotherapy protocol showed non-significant changes in the global health status scale score, functional scale scores, and symptom scale scores of insomnias, appetite loss, and diarrhea from baseline values. This may be due to that l-carnitine (LC) plays an important role in the metabolism of fatty acids, and LC deficiency is associated with a feeling of weakness or general fatigue. Cancer patients receiving chemotherapy often develop l-carnitine deficiency, which is considered to be a factor contributing to general fatigue. [35]. There also was an improvement in body image score compared to the control group this explained as chemotherapy-induced damage of the carnitine system, and secondary deficiency of this molecule may cause fatigue due to impaired energy metabolism and thus bad impact on the self-confidence of women with breast cancer [35]. Thus, restoration of the carnitine pool may alleviate the body image score of cancer patients. Our results are in harmony with Shindo et al. who studied the effect of l-carnitine on the quality of life of cancer patients receiving chemotherapy and reported significant improvement from the control group [36].

MATSUI et al. also studied the impact of l-carnitine on the quality of life of cancer patients with chemotherapy reporting improvement [35].

These studies open the way for more research on the l-carnitine impact on health-related quality of life of cancer patients, as it is a constrain of chemotherapy.

Regarding the administration of silymarin with anthracycline contains chemotherapy, our results showed that there was a non-significant change in global health status score, functional scale scores, and symptom scale scores including (fatigue,

insomnia, appetite loss, and constipation) from the baseline. This may be interpreted as silymarin has been found to be a very potent antioxidant, supporting native cellular antioxidant mechanisms such as glutathione (GSH) and superoxide dismutase by scavenging free radicals and reactive oxygen species (ROS) [37]. This can partly explain the efficacy of silymarin in hepatic damage due to disease or poisons because this antioxidant action may reduce oxidative stress associated with lipid insults that suppress lipid peroxidation (and thus cell death). The general anticancer effects of flavonoids collectively as well as the high antioxidant ability of silymarin, there was a strong interest in modifying silymarin for use as a chemoprotective agent. [37].

Our study is the first to study the effect of silymarin on the health-related quality of life of cancer patients. There was also a non-significant

There also was an improvement in body image score compared to the control group, which may be due to the ability of silymarin to eliminate toxins that have undesirable effects on the mental status and self-pride sense of the patients.

More studies should be done in a similar population in order to analyzes the long-term HRQoL effects of silymarin and l-carnitine on anthracycline-based chemotherapy

Physicians and healthcare professionals should often evaluate patients for side effects of preventive treatment and use symptom scales. Screening can also take into account patients' views of global health status and QoL, physical functioning, job functioning, and emotional and social functioning. In this context, basic communication skills and sympathy in the psychosocial evaluation are significant.

It is important to understand the patient and the family objectives in order to help the therapy tailor to its needs and to make ensure that we support the entire person, including cancer care and wellbeing preferences into consideration during therapy. Minimizing the adverse effects of medication and introducing strategies to help the patient overcome this process is critical for enhancing HRQoL. We must adapt our care strategy to the needs of each patient with this awareness.

Conclusions

In BC cases, the HRQoL of chemotherapy is usually worse during the third month relative to the time before therapy starts. The addition of l-carnitine and silymarin to anthracycline- based chemotherapy showed improvement in health-related quality of life of cancer patients and provided the basis for the design of future placebo-controlled supplementation studies in this population.

Conflicts of interest

The contributors cannot reveal conflicts of interest.

Funding statement

The writers provided no financial support for this article's study, authorship, and/or publishing.

All authors share the data underlying the findings of their manuscripts. Data sharing allows researchers to verify the results of an article, replicate the analysis, and conduct secondary analyses.

References

1. Jemal A, Vineis P, and Bray F, et al (2014) The Cancer Atlas 2nd edn (Atlanta: American Cancer Society) [www.cancer.org/canceratlas]
2. Ferlay J, Soerjomataram I, and Dikshit R, et al (2015) Cancer incidence and mortality worldwide: sources, methods and major

patterns in GLOBOCAN 2012 Int J Cancer 136 E359–E386 <https://doi.org/10.1002/ijc.29210>

