Effects of Tamoxifen on Premenopausal Breast Cancer Patients in Terms of Anxiety, Depression, Quality of Life and Sexual Satisfaction

Premenapozal Meme Kanseri Hastasında Tamoksifenin Anksiyete, Depresyon, Yaşam Kalitesi ve Cinsel Doyum Üzerine Etkisi

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ÖZET

Amaç: Bu çalışmada premenapozal meme kanserli hastalarda tamoksifenin etkilerini, anksiyete, depresyon, yaşam kalitesi ve cinsel doyumları açısından belirlemek amaçlandı.
Yöntem: Adjuvan tamoksifen kullanan 67 premenapozal meme kanserli kadın çalışmaya dahil edildi ve veriler yüzyüze görüşme sırasında bir dizi formlar kullanılarak toplandı. Çalışmada, sosyo-demografik bilgi formu, Hastane Anksiyete ve Depresyon Ölçeği (HADS), Golombok-Rust Cinsel Doyum Ölçeği (GRCDÖ) ve Yaşam Kalitesi Ölçeği (EORTC-QoL-C30) uygulandı.
Bulgular: Hastaların %46.26'sında depresyon, %40.29'unda yüksek seviyede anksiyete saptandı. Fiziksel, rol, bilişsel, duygusal ve sosyal işlevsellik ve global yaşam kalitesi alt skorları, anksiyete seviyeleri yüksek hastalarda düşük bulundu. Depresyon skorları yüksek olan hastalarda, fiziksel işlevsellik ve global yaşam kalitesi alt skorları dışındaki tüm işlevsellik skalaları istatistiksel olarak düşük bulundu. Anksiyete seviyeleri yüksek olan hastalarda, tüm GRCDÖ altskorları yüksekti. Fakat istatiksel olarak fark sadece iletişim, doyum, dokunma ve anorgasmi alt skorlarında gözlemlendi. Depresyon seviyeleri yüksek olan hastalarda tüm GRCDÖ alt skorları yüksekti. Fakat istatiksel olarak fark sadece iletişim, doyum, dokunma ve anorgasmi alt skorlarında gözlemlendi.
Sonuç: Meme kanseri ve uzun dönemli adjuvant tedaviler, hastaların sadece klinik durumlarını değil psikososyal ve psikoseksüel durumlarını da etkilemektedir. Bu nedenle, bu durumların farkında olunması, meme kanserli hastaların yaşam kalitesini yükseltecektir.
Anahtar Kelimeler: Depresyon; Anksiyete; Yaşam kalitesi; Cinsel doyum; Meme kanseri

ABSTRACT

Objective: In this study, we aimed to determine the effects of tamoxifen on premenopausal breast cancer patients in terms of anxiety, depression, quality of life (QoL) and sexual satisfaction.
Methods: Sixty-seven premenopausal patient with breast cancer using adjuvant tamoxifen were participated in the study and the data were collected by using a series of forms that completed during face-to-face interviews. The form that consists of socio-demographic characteristics of the pateints, the Hospital Anxiety and Depression Scale (HADS), Golombok-Rust Inventory of Sexual Satisfaction (GRISS) and European Organization for Research on Treatment of Cancer Questionnaires Quality of Life-C30 (EORTC-QoL-C30) were applied to the participants.
Results: We determined that 46.26% of the patients had depression and 40.29% had high anxiety levels. Physical, role, cognitive, emotional and social functioning and global QoL subscores were also found to be low in patients whose anxiety levels were high. In patients whose depression scores were high, all the functioning scales, except physical functioning scale and global QoL subscores of EORTC-QLQ-C30 were found statistically significantly low. All the GRISS subscores were higher in the patients whose anxiety levels were high. However, statistical significance was observed only in the communication, satisfaction, touch and anorgasmi subscores. All the GRISS subscores were higher in the patients who had high depression level. But the statistical significance was found only in communication, satisfaction, touch and anorgasmi subscores.
Conclusion: Breast cancer and its long-term adjuvant treatments affect not only the patients' clinical status but also their psychosocial and psychosexual aspects. Therefore, being aware of these aspects and management of them may increase the quality of life of breast cancer patients.
Key words: Depression; Anxiety; Sexual satisfaction; Quality of life; Breast cancer

