Does fasting during Ramadan trigger non-adherence to oral hormonal therapy in breast cancer patients?

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Introduction
Breast cancer (BC) is the commonest malignancy among females both in developed and developing countries [1]. In Egypt, BC represents 35% of female cancers [2]. Two thirds of BCs are positive for estrogen receptors (ER) and/or progesterone receptors (PgR) and thus can be treated with endocrine manipulations. ER blockers like tamoxifen (TAM) or aromatase enzyme inhibitors (AIs) are the most commonly used oral hormonal treatments (OHT). However, to derive the maximum benefit, these oral
drugs should be used continuously for 5 years in the adjuvant setting. With a duration of 1, 2 and 5 years of adjuvant TAM, recurrences decrease by 12%, 29% and 47%, respectively [3].

As with other chronic medications [4], compliance/adherence with OHT in BC is a major issue as it drops progressively with time from 83% in first year to 50% in the 4th year [5]. Factors associated with non-adherence include adverse side-effects, complex schedules, long treatment duration, demographic factors and financial constraints [6]. Non-adherence can be unintentional (e.g. when patients merely forget to take their medications) or intentional when they choose not to take them [7]. Intentional non-adherence can be due to lack of information about advantages and disadvantages of treatment, lack of obvious and immediate benefits as in the adjuvant setting, and seeing oneself not in need of treatment [4]. Non-adherence can signal treatment discontinuation and both are associated with lower 10-year survival rates (77.8% and 73.6%, respectively) than that of adherent patients (81.7%) [8].

During the ninth lunar month in the Arabic calendar (Ramadan), Muslims eating behavior changes as they refrain from eating and drinking from dawn till sunset. Thus, oral drugs that used to be taken during daytime have to be shifted to the night. This change may be associated with non-adherence or discontinuation that may continue afterward and have negative consequences with increased recurrences and or shortened survival.

Information on compliance with oral endocrine therapies during Ramadan is lacking. Thus we conducted this study to estimate adherence to TAM and AIs during Ramadan compared to its preceding month.

Patients and methods

This study was conducted at the out-patient clinic of the Medical Oncology Department of the Egyptian National Cancer Institute (NCI-Egypt) during Ramadan 2010. All patients consented to participate in the study that was approved by the institutional review board.

One-hundred and thirty-nine adult female patients with BC were interviewed by the first author (AZ) during their routine follow up appointments. Selection criteria were a confirmed diagnosis of BC of any stage, ER and/or PR positive, receiving OHT that is the same for at least 2 months prior to Ramadan.

They were asked how many days they were non-fasting during Ramadan and how many days they did not receive their OHT both during Ramadan and the preceding month. When missing OHTs, they were further asked whether they unintentionally forgot or they intentionally chose not to take them. Data of patients’ age, type of hormonal therapy, disease stage and aim of therapy were extracted from the patients’ files.

Outcomes were treatment adherence and predictors of non-adherence. Adherence was calculated as the numbers of days receiving the medications divided by the total days and expressed as percentage. Patients were considered adherent or non-adherent if they received ≥80% or <80% of their medications, respectively [9]. Adherence was divided into complete or partial if patients received 90–100% or 90–<90% of their medications. Non-adherence was divided into intentional and unintentional.

Statistical analysis

All data were analyzed using SPSS® v15 software (Chicago, USA). The dependent variable ‘adherence during Ramadan’ was then subjected to Chi-squared test analysis to identify any association with relevant factors (age, performance status, presence of metastases, type of hormonal therapy and adherence in the month preceding Ramadan) which were then entered into a logistic regression analysis.

Results

The study included 139 female patients with BC. The median age was 50 years (Table 1). Most patients were postmenopausal (60%) with good performance status (PS 0-1 in 80%) and non-metastatic disease (81%). The median number of fasting days was 18. OHT was given as adjuvant therapy in 81% and TAM was given in 64% while AIs in 36%. Fasting 80% or more of Ramadan was encountered in 93% of patients. One fifth of the patients presented with metastatic disease and most of them had single metastasis. Almost half of the patients were receiving OHT for a duration up to 2 years.

Adherence to OHT during Ramadan was 94.2% compared to 95.7% prior to Ramadan (p = 0.77) with higher but insignificant rate of intentional non-adherence prior to Ramadan (p = 0.92, Table 2). Adherence was complete in 97% of patients both during and before Ramadan (p = 0.74). Six out of the eight patients recognized as non-adherent to OHT during Ramadan were also non-adherent in the preceding month. Six of the eight non-adherent patients during Ramadan were on TAM and four of them (67%) intentionally opted not to take the drug because of side effects that were mostly hot flushes and epigastric pains. All non-adherences with AIs were unintentional and mostly related to missing their prescriptions.

