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Cancer information overload may be a crucial determinant of adjuvant aromatase inhibitor adherence

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Abstract. – OBJECTIVE: Medication non-adherence is the leading preventable cause of death among cancer patients. We aimed at investigating whether an online search on cancer treatments creates information overload and to determine the effect of online search on treatment adherence in postmenopausal breast cancer (BC) patients receiving adjuvant aromatase inhibitor (AI) treatment.

PATIENTS AND METHODS: A total of 103 patients completed the demographic and medical information form, Cancer Information Overload (CIO) scale, Hospital Anxiety Depression Scale (HADS), and Modified Medication Adherence Questionnaire (MAQ).

RESULTS: More than half of the patients (n=55, 53.4%) performed an additional online search on BC treatment. Median HADS-Anxiety scores, HADS-Depression scores, CIO scores, and percentage of patients with a low MAQ status were 10.00 (7.00-13.00) and 4.00 (3.00-6.75) (p<0.001), 11.00 (6.00-14.00) and 4.00 (2.00-6.00) (p<0.001), 24.00 (17.00-28.00) and 12.00 (10.00-15.00) (p<0.001), and 63.6% (n=35) and 39.6% (n=19) (p=0.018) for the searcher and non-searcher groups, respectively. Co-morbidity(s) (OR 2.407, 95% CI 1.017-5.700, p=0.046) and CIO score (OR 1.126, 95% CI 1.006-1.259, p=0.039) were independent predictive factors of a low MAQ score.

CONCLUSIONS: CIO is one of the main determinants of non-adherence to adjuvant AI treatment. An additional online search on cancer treatment may negatively contribute to patients' CIO, depression, and anxiety levels and does not seem to be beneficial for treatment adherence.

Key Words:
Cancer information overload, Internet, Medication non-adherence, Treatment, Postmenopausal breast cancer, Adjuvant aromatase inhibitor.

Introduction

The internet is a useful tool for storing patients' medical records and accessing them quickly, educating patients about their diseases, and communicating with health care professionals. In addition, digital health interventions can contribute to supportive care for cancer patients[1]. Most cancer patients have long used the internet as their primary source of information[2]. However, searching for diseases and their treatments on the internet can also have negative consequences. A recent study[3] has shown that 32.5% of the information about cancer treatments on social media is misinformation, and 30.5% is harmful. Similarly, social media misinformation on vaccines increases vaccine hesitancy and disrupts the fight against the COVID-19 pandemic[4].

Information overload generally refers to problems related to an overabundance of information, growth of media resources, increased diversity of views, and expansion of communication networks[5]. Cancer information overload (CIO) has been defined as feeling overwhelmed by excessive information about cancer in the information environment[6]. Cancer information avoidance (CIA) occurs when acquired information causes emotional distress, leading people to avoid the information[7]. As the internet is the most commonly used resource for researching diseases, CIA is most commonly seen among internet researchers[8].

Breast cancer (BC) is the most common malignancy in women and the second leading cause of death after lung cancer[4]. Medication non-adherence, which the World Health Organization lists as the leading cause of preventable death, is also an adverse prognostic factor in BC[9]. Aromatase

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inhibitors (AIs; letrozole, anastrozole, exemestane) are currently prescribed for more than 80% of postmenopausal women with estrogen receptor-positive BC[10]. Large-scale clinical trials[11,12] have shown that AI therapy for postmenopausal women with surgically treated BC significantly reduces BC recurrence and improves survival. Unfortunately, nearly 10% of patients receiving adjuvant AI discontinue their treatment each year without consulting a physician, with approximately half of the patients completing the planned five-year adjuvant therapy[13]. Non-adherence to hormonal treatment has been associated with early recurrence in BC patients receiving adjuvant AIs[14].

There are insufficient data about the effect of CIO on cancer medication adherence. Researching cancer treatments online can have a negative effect on CIO and increasing CIO can also negatively affect treatment compliance. We aimed at investigating whether research on cancer treatment, in addition to the medical information provided by physicians from the internet (i.e., social media, blogs, video streaming sites), can create an information overload and its effect on treatment adherence in postmenopausal women receiving adjuvant AI treatment for surgically treated BC.

