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ORIGINAL ARTICLE

The impact of structured education of breast cancer patients receiving capecitabine on mental disorders

Dusanka Tadic[1], Slavica Djukic-Dejanovic[2], Zorica I. Tomasevic[3], Danijela Djokovic[4], Vladimir Janjic[4]

[1]Academy for Applied Studies Belgrade, Department of Higher Medical School, Belgrade, Serbia; [2]University of Kragujevac, Faculty of Medical Sciences, Kragujevac, Serbia; [3]Institute for Oncology and Radiology of Serbia, Department of Medical Oncology, Belgrade, Serbia; [4]University of Kragujevac, Faculty of Medical Sciences, Clinic of Psychiatry, Clinical Centre "Kragujevac", Kragujevac, Serbia.

Summary

Purpose: *This study was conducted to assess the impact of structured education of breast cancer patients receiving capecitabine treatment on depression, anxiety and stress.*

Methods: *The study included 142 breast cancer patients who were receiving capecitabine at the Institute of Oncology and Radiology of Serbia in 2016 and 2017. Patients were randomized into two study groups: the experimental group had additional individual, structured, specific education, before chemotherapy by using a Serbian version of the Multinational Association of Supportive Care in Cancer (MASCC) Oral Agent Teaching Tool (MOATT V1.0), while the control group had usual standard education. Patients were followed up for 3 weeks, during their first chemotherapy cycle. Two instruments were used: specifically designed, for the purpose of this study, sociodemographic questionnaire and the Serbian version of the Depression Anxiety Stress Scales-21 (DASS 21) self-report questionnaire.*

Results: *Before starting capecitabine and education, breast cancer patients with metastatic disease had symptoms of depression (29.58%), anxiety (35.92%) and stress (21.13%), mostly mild and moderate. These symptoms were decreased in the whole group of patients after the first and the third week from education, with significant difference in depression and anxiety. Depression, anxiety and stress were decreased significantly in experimental group of patients from the initial measurement to the one-week and three-week follow-up, comparing to the control group of patients.*

Conclusions: *Structured education has a significant positive impact on depression, anxiety and stress symptoms of breast cancer patients receiving capecitabine. Therefore, it may be recommended for use in everyday clinical practice.*

Key words: *breast cancer, capecitabine, mental disorders, patient education*

Introduction

Patients suffering from cancer, especially those who are undergoing treatment, have an elevated risk of developing mental disorders compared to cancer survivors and persons without cancer [1]. Meta-analyses showed that one-third of the cancer patients in acute care hospitals develop some mental disorders [2], and that 30-40% of patients in palliative and non-palliative wards have some combination of mood disorders [3], which requires further attention. Also, two large epidemiological studies pointed out similar findings, indicating the need for offering psycho-oncological support to these patients [4,5].

Depression, anxiety and adjustments disorders are very common psychological problems of persons with cancer [2-4]. The highest prevalence

Corresponding author: Dusanka Tadic, PhD candidate. Academy for Applied Studies Belgrade, Department of Higher Medical School, Belgrade, Serbia; Cara Dusana 254 street, 11080 Belgrade, Zemun, Serbia.
Tel: +381 11 2618 120, Mob: +381 65 8240 515, Email: duska.tadic@gmail.com
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for mental disorders was observed in patients with breast cancer [4] with increased levels of depression, anxiety, or both, especially after the initial diagnosis or disease recurrence [6] and during chemotherapy [6,7]. Unfortunately, these negative emotional states among the cancer patients often are unrecognized and untreated by healthcare providers and thus may have a negative impact on their quality of life (QoL) [2,3,8-10]. Some of mental disorders, especially depression, reduces patient active participation in the treatment [3].

