This study examines whether women with breast cancer, who are adherent and non-adherent to tamoxifen, differ in their perceptions of information received during treatment. This cross-sectional study included women receiving tamoxifen as adjuvant treatment for breast cancer recruited from a teaching hospital specialised in women’s health in the state of São Paulo (Brazil). Women were interviewed and their records were reviewed for socio demographic data and clinical characteristics. We assessed tamoxifen adherence using the Morisky-Green Test, and the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Information module (EORTC QLQ-INFO25) was used to evaluate the information received by the women. The sample contained 31 women (mean age = 55.4; SD = 11.6 years). According to the Morisky-Green Test, 74.2% of the women had suboptimal tamoxifen adherence. The global score for women’s perceptions of information they received about the treatment and disease was 57.0 ±19.1 on a scale of 0 to 100, and no significant differences in scores were observed between adherents and non-adherents. A high prevalence of suboptimal tamoxifen adherence was observed. We found no significant differences between women with breast cancer who were adherent and non-adherent to tamoxifen.

Key words: medication adherence, quality of life, breast cancer, tamoxifen.

Contemp Oncol (Pozn) 2017; 21 (4): 295–298
DOI: https://doi.org/10.5114/wo.2017.72397

Analysis of information received during treatment and adherence to tamoxifen in breast cancer patients

Aline Cruz1, Aline Rodrigues1, Amanda Ferracini2, Rebeca Stahlschmidt1, Nice Silva2, Priscila Mazzola3

1Faculty of Medical Sciences (FCM), State University of Campinas, São Paulo, Brazil
2Pharmacy Service of Women’s Hospital (CAISM), State University of Campinas, São Paulo, Brazil
3Department of Pathology, State University of Campinas, São Paulo, Brazil

Introduction

The use of tamoxifen in early-stage breast cancer as adjuvant therapy has been known to improve long-term survival and reduce recurrence and mortality rates among patients with oestrogen receptor-positive breast cancer [1]. Several authors have observed high rates of non-adherence to tamoxifen and treatment persistence [2–4].

Numerous factors were found to be negatively associated with adherence and persistence: extremes of age, follow-up care with a general practitioner, higher CYP2D6 activity, switching from one form of therapy to another, and treatment side effects [5]. Furthermore, significant differences regarding beliefs about the necessity of taking tamoxifen between adherent and non-adherent patients have been observed [6]. The percentage of women who drop out after one year of treatment has previously been estimated at 15–20%, and this proportion increases to approximately 31–60% at the end of five years [5].

Relatively few studies have shown the positive effects of interventions on improvement of adherence and persistence on treatment. Some suggest that interventions in the management of tamoxifen’s adverse effects as well as patient counselling strategies that clarify the expected benefits of appropriate adherence (e.g. in reducing the recurrence of breast cancer) may be effective in increasing adherence to, and persistence with, tamoxifen treatment [6].

We therefore aimed to determine whether there are differences between women with breast cancer, who are adherent and non-adherent to tamoxifen regarding the perceived level of information received during treatment.

Material and methods

Setting and participants

The study was conducted in a university hospital specialised in women’s health located in Campinas, Brazil. Patients were recruited between January 2012 and December 2012. This study was approved by the Ethics Committee of the University of Campinas (CAEE: 1101.0.146.000-11). Written, informed consent was obtained from all participants.

Inclusion criteria were adult women (aged > 18 years) with oestrogen receptor-positive breast cancer using tamoxifen as endocrine therapy. Women who had cognitive impairment sufficient to interfere with answers to questionnaires were excluded from the study.

Data collection

The volunteers were interviewed regarding their demographic backgrounds and their clinical records were reviewed for relevant information.
on disease characteristics. Medication adherence was assessed with the Morisky-Green Test, a structured questionnaire with four items: (1) “Do you ever forget to take your medicine?” (2) “Are you careless at times about taking your medicine?” (3) “When you feel better, do you sometimes stop taking your medicine?” and (4) “Sometimes if you feel worse when you take the medicine, do you stop taking it?” [7]. Adherence was considered as adequate if all four questions were answered with a “no” and as inadequate if one or more questions were answered with a “yes”. The assessment was performed by a trained interviewer.

