



Artículo original

**Effect of Mirtazapine on Improving the Quality of Life in
Breast Cancer Patients**

**Efecto de la mirtazapina en la calidad de vida de pacientes con
cáncer de mama**

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Abstract

Introduction: Mirtazapine is an antidepressant drug with serotonergic and noradrenergic effects, which is used to treat various cancer symptoms.

Objective: Describe the effect of Mirtazapine medication on improving the quality of life in breast cancer patients, in Sabzevar, Iran.

Methods: This study was conducted as a randomized controlled clinical trial on two groups of breast cancer patients referred to the chemotherapy and radiotherapy center at Vasei Educational Hospital in Sabzevar, Iran, in 2022. After random assignment, the research had 55 patients in the intervention group (Mirtazapine) and 55 in the control group. The intervention group received Mirtazapine medication for 8 weeks under the supervision of a psychiatrist, at a daily dose of 15-30 milligrams. After 8 weeks, all patients were asked to complete a quality-of-life questionnaire again. The data was analyzed using SPSS 24 software and a t-test, and chi-square test, with a significance level of 0.05.

Results: The average age of the patients was 54.05 ± 12.91 . The two groups were homogeneous in all quantitative and qualitative variables before the intervention, and there was no significant statistical difference ($p > 0.05$).

The comparison of the average variables in the two groups in the field of quality of life after intervention has been reported to be significant ($P = 0.008$). Moreover, this comparison in the field of general health after intervention between the two research groups was not significant ($p = 0.779$). The use of Mirtazapine medication in cancer patients significantly improved sleep quality and sexual relationships, and improved their sexual function, mood, sadness, anxiety, and depression ($p < 0.001$).

Conclusion: A recent study showed that using Mirtazapine medication in cancer patients enhances sleep quality, satisfaction in sexual relationships, mood, depression, and anxiety symptoms, and overall quality of life without affecting the general health subscale.

Keywords: depression; cancer; quality of life; mirtazapine

Resumen

Introducción: la mirtazapina es un fármaco antidepresivo con efectos serotoninérgicos y noradrenérgicos que se utiliza para tratar diversos síntomas del cáncer.

Objetivo: describir el efecto de la Mirtazapina en la mejora de la calidad de vida de los pacientes con cáncer de mama.

Métodos: este estudio se realizó como un ensayo clínico controlado aleatorio en dos grupos de pacientes con cáncer de mama remitidos al centro de quimioterapia y radioterapia del Hospital Educativo Vasei de Sabzevar, Irán en 2022. Después de la asignación aleatoria, 55 pacientes formaron el grupo de intervención (mirtazapina) y 55 en el grupo de control. El grupo de intervención recibió medicación mirtazapina durante ocho semanas bajo la supervisión de un psiquiatra, en una dosis diaria de 15-30 miligramos. Después de ocho semanas, se les solicitó a todas las pacientes que completaran nuevamente un cuestionario de calidad de vida. Los datos se analizaron utilizando el software SPSS 24 y una prueba t y una prueba de chi-cuadrado, con un nivel de significancia de 0,05.



Resultados: la edad promedio de las pacientes fue de $54,05 \pm 12,91$. Los dos grupos eran homogéneos en todas las variables cuantitativas y cualitativas antes de la intervención, y no hubo diferencia estadísticamente significativa ($p > 0,05$). La comparación de las variables promedio en los dos grupos sobre la calidad de vida después de la intervención fue significativa ($p = 0,008$). Además, la salud general después de la intervención entre los dos grupos de investigación no fue significativa ($P = 0,779$). El uso de la mirtazapina en pacientes con cáncer mejoró significativamente la calidad del sueño, las relaciones sexuales y el estado de ánimo ($p < 0,001$).

Conclusión: el estudio mostró que el uso de la medicación Mirtazapina en pacientes con cáncer mejora la calidad del sueño, la satisfacción en las relaciones sexuales, el estado de ánimo, los síntomas de depresión y ansiedad y la calidad de vida en general sin afectar la subescala de salud general.