Depressed patients are especially at risk for noncompliance with medical treatment [11] which is very important if the patient is undergoing oral chemotherapy [12-14]. This way of drug administration is a great challenge for healthcare professionals, because the patient takes the medication at home, without direct supervision by physicians and nurses, where dosing and side effects monitoring becomes responsibility of the patients, family members and caregivers. If the patients do not take their medications correctly or do not take medications at all, they could not benefit from them. Noncompliance can have many consequences on patient outcomes, such as ineffective treatment, drug resistance, disease progression and side effects caused by toxicities [14]. For this reason, healthcare providers should pay much more attention to symptoms of mental disorders in this specific group of patients.

Clinical assessment and follow up of cancer patients with mental disorders, especially depression, needs a systematic approach [2,3], and providing psycho-oncological interventions [4] including specific patient education by healthcare professionals as well [2,14]. Literature suggests that education and provision of information to cancer patients in combination with psycho-emotional support can improve QoL and diminish anxiety and depression [15-17]. We strongly believe that it is of major importance for patients receiving oral chemotherapy, thus there is a need for identification of the best practice in this area.

Multinational Association of Supportive Care in Cancer (MASCC) developed and evaluated a teaching tool for patients receiving oral agents for cancer to meet the need for a comprehensive and systematic approach to patient education. MASCC Oral Agent Teaching Tool (MOATT) was designed to help clinicians in assessing and teaching patients about all aspects of oral antineoplastic treatment through structured format of education [18,19].

One of the most common prescribed oral cytotoxic agent in the treatment of metastatic breast cancer is capecitabine [20,21] and all findings about compliance and management of this drug, could be, in practice, generalized to all oral cancer therapies [22]. Education and providing information to patients receiving capecitabine has vital role in their management and active participation in this oral, home-based chemotherapy [23].

The aim of our investigation was to assess the impact of structured education of breast cancer patients who are receiving capecitabine on mental health problems such as depression, anxiety and stress (DAS).

Methods

Design and sample

The investigation has been conducted at the Institute of Oncology and Radiology of Serbia, in Belgrade, from March 2016 until November 2017. One hundred forty-two female patients over 18 years old, who had confirmed diagnosis of breast cancer and were receiving oral capecitabine, were enrolled. Eligibility criteria also included absence of any previous psychiatric diagnosis and treatment, brain metastases and life expectancy for more than 6 months as well. The research was approved by the Ethics Committee of the Institute and informed consent about participation in the study was obtained from each patient.

An experimental, prospective analytical study was performed. After patients were informed and consented for participation, they were randomized into two groups, the experimental and control group. The experimental group had additional individual, structured, specific education, before starting chemotherapy, by using a Serbian version of the MOATT V1.0 and the control group had usual, standard education, given in routine clinical practice. Patients were followed up for 3 weeks during their first chemotherapy cycle.

Data collection

Data were collected using specifically designed, for the purpose of this study, sociodemographic questionnaire and the Serbian version of the Depression Anxiety Stress Scales-21 (DASS 21) self-report questionnaire.

The sociodemographic questionnaire consisted of 11 items: age, educational level, employment status, environment, residence, marital status, parenthood, people living together, economic status, family relationship, family participation in treatment, person who provides the greatest support, the impact of illness on contacts with relatives and friends and organizing free time. All patients were asked to answer the sociodemographic questionnaire before education.

The DASS 21 self-report questionnaire was used in order to evaluate the symptoms of DAS. This instrument contains a set of 3 self-reported scales, each consisting of 7 items, designed to measure the negative emotional states of DAS over the past week. The Depression scale evaluates dysphoria, hopelessness, devaluation of life, self-deprecation, and lack of interest/involvement, anhedonia and inertia. The Anxiety scale evaluates autonomic arousal, skeletal muscle effects, situational anxiety and

