Assessment of Health Beliefs Among Iraqi Breast Cancer Patients in Baghdad using either Tamoxifen or Trastuzumab

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Abstract

Breast cancer is the most diagnosed form of malignant tumor in Iraqi women. Tamoxifen and Trastuzumab are highly effective adjuvant therapies for breast cancer.

The objectives of this study were to define the patient's belief in Tamoxifen or Trastuzumab when used as adjuvant therapies and to determine the variation in beliefs between the two medications in a sample of Iraqi breast cancer patients. The cross-sectional survey was conducted using the belief about the medication-specific (BMQ-Specific) questionnaire. Ninety-seven participants (sixty-seven Tamoxifen, thirty Trastuzumab) participated in this study. The mean of specific-necessity scale for Tamoxifen was (3.7) and for Trastuzumab (4). The findings showed a high necessity for both medicines, and there were no significant differences in the scale of necessity between the two treatments. Regarding the scale of concern, the Trastuzumab group's values are higher (3.35) than Tamoxifen (3). Most participants who use Tamoxifen or Trastuzumab strongly agree with or agree with all the questions on the necessity scale with higher percentages for Trastuzumab. Besides, the concern scale results showed the percentage of patients who agree / strongly agree is higher in the Trastuzumab group. For the correlation between the necessity or concern score, the result showed only one significant negative correlation (R=-0.366, P-value=0.011) between the necessity score and the age of the participants for Tamoxifen users. In Conclusion, this survey clearly showed a high level of necessity and a high level of concern regarding the use of two effective adjuvant therapies for women with breast cancer, Tamoxifen and Trastuzumab. Furthermore, this study shows that while the level of need for Tamoxifen is higher than for Trastuzumab, there were no significant variations between them.

Key words: Breast cancer, Tamoxifen, Trastuzumab, Beliefs, Necessity, Concern.

تقييم المعتقدات الصحية بين مرضى سرطان الثدي العراقيين في بغداد المستخدمين لعقاري تاموكسيفين أو تراستوزوماب

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الخلاصة

سرطان الثدي هو الورم الخبيث الأكثر تشخيصا لدى النساء العراقيات. ويعتبر عقار تاموكسيفين وتراستوزوماب علاج مساعد فعال للغاية لسرطان الثدي . كانت أهداف هذه الدراسة هي تحديد اعتقاد المريض في عقاري تاموكسيفين أو تراستوزوماب عند استخدامه كعلاج مساعد وتحديد الاختلاف في الاعتقاد بين الدواءين في عينة من مرضى سرطان الثدي العراقيين. تم إجراء المسح المقطعي باستخدام استبيان المعتقدات حول الدواء المحدد (BMQ-specific.). شارك في هذه الدراسة سبعة وتسعون مشاركًا (سبعة وستون يستخدمون تاموكسيفين ، وثلاثون يستخدمون تراستوزوماب) وكان متوسط مقياس الضرورة المحددة لتاموكسيفين (٣،٧) وللتراستوزوماب (٤). أظهرت النتائج ضرورة قصوى لكلا الدوائين ، ولا توجد فروق ذات دلالة إحصائية في مقياس الضرورة بين العلاجين. فيما يتعلق بمقياس القلق ، فإن قيم مجموعة التراستوزوماب كانت أعلى (٣،٣٥) من عقار تاموكسيفين (٣). يتفق معظم المشاركون الذين يستخدمون عقار تاموكسيفين أو تراستوزوماب بشدة مع جميع الأسئلة المتعلقة بمقياس الضرورة. إلى جانب ذلك ، أظهرت نتائج مقياس القلق أن النسبة المئوية للمرضى الذين يوافقون / يوافقون بشدة أعلى في مجموعة تراستوزوماب. بالنسبة للعلاقة بين درجة الحاجة أو القلق ، أظهرت النتيجة ارتباطًا سلبيًا واحدًا فقط (**R = -0.366**، ، **P-value = 0.011**) بين درجة الضرورة وعمر المشاركين لمستخدمي عقار تاموكسيفين. في الختام ، أظهر هذا المسح بوضوح مستوى عالٍ من الضرورة ومستوى عالٍ من القلق فيما يتعلق باستخدام اثنين من العلاجات المساعدة الفعالة للنساء المصابات بسرطان الثدي ، عقار تاموكسيفين وتراستوزوماب. علاوة على ذلك ، تُظهر هذه الدراسة أنه في حين أن مستوى الحاجة إلى عقار تاموكسيفين أعلى منه في عقار تراستوزوماب ، لم تكن هناك اختلافات كبيرة بينهما.