Patients and Methods

This is a cross-sectional observational descriptive study. It was conducted in the medical oncology clinic of a tertiary referral centre after receiving approval from the Local Ethics Committee (UHS Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee, Document No: 2021-01/ 955, Date: 13.01.2021). Postmenopausal women with a diagnosis of surgically treated BC who had been receiving adjuvant AI therapy for at least one year were included in the study. Patients who receive tamoxifen were excluded to minimize compliance problems due to drug properties and to obtain a homogeneous study population. The patients did not have a known psychiatric disease or treatment history, co-morbidities that posed a life-threatening risk, or joint diseases that cause severe morbidity. All patients were over 18 years of age, literate, able to communicate, and able to fully understand what they read. An informed consent form, demographic and medical information form, hospital anxiety depression scale (HADS), Cancer Information Overload (CIO) Scale, and Modified Medication Adherence Questionnaire (MAQ) were given to the patients in a printed form. They were asked to fully complete the study scales in a quiet environment. Data from 103 patients who agreed to participate in the study, signed the informed consent form, and filled out the study scales completely and consistently were evaluated. The data of 29 patients who filled in the study scales incompletely or inconsistently (i.e., giving the same answer to all questions) were excluded.

Instruments

Demographic and Medical Information Form

The demographic information form included questions about the participants' age, marital status, educational status, employment status, and co-morbidities (chronic diseases that did not pose a life-threatening risk and were being treated with medication, such as hypertension, diabetes mellitus, migraine). In addition, this form included questions about whether patients conducted a search on their treatment on the internet (i.e. social media, blogs, and video streaming sites) in addition to the medical information provided by physicians. Another question was whether patients experienced symptoms (musculoskeletal pain, weakness, hot flushes, nausea) in the last six months that might be associated with AI treatment.

Cancer Information Overload Scale (CIO)

The CIO Scale consists of eight items with a four-point Likert-type rating ranging from strongly agree to strongly disagree[6]. A minimum of 8 and a maximum of 32 points can be obtained from the scale. The original scale is one-dimensional and evaluates the information load of the person regarding cancer. A high score on the scale indicates information overload. Inci et al[15] demonstrated the validity and reliability of the Turkish version of the CIO Scale.

Hospital Anxiety Depression Scale (HADS)

Zigmond and Snaith[16] developed the HADS to determine the risk, level, and changes in the severity of anxiety and depression of patients who applied to primary health care services due to physical illness. Aydemir[17] demonstrated the validity and reliability of the Turkish version of this scale. The HADS is a questionnaire consisting of 14 questions. Seven of the questions measure anxiety, while the other seven measure depression. Responses are evaluated using a four-point Likert scale ranging from 0 to 3.

Modified Medication Adherence Questionnaire (MAQ)

The MAQ was developed by Morisky et al[18] as a four-item questionnaire to assess adherence to antihypertensive drug therapy. Vural et al[19] confirmed the validity and reliability of the Turkish version of the scale, which was later modified by adding two new questions. The modified MAQ consists of two subscales measuring treatment compliance motivation and knowledge level. We used the motivation subscale in our study, which included three questions: Q1) Do you ever forget to take your medication?; Q2) Are you careless at times about taking your medicine?; Q3) Do you sometimes forget to refill your prescription medicine on time? The answer choices were 'Yes' and 'No'. A total score was calculated by giving 1 point to 'No' answers. A scale score of 0 or 1 indicated low motivation, while a score >1 was considered high motivation.

Statistical Analysis

Statistical analysis was performed using SPSS software (SPSS for Windows, version 24.0., IBM Corp., Armonk, NY, USA). Numeric data were presented as medians (interquartile range; IQR), and categorical data were presented as frequencies (percentages). First, the patients were divided into two subgroups (with and without additional research for BC treatment), and the groups were compared in terms of sociodemographic characteristics, drug side effects, and study scale scores. Second, the patients were divided into MAQ-high and MAQ-low subgroups to again compare sociodemographic characteristics, drug side effects, and study scale scores. A comparative analysis

Table I. Main patients' characteristics.