Table 1. Patient characteristics

Characteristics	*Whole group*	*Groups*		*Pearson x^2 test*
	n (%)	*Experimental n (%)*	*Control n (%)*	
Age (years)				* W=2087.5 p=0.07745
Mean (SD)	61.96 (10.6)	60.18 (11.45)	63.75 (9.42)	
Median (range)	62.5 (33-86)	62 (33-86)	65 (39-84)	
Age (categories)				x^2_1=2.33 p=0.12707
≤60	61 (42.96)	35 (49.30)	26 (36.62)	
>60	81 (57.04)	36 (50.70)	45 (63.38)	
Educational level				x^2_3=5.14 p=0.1614
Primary school	28 (19.72)	19 (26.76)	9 (12.68)	
Secondary school	68 (47.89)	30 (42.25)	38 (53.52)	
High school	15 (10.56)	6 (8.45)	9 (12.68)	
Faculty#	31 (21.83)	16 (22.54)	15 (21.13)	
Employment status				x^2_1=0.76 p=0.3826
Employment	13 (9.15)	8 (11.27)	5 (7.04)	
Unemployment/retired	129 (90.85)	63 (88.73)	66 (92.96)	
Environment				x^2_1=0.76 p=0.3817
Urban	91 (64.08)	48 (67.61)	43 (60.56)	
Suburban/Rural	51 (35.92)	23 (32.39)	28 (39.44)	
Residence				x^2_1=0.75 p=0.386
Belgrade	111 (78.17)	53 (74.65)	58 (81.69)	
Province	30 (21.13)	17 (23.94)	13 (18.31)	
No data	1 (0.70)	1 (1.41)	0 (0)	
Marital status				** p=0.3523
Married	80 (56.34)	42 (59.15)	38 (53.52)	
Single	8 (5.63)	6 (8.45)	2 (2.82)	
Divorced	12 (8.45)	5 (7.04)	7 (9.86)	
Widow	40 (28.17)	17 (23.94)	23 (32.39)	
No data	2 (1.41)	1 (1.41)	1 (1.41)	
Parenthood				x^2_1=0.05 p=0.82007
No	17 (11.97)	8 (11.27)	9 (12.68)	
Yes	124 (87.32)	62 (87.32)	62 (87.32)	
No data	1 (0.70)	1 (1.41)	0 (0)	
Number of children				* W=1960 p=0.4215
Mean (SD)	1.89 (0.63)	1.95 (0.69)	1.83 (0.56)	
Median (range)	2 (1-5)	2 (1-5)	2 (1-3)	
No data	21 (14.79)	10 (14.08)	11 (15.49)	
People living together				x^2_1=3.55 p=0.05938
Alone	27 (19.01)	9 (12.68)	18 (25.35)	
Not alone##	114 (80.28)	61 (85.92)	53 (74.65)	
No data	1 (0.70)	1 (1.41)	0 (0)	
Economic status				x^2_1=1.72 p=0.19015
Under average	47 (33.10)	27 (38.03)	20 (28.17)	
Average/above average	94 (66.20)	43 (60.56)	51 (71.83)	
No data	1 (0.70)	1 (1.41)	0 (0)	
Total	142 (100)	71 (100)	71 (100)	-

* Wilcoxon rank sum test, ** Fisher Exact test, #higher education, MSc, PhD; ##family, home, other

subjective experience of anxious affect. The Stress scale evaluates difficulty in relaxing, nervous arousal and being easily upset/agitated, irritable/over-reactive and impatient. Patients were asked to use 4-point severity/frequency scales to rate the extent to which they have experienced each state over the past week, from 0 ("did not apply to me at all") to 3 ("applied to me very much, or most of the time"). Scores for DAS are calculated by summing the scores for the relevant items and ranging from 0 to 21 on each scale. Rating of severity by using the cut-off scores have been developed for defining normal, mild, moderate, severe and extremely severe scores for each scale, which means degree of symptom severity, not a level of disorder. The DASS 21 is a short version of DASS, suitable for brief evaluating unpleasant emotional conditions, core symptoms of DAS [24]. It has been psychometrically evaluated in the Serbian population and the results demonstrated that the DASS 21 is a reliable and valid measure of unpleasant emotional states [25]. Also, it has been examined in oncologic settings and the results supported psychometric properties of the DASS 21 for measuring psychological distress in cancer patients [26].