الكلمات المفتاحية: سرطان الثدي، تاموكسفين ، تراستوزوماب ،المعتقدات،الحاجة، القلق.

Introduction

Breast cancer is one of the most prevalent cancers among women[1]. Breast cancer is also the most frequently diagnosed type of malignant tumor in Iraqi women and the leading cause of death for women due to malignant neoplasm[2].

Moreover , metastasized breast cancer, despite extensive studies, remains an incurable condition with an estimated survival time of around two years[3]. For breast cancer treatment; surgery,

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chemotherapy, adjuvant hormones, and radiotherapy may be used[4]. In general, several variables, including the pathological features of breast cancer, the demographic and clinical characteristics of patients, and the chances of recurrence decide treatment choice [5,6].

As a role, breast cancer therapies such as chemotherapy, radiation, or surgery are usually accompanied by hormonal therapy[7].

Adjuvant endocrine therapy is adequate and sufficient for almost any woman with positive breast cancer with estrogen receptors (ER) and/or progesterone receptor(PR), rendering adjuvant endocrine therapy the most widely prescribed cancer therapy[8].

Tamoxifen, a selective estrogen receptor modulator (SERM), was the standard adjuvant endocrine therapy that can be used for five years, according to the American Society of Clinical Oncology Clinical Practice[8].

Furthermore, Tamoxifen is used to treat both early and advanced estrogen receptor-positive (ER-positive or ER+) breast cancer in pre-and postmenopausal women[9].

On the other hand, Trastuzumab (Herceptin; Genentech, San Francisco, CA) was a monoclonal antibody tested in human clinical trials as a therapy for metastatic breast cancer patients overexpress human epidermal growth factor receptor 2(HER2)[10].

A variety of studies have shown that additional administration of Trastuzumab to adjuvant chemotherapy substantially reduces recurrence rates and that Trastuzumab is tolerable for cardiac side effects[11–13].

The administration of Trastuzumab for one year in addition to adjuvant chemotherapy is standard practice nowadays[13].

Nevertheless, adjuvant endocrine therapies are noted to have a substantial side effect profile that may negatively impact the quality of life and have been cited as obstacles to enduring care[14].

The clinical challenge of adjuvant drug therapy for metastasized breast cancer primarily pursues two goals: first, achieving high effectiveness in progression-free survival and avoiding therapy-induced and disease-related side effects at the same time is essential; second, preserving the best possible quality of life of the patient[15].

Furthermore, the patient beliefs concerning the use of adjuvant therapy and pain and treatment duration were the most salient obstacles for using these medications[16]. Adherence to oral endocrine therapy for preventing and treating breast cancer is one of the substantial challenges for health care practitioners[16]. Since Tamoxifen or Trastuzumab can only achieve therapeutic benefits when taken as prescribed, it is necessary to examine patient non-compliance with treatments[16].

As well-known, patients with breast cancer who do not adhere to adjuvant therapy (i.e., take their medication as directed) and not persist (i.e., take their medication for the required duration) have worse prognoses[17]. Furthermore, studies of the relationship between demographic data (i.e., age and gender) and medications adherence have shown inconsistent results. However, poor adherence can be attributed to long treatment duration and lifestyle changes such as sleeping routines, social status, or mealtime [17,18].

Accordingly, It is crucial to study the patient's beliefs about their medication because there is a possible association between beliefs and adherence to adjuvant therapy for treating breast cancer[19].