Parameter	n	%
Age§	57.0	52.0-62.0
Employment status		
Unemployed	89	86.4
Employed	14	13.6
Marital status		
Single	27	26.2
Married	76	73.8
Educational status		
Primary and secondary school	59	57.3
High school / University	44	42.7
Co-morbidity(s)		
No	56	54.4
Yes	47	45.6
Additional research for BC treatment		
No	48	46.6
Yes	55	53.4
Musculoskeletal pain		
No	43	41.7
Yes	60	58.3
Weakness		
No	46	44.7
Yes	57	55.3
Hot flushes		
No	47	45.6
Yes	56	54.4
Nausea		
No	54	52.4
Yes	49	47.6
HADS-A§	7.0	4.0-11.0
HADS-D§	6.0	3.0-12.0
MAQ		
Low	54	52.4
High	49	47.6
CIO§	16.0	12.0-25.0

BC, breast cancer; §Given as median (range IQR); BC, breast cancer; HADS-A, Hospital Anxiety and Depression Scale nxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale Depression Subscale; MAQ, Modified Medication Adherence Questionnaire; CIO, Cancer Information Overload Scale.

Table II. Comparative evaluation of the groups with and without additional research for breast cancer treatment in terms of drug side effects and study scale scores.

	Additional research for BC treatment		
Parameter	**Yes (n=55)**	**No (n=48)**	***p*-value**
Musculoskeletal pain[ε]	43 (78.2)	17 (35.4)	**<0.001**
Weakness[ε]	41 (74.5)	16 (33.3)	**<0.001**
Hot flushes[ε]	42 (76.4)	14 (29.2)	**<0.001**
Nauseaε	32 (58.2)	17 (35.4)	**0.029**
HADS-A[§]	10.00 (7.00-13.00)	4.00 (3.00-6.75)	**<0.001**
HADS-D[§]	11.00 (6.00-14.00)	4.00 (2.00-6.00)	**<0.001**
MAQ-low[ε]	35 (63.6)	19 (39.6)	**0.018**
CIO[§]	24.00 (17.00-28.00)	12.00 (10.00-15.00)	**<0.001**

BC, breast cancer; [ε]Given as number (%); [§]Given as median (range IQR); HADS-A, Hospital Anxiety and Depression Scale Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale Depression Subscale; MAQ, Modified Medication Adherence Questionnaire; CIO, Cancer Information Overload Scale.

was performed using Pearson's Chi-square test and the Mann-Whitney U test for categorical and nonparametric numerical data. Multivariate logistic regression analysis was performed using variables with a *p*-value below 0.2 in the univariate analysis to determine independent factors predicting low MAQ subscale scores. All statistical tests were two-sided, and *p*-values < 0.05 were considered statistically significant.

Results

A total of 132 postmenopausal female patients with surgically treated BC who were receiving adjuvant AI therapy between January 2021 and August 2021 were included in the study. Of these, 103 fully completed the study scales and were evaluated. Table I shows the main patient characteristics. The median age of the patients was 57.0 (IQR 52.0-62.0). Most patients (86.4%) were unemployed, and most were married (73.8%). The patients' highest level of educational attainment was categorized as primary school (42.7%), secondary school (14.6%), high school (27.2%), and university graduate (15.5%). Nearly half (47.6%) of the patients had co-morbidities. In addition, more than half (53.4%) searched the internet for information about their treatment in addition to that received from their doctors. The percentages of patients with musculoskeletal pain, weakness, hot flushes, and nausea likely to be related to AI treatment were 58.3%, 55.3%, 54.4%, and 47.6%, respectively. The median study scales scores were as follows: HADS-A, 7.0 (IQR 4.0-11.0); HADS-D, 6.0 (IQR 3.0-12.0); CIO, 16.0 (IQR 12.0-25.0). Of the patients, 54 (52.4%) had a low MAQ score, and 49 (47.6%) had a high MAQ score.