3. Anampa J, Makower D, and Sparano JA (2015) Progress in adjuvant chemotherapy for breast cancer: an overview BMC Med 13 195 <https://doi.org/10.1186/s12916-015-0439-8> PMID: 26278220 PMCID: 4538915
4. Chopra I and Kamal KM (2012) A systematic review of quality of life instruments in long-term breast cancer survivors Health Qual Life Outcomes 10 14 <https://doi.org/10.1186/1477-7525-10-14> PMID: 22289425 PMCID: 3280928
5. Ferreira RG and Franco LF de R (2017) Efeitos colaterais decorrentes do tratamento quimioterápico no câncer de mama: revisão bibliográfica Rev da Univ Val do Rio Verde <https://doi.org/10.5892/ruvrd.v15i2.3759>
6. Stanton AL, Rowland JH, and Ganz PA (2015) Life after diagnosis and treatment of cancer in adulthood: contributions from psychosocial oncology research Am Psychol 70 159–174 <https://doi.org/10.1037/a0037875> PMID: 25730722
7. WHOQOL Group (1994) Development of the WHOQOL: rationale and current status Int J Ment Health 23 24–56 <https://doi.org/10.1080/00207411.1994.11449286>
8. Food and Drug Administration (2006) Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance Health Qual Life Outcomes 4 79 <https://doi.org/10.1186/1477-7525-4-79> PMID: 17034633 PMCID: 1629006
9. Guyatt GH, Feeny DH, and Patrick DL (1993) Measuring health-related quality of life Ann

- Intern Med 118 622–629 <https://doi.org/10.7326/0003-4819-118-8-199304150-00009> PMID: 8452328
10. Sayed -Ahmed MM. Role of carnitine in cancer chemotherapy-induced multiple organ toxicity. Saudi pharmaceutical journal. October 2010;18(4) Pages 195-206
 11. Surai, P.F. Silymarin as a Natural Antioxidant. An Overview of the Current Evidence and Perspectives. Antioxidants 2015, 4, 204-247.
 12. Frassová Z, Rudá-Ku erová J. Milk Thistle (Silybum Marianum) as a supportive Phytotherapeutic agent in Oncology. Klin Onkol. 2017, 30(6), 426-432.
 13. Zou, H.; Zhu, X.X .; Zhang, G.B.; Ma, Y.; Wu, Y.; Huang, D.S. Silibinin: an old drug for hematological disorders. Oncotarget 2017 Jul 11; 8(51): 89307-89314.
 14. Fayers P, Aaronson N, and Bjordal K, et al (2001) The EORTC QLQ-C30 Scoring Manual 3rd edn (Brussels: European Organisation for Research and Treatment of Cancer) [<https://www.eortc.org/app/uploads/sites/2/2018/02/SCmanual.pdf>]
 15. Montazeri A (2008) Health-related quality of life in breast cancer patients: a bibliographic review of the literature from 1974 to 2007 J Exp Clin Cancer Res 27 32 <https://doi.org/10.1186/1756-9966-27-32> PMID: 18759983 PMCID: 2543010
 16. Fanakidou I, Zyga S, and Alikari V, et al (2018) Mental health, loneliness, and illness perception outcomes in quality of life among young breast cancer patients after mastectomy: the role of breast reconstruction Qual Life Res 27 539–543 <https://doi.org/10.1007/s11136-017-1735-x>
 17. Leinert E, Singer S, and Janni W, et al (2017) The impact of age on quality of life in breast cancer patients receiving adjuvant chemotherapy: a comparative analysis from the prospective multicenter randomized ADEBAR trial Clin Breast Cancer 17 100–106 <https://doi.org/10.1016/j.clbc.2016.10.008>
 18. Gaton-Johansson F, Watkins CC, and Kanu IK, et al (2015) The effects of symptoms on quality of life during chemotherapy in africanamerican women with breast cancer J Natl Black Nurses Assoc 26 7–16
 19. Tachi T, Teramachi H, and Tanaka K, et al (2015) The impact of outpatient chemotherapy-related adverse events on the quality of life of breast cancer patients PLoS One 10 e0124169 <https://doi.org/10.1371/journal.pone.0124169> PMID: 25915539 PMCID: 4410996
 20. Binotto M , Reiner T , Werutsky G, Zaffaroni F and Schwartzmann G (2020) Health-related quality of life before and during chemotherapy in patients with early-stage breast cancer *ecancer* 2020, 14:1007; www.ecancer.org; DOI: <https://doi.org/10.3332/ecancer.2020.1007>
 21. Barbosa PA, Cesca RG, and Pacífico TED, *et al* (2017) Quality of life in women with breast cancer, after surgical intervention, in a city in the zona da mata region in Minas Gerais, Brazil *Rev Bras Saúde Matern Infant* 17 385–399 <https://doi.org/10.1590/1806-93042017000200010>
 22. Perroud HA, Alasino CM, and Rico MJ, et al (2016) Quality of life in patients with metastatic breast cancer treated with metronomic chemotherapy *Futur Oncol* 12 1233–1242 <https://doi.org/10.2217/fon-2016-0075>