Likewise, incorporating health beliefs into research and clinical practice can help to elucidate challenges the patients face while initiating and continuing use of adjuvant endocrine therapy[18].

Enhancing medication-based beliefs seems especially relevant to the strategy of patients' behavior modification to improve their medication adherence [20].

In Iraq, Tamoxifen is used widely among Iraqi patient as an adjuvant hormonal treatment option with ER and/or PR positive tumor while Trastuzumab, as a biological therapy, was suggested with HER2 positive patients[21].

The objectives of this study were to define the patient's belief in Tamoxifen or Trastuzumab when used as adjuvant therapies and to determine the variation in beliefs between the two medications in a sample of Iraqi breast cancer patients.

Patient and Method

Study design

A cross-sectional survey was completed by using the BMQ-Specific questionnaire[22].

The research assistant physician does data collection. The collection began in March 2018 and continued until August 2020. Patients with breast cancer who have been attending an oncology consultation hospital in Baghdad and using either Tamoxifen or Trastuzumab alone as an adjuvant therapy for a period of between one month and twelve months have been asked to join this study by a research assistant physician.

The research assistant briefly clarified the research objectives to the patient and assessed whether the eligibility criteria had been met. If they agreed to participate in the study and since the authors used the English version of the questionnaire, the research assistant physician interpreted the questions to the Arabic language with their choices and wrote down the patient choices in the questionnaire paper.

The inclusion criteria include 1- women with early or metastatic breast cancer treated with Trastuzumab alone and not in combination with chemotherapy.

2- Women with early estrogen receptor-positive (ER-positive or ER+), metastatic and adjuvant breast cancer, both pre-and postmenopausal.

3- The treatment period should not be less than one month or longer than twelve months to prevent a disparity in the duration of treatment between the two medications.The total number of patients who met the eligibility requirements and asked to enter this study was 123, and only 97 (67 with Tamoxifen and 30 with Trastuzumab) were eligible to participate in this study. The response rate is 78.8%.

The BMQ-Specific questionnaire:

The BMAQ-specific contains two 5-item factors: the Specific-Necessity measure assessing concerns about prescribed medications based on beliefs about the possibility of dependency and long-term toxicity, and the Disturbing Effects subscale assessing concerns about prescribed medications based on beliefs about the danger of dependence and long-term toxicity (Specific-Concerns)[23].

Respondents rate how much they agree or disagree with each argument using a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree. In sum, the scores for both scales are added up to provide a total ranking. In general, the total point score reflects the score along with the Necessity and Concern scale from 5 to 25. Stronger beliefs suggest higher test scores[23].

Data analysis

The data were analyzed using IBM SPSS Statistics Version 26 (IBM Corp., Armonk, New York, USA) and GraphPad Prisma Version 7.04. Descriptive statistics including mean, standard deviation, frequency and percentage have been obtained for both continuous and categorical variables as appropriate. The associations of concern scores, necessity scores with the patient's age and duration of treatment were evaluated using bivariate correlations. Two-tailed independent t-tests were used to identify whether there was a significant difference in beliefs between the two groups. P-values equal or less than 0.05 were considered significant.Ethical Approval: Permissions were obtained from the Ethical and Scientific Committee in Baghdad University – College of Pharmacy. A verbal consent was taken from all the participants. The data collection questionnaire was anonymous, and data confidentiality was maintained throughout the study.

Results

Demographic data for all participants are presented in table 1 showing that for Tamoxifen, the sample had a mean age of (53 ±13 years) compared to a mean age of (52 ±13 years) for Trastuzumab. Most of the participants were married (59.7% for Tamoxifen, 70% for Trastuzumab), while the remaining groups were either single or divorced/separated, where the latter had the lowest percentage (10.4 for Tamoxifen, 6.6% for Trastuzumab).Regarding Tamoxifen participants' education status: Almost two-thirds of the participants graduated from high school (34.3%) or awarded the bachelor's degree (34.3%). Only (13.4%) had no schooling.