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Introduction

Breast cancer (BC) is the second most common cancer and the second leading cause of cancer deaths in women (1). Treatment of breast cancer contains three main modalities; surgery, radiotherapy and chemotherapy (2). Besides, hormonal therapy has also an important role in the treatment of breast cancer. Among the hormonal agents, tamoxifen is the most commonly used drug in the premenopausal setting. Tamoxifen can be administered as adjuvant, neoadjuvant or palliative intent.

Although breast cancer patients have high survival rate mainly because of the developments in medical technology and understanding its tumor biology, treatment-related side effects may still lead to physical and psychological distress in the breast cancer survivals (3,4). In one of the study, psychiatric disorders were observed in about half (47%) of the cancer patients (5). Depression and anxiety in cancer patients were also estimated ranging from 1.5% to 50% and from 20% to 50%, respectively (6,7). Depression and anxiety rates are highly correlated in women with BC and most of them suffer from both types of symptoms (8). Breast cancer patients with depression and anxiety often increase physical side effects and may experience reduced quality of live (QoL) (9). Additionally, many studies showed that there was a significant correlation between sexual problems and reduced QoL among younger BC survivors (10,11). Moreover, these negative mood states significantly increase the risk of mortality in women with BC (12).

Tamoxifen, an anti-estrogenic agent, improves survival of premenopausal early-stage breast cancer female patients. It often results in menopausal symptoms, permanent infertility or the need to delay pregnancy (13-15). However, it is still unclear whether tamoxifen has a positive or adverse effect on sexual functioning (16,17). In a related study with limited number of patients, it is reveald that treatment with tamoxifen may not lead to contribute sexual problems (18). On the contrary, when vaginal smears were obtained before and after tamoxifen treatment, it is found that this drug has estrogen agonist effect on vaginal mucosa (19). So, treatment with tamoxifen may cause vaginal atrophy and problems with sexual desire.

Especially in recent years, despite the increase in the number of studies examining the psychosocial and psychosexual changes in the women diagnosed with breast cancer, there are few studies that investigated the effects of tamoxifen with respect to these aspects. So, we aimed to evaluate the effects of adjuvant tamoxifen treatment on anxiety, depression, QoL and sexual satisfaction of the premenopausal breast cancer patients.

Materials and Methods

Patient Selection

Sixty-seven premenopausal breast cancer patients treated with adjuvant tamoxifen in medical oncology clinics of Izmir Katip Celebi University Atatürk Research and Training Hospital were enrolled in this study. Breast cancer patients who did not have a partner were excluded. Seventy-one eligible women with breast cancer were asked to participate in the study and four of them denied answering the questionnaires. So, 67 patients were selected for this study.

Data collection

The data were collected using a series of forms completed during face-to-face interviews by trained interviewers for determination of the psychological status, sexual satisfaction, and quality of life of the patients. The participants were informed about the study. Informed consent was applied and no interview was conducted without the written consent of the patient. Participants were asked to complete four questionairres. The first form consisted of questions regarding *the socio-demographic characteristics and medical history of the patients.*

The second form was the *Hospital Anxiety and Depression Scale (HADS)* The Hospital Anxiety and Depression Scale is a self-assessment scale that has been developed and found to be a reliable instrument for detecting states of depression and anxiety in the setting of a hospital medical outpatient clinic. It is suggested that the introduction of HADS into general hospital practice would facilitate the large task of detection and

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management of emotional disorder in patients under investigation and treatment in medical and surgical departments. This scale is made up of 14 items consisting of HADS-A (Anxiety, 7 questions) and HADS-D (Depression, 7 questions) subscales (20). Each item on the questionnaire is scored from 0-3 and this means that a person can score between 0 and 21 for either anxiety or depression and an overall total score ranging from 0 to 42 with higher scores indicating greater levels of depression and anxiety. The HADS was translated in to Turkish by Aydemir O. et al (21). After satisfied validity and reliability studies, it was reported as a suitable tool for the Turkish population. The reliability coefficient of the anxiety and depression HADS subscales for the Turkish patient group was 0.85 and 0.78, respectively (21).