Palabras clave: depresión; cáncer; calidad de vida; mirtazapina

Introduction

Breast cancer (BC) is the most common and second leading cause of cancer-related death among women aged 35 to 54 years. According to the latest WHO report in 2020, 2.3 million (11.7 % of newly diagnosed) women worldwide were diagnosed with breast cancer and 685,000 deaths were recorded as a result of the disease.⁽¹⁾ In general, breast cancer treatment is divided into two groups: local treatment including surgery and radiotherapy, and systematic treatment groups such as adjuvant and neoadjuvant chemotherapy, immunotherapy, and hormone therapy. The main chemotherapy drugs include Doxorubicin, Cyclophosphamide, and Taxanes, which are often used in combination with each other to treat breast cancer.⁽²⁾ Recent advances in the management of breast cancer treatment have made the treatment of this cancer improve the overall survival of patients.⁽³⁾ However, the use of these treatments has side effects that reduce the quality of life of patients in the long term.

One of the most important issues in clinical research is the assessment of the quality of life (QOL), which includes patient's feelings about their ability to perform physical, emotional, and social functions.⁽⁴⁾ The increase in the prevalence of cancer in recent years and its effects on the physical, psychological, and social dimensions of human life have caused cancer to be recognized as a major health problem of the century. Breast cancer, as the most common female cancer, has an important role in this problem. The impact of treatment methods on the survival of breast cancer patients is an important goal in health care as well as their mental and psychological health in studies due to the high prevalence of breast cancer in women and the therapeutic advances that have led to the long survival of patients.⁽⁵⁾ Paying attention to other aspects of breast cancer, including the side effects of treatment that affect the quality of life of patients, can help improve the quality of life and mental health of patients. One of the common side effects in breast cancer patients is depression, which affects the quality of life in these patients. According to the report of Pilevarzadeh et al., the global prevalence of depression is 32.2 % among breast cancer patients,⁽⁶⁾ the management of this complication can improve the quality of life and increase the survival of cancer patients.



Mirtazapine is an antidepressant drug with serotonergic and noradrenergic effects, which is used to treat various symptoms of cancer, such as depression, as well as in the treatment of sleep and appetite disorders.⁽⁷⁾ In recent years, researchers have begun to study the antioxidant activity of mirtazapine along with its anti-depressant effects.⁽⁸⁾ Despite the very low risks of using this drug, some studies report side effects such as dry mouth, increased appetite, and weight gain.^(9, 10) Considering the roles of mirtazapine in the management of some psychological disorders such as depression and its effects on improving the quality of life of patients with breast cancer. This study aimed to describe the effect of Mirtazapine on improving the quality of life for cancer patients in Sabzevar, Iran.

Methods

This study was conducted as a randomized controlled clinical trial on two groups of breast cancer patients referred to the chemotherapy and radiotherapy center at Vasei Educational Hospital of Sabzevar, Iran in 2022. After random assignment, the research had 55 patients in the intervention group (Mirtazapine) and 55 in the control group.

Sample size

The sample size was calculated using the formula for the experimental survey.¹¹ In this study, random allocation was used. With a margin of error = 0.05 and = 10 %, an expected power of 90 %, a Z value of 1.28. Participants were 55 patients in each group in Iran.

$$n = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

Inclusion criteria: 1- Diagnosis of cancer (both new cases and patients visiting for follow-up) 2- Not using sleeping pills simultaneously 3- Major depressive disorders according to DSM IV criteria.

Exclusion criteria: 1- Inaccessibility to the patient due to migration from the area and... 2- Failure to adhere to a regular treatment plan 3- In case of side effects: Common: Unusual dreams/anxiety/joint pain and dizziness/sleepiness/dry mouth/fatigue/insomnia/increased appetite/edema/orthostatic hypotension/tremor/weight gain/agitation/anxiety/headache/dizziness/nausea and vomiting Uncommon: Delusions/mania/syncope/movement disorders/ Rare: Aggression/pancreatitis/sudden muscle contractions

Uncertain occurrence: Acute angle closure glaucoma/blood disorders/seizures/dysarthria/hyponatremia/increased salivation/inappropriate anti-diuretic hormone secretion/sedative effects at the start of treatment/Steven Johnson syndrome 4- Not taking medication and following the intervention.