Age, performance status, presence of metastases, type and duration of hormonal therapy and history of adherence in the month preceding Ramadan were assessed for their effects on adherence to OHT during Ramadan (Table 3). Non-adherence to OHT prior to Ramadan and a shorter duration of OHT (≤2 years) were associated with non-adherence to OHT during Ramadan (p < 0.001 and 0.003, respectively). This was shown only in univariate analysis and was lost in multivariate analysis.

Discussion

Long-term daily OHT in BC reduces recurrences and increases survival. However, adherence to these medications is essential to derive the mentioned benefits [10]. While adherence to OHT in BC patients was assessed in many trials, little is known about adherence during the fasting month of Ramadan when eating behaviors of fasting patients change with a possibility of increased non-adherence.

This study assessed short term adherence to OHTG over a period of two months; Ramadan and its preceding month. Thus it differs from other studies [5,6,9] that assessed long term adherence. We assessed adherence among patients regularly attending their routine appointments, thus we could not assess the fraction that opted to permanently discontinue their medications as those would not be accessible. Short-term compliance, as in our study, needs to be correlated with long term adherence and this issue needs further attention and research.

Given the high illiteracy rates among Egyptian females [11], we felt that a self-administered questionnaire would be difficult
to complete. Higher than actual adherence figures might result from exaggeration of adherence claims to satisfy the interviewer or to obviate a possible blame [10]. However, the interview was conducted in friendly circumstances to allow patients...
reveal as much normal information as possible. Patients were reassured that their answers, whatever they are, will never affect their treatments negatively.

The majority of patients (94%) were adherent to their OHT during Ramadan which is slightly (and insignificantly) lower than the non-fasting months (96%). Patients usually change the timing to match the change in the eating patterns, i.e. instead of taking the drugs during day time, they shift this to the night time where eating and drinking are religiously allowed. Maintaining adherence to OHT during Ramadan is facilitated by the non-complex schedules of these medications and the relative lack of their side effects [6]. Moreover as the first meal after a full-day fast is usually indoors gathering all family members, patients will easily access their medications and receive reminders and support from family.

The rates of adherence to OHT in our study are similar to those reported by other researchers in the short-term [6,11,12]. This reflects the short duration of the study and hence the ease of recalling adherence information by the patients. Also, many of the negative predictors of poor adherence are obviated in the current study [4]. The negative impact of low socioeconomic on adherence in the current study was abolished as most aspects of the medical care of the interviewed patients (including medical exams, laboratory and radiologic investigations as well as medications) were provided free of charge. Moreover, the crowded clinics and the long waiting time allows a significant time for contact with and observation of other patients. This might enhance compliance through something similar to psychological group support techniques. Patients on OHT may recall their unfavorable experiences with chemotherapy and realized how other patients do poorly upon relapse and these two factors provide an incentive for adherence to avoid getting relapse and further receiving chemotherapy.

Adherence in the month preceding Ramadan was significantly associated with adherence during Ramadan (P < 0.001). This may reflect the patient personality; as compliers prior to Ramadan will mostly remain compliant during Ramadan. A shorter duration of OHT was associated with non-adherence during Ramadan (p < 0.003). While this contradicts with studies that showed that compliance decreases with the longer duration of OHT use, it reflects a fact that patients who are using OHT for a longer time are more accustomed to the drugs and less likely to drop them during Ramadan. Age was not a factor as most of our patients (~90%) were below the age of 65. Similarly performance status (PS) had no influence as most of the patients (80%) were in the favorable group (PS 0–1) and only a minority (4%) had a PS of 3. Type of hormonal therapy had no influence on adherence. This may be explained by simple administration schedule (once daily) of both TAM and AIs. Metastases had no influence on adherence. This is because most of those patients eligible for OHT either had bone metastases or slowly progressive visceral disease. Thus most of them are stable for long periods.

Similar to previous studies [4,13,14], adherence to OHT in our study did not differ with TAM or AIs. The lower adherence rates reported by Ziller et al. [9] with AIs compared to TAM were debated mostly with the small numbers included in their study [5].

Intentional non-adherence was insignificantly lower during Ramadan compared to its preceding month (50% vs. 67%). Intentional non-adherences in Ramadan and the prior month were related to TAM and its side-effects. Those non-adherent patients preferred to continue fasting than getting the treatments. However, the differences were statistically insignificant and the absolute numbers were small.

In conclusion, Egyptian BC patients receiving OHT have high rates of short-term adherence to these medications. Fasting does not appear to decrease this adherence and thus, in the absence of a contraindication, patients should not be discouraged to fast if they wish.

Conflict of interest statement
None declared.
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References