Original Paper

Adherence to Aromatase Inhibitors among Postmenopausal Breast Cancer Patients in Middle Euphrates Region of Iraq

Ahmed Mjali[1*], Alyaa Hadi Oudah[1], Haider Hasan Jaleel Al-Shammari[2], Nareen Tawfeeq Abbas[3]

[1]Department of Hematology /Oncology, Al- Hussein Medical City, Karbala, Iraq.
[2]Baghdad University, College of Medicine, Baghdad, Iraq.
[3]Hiwa Hematology/Oncology Hospital, Sulaymaniyah, Iraq.

Abstract

Background: Aromatase inhibitors AIs, are now widely used hormonal therapy in postmenopausal breast cancer patients with hormone receptors positive because of their clinical effectiveness in both adjuvant and metastatic setting. Adherence to therapy and compliance with professional instructions are critical in the management since poor compliance to treatment leading to inferior outcomes. **Aims:** To determine the adherence of patients to AIs therapy and factors associated with non-adherence among breast cancer patients in Middle Euphrates region of Iraq.
Methods: This study was conducted in Al-Hussein cancer center in Karbala province of Iraq, between January 2020 and December 2020. There were 101 breast cancer patients treated with AIs, their adherence was assessed by using the validated Morisky Medication Adherence Scale (8-MMAS).
Results: Majority of patients had a high adherence in (62.38%) while (37.62%) of our patients were suboptimal adherence. Forgetfulness was the main cause of poor adherence in (71.05%) of patients. Bone and joint pain were the most frequent side effect among our patients. There was no significant association between age, educational level, marital status, income, parity, prior treatment and adherence (p-vale > 0.05).
Conclusion: These data suggest that more than one third of the patients have suboptimal adherence to Aromatase inhibitors. The factors associated with poor adherence were unintentional (forgetfulness), but also included intentional factors, such as drug inconvenience and avoidance of adverse effects. Paying attention to the factors found in this study might help to improve outcomes among breast cancer patients.
Key words: Aromatase inhibitors, Adherence, Breast cancer, Karbala Governorate, Iraq.

Introduction

Breast cancer is one of the most common types of cancer in women around the world, as well as one cause of the highest death rates.(1) There are three important breast cancer markers: hormonal receptors (estrogen receptor (ER) status and progesterone receptor (PR) status), and human epidermal growth factor receptor 2 (HER2). Those receptors are helpful in disease prognosis and make decisions about therapy.(2, 3)

Aromatase inhibitors (AIs) are effective drugs that stop the production of estrogen in postmenopausal women. They work by blocking the enzyme aromatase, which turns the hormone androgen into small amounts of estrogen in the body, this means that less estrogen is available to stimulate the growth of cancer cells. Nowadays AIs is a standard treatment in early and advanced breast cancer in postmenopausal women who have a hormonal positive test.(4,5)Although AIs is an effective drug in treating breast cancer with a significant

*For correspondence email: ahmedmajly@yahoo.com

improvement in disease free survival, failure to adherence impedes its effectiveness. In developed countries only half of the patients adhere to the treatment, making poor compliance as one of the important problems in the treatment plan.[6,7] There are many reasons for poor adherence, some of which are related to the patients and it is the largest part, others related to either treatment side effects or health care providers.[8]

Several methods are used to determine patients' adherence to treatment, one of the most common used methods is the eight items Morisky method adherence scale (MMAS-8). It is a tool for checking patients adherence to a specific treatment, it was consisted from four questions then developed into 8-questions and was used in different fields of diseases including oncology.[9-13]

In the present study, we try to assess the adherence to AIs among Iraqi breast cancer patients, specifically in the Middle Euphrates region. This study will help us to identify factors that lead to poor adherence to treatment and improve breast cancer treatment strategies in our country.

Methodology

Study design and participants

This is a cross-sectional study conducted at Al-Hussein Cancer Center in Karbala province in Iraq on 101 breast cancer patients during the period between January 2020 and December 2020. This center was established in November 2011 with oncology and hematology departments. It covers Karbala population in addition to other patients from the Middle Euphrates region of Iraq.[14]

Data collection

Information was collected through a questionnaire filled during individual interview between the nurses and the breast cancer patients' who regularly visit our center for treatment or follow up. The questionnaire included three sections, A, B and C. Section A contained socio-demographic information including age, marital status, duration of marriage, number of pregnancies, family history, level of education, and family income. Regarding income, patients were divided into: low-income class for those who earned less than 500,000 Iraqi Dinars (IQD) per month and middle - high income class for those who earned over 500,000 Iraqi Dinars (IQD) per month.[15] Section B contained questions about the treatment details. Section C contained the eight questions of Morisky medication adherence scale (8-MMAS) where the questions were translated into Arabic.