Patients who performed additional searches on BC treatment on the internet (n=55, 53.4%) had more AI side effects than those who did not (n=48, 46.6%). The characteristics of the researcher and non-researcher groups were as follows: median age: 56.0 (IQR 52.0-61.0) *vs.* 57.5 (53.5–64.0) (p=0.228); those who were employed: 11 (20%) *vs.* 3 (6.3%) (p=0.049); those who were married: 41 (74.5%) *vs.* 35 (72.9%) (p=1,000); those who completed high school/university education: 22 (40%) *vs.* 22 (45%) (p=0.690); and those with any co-morbidity: 27 (49.1%) *vs.* 20 (41.7%) (p=0.553). The median HADS-A, HADS-D, and CIO scores were significantly higher in the researcher group than in the non-researcher group. Twenty (36.4%) patients in the researcher group and 29 (60.4%) in the non-researcher group had high MAQ scores (p=0.018). A comparative evaluation of the researcher and non-researcher groups in terms of drug side effects and study scale scores is shown in Table II.

The rates of having a co-morbidity were 34.7% in the MAQ-high group and 55.6% in the MAQ-low group (p=0.047); for additional research on BC treatments, they were 40.8% and 64.8% (p=0.018); and for musculoskeletal pain rates they were 46.9% and 68.5% (p=0.03). The median HADS-A scores were 6.00 (IQR 3.50-10.00) and 8.50 (IQR 3.75-12.00) (p=0.105) for the MAQ-high group and the MAQ-low group, respectively. The median HADS-D scores were 5.00 (IQR 2.50-8.00) and 9.50 (IQR 3.00-14.00) (p=0.027), respectively, while the median CIO scores were 14.00 (IQR 10.50-19.00) and 22.00 (IQR 12.75-27.00) (p=0.003). Table III shows the compara-

Table III. Comparative evaluation of groups with high and low MAQ scores in terms of sociodemographic parameters, aromatase inhibitor side effects, and study scale scores.

Parameter	MAQ-high (n=49)	MAQ-low (n=54)	*p*-value
Age[§]	58.0 (52.5-61.5)	56.0 (52.0-65.0)	0.963
Employment status[ε]			0.251
Unemployed	40 (81.6)	49 (90.7)	
Employed	9 (18.4)	5 (9.3)	
Marital status[ε]			0.658
Single	14 (28.6)	13 (24.1)	
Married	35 (71.4)	41 (75.9)	
Educational status[ε]			0.694
Primary education	27 (55.1)	32 (59.3)	
High school/University	22 (44.9)	22 (40.7)	
Co-morbidity(s)[ε]			**0.047**
No	32 (65.3)	24 (44.4)	
Yes	17 (34.7)	30 (55.6)	
Additional research for BC treatment[ε]			**0.018**
No	29 (59.2)	19 (35.2)	
Yes	20 (40.8)	35 (64.8)	
Musculoskeletal pain[ε]			**0.030**
No	26 (53.1)	17 (31.5)	
Yes	23 (46.9)	37 (68.5)	
Weakness[ε]			0.239
No	25 (51.0)	21 (38.9)	
Yes	24 (49.0)	33 (61.1)	
Hot flushes[ε]			0.327
No	25 (51.0)	22 (40.7)	
Yes	24 (49.0)	32 (59.3)	
Nausea[ε]			0.431
No	28 (57.1)	26 (48.1)	
Yes	21 (42.9)	28 (51.9)	
HADS-A[§]	6.00 (3.50-10.00)	8.50 (3.75-12.00)	0.105
HADS-D[§]	5.00 (2.50-8.00)	9.50 (3.00-14.00)	**0.027**
CIO[§]	14.00 (10.50-19.00)	22.00 (13.00-27.00)	**0.001**

BC, breast cancer; [ε]Given as number (%); [§]Given as median (range IQR); BC, breast cancer; HADS-A, Hospital Anxiety and Depression Scale Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale Depression Subscale; MAQ, Modified Medication Adherence Questionnaire; CIO, Cancer Information Overload Scale.

tive evaluation of the groups with high and low MAQ scores with regard to sociodemographic parameters, AI side effects, and study scale scores.