For Trastuzumab, One-third of the participants had earned the degree of bachelor whereas only (16.6%) had left full-time education.

The participants took Tamoxifen for a mean of (8.4±2.3 months) while the mean was (7.6±2.2 months) for Trastuzumab.

Table 1. Demographic data for the participants.

Parameter		Tamoxifen (n=67)	Trastuzumab (n=30)
Age (Mean ±SD)		53±13	52±13
Duration of treatment (months) (Mean ±SD)		8.4±2.3	7.6±2.2
Marital status No. (%)	Single	20 (29.8%)	6 (20%)
	Married	40 (59.7%)	21 (70%)
	Divorce/ Widow	7 (10.4%)	2 (6.6%)
Education No. (%)	Illiterate	9 (13.4%)	5 (16.6%)
	Primary School	12 (17.9%)	8 (26.6%)
	Secondary School	23 (34.3%)	7 (23.3%)
	University	23 (34.3%)	10 (33.3%)

The findings showed a high necessity for both medicines, as seen in Table 2, and there were no significant differences in the scale of necessity between the two medicines.

Table 2. Specific-Necessity (BMQ-SN) for both Tamoxifen and Trastuzumab.

Questions	Tamoxifen	Trastuzumab	P-Value
My health, at present, depends on my medicines.	3.820	4.33	0.0876
My life would be impossible without my medicines	3.626	4.2	0.0960
Without my medicines, I would be very ill	3.895	3.966	0.1240
My health in the future will depend on my medicines.	3.746	3.933	0.0699
My medicines protect me from becoming worse	3.626	3.733	0.8169

The mean of specific-necessity scale for Tamoxifen was (3.7) and for Trastuzumab (4) as observed in fig (1). While the mean of specific-concern scale for Tamoxifen (3) and trastuzumab (3.35) as indicated in fig (2).
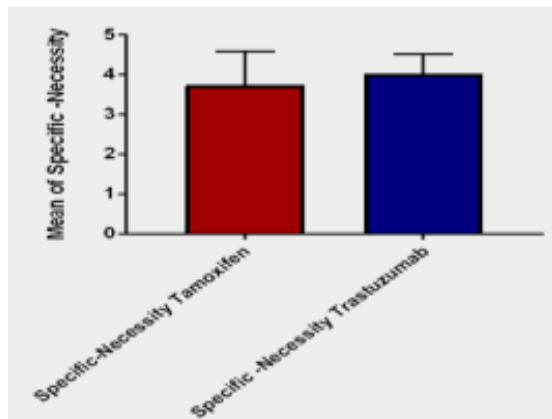

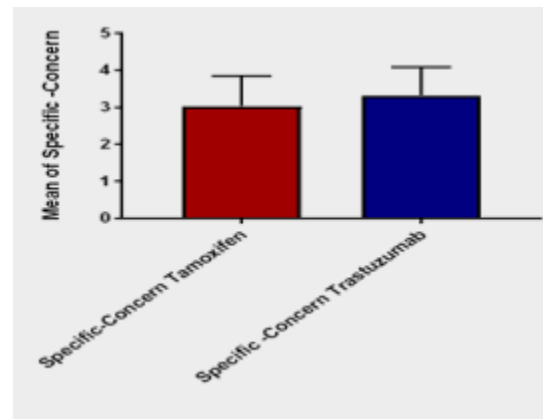**Figure 2. Mean of Specific-Concern for Tamoxifen and Trastuzumab.**

Figure 1. Mean of Specific-Necessity for Tamoxifen and Trastuzumab.

Regarding the scale of concern, the values in the Trastuzumab group are higher. Although, except for one question, there were no significant differences between the two medicines as seen in Table 3.

Table 3. Specific Concern (BMQ-SC) for both Tamoxifen and Trastuzumab.

Questions	Tamoxifen	Trastuzumab	P-value
Having to take medicines worries me.	3.119	3.4	0.4032
I sometimes worry about the long-term effects of my medicines	3.208	3.3	0.3818
My medicines are a mystery to me.	3.358	3.53	0.0421*
My medicines disrupt my life.	2.805	3.2	0.2118
I sometimes worry about becoming too dependent on my medicines	2.805	3.33	0.3150

* Significant difference between the Tamoxifen and Trastuzumab groups ($p < 0.05$).

