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Association between self-report adherence measures and oestrogen suppression among breast cancer survivors on aromatase inhibitors

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Abstract   *Purpose:* Poor adherence to oral adjuvant hormonal therapy for breast cancer is a common problem, but little is known about the relationship between self-report adherence measures and hormonal suppression. We evaluated the relationship of three self-report measures of medication adherence and oestrogen among patients on aromatase inhibitors (AIs).
Materials and methods: We recruited 235 women with breast cancer who were prescribed AI therapy. Participants self-reported AI adherence by completing the following: (1) a single item asking whether they took an AI in the last month, (2) a modified Morisky Medication Adherence Scale-8 (MMAS-8) and (3) the Visual Analog Scale (VAS). Serum estrone and estradiol were analysed using organic solvent extraction and Celite column partition chromatography, followed by radioimmunoassay.
Results: Ten percent of participants reported they had not taken an AI in the last month and among this group, median estrone (33.2 pg/ml [interquartile range (IQR) = 22.3]) and estradiol levels (7.2 pg/mL [IQR = 3.3]) were significantly higher than those in participants who reported AI use (median estrone = 11.5 pg/mL [IQR = 4.9]; median estradiol = 3.4 pg/mL [IQR = 2.1]; $p < 0.001$). This relationship held when controlling for race and AI drug type.

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Conclusions: A single-item monthly-recall adherence measure for AIs was associated with oestrogen serum levels. This suggests that patient-reported monthly adherence may be a useful measure to identify early non-adherence behaviour and guide interventions to improve patient adherence to hormonal treatment.

1. Introduction

Breast cancer is one of the most common cancers among women in the United States, with an estimated 235,000 cases diagnosed in 2014 [1]. Though breast cancer treatments are typically effective, recurrence is often a concern. Oral adjuvant hormonal therapy has been shown to decrease the recurrence rate and increase the overall survival rate of hormone receptor positive breast cancer [2,3]. Aromatase inhibitors (AIs), the newest class of these drugs developed for post-menopausal women, help prevent recurrence by reducing circulating levels of oestrogen which at high levels can stimulate growth of breast tumour tissue [4].

Non-adherence is a common problem for women undergoing hormonal treatment [5–7]. Early discontinuation of adjuvant hormonal therapy (adjusted hazard ratio [HR], 1.26; 95% confidence interval (CI), 1.09–1.46), as well as frequent missed doses among those who have continued therapy ([HR], 1.49; 95% CI, 1.23–1.81), have each been shown to be independently associated with increased mortality even after controlling for age and disease factors [8]. Consequently, measuring adherence to AIs has been recognised as an important element of patient care, from both research and clinical perspectives [9].

Though there is no gold standard for assessing medication adherence [10], pharmacy refill data and electronic bottle monitoring are often considered superior approaches among the methods available. Unfortunately, they are either labour intensive or expensive to implement, making them impractical for many clinicians and researchers. Self-report adherence measures, on the other hand, are relatively easy and inexpensive to collect; and though potentially subject to recall and reporter bias, they have been found to be reliable and valid among chronically ill populations. For example, self-report measures for medication adherence have been found to predict biological and physiological outcomes, including CD4 count among HIV patients [11] and blood pressure levels among hypertensive patients [12].

Currently, the relationship between self-report adherence measures and hormonal suppression among breast cancer patients on AIs is unknown. The primary purpose of this study was to determine whether self-reported adherence to AIs is associated with patients' serum oestrogen levels. As a secondary aim, we examined the relationship between patients' self-reported adherence behaviour and their mood and anxiety levels to further understand the relationship between difficulties patients report with AI adherence and their distress levels.

2. Methods

2.1. Participants

Participants were drawn from the Wellness after Breast Cancer (WABC), a large ongoing study examining genetic determinants of symptom distress and disease outcomes among postmenopausal women with hormone receptor positive breast cancer on AIs [13]. Our analysis focused on 235 participants of the WABC cohort for whom oestrogen serum levels were available. These women were not selected for any characteristics, but were rather a subset of women recruited during the study period when funds were available to conduct the oestrogen assays. No differences were found in baseline characteristics (age, race, BMI, marital status or education) between the subset represented in this study and the rest of the sample. The sample included women who were currently on an AI as well as women who had self-reported premature discontinuation of their AI treatment.

This study was conducted with the approval of the Institutional Review Board of the University of Pennsylvania and all participants provided written informed consent. Research assistants recruited participants in two breast cancer clinics, one situated in an academic tertiary care teaching hospital and the other in a community hospital. Eligibility criteria were (1) female sex; (2) age 18 or older; (3) history of stage I, II or III breast cancer and (4) current use of a third-generation AI for at least 6 months or premature discontinuation of an AI; (5) postmenopausal; (6) completed primary cancer treatments (surgery, chemotherapy and radiotherapy) and (7) able to understand written English and participate in an informed consent process.

2.2. Measures

Participants completed measures of AI adherence in addition to measures of pain, AI side-effects, emotional wellbeing, sleep and fatigue, physical functioning and physical activity. Participants also provided information