Table 1. The 8-items MMAS.[9,10]

1	Do you sometimes forget to take your breast cancer oral medication?	No	Yes
2	People sometimes miss taking their medications for reasons other than forgetting. Thinking over the past two weeks, were there any days when you did not take your breast cancer oral medication?	No	Yes
3	Have you ever cut back or stopped taking your breast cancer oral medication without telling your doctor because you felt worse when you took it?	No	Yes
4	When you travel or leave home, do you sometimes forget to bring along your breast cancer oral medication?	No	Yes
5	Did you take your breast cancer oral medication yesterday?	No	Yes
6	When you feel like your breast cancer is under control, do you sometimes stop taking your medication?	No	Yes
7	Taking medication every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your breast cancer treatment plan?	No	Yes
8	How often do you have difficulty remembering to take all your medications?	Never/Rarely Once in a while Sometimes Usually All the time	

The answer of the first seven questions is either yes or no. Only in the fifth question, if the answer is yes, the scale gets one point, and if the answer is no, it gets zero, in the remaining six questions, if their answer is no, then the scale gets one point for each answer, and if their answer is yes, it gets zero. The eighth question consists of five branches if the answer is never, the scale gets one point, once in a while gets 0.75, sometimes gets 0.5, usually gets 0.25, and all the time gets zero. The sum of all the points of the questions ranges from zero to eight. AIs adherence is classified as high adherence (score 8 points), medium adherence (score 6-7 points), and low adherence (score below the 6).[9,10]

Inclusion / Exclusion criteria

All postmenopausal breast cancer patients with positive hormonal receptor who attended the center between January 2020 and December 2020 for hormonal therapy were included in this study. All patients participating in the research had been taking the drug for at least 2 months, so most of them recovered from the side effects of radiation or surgery, if they did it. Any patient with inconclusive results was excluded from the study.

Ethical considerations

Institutional review board (IRB) approval was obtained from the Ethics Committee at Al- Hussein Medical City, Karbala, Iraq. Each patient was informed about the objectives of study prior to interview and the participation was voluntarily.

Statistical analysis

Data were analyzed by using the Social Sciences of Statistical Package (SPSS) version 20, Chi square procedure was being used to identify the significant differences at the level of significance < 0.05. Descriptive statistics of the variables were expressed as percentage, meaan, and ratio.

Results

There were 101 post-menopausal patients with hormone receptors positive breast cancer were enrolled in the present study. Overall mean age of patients was (61.81± 8.15) years and the range (45-84) years. Out of 101 patients, there were 55 patients (54.45%) married, 40 patients (39.6%) widowed, 4 patients (3.96%) single, 2 patients (1.98%) divorced. The majority of patients are found to be low income in 66 patients (65.34%) and 42 patients (41.58) were illiterate.

Overall, the mean MMAS-8 score of the patient was 7.42±0.99, where the range was (1-8). Regarding patients adherence level, 63 patients (62.38%) had a high level of adherence, followed by 35 patients (34.65%) patients with medium level of adherence and 3 patients (2.97%) with low level of adherence as shown in (figure 1).

There was no correlation between duration of treatment, level of education, income, parity or type of treatment and adherence level (P value >0.05) for each (table 2). Among 38 patients with suboptimal adherence, the most common reason for poor adherence to AIs was forgetfulness in 71.05% followed by inconvenience in 50%, side effects in 31.58%, unavailability of drug in 13.16%, hopelessness in 7.89%, and misunderstand medication instructions in 2.63% as shown in (figure 2).

The most common reported side effects of AIs was bone and joint pain in 56 patient (55.44%), followed by fatigue in 12 patients (11.88%), nausea in 11 patients (10.89%), hot flashes in 10 patients (9.9%) and headache in 7 patients (6.93%). Other side effects, and their percentages are shown in (table 3).