The multivariate binary logistic regression analysis, which included factors with a *p*-value of 0.2 in the univariate statistical analysis, showed that CIO score (OR 1,126, 95% CI 1.006-1.259, *p*=0.039) and having a co-morbidity (OR 2.407, 95% CI 1.017-5.700, *p*=0.046) were independent predictive factors of a low MAQ score. Table IV presents the multivariate binary logistic regression analysis results, including factors that may predict a low MAQ score.

Discussion

The current study involved patients receiving adjuvant AI for surgically treated BC. The results showed that co-morbidity(s) and CIO are the main predictors of low motivation for AI treatment adherence. Additionally, in the searcher group (patients who searched on the internet for additional information beyond what they received from their physicians about their treatments), AI side effects were more frequent, and HADS-A, HADS-D, and CIO scores as well as the probability of being in the MAQ-low group were significantly higher than in the non-searcher group.

A study by Sutton et al[20] that included 572 women with BC receiving adjuvant endocrine therapy showed that higher ratings of patient-provider communication were associated with lower concern and higher necessity beliefs. Moreover, the study showed stronger concern beliefs were related to more treatment-related symptoms and lower patient satisfaction[20]. Similarly, our study found that patients seeking additional treatment

Table IV. Multivariate binary logistic regression analysis results which contain factors may predict a low MAQ score.

Parameter	OR	95% CI		*p*-value
		Lower	Upper	
Co-morbidity(s)	2.407	1.017	5.700	**0.046**
Additional research for BC treatment	1.185	0.397	3.538	0.761
Musculoskeletal pain	1.490	0.535	4.145	0.445
HADS-A score	0.875	0.725	1.056	0.164
HADS-D score	1.043	0.887	1.228	0.609
CIO score	1.126	1.006	1.259	**0.039**

CI, Confidence Interval; OR, Odds Ratio; BC, breast cancer; HADS-A, Hospital Anxiety and Depression Scale Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale Depression Subscale; CIO, Cancer Information Overload Scale.

information experienced more AI side effects along with high depression and anxiety scale scores. These results may be an indirect indicator of insufficient treatment information provided by physicians or limitations related to physician-patient communication. However, patients who experience intense drug side effects, even if they have received sufficient information about their treatment, may seek more information or alternative treatment methods to relieve the side effects. Several studies[21,22] have shown that negative psychiatric symptoms, such as anxiety and depression, decrease treatment adherence. Similarly, we observed that patients seeking additional information about treatments in our study population had higher depression, anxiety, and CIO scale scores. Moreover, these patients were less motivated to adhere to their treatments. However, the findings of our study do not allow us to distinguish whether seeking additional information on the internet is a cause or a consequence of psychiatric conditions (i.e., depression, anxiety). Jacob Arriola et al[23] showed that more frequent doctor communication could shape patients' beliefs and awareness regarding the importance of adjuvant endocrine therapy and may be associated with greater treatment adherence. Kahn et al[24] demonstrated that patient-centered communication was a primary mediator of long-term adherence to tamoxifen use in patients with BC. It can be argued that seeking information from non-physician sources on the internet, where the information is erroneous and harmful[3], does not contribute positively to adjuvant AI treatment adherence. This erroneous and harmful information may create confusion, anxiety, depression, and information overload, impairing treatment compliance. In addition, the patient's passive position in this type of communication may also negatively affect treatment adherence.

Non-adherence to cancer treatment is the leading preventable cause of cancer-related deaths[9]. The review by Murphy et al[25] reported adherence rates of 41-72% and discontinuation rates of 31-73% at the end of five years of adjuvant hormonal therapy among BC survivors. In a large population-based study, the completion rate of five years of adjuvant endocrine therapy was only 49%[26]. In our study, we observed that slightly less than half of the patients had a high MAQ score, and treatment adherence was poor in our patients, as in the literature. A recent systematic review provided strong evidence of the adverse clinical outcomes (i.e., disease recurrence, disease progression/metastasis, and mortality) of non-adherence to early systemic BC treatments[27]. An economic analysis[28] from Scotland showed that an average BC patient with low tamoxifen adherence had increased healthcare costs (by £5,970). Identifying and correcting the factors impairing treatment adherence in cancer patients will improve treatment success and decrease cancer mortality and treatment costs. However, the literature lacks data on the relationship between treatment adherence and psychiatric status, beliefs, and feelings about treatment.