Data collection tools:



World Health Organization Quality of Life Questionnaire⁽¹²⁾

Physical Health Subscale: The sum of scores for questions 3, 4, 10, 15, 16, 17, 18 in the questionnaire. The score range for this subscale will be between 7 and 35, with a difference of 28.

Mental Health Subscale: The sum of scores for questions 5, 6, 7, 11, 19, 26 in the questionnaire. The score range for this subscale will be between 6 and 30, with a difference of 24.

Social Relationships Subscale: The sum of scores for questions 20, 21, and 22 in the questionnaire. The score range for this subscale will be between 3 and 15, with a difference of 12.

Environmental Health Subscale: The sum of scores for questions 8, 9, 12, 13, 14, 23, 24, 25 in the questionnaire. The score range for this subscale will be between 8 and 40, with a difference of 32.

Overall Quality of Life and General Health: The sum of scores for questions 1 and 2 in the questionnaire. The score range for this subscale will be between 2 and 10, with a difference of 8.

Method for determining the reliability of the tool: This questionnaire was developed by the World Health Organization and Nazari and colleagues demonstrated the validity and reliability of the Persian version through a study.

The intervention group received Mirtazapine medication for 8 weeks under the supervision of a psychiatrist, at a daily dose of 15-30 milligrams. After 8 weeks, all patients were asked to complete a quality-of-life questionnaire again.

To describe quantitative variables based on conditions, the mean (standard deviation) was used, and for qualitative variables, frequency report (percentage) was used. To compare the average quantitative outcomes between two study groups, the t-test or its non-parametric equivalent, the Mann-Whitney test, was used. To compare qualitative factors between study groups, the chi-square test or Fisher's exact test was applied. The data obtained from the study was analyzed using SPSS software version 24, and a significance level of 0.05 was considered.

All participating parents provided informed consent, and the project adhered to the ethical code: IR.MEDSAB.REC.1399.192. The project was registered under the IRCT code: IRCT20210425051075NN1.

Results

In this research, 110 cancer patients referred to the Chemotherapy and Radiotherapy Center in Iran with an average age of 54.05 years and a standard deviation of 12.91 participated. Frequency distribution of education and marital status in two intervention and control groups using the Chi-



square test showed no significant difference between these two groups in terms of education level and marital status ($P = 0.897$). According to the variables of the study (quality of sleep, life expectancy, enjoyment of life, satisfaction with sexual relations, and improvement of sad and hopeless mood and anxiety and depression), the questions of the questionnaire were divided into 6 groups: the question related to the quality of life (question 1), general health (question 2), physical health (questions 3, 4, 10, 15, 16, 17, 18), psychological health (questions 5, 6, 7, 11, 19, 26), social relations (questions 20, 21, 22) and social environment (8, 9, 12, 13, 14, 23, 24, 25). The results of completing the questionnaires were analyzed using the Mann-Whitney test and the average variables of the questionnaires were compared in the intervention and control groups (table 1).

Table1. Comparison of average questionnaire variables in two intervention and control groups in cancer patients

Variable	Group	N	M	SD	SEM
Quality of life (pre intervention)	Education	55	3.2545	.72567	.09785
	control	55	3.2000	.96992	.13078
General health subscale (pre intervention)	Education	55	3.0909	.84487	.11392
	control	55	3.8909	4.08100	.55028
Physical health subscale (pre intervention)	Education	55	20.8727	4.80376	.64774
	control	55	20.4182	4.52847	.61062
Psychology health subscale (pre intervention)	Education	55	17.6364	2.69680	.36364
	control	55	18.1636	2.80716	.37852
Social health subscale (pre Intervention)	Education	55	9.4909	1.63155	.22000
	control	55	9.2727	1.89985	.25618
Environment health subscale (pre intervention)	Education	55	27.4909	4.36685	.58883
	control	55	25.1273	3.46439	.46714
Quality of life subscale (post intervention)	Education	55	3.5273	.57267	.07722
	control	55	3.1636	.81112	.10937
General health subscale (post intervention)	Education	55	3.3818	.56078	.07562
	control	55	3.3455	.77503	.10451
Physical health subscale (post intervention)	Education	55	22.8545	3.84138	.51797
	control	55	20.1455	4.31800	.58224
Pshychology health subscale (post intervention)	Education	55	19.8727	2.25302	.30380
	control	55	17.5273	2.87296	.38739
Social health subscale (post intervention)	Education	55	10.2909	1.79168	.24159
	control	55	9.2000	2.12045	.28592
Environment health subscale (post intervention)	Education	55	27.6364	4.34768	.58624
	control	55	25.0182	3.58232	.48304