Discussion

Worldwide, breast cancer is the most commonly diagnosed cancer and the main cause of cancer death. In Iraq it is the most common cancer in female presenting more than 40% of newly diagnosed cancer cases, making treatment of breast cancer is a great challenge to health workers in our country.[16-18]

Table 2. The association between clinical characteristics of the patients and their adherence levels

Factor		Overall n (101)	High (n=63)	Medium (n=35)	Low (n=3)	p-value
Age (year)	Mean±SD	61.86± 8.15	63.07±8.85	59.88±6.4	59.33±8.5	0.147
Age group, N (%)	< 60 years	44 (43.56%)	24 (38.10%)	18 (51.43%)	2 (66.67%)	0.316
	≥ 60 years	57 (56.44%)	39 (61.90%)	17 (48.57%)	1 (33.33%)	
Years since diagnosis	Mean±SD	2.95 ± 2.35	3.05 ± 2.34	2.78 ± 2.44	4.46±0.62	0.389
MMAS-8 score	Mean±SD	7.42 ± 0.99	8 ± 0.00	6.68 ± 0.49	3.83 ±2.46	0.001*
Duration of AI, N (%)	≤ 2 Years	55 (54.45%)	37 (58.73%)	18 (51.43%)	0	0.592
	> 2 Years	46(45.54%)	26 (41.27%)	17 (48.57%)	3 (100%)	
Education level, N (%)	Illiterate	42 (41.58%)	26 (41.27%)	13 (37.14%)	3 (100%)	0.408
	Primary	15 (14.85%)	13 (20.63%)	2 (5.72%)	0	
	Secondary	23 (22.77%)	13 (20.63%)	10 (28.57%)	0	
	Institute graduate	17 (16.83%)	10 (15.88%)	7 (20%)	0	
	Higher education	4 (3.96%)	1 (1.59%)	3 (8.57%)	0	
Marital status, N (%)	Single	4 (3.96%)	3 (4.76%)	1 (2.86%)	0	0.147
	Married	55 (54.45%)	36 (57.14%)	17 (48.57%)	2 (66.67%)	
	Divorced/separated	2 (1.98%)	1 (1.59%)	1 (2.86%)	0	
	Widowed	40 (39.60%)	23 (36.51%)	16 (45.71%)	1 (33.33%)	
Income, N (%)	≥ 500000 IQD	35 (34.65%)	20 (31.75%)	15 (42.86%)	0	0.494
	< 500000 IQD	66 (65.34%)	43 (68.25%)	20 (57.14%)	3 (100%)	
Parity, N (%)	Multiparous	84 (83.17%)	50 (79.36%)	31 (88.57%)	3 (100%)	0.541
	Primiparous	4 (3.96%)	4 (6.35%)	0	0	
	Nulliparous	13 (12.87%)	9 (14.29%)	4 (11.43%)	0	
Chemotherapy, N (%)	Yes	77 (76.24%)	45 (71.43%)	30 (85.71%)	2 (66.67%)	0.260
	No	24 (23.76%)	18 (28.57%)	5 (14.29%)	1 (33.33%)	
Surgery, N (%)	Bilateral mastectomy	5 (4.95%)	3 (4.76%)	2 (5.71%)	0	0.755
	Mastectomy	72 (71.29%)	46 (73.02%)	23 (65.72%)	3 (100%)	
	Lumpectomy	18 (17.82%)	10 (15.87%)	8 (22.86%)	0	
	No	6 (5.94%)	4 (6.35%)	2 (5.71%)	0	
Radiation, N (%)	Yes	62 (61.39%)	37 (58.73%)	24 (68.57%)	1 (33.33%)	0.377
	No	39 (38.61%)	26 (41.27%)	11 (31.43%)	2 (66.67%)	
* significance differences (P<0.05)						