The study of Bright et al[29] showed that the patient-oncologist relationship, belief in the necessity of treatment, and negative endocrine therapy-related emotions are predictive factors of treatment adherence. Further, the majority of participants reported recalling something a doctor had said (60%) regarding facilitative strategies for treatment adherence[29]. Numerous studies[23,24,30,31] have highlighted the importance of the doctor-patient relationship for adjuvant

endocrine therapy adherence. We found that patients who did not perform additional searches on the internet for information beyond what they received from their physician showed a better adherence to treatment. Although communication quality was not the primary aim of our study, it could be an indirect indicator of adequate doctor-patient communication. However, various reasons, especially drug side effects, may explain the low treatment adherence motivation scores. In the univariate analysis, we observed that patients with low treatment adherence scores had higher rates of co-morbidity(s), additional internet information searches, AI side effects, depression, anxiety, and CIO scores than those with high adherence scores. In the multivariate analysis, only co-morbidity(s) and CIO scores predicted low adherence motivation. The study of Quinn et al[32] revealed that suboptimal treatment adherence was associated with young age, employment status, low perceived emotional support, and using the internet to read about BC. Patients often believe that other patients know better and are the best source of information about their disease[33]. Accordingly, the most frequently researched sources on the internet are inevitably social media, blogs, and video streaming sites, which are often non-physician or non-scientific sources. Learning about the negative experiences of other patients can cause them to feel anxious about their situation, even if they have no similarities.

Obamiro et al[34,35] identified health information overload as a significant predictor of poor oral anticoagulant knowledge and a negative predictor of oral anticoagulant adherence. In addition, health information overload is associated with patient confusion, and confused patients have a stronger inclination to narrow down their possible decision alternatives hastily[36]. It is inevitable for a confused person to feel anxiety. Chae et al[37,38] demonstrated a relationship between anxiety and CIO and showed that the active use of information from media channels negatively predicts CIO. In our study, we observed that having a co-morbidity and high CIO scores were independent predictors of low treatment adherence motivation. Numerous studies[39-43] of BC patients have shown that having a co-morbidity is an adverse factor for adjuvant endocrine therapy adherence. To the best of our knowledge, no studies have evaluated the relationship between treatment adherence and CIO in cancer patients so far[44,45]. This is important as we believe that CIO may create confusion and anxiety in cancer patients, disrupting treatment adherence and may be a primary factor determining treatment adherence. Although their findings were not statistically significant, Jensen et al[46] showed that high levels of uncertainty about treatment and newspaper stories resulted in high CIO. Similarly, in our study, patients who researched on the internet had high scores on the anxiety, depression, and CIO scales. In another study by Jensen et al[47], individuals with a high level of CIO were less likely to file a cancer screening claim. Additional internet research may increase CIO but not have a further impact treatment adherence.

Conclusions

The internet may provide some benefits in terms of disease management, patient education, and medical information storage for patients. However, non-physician/non-scientific resources on the internet may contain a high proportion of misinformation or harmful medical information. Our study suggested that patients' searches for information about their treatments on the internet may cause CIO, depression, and anxiety. We also observed that searches on the internet did not positively contribute to treatment adherence. For patients receiving adjuvant AIs who have been diagnosed with early-stage breast cancer, CIO and the presence of a co-morbidity(s) requiring medication are the main determinants of treatment non-adherence. Protecting patients from false and harmful information about cancer treatment on the internet could reduce CIO and increase treatment adherence.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Pınar Eraslan provided the study's conception and design. Material preparation, data collection and analysis were performed by Gülnihal Tufan. Pınar Eraslan drafted the manuscript. All authors read and approved the final manuscript.

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Ethics Approval
The study has been performed under the ethical standards of the Declaration of Helsinki. It was conducted in the medical oncology clinic of a tertiary referral centre after receiving approval from the local ethics committee (UHS Dr Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Ethics Committee, Document No.: 2021-01/955, Date: 13.01.2021).

Informed Consent
Informed consent was obtained from all individual participants included in the study.

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