The third form was the *Golombok-Rust Inventory of Sexual Satisfaction (GRISS)*. The Golombok-Rust Inventory of Sexual Satisfaction (22) is a 28-item questionnaire used to evaluate the quality of the sexual life and sexual dysfunction. It has two different types for males and females. The female form includes 7 subscales as frequency, communication, satisfaction, avoidance, touch, vaginismus and anorgasmi. The male form includes impotence and premature ejaculation instead of anorgasmi and vaginismus. A score of 5 points or higher in any category reveals sexual dysfunction. A validation and reliability study of GRISS in Turkish population was done by Tugrul C. et al (23). In our study we used only the female form.

The fourth form was *European Organization for Research on Treatment of Cancer Questionnaires Quality of Life-C30* (EORTC-QOL-C30): The EORTC QOL-C30 is a questionnaire developed to assess the quality of life of cancer patients. It consists of 30 items that measure the quality of life of cancer patients into three major domains: functional scales, global health/quality of life and symptom scales (24). Functional scales consist of physical (five items), social (two items), emotional (four items), role (two items) and cognitive (two items) items. Quality of Life scale consists of two items. There are also nine symptom scales associated with fatigue (three items), nause and vomiting (two items), pain (two items), dyspnea, insomnia, appetite loss, diarrhea and constipation (one each items) (25). A validation and reliability study of EORTC-QOL-C30 in Turkish population was done by Beser and Oz (26).

Statistical analysis

All data were analyzed by using SPSS for Windows version 20.0. Descriptive statistics summarized frequencies and percentages for categorical variables, mean and standard deviation for continuous variables. Independent samples T-tests were used to compare categorical variables. A value of $p<0.05$ was considered as significant.

Results

The mean age of breast cancer patients was 42.7±4.7 (range, 34–50). Among the patients, local disease (44.8%) and locally advanced disease (55.2%) was nearly equally distributed. Most of the patients (71.6%) had primary education while only 6% of them were graduated from university. Thirty-seven patients (55.2%) had cancer history in their families. The demographic and clinical characteristics of the 67 female breast cancer patients were shown in Table 1.

Table 1. Demographic and clinical characteristics of the patients

Demographic and Clinical Characteristics	Patients (n=67)
Age (mean±SS) (min-max)	42.7±4.7 (34-50)
Education	
Primary Education	48 (71.6%)
High School	15 (22.4%)
University	4 (6%)
Monthly income	
<1000 TL	29 (43.3%)
≥1000 TL	38 (56.7%)
Cancer History of Family	
Yes	37 (55.2%)
No	30 (44.8%)
Type of Surgery	
Modify Radical Mastectomy	30 (44.8%)
Breast Conservation Surgery	37 (55.2%)
Disease Stage	
Local Disease	30 (44.8%)
Locally Advanced Disease	37 (55.2%)

The mean HADS-A and HADS-D scores of the patients were 8.85±6.53 and 6.79±5.91, respectively. The mean global quality of life score was 61.07±32.51, fatigue score was 50.5±38.81 and pain score was

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24.38±29.5. The vaginismus and anorgasmi scores (3.32±1.72, 3.94±2.48) were found higher than the other subscores of GRISS. Among all, 46.26% of the patients showed results above the cut-off for depression and 40.29 % had high anxiety above the cut-off. The mean scores of HADS, EORTC-QLQ-C30 and GRISS of the patients were shown in Table 2.