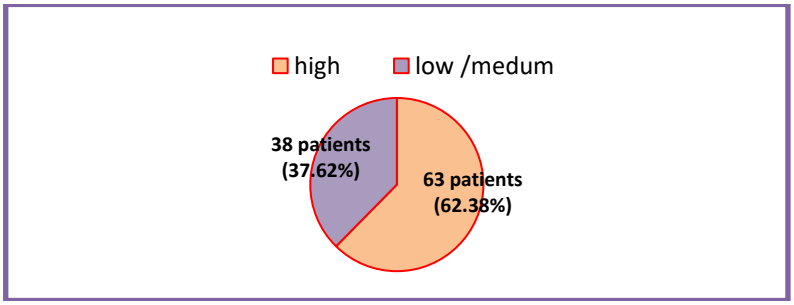

Figure 1. Adherence of patients according to 8-MMAS

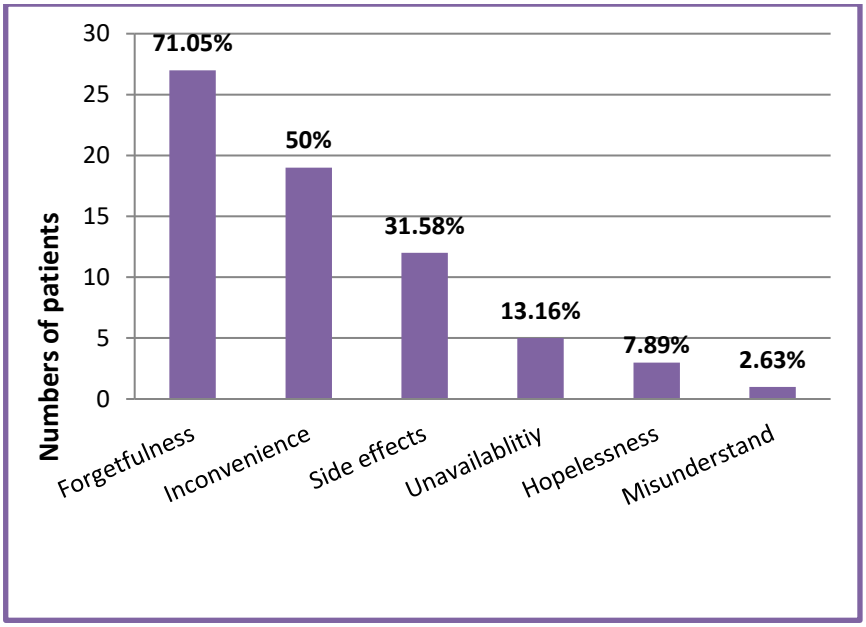

Figure 2. Causes of poor- adherence to AIs.

Table 3. Reported side effects of AIs among our patients

Side effects	N (%)
Bones, joints pain	56 (55.45%)
Fatigue	12 (11.88%)
Nausea	11 (10.89%)
Hot flashes	10 (9.90%)
Headache	7 (6.93%)
Mood disturbances	5 (4.95%)
Dizziness	4 (3.96%)
Stomach pain	3 (2.97%)
Shortness of breath	3 (2.97%)
Peripheral edema	3 (2.97%)
Weight gain	2 (1.98%)
Hair thinning	2 (1.98%)

Poor compliance to treatment had negative impact on cancer patients, understanding factors that lead to incompliance may help to improve treatment outcomes and decrease complications.[19,20]

In our region 62.38% of patients had good adherence to AIs, these results may be somewhat similar to studies in US (62%), little lower than Europe (69%).[21-23] While our results were higher than in Latin America (44%).[12]

The major cause of poor adherence to AIs in this study was forgetfulness (65.79%) and this cause was similar in Singapore and Latin America.[24,25] While previous research in our province suggested the unavailability of drug was the main cause of poor adherence.[11]

There were several factors may influence the degree of adherence among cancer patients including age, gender, marital status, income and type of treatment.[26] In this study there was no correlation between age and adherence, that disagree with previous studies in US and Europe suggested that old age patients were more adherent than young patients.[22,27]

This study revealed that no association between parity and adherence among our patients, while in Latin America, nulliparous women were better adherence than multiparous women.[12] On other hand

there was no correlation between marital status and adherence in our study but in previous study in US unmarried women tend to be more adherent than married.[21] While in Europe married women were more adherent.[(22)]

In the present study, adherence was not affected by type of prior treatment, duration of treatment, income or education level. This agreed with previous studies in Europe, US, Latin America and Singapore. [(12,13,21,22, 25)]

Drugs side effects had poor impact on cancer patients compliance, recognition of these side effects and urgent treatment leading to improve patients compliance.[28, 29] Bone pain and join pain was the most common side effect that presented in more than half of our patients. Same results in previous studies in US and Europe where musculoskeletal symptoms were the most frequent among patients who receive AIs.[(30,31)]

This study has to be evaluated in light of its strengths and limitations. The main strength of our study is that it is among few studies addressing adherence level of Iraqi patients, presenting factors that lead to poor adherence. As for the limitations, the study was cross-sectional in one center and the sample size was relatively small. Accordingly, the sample taken may not be representative of the whole population in Iraq and thus the generalizability of this study is limited.

Conclusion

The level of adherence to Aromatase inhibitors in our region is suboptimal, the main reason for poor adherence was forgetfulness. There was no significant association between age, education level, duration of treatment, marital status, income or previous treatment with adherence among our patients. Future studies in other parts of Iraq are recommended to identify the factors that lead to poor adherence. Improving patient knowledge or beliefs regarding treatment are very important to increase adherence and improve treatment outcomes in our country.

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