M= mean SD= estándar desviation SEM= standar error mean

The results of this comparison showed that the average variables in the field of psychological health before the intervention did not differ significantly between the two intervention and control groups (P value = 0.317), but after the intervention, it was significantly different ($P < 0.001$). And the participants of the intervention group had a higher average. This comparison also showed that the average variables in the field of physical health were not significantly different between the two groups ($p = 0.611$), but after the intervention, this difference became relatively significant ($p = 0.001$). In the field of social relations, the average difference of the study variables between the two intervention and control groups was not significant before the intervention ($p = 0.520$), but after the



end of the intervention, it became relatively significant ($p = 0.004$). In the field of social environment, before the intervention, the difference in the average of the variables between the two groups was almost significant (p value = 0.002) and after the end of the intervention, it became significant as well ($P = 0.001$). The comparison of the average variables in the two groups in the field of quality of life before intervention ($p = 0.739$) and after ($p = 0.008$) has been reported to be significant. Also, this comparison in the field of general health before ($p = 0.157$) and after ($p = 0.779$) intervention between the two research groups was not significant (table 2).

Table 2. Independent Samples Test in two intervention and control groups in cancer patients

Independent Samples Test										
Questionnaire variables		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	p	t	df	Sig. (2-tailed)	MD	SED	95% confidence interval of the difference	
									Lower	Upper
Quality of life (Pre Intervention)	Education	3.732	.056	.334	108	.739	.05455	.16334	-.26922	.37831
	Control			.334	100.032	.739	.05455	.16334	-.26951	.37860
General health Subscale (Pre Intervention)	Education	1.425	.235	1.424	108	.157	-.80000	.56195	-1.91388	.31388
	Control			1.424	58.620	.160	-.80000	.56195	-1.92461	.32461
Physical Subscale (Pre Intervention)	Education	.195	.660	.511	108	.611	.45455	.89018	-1.30995	2.21904
	Control			.511	107.626	.611	.45455	.89018	-1.31002	2.21911
Psychology Subscale (Pre Intervention)	Education	.088	.767	1.005	108	.317	-.52727	.52489	-1.56769	.51314
	Control			1.005	107.827	.317	-.52727	.52489	-1.56771	.51316
Social Subscale (Pre Intervention)	Education	.305	.582	.646	108	.520	.21818	.33768	-.45115	.88751
	Control			.646	105.590	.520	.21818	.33768	-.45132	.88769
Environment Subscale (Pre Intervention)	Education	3.431	.067	3.145	108	.102	2.36364	.75162	.87379	3.85348
	Control			3.145	102.687	.102	2.36364	.75162	.87292	3.85435
Quality of life (Post Intervention)	Education	1.270	.262	2.716	108	.008	.36364	.13388	.09826	.62902
	Control			2.716	97.120	.008	.36364	.13388	.09792	.62935
General health Subscale (Post Intervention)	Education	4.794	.031	.282	108	.779	.03636	.12899	-.21932	.29205
	Control			.282	98.379	.779	.03636	.12899	-.21961	.29233
Physical Subscale (Post Intervention)	Education	.814	.369	3.476	108	.001	2.70909	.77929	1.16440	4.25378
	Control			3.476	106.556	.001	2.70909	.77929	1.16416	4.25402
Psychology Subscale (Post Intervention)	Education	2.476	.119	4.764	108	.000	2.34545	.49230	1.36962	3.32129
	Control			4.764	102.192	.000	2.34545	.49230	1.36899	3.32191
Social Subscale (Post Intervention)	Education	.493	.484	2.914	108	.004	1.09091	.37432	.34894	1.83288
	Control			2.914	105.073	.004	1.09091	.37432	.34871	1.83311
Environment Subscale (Post Intervention)	Education	3.176	.078	3.447	108	.001	2.61818	.75961	1.11250	4.12386
	Control			3.447	104.189	.001	2.61818	.75961	1.11188	4.12448