Table 2. The mean scores of HADS, EORTC-QLQ-C30 and GRISS of the patients

	mean±SD
HAD Anxiety score	8.85±6.535
HAD Depression score	6.79±5.915
Total HAD	15.64±11.43
Physical functioning	65.84±24.95
Role functioning	72.28±33.08
Cognitive functioning	63.93±36.44
Emotional functioning	58.95±35.74
Social functioning	66.66±37.93
Global quality of life	61.07±32.51
Fatigue	50.5±38.81
Pain	24.38±29.05
Nausea and vomiting	21.64±34.93
Dyspnea	17.99±29.2
Insomnia	27.36±40.17
Appetite loss	22.88±36.33
Constipation	14.42±29.14
Diarrhea	6.96±24.29
Financial problems	29.84±41.49
Avoidance	2.4±2.12
Frequence	2.78±1.13
Vaginismus	3.32±1.72
Satisfaction	2.04±1.7
Communication	2.17±1.81
Anorgasmi	3.94±2.48
Touch	2.4±2.29

HADS: Hospital Anxiety and Depression Scale
GRISS: Golombok-Rust Inventory of Sexual Satisfaction
EORTC- QoL-C30: European Organization for Research on Treatment of Cancer Questionnaires Quality of Life-C30

The comparison of the EORTC-QLQ-C30, GRISS scores and anxiety levels of the patients were shown in Table 3 and 4. It was determined that physical, role, cognitive, emotional and social functioning and global

Table 3. Comparison of the EORTC QLQ-C30 scores and anxiety levels of the patients

Physical functioning		
anxiety ≥ 10	57.38±26.17	**0.021**
anxiety <10	71.5±22.68	
Role functioning		
anxiety ≥ 10	59.5±35.32	**0.008**
anxiety<10	80.9±28.83	
Cognitive functioning		
anxiety ≥10	52.47±35.93	**0.03**
anxiety<10	71.6±35.14	
Emotional functioning		
anxiety ≥ 10	36.11±31.9	**0.001**
anxiety <10	74.37±29.6	
Social functioning		
anxiety ≥ 10	58.64±39.5	0.156
anxiety <10	72.08±36.27	
Global quality of life		
anxiety ≥ 10	44.14±32.26	**0.001**
anxiety <10	72.49±27.62	
Pain		
anxiety ≥ 10	26.54±27.4	0.62
anxiety <10	22.9±30.35	
Nausea and vomiting		
anxiety ≥ 10	20.9±34.46	0.9
anxiety <10	22.08±35.67	
Dyspnea		
anxiety ≥ 10	24.69±33.13	0.119
anxiety <10	13.33±25.64	
Insomnia		
anxiety ≥ 10	41.97±44.9	**0.013**
anxiety <10	17.5±33.75	
Appetite loss		
anxiety ≥ 10	24.68±36.5	0.741
anxiety <10	21.66±36.63	
Constipation		
anxiety ≥ 10	11.1±24.45	0.448
anxiety <10	16.66±32.02	
Diarrhea		
anxiety ≥ 10	8.64±27.09	0.64
anxiety <10	5.83±22.5	
Financial problems		
anxiety ≥ 10	39.5±44.37	0.118
anxiety <10	23.3±38.63	

EORTC- QoL-C30: European Organization for Research on Treatment of Cancer Questionnaires Quality of Life-C30

QoL subscores were low in the patients whose anxiety levels were high whereas pain, dyspnea, insomnia, appetite loss, diarrhea subscores were higher in the patients who has high anxiety levels. When we analyzed the results in terms of EORTC-QLQ-C30, we found statistical significance in the physical, role, cognitive and emotional functioning, global QoL and insomnia subscores of the patients (Table 3). All the GRISS subscores were found higher in the patients whose anxiety levels were high. However, statistical significance was found only in the communication, satisfaction, touch and anorgasmi subscores (Table 4).