Table 4 indicates that most participants who use Tamoxifen or Trastuzumab strongly agree with or agree with all the questions on the scale of necessity. The percentage is higher in the Trastuzumab group for all the questions.

Also, the concern scale results showed that the percentage of patients who agree / strongly agree is higher in the Trastuzumab group, as seen in table 5.

Table 4. Percentages of Tamoxifen and Trastuzumab users agreeing /strongly agreeing with Beliefs about Medicines Questionnaire -Necessity statements.

Necessity scale	Percentage agreeing or strongly agreeing for Tamoxifen group (n = 67)	Percentage agreeing or strongly agreeing for Trastuzumab group (n = 30)
My health, at present, depends on my medicines	69%	93%
My life would be impossible without my medicines	74%	80%
Without my medicines, I would become very ill	68%	73%
My health in the future will depend on my medicines	64%	77%
My medicines protect me from becoming worse	61%	63%

Table 5. Percentages of Tamoxifen and Trastuzumab users agreeing /strongly agreeing with Beliefs about Medicines Questionnaire -Concern statements.

Concerns scale	Percentage agreeing or strongly agreeing for Tamoxifen group (n = 67)	Percentage agreeing or strongly agreeing for Trastuzumab group (n = 30)
Having to take medicines worries me	36%	50%
I sometimes worry about the long-term effects of my medicines	49%	53%
My medicines are a mystery to me	44%	48%
My medicines disrupt my life	33%	50%
I sometimes worry about becoming too dependent on my medicines	36%	53%

Regarding the association between the necessity or concern score for Tamoxifen users, the result showed only one significant negative correlation (R=-0.366, P-value=0.011) between the necessity score and the age of the participants as shown in the table 6.

The concern score for Tamoxifen users showed a non-significant positive association with age of participants as shown in the table 6.

Regarding the association between the length of treatment of Tamoxifen and the necessity or concern score, the results showed a non-significant negative correlation (table 6).

The study also observed a non-significant positive correlation between the age of Trastuzumab users and the requirement score, although the findings showed a non-significant negative correlation between age and concern score or length of treatment for both necessity and concern score (table 6).

Table 6. The correlation between age, duration of treatment and necessity or concern scale for both Tamoxifen and Trastuzumab.

Parameter		Tamoxifen		Trastuzumab	
		R	P-value	R	P-value
Age	Necessity	-0.366*	0.011	0.144	0.449
	Concern	0.026	0.864	-0.029	0.879
Duration of treatment	Necessity	-0.110	0.465	-0.244	0.194
	Concern	-0.077	0.609	-0.236	-0.236

* Significant difference between the Tamoxifen and Trastuzumab groups (p<0.05).

Discussion

It is crucial to improve the treatment of women provided with adjuvant therapy and find ways to prolong the length of therapy to reduce recurrence and mortality[20].

Compared to socio-demographic variables, patient beliefs about his medication were a powerful predictor of reported adherence[24].

Moreover, individuals' beliefs about their medicine are modifiable drivers of decision-making about treatment[25].

From a current systematic review that looked at the impact of various health beliefs on drug adherence, patients' beliefs and their relationship to drug adherence appear to vary unpredictably across cultures and across populations[26] It is therefore important to examine Iraqi patients' beliefs and assess the level of needs and concern for their treatment.

The Belief about Medicine Questionnaire (BMQ) is a reliable test for measuring patients' beliefs in various populations[27].

This study investigates the beliefs concerning Tamoxifen and Trastuzumab, which are two effective and widely used adjuvant therapies prescribed for breast cancer patients. According to a study conducted in Iraq[21] investigating treatment options and follow-up among Iraqi breast carcinoma patients, the findings regarding hormone therapy showed that Tamoxifen was provided as an adjuvant treatment choice in (63.5%) of patients. In comparison, Trastuzumab was recommended in (27.4%) of patients with HER2-positive patients[21]. The findings of the current study have shown that the participants are primarily between 40-60 years of age and that, in line with previous studies[21,28] conducted in Iraq, which showed the peak age frequency for breast cancer patients is between 40-60.