All patients were asked to answer the DASS 21 self-report questionnaire before education (initial measurement) and after education, at the end of the first week (I measurement) and the third week (II measurement).

Interventions

MOATT is a teaching tool prepared to assist healthcare professionals in the assessment and education of patients about all aspects of oral antineoplastic treatment through structured format of education. The tool also enables clinicians to ensure that patients know and understand their treatment and that all key aspects of patient assessment and teaching are addressed. This valuable instrument has 4 sections: key assessment questions, patient education, drug specific information and evaluation. The first section contains key assessment questions for assessing the patient's knowledge of the treatment plan, current medications and ability to obtain and take the drug. The second section has generic patient education for all oral antineoplastic agents such as storage, handling, disposal, system to remember to take the drug and actions to take if problem occurs, such as missed dose. The third section provides the drug-specific

Table 2. Social interactions

Characteristics	*Whole group*	*Groups*		*Pearson x^2 test*
	n (%)	*Experimental n (%)*	*Control n (%)*	
Family relationships	21 (14.79)			x^2_2=3.13 p=0.2087
Poor/Satisfactory	21 (14.79)	11 (15.49)	10 (14.08)	
Good	55 (38.73)	32 (45.07)	23 (32.39)	
Very good	62 (43.66)	26 (36.62)	36 (50.70)	
No data	4 (2.82)	2 (2.82)	2 (2.82)	
Family participation in treatment				x^2_1=1.14 p=0.2849
No/partly	27 (19.01)	16 (22.54)	11 (15.49)	
Yes	115 (80.99)	55 (77.46)	60 (84.51)	
Greatest support				** p=0.72059
Nobody	6 (4.23)	4 (5.63)	2 (2.82)	
Partner	59 (41.55)	30 (42.25)	29 (40.85)	
Children	61 (42.96)	28 (39.44)	33 (46.48)	
Others#	16 (11.27)	9 (12.68)	7 (9.86)	
Less social contacts due to illness				x^2_1=3.08 p=0.0789
No	92 (64.79)	51 (71.83)	41 (57.75)	
Partly/yes	50 (35.21)	20 (28.17)	30 (42.25)	
Organizing free time				x^2_2=0.11 p=0.9469
Always	76 (53.52)	38 (53.52)	38 (53.52)	
Sometimes	55 (38.73)	28 (39.44)	27 (38.03)	
Never	11 (7.75)	5 (7.04)	6 (8.45)	
Total	142 (100)	71 (100)	71 (100)	

** Fisher Exact test; #parents, sister/brother, relatives, others

information for the specific treatment that the patient is receiving such as drug name, dose and schedule, where the drug should be stored, potential side effects and management of them, precautions, drug and food potential interreactions as well as when and whom to call with questions. The last section lists the questions that may be asked to ensure that the patient understands the information provided. The tool contains an additional page with drug-specific information that can be given to the patient [18,19].

Patients were educated using the Serbian version of the MOATT V1.0. Individual, structured education was provided before starting oral chemotherapy and lasted about 30 min. The drug-specific information and written instructions for taking the medication was given to each patient.

Statistics

For normality of distribution data testing, the Normal Q-Q Plot and Histogram graphics were used, as well as Kolmogorov-Smirnov and Shapiro-Wilk tests. The data were analyzed using descriptive statistics (frequencies, percentages, mean, median, standard deviation and range), Pearson x^2 test, Fisher exact test and Wilcoxon rank sum test (to assess significant differences between groups), Wilcoxon signed rank test and McNemar test (to test the significant differences between repeated measurements within groups), depending on data type and distribution. For the level of statistical significance the value α=0.05 was adopted. Statistical analyses was carried out using statistical programme R version 3.3.2 (2016-10-31) - "Sincere Pumpkin Patch"; Copyright (C) 2016 The R Foundation for Statistical Computing; Platform: x86_64-w64-mingw32/x64 (64-bit); (available at: www.r-project.org; downloaded: 21.01.2017).