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Table 4. Comparison of the GRISS scores and anxiety levels of the patients

	Patient	**p**
Frequency		
anxiety ≥ 10	3.1±0.9	0.061
anxiety <10	2.57±1.19	
Communication		
anxiety ≥ 10	2.7±1.75	**0.026**
anxiety <10	1.7±1.75	
Satisfaction		
anxiety ≥ 10	2.7±1.9	**0.008**
anxiety <10	1.6±1.3	
Avoidance		
anxiety ≥ 10	2.93±2.13	0.094
anxiety <10	2.05±2.06	
Touch		
anxiety ≥ 10	3.22±2.69	**0.014**
anxiety <10	1.84±1.82	
Vaginismus		
anxiety ≥ 10	3.31±1.64	0.963
anxiety <10	3.3±1.78	
Anorgasmi		
anxiety ≥ 10	4.72±2.26	**0.033**
anxiety <10	3.41±2.5	

GRISS: Golombok-Rust Inventory of Sexual Satisfaction

The comparison of the EORTC-QLQ-C30, GRISS scores and depression levels of the patients were shown in Table 5 and 6. In the patients whose depression scores were high, all the functioning scales, except physical functioning scale, and global quality of life subscores of EORTC-QLQ-C30 were found statistically significantly low. All the symptom subscores were found high in the patients who had high depression levels. The result was also similar with respect to anxiety level, all the subscores of GRISS were determined higher in the patients whose depression levels were high. Statistically significant difference was observed only in pain, dyspnea, insomnia, appetite loss and financial problems (Table 5). All the GRISS subscores were higher in the patients who had high depression level. But statistical significance was found only in communication, satisfaction, touch and anorgasmi subscores (Table 6).

Table 5. Comparison of the EORTC-QLQ-C30 scores and depression levels of the patients

	Patient	**p**
Physical functioning		
depression ≥ 7	60.77±24.56	0.124
depression <7	70.2±24.8	
Role functioning		
depression ≥ 7	62.37±35.87	**0.022**
depression <7	80.82±28.27	
Cognitive functioning		
depression ≥ 7	45.43±35.9	**0.001**
depression <7	79.85±28.8	
Emotional functioning		
depression ≥ 7	39.25±33.27	**0.001**
depression <7	75.9±28.64	
Social functioning		
depression ≥ 7	53.2±40	**0.006**
depression <7	78.24±32.31	
Global quality of life		
depression ≥ 7	47.04±30.7	**0.001**
depression <7	73.15±29.28	
Pain		
depression ≥ 7	34.9±33.14	**0.005**
depression <7	15.28±21.59	
Nausea and vomiting		
depression ≥ 7	26.88±39.35	0.257
depression <7	17.12±30.46	
Dyspnea		
depression ≥ 7	28.49±35	**0.005**
depression <7	8.79±19.3	
Insomnia		
depression ≥ 7	40.86±46.9	**0.01**
depression <7	15.73±29.26	
Appetite loss		
depression ≥ 7	33.32±43.03	**0.028**
depression <7	13.88±26.87	
Constipation		
depression ≥ 7	17.2±32.06	
depression <7	12.03±26.6	0.473
Diarrhea		
depression ≥ 7	28.49±35	0.862
depression <7	8.79±19.3	
Financial problems		
depression ≥ 7	40.86±46.11	**0.043**
depression <7	20.36±34.98	

EORTC- QoL-C30: European Organization for Research on Treatment of Cancer Questionnaires Quality of Life-C30

Table 6. Comparison of the GRISS scores and depression levels of the patients

	Patient	**P**
Frequency		
depression ≥ 7	2.9±1.06	0.170
depression <7	2.6±1.18	
Communication		
depression ≥ 7	2.7±1.69	**0.025**
depression <7	1.7±1.8	
Satisfaction		
depression ≥ 7	2.64±1.92	**0.006**
depression <7	1.53±1.3	

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Avoidance		
depression ≥ 7	2.72±2.11	0.265
depression <7	2.13±2.12	
Touch		
depression ≥ 7	3.15±2.55	**0.011**
depression <7	1.75±1.85	
Vaginismus		
depression ≥ 7	3.71±1.81	0.081
depression <7	2.9±1.58	
Anorgasmi		
depression ≥ 7	4.69±2.44	**0.02**
depression <7	3.29±2.35	