$P < 0.05$ MD= mean difference SED= standard error difference

Discussion

The results of this research showed that the use of mirtazapine significantly ($p < 0.001$) improved the sleep quality of participants in the intervention group. These results are consistent with the findings of Konkoutaran and colleagues,⁽¹³⁾ who studied the effects of mirtazapine on improving sleep quality and reducing anxiety and depression symptoms in cancer patients ($p < 0.001$). Additionally, Kim and



colleagues⁽¹⁴⁾ conducted a study in 2008 to assess the effectiveness of oral mirtazapine tablets for nausea and sleep disturbances, common and distressing symptoms of cancer, showing that this medication improves sleep quality in these patients. These results align with the findings of our research.

In the field of general health before ($p = 0.157$) and after ($p = 0.779$) intervention between the two research groups was not significant ($p > 0.05$). These results are consistent with the findings of Claudia Chaves¹⁵ the “General Health” domain (domain 4) showed a negative correlation with the CDQ. These results are not consistent with the findings of studies.⁽¹⁶⁻¹⁸⁾

The results of the study also showed that the use of mirtazapine significantly ($p = 0.004$) improved mood, irritability, anxiety, and depression in breast cancer patients. In 2020, when examining studies on the impact of mirtazapine on improving the quality of life in cancer patients, it was consistent.

The results of the study by Economus and colleague,⁽¹⁹⁾ which aimed to evaluate the effectiveness of mirtazapine in reducing multiple symptoms simultaneously in advanced cancer patients experiencing a major depressive episode, compared to a group receiving escitalopram, another antidepressant, were also consistent with the findings of our research. Zaini and colleague⁽²⁰⁾ also conducted a study in 2017 to investigate the effects of mirtazapine on the physical and mental symptoms of cancer patients, showing that mirtazapine improves the mental symptoms of these patients, including depressive and anxiety symptoms. Arsoyi and colleagues⁽²¹⁾ also conducted a study in 2008 to examine the effect of mirtazapine on depression symptoms in cancer patients, with the results demonstrating that this medication significantly impacts the improvement of depressive symptoms in these patients.

The examination of the results of this study showed that the use of the drug mirtazapine somewhat contributes to improving the satisfaction of cancer patients with their sexual relationships ($p = 0.06$). These findings are consistent with the results of the study by Davis and colleagues⁽²²⁾ in 2002, which focused on treating quality of life symptoms in cancer patients and demonstrated that mirtazapine leads to an 11 % improvement in sexual function in these patients, positively affecting their satisfaction with their sexual relationships.

The results of this research also indicated that the significant use of mirtazapine increases pleasure and satisfaction in the lives of cancer patients ($p < 0.001$). These results align with the findings of the study by Theobald and colleagues,⁽²³⁾ which examined the effect of mirtazapine on anxiety symptoms and quality of life in cancer patients and showed that this drug is effective in improving the quality and satisfaction of life in these patients.

Conclusion

The results of this study indicated that the use of mirtazapine in cancer patients significantly leads to improving sleep quality, lifting mood, reducing feelings of hopelessness, anxiety, and depression, as well as increasing enjoyment of life and its overall quality. In the field of general health intervention



between the two research groups was not significant. Additionally, mirtazapine has positive effects on increasing the satisfaction of cancer patients with their sexual relationships and enhancing their sexual function. The results of this study can be beneficial in treating symptoms such as sleep disorders, sexual dysfunction, mood disturbances, and anxiety symptoms in cancer patients, leading to an improvement in their quality of life.

The use of a larger and more diverse sample population, including individuals with various types of cancer, can help better support the results of this study.

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Ethics approval

Ethical approvals in this study, all procedures performed on human samples were conducted following the relevant guidelines and regulations of the Helsinki Declaration. The study protocol was approved by the Research Ethics Committee (IR.MEDSAB.REC.1399.192) in Sabzevar Iran.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding authors on reasonable request.

Conflict of Interest disclosure: The authors declare that there are not conflicts of interest

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Authors' contributions

All authors read and approved the manuscript.

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