Results

The study included 142 female patients, randomly divided into experimental and control group. The mean age of the total sample was 61.96±10.6 years. Almost half of the patients were secondary school-graduated and the majority of them were unemployed or retired. More than half of them lived in urban environment and were married,

Table 3. Depression, anxiety and stress in the whole group between measurements

Characteristics	*Measurements*				
	Initial measurement	*I measurement*		*II measurement*	
	Before n (%)	*After 1 week* n (%)	*Test (Init. vs I)*	*After 3 week* n (%)	*Test (Init. vs II)*
Depression (score)			*V=2981.5 p=0.074803		*V=2736 p=0.01931
Mean (SD)	3.25 (2.85)	2.95 (3.18)		2.71 (3.05)	
Median (range)	3 (0-18)	2 (0-21)		2 (0-18)	
Depression (categories)			**x^2_1=5.9394 p=0.01481		**x^2_1=5.9211 p=0.01496
Normal	100 (70.42)	115 (80.99)		116 (81.96%)	
Depression#	42 (29.58)	27 (19.01)		26 (18.31%)	
Anxiety (score)			*V=2881 p=0.10211		*V=2808 p=0.07669
Mean (SD)	2.96 (2.53)	2.8 (2.84)		2.65 (2.5)	
Median (Range)	2 (0-20)	2 (0-18)		2 (0-14)	
Anxiety (categories)			**x^2_1= 6.2439 p= 0.01246		**x^2_1= 5.9535 p= 0.01469
Normal	91 (64.08)	108 (76.06)		108 (76.06%)	
Anxiety#	51 (35.92	34 (23.94)		34 (23.94%)	
Stress (score)			*V=2849 p=0.45525		*V=3336.5 p=0.39501
Mean (SD)	5.31 (3.25)	5.21 (3.54)		5.08 (3.27)	
Median (range)	5 (0-21)	5 (0-20)		5 (0-18)	
Stress (categories)			**x^2_1=0.48485 p=0.4862		**x^2_1=0.43243 p=0.5108
Normal	112 (78.87)	117 (82.39)		117 (82.39%)	
Stress#	30 (21.13)	25 (17.61)		25 (17.61%)	
Total	142 (100)	142 (100)		142 (100)	

* Wilcoxon signed rank test, ** McNemar test, #mild, moderate, severe, extremely severe

Table 4. Depression, anxiety and stress between groups

Measures	*Characteristics*	*Whole group*	*Groups*		*Pearson x^2 test*
		n (%)	*Experimental n (%)*	*Control n (%)*	
(before)	Depression (score)				* W=2781.5 p=0.2835
	Mean (SD)	3.25 (2.85)	3.54 (3.07)	2.97 (2.6)	
	Median (range)	3 (0-18)	3 (0-18)	2 (0-10)	
	Depression (categories)				x^2_1=1.22 p=0.2699
	Normal	100 (70.42)	47 (66.20)	53 (74.65)	
	Depression#	42 (29.58)	24 (33.80)	18 (25.35)	
	Anxiety (score)				* W=2943.5 p=0.0807
	Mean (SD)	2.96 (2.53)	3.39 (2.96)	2.54 (1.93)	
	Median (range)	2 (0-20)	3 (0-20)	2 (0-7)	
	Anxiety (categories)				x^2_1=1.49 p=0.2208
	Normal	91 (64.08)	42 (59.15)	49 (69.01)	
	Anxiety#	51 (35.92)	29 (40.85)	22 (30.99)	
	Stress (score)				* W=3198 p=0.0054
	Mean (SD)	5.31 (3.25)	6.07 (3.5)	4.55 (2.8)	
	Median (range)	5 (0-21)	5 (0-21)	4 (0-12)	
	Stress (categories)				x^2_1=8.28 p=0.004001
	Normal	112 (78.87)	49 (69.01)	63 (88.73)	
	Stress#	30 (21.13)	22 (30.99)	8 (11.27)	
nt	Depression (score)				* W= 1525.5 $p=4.04\times10^{-5}$
	Mean (SD)	2.95 (3.18)	1.83 (1.64)	4.07 (3.89)	
	Median (range)	2 (0-21)	2 (0-9)	3 (0-21)	
	Depression (categories)				**$p=6.15\times10^{-7}$
	Normal	115 (80.99)	69 (97.18)	46 (64.79)	
	Depression#	27 (19.01)	2 (2.82)	25 (35.21)	
	Anxiety (score)				* W=1598.5 p= 0.00013
	Mean (SD)	2.8 (2.84)	1.82 (1.53)	3.79 (3.46)	
	Median (range)	2 (0-18)	2 (0-7)	3 (0-18)	
	Anxiety (categories)				**$p=2.92\times10^{-7}$
	Normal	108 (76.06)	67 (94.37)	41 (57.75)	
	Anxiety#	34 (23.94)	4 (5.63)	30 (42.25)	
	Stress (score)				* W=1688.5 p= 0.0006
	Mean (SD)	5.21 (3.54)	4.2 (2.41)	6.22 (4.17)	
	Median (range)	5 (0-20)	4 (0-12)	7 (0-20)	
	Stress (categories)				**$p=3.56\times10^{-5}$
	Normal	117 (82.39)	48 (95.77)	49 (69.01)	
	Stress#	25 (17.61)	3 (4.23)	22 (30.99)	
	Depression (score)				* W=1308 $p=5.16\times10^{-7}$
	Mean (SD)	2.71 (3.05)	1.44 (1.37)	3.99 (3.69)	
	Median (range)	2 (0-18)	1 (0-4)	4 (0-18)	