23. Ho SSM, So WKW, and Leung DYP, et al (2013) Anxiety, depression and quality of life in Chinese women with breast cancer during and after treatment: a comparative evaluation *Eur J Oncol Nurs* 17 877–882 <https://doi.org/10.1016/j.ejon.2013.04.005> PMID: 23727448
24. Pierrisnard C, Baciuchka M, and Mancini J, et al (2018) Body image and psychological distress in women with breast cancer: a French online survey on patients' perceptions and expectations *Breast Cancer* <https://doi.org/10.1007/s12282-017-0828-2>
25. Tang L, Fritzsche K, and Leonhart R, et al (2017) Emotional distress and dysfunctional illness perception are associated with low mental and physical quality of life in Chinese breast cancer patients *Health Qual Life Outcomes* 15 231 <https://doi.org/10.1186/s12955-017-0803-9> PMID: 29191208 PMCID: 5709963
26. Zhang Y, Fritzsche K, and Leonhart R, et al (2014) Dysfunctional illness perception and illness behaviour associated with high somatic symptom severity and low quality of life in general hospital outpatients in China *J Psychosom Res* <https://doi.org/10.1016/j.jpsychores.2014.06.005> PMID: 25149028
27. Winters ZE, Haviland J, and Balta V, et al (2013) Integration of patient-reported outcome measures with key clinical outcomes after immediate latissimus dorsi breast reconstruction and adjuvant treatment *Br J Surg* 100 240–251 <https://doi.org/10.1002/bjs.8959>
28. Kroenke CH, Kwan ML, and Neugut AI, et al (2013) Social networks, social support mechanisms, and quality of life after breast cancer diagnosis *Breast Cancer Res Treat* 139 515–527 <https://doi.org/10.1007/s10549-013-2477-2> PMID: 23657404 PMCID: 3906043
29. Lindau ST, Abramsohn EM, and Baron SR, et al (2016) Physical examination of the female cancer patient with sexual concerns: what oncologists and patients should expect from consultation with a specialist *CA Cancer J Clin* 66 241–263 <https://doi.org/10.3322/caac.21337> PMID: 26784536 PMCID: 4860140
30. Hall E, Cameron D, and Waters R, et al (2014) Comparison of patient reported quality of life and impact of treatment side effects experienced with a taxane-containing regimen and standard anthracycline based chemotherapy for early breast cancer: 6year results from the UK TACT trial (CRUK/01/001) *Eur J Cancer* 50 2375–2389 <https://doi.org/10.1016/j.ejca.2014.06.007> PMID: 25065293 PMCID: 4166460
31. Jolly TA, Williams GR, and Bushan S, et al (2016) Adjuvant treatment for older women with invasive breast cancer *Women's Heal* 12 129–145 quiz 145–146
32. Savard J, Ivers H, and Savard M-H, et al (2015) Cancer treatments and their side effects are associated with aggravation of insomnia: results of a longitudinal study *Cancer* 121 1703–1711 <https://doi.org/10.1002/cncr.29244> PMID: 25677509
33. Laviano A, Koverech A, and Seelaender M (2017) Assessing pathophysiology of cancer anorexia *Curr Opin Clin Nutr Metab Care* 20 340–345 <https://doi.org/10.1097/MCO.0000000000000394> PMID: 28598896

34. Velikova G, Booth L, and Smith AB, et al (2004) Measuring quality of life in routine oncology practice improves communication and patient well-being: a randomized controlled trial *J Clin Oncol* 22 714–724 <https://doi.org/10.1200/JCO.2004.06.078>
35. MATSUI H, EINAMA T, SHICHI S, et al (2018) L-Carnitine supplementation reduces the general fatigue of cancer patients during chemotherapy *MOLECULAR AND CLINICAL ONCOLOGY* 8: 413-416
36. Shindo T & Kobayashi K & Tanaka T & Masumori N et al (2019) Can levocarnitine supplementation improve fatigue caused by sunitinib as a treatment for renal cell carcinoma? A single-center prospective pilot study *Supportive Care in Cancer* 27:1491–1496 <https://doi.org/10.1007/s00520-018-4521-6>
37. Ting H, Deep G, and Agarwal R (2013) Molecular Mechanisms of Silibinin-Mediated Cancer Chemoprevention with Major Emphasis on Prostate Cancer *The AAPS Journal*, Vol. 15, No. 3,707-716