GRISS: Golombok-Rust Inventory of Sexual Satisfaction

Discussion

In BC, patients may experience physical loss, emotional distress, destruction in family, work and social roles. It may also cause uncertainty about changes in a woman's body image and treatment options. Besides, these intense and long-time treatments and its adverse effects could lead to psychosocial and sexual problems and could result in reduced quality of life for breast cancer patients (27). As cancer is a chronic disease, the quality of life can be affected in various dimensions including the physical, psychological, social, functional and sexual (28). In this study, we evaluated depression, anxiety, quality of life and sexual satisfaction of the premenopausal breast cancer patients treated with adjuvant tamoxifen.

In women with early breast cancer, the prevalence of depression, anxiety or both in the year after diagnosis is about twice that of the general female population. We found that 46.26% of the patients showed results above the cut-off level for depression and 40.29% had high anxiety levels. In a study conducted by Pandey et al. (2), depression range was found as low as 16.2%. Lim et al. reported that nearly 60% of cancer patients may experience feelings of anxiety and depression (29) whereas Thewes et al found that 32% of the patients showed results above the cut-off level for depression and 14% had high anxiety levels (30).

In our study we also examined the relation between depression and anxiety level, and quality of life. We found that the women with high anxiety levels had low physical, role, cognitive, emotional and social functioning and global quality of life subscores. In the patients whose depression scores were high, all the functioning scales, except physical functioning scale, and global quality of life subscores of EORTC-QLQ-C30 were found statistically significantly low. All the symptom subscores were found high in the patients who had high depression levels. Statistical significance was determined only in pain, dyspnea, insomnia, appetite loss and financial problems.

Tamoxifen improves survival for premenopausal women diagnosed with early-stage breast cancer. However, it also have many unpleasant side-effects including menopausal hot flashes, other vasomotor symptoms, cognitive problems, loss of bone-mineral density, changes in body image and sexual function, vaginal dryness and altered plans for child-bearing (31). The drug has estrogen agonist effect and theoretically, treatment with tamoxifen could result in vaginal atrophy and problems with desire (32). But it is unclear that whether tamoxifen has a favorable or unfavorable effect on sexual functioning (33).

Sexual satisfaction of the patients who were treated with adjuvant tamoxifen according to depression and anxiety levels was also analyzed in this study. All the patients who had high depression and anxiety levels had higher subscores of GRISS. Statistical significance was in communication, satisfaction, touch and anorgasmi subscores of the patients who had higher depression and anxiety levels. Schover et al. stated that the women who had received adjuvant chemotherapy had higher incidence of sexual dysfunction (vaginal dryness, dyspareunia and decreased libido) than the women who were treated with either adjuvant tamoxifen or no additional systemic therapy. It was also determined that the incidence of sexual dysfunction in women treated with tamoxifen was similar with the patients who did not receive any systemic therapy (34). In the study of McCaughan et al., it is found that the women who were treated with hormonal therapy did not experience significantly different levels of sexual dysfunction than the women who were not treated with hormonal therapy (35). Similarly, Ganz et al. examined the relation between tamoxifen usage and sexual functioning in breast cancer survivors and they revealed no difference in sexual functioning between women treated with or

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without tamoxifen (36). In contrast with these studies, Joanne et al observed that women treated with tamoxifen could experience symptoms of sexual dysfunction (19).

Limited number of the patients and different follow-up intervals of the patients were the major limitations of our study. The other limitation was we didn't know the anxiety and depression scores of the patients before using tamoxifen. However, detailed analysis of the effects of adjuvant tamoxifen treatment on our premenopausal breast cancer patients gave us important clues about how to identify these problems and manage them before they were apparent. In conclusion, breast cancer and its long-term adjuvant tamoxifen treatment affects not only the patients' clinical status but also their psychosocial and psychosexual aspects. Thus, being aware of these aspects and taking precautions may increase the quality of the breast cancer patients.

Conflict of Interest: None

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