Continued on the next page

Measures	*Characteristics*	*Whole group*	*Groups*		*Pearson x^2 test*
		n (%)	*Experimental n (%)*	*Control n (%)*	
II measurement	Depression (categories)				**p=1.79×10^{-9}
(after 3. week)	Normal	116 (81.96)	71 (100)	45 (63.38)	
	Depression#	26 (18.31)	0 (0)	26 (36.62)	
	Anxiety (score)				* W=1541 p=5.01×10^{-5}
	Mean (SD)	2.65 (2.5)	1.69 (1.27)	3.62 (3.02)	
	Median (range)	2 (0-14)	1 (0-5)	3 (0-14)	
	Anxiety (categories)				**p=3.92×10^{-11}
	Normal	108 (76.06)	70 (98.59)	38 (53.52)	
	Anxiety#	34 (23.94)	1 (1.41)	33 (46.48)	
	Stress (score)				* W=1443 p=9.67×10^{-6}
	Mean (SD)	5.08 (3.27)	3.89 (1.92)	6.28 (3.86)	
	Median (range)	5 (0-18)	4 (0-8)	7 (0-18)	
	Stress (categories)				**p=1.76×10^{-7}
	Normal	117 (82.39)	70 (98.59)	47 (66.20)	
	Stress#	25 (17.61)	1 (1.41)	24 (33.80)	
-	Total	142 (100)	71 (100)	71 (100)	-

* Wilcoxon rank sum test, ** Fisher Exact test, #mild, moderate, severe, extremely severe

87.32% were parents with 1-5 children, 80.28% lived with somebody and 66.20% had average or above average economic status. There was no significant difference between groups regarding the patient characteristics (Table 1).

The majority of patients had good and very good family relationships and family members participated in their treatment. The greatest support to patients during their treatment was provided by children and partner. Most patients had no less social contacts due to illness and more than half of them always organized their free time. There was no statistically significant difference between groups regarding the patient social interactions (Table 2).

Mean DAS scores in the whole group of patients before education were 3.25, 2.96 and 5.31, respectively. After the first and the third week from education, mean DAS scores were decreased with significant difference in mean depression score between initial and II measurement (p=0.01931) (Table 3). The percentages of patients with mild, moderate, severe and extremely severe symptoms of DAS in both groups at the initial measure were 29.58% for depression, 35.92% for anxiety and 21.13% for stress. Most patients had mild and moderate symptoms of depression (19.01% and 9.86%, respectively), anxiety (22.54% and 9.86%, respectively) and stress (13.38% and 6.34%, respectively), while much less patients had severe or extremely severe symptoms of depression (0% and 0.70%, respectively), anxiety (2.82% and 0.70%, respectively) and stress (0.70% and 0.70%, respectively).