While there was a higher value of necessity and concern in patients using Tamoxifen, the outcome clearly showed a significant higher necessity values, which means the patients' needs for Tamoxifen exceed their fear from taking this medicine. The findings are consistent with those of a previous study conducted by Elizabeth et al.[29], which shows that patients with strong need for Tamoxifen have good adherence.

While it is in contrast with Rachael et al., study that demonstrated a low necessity for Tamoxifen[30].

Regarding Trastuzumab, the value for necessity is additionally significantly higher than the concern value. This study was the first study that assesses the patient's beliefs about Trastuzumab, so there were no prior results to compare with. The expected reasons for these results are the well-tolerated side effect profiles and the comorbidities which are also crucial in patient's acceptance for Tamoxifen [31] and Trastuzumab [32].

Regarding the difference in necessity score or concern score between Tamoxifen and Trastuzumab, the current study revealed that there was no significant variation between the two medications. This could be related to the patients' positive experiences with both medications; in addition, most of them were not exposed to an undesirable side effect. The positive experiences were reflected from the high level of necessity with both medications.

Another factor that may cause this increase in the necessity for both medications is the physicians' prolonged experience with these medications and their knowledge that both medications were approved to be essential to prevent cancer recurrence with a well tolerable history of safety and effectiveness in improving the survival[33].

The physicians' confidence could be reflected as a positive overview in their patients as belief is a modifiable variable[34].

Moreover, both drugs are offered freely to the patients in Iraq[21], which may be the reason why the necessity is higher than the concern values.

Patients' awareness about the side effect of their medication is another factor that can influence the patient response, which can affect the degree of the concern level.

One question in concern part of the BMQ-specific questionnaire revealed a significant difference in responses between patients: "My medicines are a mystery to me," where there was a higher level of concern about this question in the Trastuzumab group. This can be explained by the insufficient information of the medication given by medical staff to the patient.

Patient's understanding of his drugs and their predicted adverse effects may be attributed to his belief as patients with negative medication beliefs may be vulnerable to misattributing symptoms and stopping medication afterwards[35].

A low side-effect profile may explain the low level of concern plus no deleterious influence of Trastuzumab[36] or Tamoxifen[37] on the health-related quality of life has been reported.

The only negative association was found between the necessity scale and the patients' age in the Tamoxifen group. Failure to find a positive or negative correlation might be related to the limited number of patients who participated in this study or short treatment duration. This study was the first study attempted to find a correlation between age, duration of treatment and scale of need or concern, so that no prior studies can be compared.

Understanding the reasons behind a varying degree of need and concern among patients is crucial in providing optimal health advice and guidance[38].

Limitations of this study include: firstly, the small number of participants which could be linked to the inclusion – exclusion criteria that excluded many participants such as those with longer medication use (more than one year) or those using combination therapy to prevent any bias that may influence beliefs. Secondly, the use of the questionnaire English version since it is a validated version[23]. Thirdly, the biases that may arise during patient comprehension of the questions may account as another drawback. In addition, the authors did not discuss the quality of contact between the clinician and the patient, which could affect women's awareness, comprehension and beliefs about the two medications.

Conclusion

This survey clearly showed a high level of necessity and concern regarding the use of two effective adjuvant therapies for women with breast cancer, Tamoxifen and Trastuzumab. Furthermore, this study showed that while the level of need for Tamoxifen is higher than for Trastuzumab, there were no significant variations between them. Considering the level of concern, the results for Trastuzumab were higher, but not significant compared to the level of concern for Tamoxifen. The age and length of treatment are not significantly correlated with the degree of necessity or even concern. Physicians should evaluate patients' beliefs, and it might be helpful to follow educational programs to attempt for changing them.

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