The severity of symptoms were decreased on the I and II measurement, with significance in depression and anxiety between initial and I measurement (p=0.01481 and p=0.01246, respectively), and between initial and II measurement (p=0.01496 and p=0.01469, respectively) (Table 3).

Before education, there was significant difference between groups regarding mean stress score (p=0.0054) and stress categories (p=0.004001). Mean stress score and number of patients with mild, moderate, severe and extremely severe symptoms of stress were significantly higher in the experimental group comparing to the control group. No significant difference between groups regarding depression and anxiety was seen. One week after education, there was significant difference between groups in mean DAS scores (p=4.04×10^{-5}, p=0.00013 and p=0.0006, respectively), as well as in DAS categories (p=6.15×10^{-7}, p=2.92×10^{-7} and p=3.56×10^{-5}, respectively). Furthermore, three weeks after education there was also significant difference between groups in mean DAS scores (p=5.16×10^{-7}, p=5.01×10^{-5} and p=9.67×10^{-6}, respectively), as well as in DAS categories (p=1.79×10^{-9}, p=3.92×10^{-11} and p=1.76×10^{-7}, respectively). Therefore, DAS decreased significantly in the experimental group from initial measurement to the one-week and three-week follow-up, comparing to the controls (Table 4).

Discussion

It is known that breast cancer patients have a high risk of developing psychological morbidity. A large-scale epidemiological study showed that mental disorders were present in 42% of breast cancer patients [4]. Higher frequencies of anxiety and depression were observed in patients receiving chemotherapy as a single treatment option [9]. A prospective, multicenter cohort study showed that beginning of adjuvant chemotherapy results with high prevalence of anxiety (49.8%) and depression (36.6%) [27]. A Greek cohort study also pointed to the fact that high percentage of breast cancer patients who receive chemotherapy, radiotherapy or both treatments are depressed (38.2%) and anxious (32.2%) [28]. A Swedish longitudinal study reported that 36% of oncology patients had anxiety or depression symptoms on screening at the time of their first visit at an oncology department [10]. Our results also showed that breast cancer patients with metastatic disease, before starting capecitabine therapy have symptoms of depression (29.58%), anxiety (35.92%) and stress (21.13%), ranging from mostly mild, then moderate symptoms, and least severe or extremely severe symptoms. Higher level of symptom severity (moderate, severe and extremely severe) was found in 31.68% of patients (depression 10.56%; anxiety 13.38%; stress 7.74%).

Many studies reported that provision of information or patient education with psycho-emotional support could reduce psychological problems of cancer patients and improve QoL [15-17,29-33]. A prospective cohort study of female breast cancer patients showed that patient satisfaction with received information may reduce subsequent depression and anxiety and *vice versa* [34]. Satisfied and well informed patients in general have a better health-related QoL, and lower levels of anxiety and depression [16]. A recent observational study showed that patients who are undergoing oral chemotherapy, mostly capecitabine, would like to receive more specific information related to their treatment and its impact on different aspects of their daily life [35].

The optimal method for providing patient education and psycho-oncological support is still unknown. Faller et al [36] found that different types of psycho-oncologic interventions are related to significant, small-to-medium effects on emotional distress and QoL in adult cancer patients. A meta-analysis from China [37] also showed that psychological interventions have large effects on depression and anxiety. A recent systematic review showed the range of the various types of psychosocial interventions for advanced cancer patients including the education-only interventions. The authors reported a progress in meeting the psychosocial needs of cancer patients, although some psychosocial interventions still need the evidence for their effectiveness [38].

The impact of structured education of breast cancer patients receiving capecitabine on DAS were examined in this study. Most studies regarding educational interventions of patients on oral chemotherapy assessed medication adherence, knowledge and symptom management [39-44]. To our knowledge, this is the first study to evaluate the impact of structured education on DAS in breast cancer patients on oral capecitabine treatment. Our results showed that structured education significantly reduces symptoms of DAS in our patients, which has similarities and differences with the results of other researches due to differences in the methodology, such as type of intervention, instruments for assessment of psychological disorders, time to follow-up, outcome measures and sample characteristics.

There is evidence that nurse-led prechemotherapy education significantly reduces generalized anxiety about treatment, when comparing the patient responses before teaching visit with those at the beginning of the second cycle of chemotherapy [45]. Another study [46] showed that patients with elevated distress who attended nurse-led (ChemoEd) prechemotherapy education had significant decrease in distress before the first cycle of chemotherapy comparing to baseline. Similarly to our results, this group of authors pointed out that patients with low level of distress may need less intensive education comparing to those with high level of distress who need more intensive intervention and follow-up. A longitudinal study [10] of a screening, assessment and psychosocial support interventions in oncology patients showed that anxiety and depression had been decreased after subsequent psychosocial support over time, with significance in anxiety from baseline to one-month follow-up, and depression from baseline to the six month follow-up. In contrast to our results, no significant differences between the standard and intervention group were reported at any time point. Namely, the authors found that patients with clinical assessment and the support intervention do not have an improvement in depression and anxiety, comparing to patients in standard care group [10].

Molassiotis et al [47] showed that home care nursing program in cancer patients receiving oral chemotherapy has higher improvement in anxiety than patients on standard care program, the anxiety being improved in both groups all the time but this

was not true regarding depression. These authors suggested that "the most crucial time to provide a supportive care intervention in patients receiving capecitabine is during the first two cycles of treatment", as it was found in our study. Another study that also examined the effect of structured, active, home-based program related to oral chemotherapy showed association of this program with improvements in the QoL of patients, adherence to the treatment and symptom management [48].

A recent study showed that patients receiving oral chemotherapy benefit from a standardized patient education program provided by specially trained oncology nurses. According to these results, patients in the intervention group have fewer side effects and less frequently interrupted the therapy, compared to the standard care group [49]. Mollaoglu also concluded that chemotherapy patients who received structured and planned education had significant decreases in the frequencies of psychological symptoms, such as distress/anxiety and pessimism/unhappiness, and unusual fatigue and sleeping problems as well [50].

We assumed that the reasons for the reduction of DAS symptoms in our patients are related to the experience of better care, support and more time from the health care provider, better understanding the treatment plan, schedule and adverse events, the knowledge about handling the medication, means of remembering to take the drug, actions to take if problem occurs and provider contact information. Furthermore, the majority of patients were identified as having mild level of DAS symptoms, which means that they had less severe symptoms. These patients, as mentioned before, might benefit much more from less intensive treatment such as education and provision of information than patients with higher level of DAS symptoms.

Although our study suggests that structured education is superior to standard education, there are some limitations, first being the use of self-reported questionnaire for DAS symptom assessment. Although the DASS 21 may contribute to the diagnosis, it cannot replace a clinical interview. However, our suggestion is that DASS 21 self-reported questionnaire, as a not time-consuming tool, may serve in everyday practice as a first step in a process of clinical assessment and follow-up of cancer patients who experienced DAS symptoms. Second potential limitation is the short time of follow-up of patients, so there is a need of further studies with longer follow-up.

Our study demonstrated that structured education has a significant positive impact on DAS symptoms of breast cancer patients undergoing capecitabine treatment. Considering that patients could benefit from this individual, systematic approach, we can recommend its implementation in everyday clinical practice. Our findings also showed that there is a need for clinical assessment of mental disorders in breast cancer patients, especially before and during chemotherapy, and also a need of identification of those patients who require further attention.

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Conflict of interests

The authors declare no conflict of interests.

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