Women’s perceptions of how much information was received about the disease and treatment were ascertained with The European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire, Information module EORTC QLQ-INFO25, a self-report measure with a four-point Likert scale response format: 1 = “not at all”, 2 = “a little”, 3 = “quite a bit”, and 4 = “very much” [8]. Scores on this instrument were then linearly transformed into a 0–100 scale, according to the procedure outlined in the EORTC manual [9].

Statistical analysis
Analyses were conducted using the Statistical Package for the Social Sciences (SPSS) 16.0. Comparisons were performed with the Student’s t-test (two-tailed test; significance threshold: 0.05).

Results
We interviewed a total of 37 women, six of whom were excluded because they did not answer any questions in a module of the INFO25 questionnaire. The demographic and clinical characteristics of the remaining women are shown in Table 1.

Study participants answered the Morisky-Green questionnaire assessment, at the beginning and at the end of one year follow-up, and were classified as ‘total adherence’ (score = 4) or ‘non-adherence’ (score < 4).

The Morisky-Green test showed that only eight (25.8%) women were considered fully adherent to tamoxifen. The other 23 women had answered “yes” to one or two questions in the test and were considered non-adherent to hormonal therapy.

An important reason for non-adherence was forgetting to take the medication. Various guidelines have been conducted to provide strategies to remind women to take their medication: establishment of a schedule when the patient is at home and it is time to take the medicine (many volunteers taking the drug after dinner and during the weekends, when they were not at home, stopped taking the pill), guidance to set the alarm clock to the time of administration, leave the drug box in a visible place, or a reminder in the refrigerator, etc.

Many important problems regarding the use of tamoxifen were solved, and directions were given to the most frequently asked questions, such as: what to do in case of forgetting a dose, the importance of the administration at the right time, how to act in case of a delay in taking the dose.

Scores obtained by the INFO25 questionnaire are presented in Table 2. The global score was calculated according to the method adopted by Singer et al. (2013) [10].

We found no significant differences between adherent and non-adherent women in their perceptions of the information they received (Table 3).

Discussion
We investigated if there are differences among women with breast cancer receiving tamoxifen concerning their adherence and perception of information received during the treatment. In a recent systematic review of the literature, Murphy et al. noted tamoxifen adherence rates ranging between 41 and 88% in various studies/samples of breast cancer patients [5].

These large studies that found high adherence rates among women taking tamoxifen point to another problem in this type of therapy: a low persistence in the use of this drug. In Murphy’s review, after analysis of six studies evaluating the abandonment of treatment with tamoxifen in patients with breast cancer, it was observed that discontinuation in the first year is about 15–20% rising to 31–60% at the end of five years [5].

| Parameter | Value |
|-----------|-------|
| Age (years), average (SD) | 55.4 (11.6) |
| Marital status | 17 (54.8%) Married, 14 (45.2%) Unmarried |
| Education level | 14 (45.2%) Less than 8 years, 9 (29.0%) 8–11 years, 8 (25.8%) More than 11 years |
| Tumour stage | 16 (51.6%) I, 8 (25.8%) II, 7 (22.6%) III, 0 (0%) IV |
| Time of tamoxifen treatment (months), mean (SD) | 23.1 (12.5) |

SD – standard deviation

| Scale | Mean (SD) |
|-------|-----------|
| Information about the disease | 51.4 (27.3) |
| Information about medical tests | 58.4 (27.8) |
| Information about treatment | 56.5 (26.8) |
| Information on other health services | 42.5 (26.9) |
| Satisfaction with the amount of information received | 62.4 (25.4) |
| Helpfulness of information | 75.3 (22.7) |
| Global score | 57.0 (19.1) |

SD – standard deviation

Table 1. Demographic and clinical characteristics of patients (n = 31)

Table 2. Scores on various items comprising the EORTC QLQ-INFO25
We observed full adherence in only 25.8% of the women, a lower rate than we had anticipated. However, the differences in rates may be due to the different methodologies employed in evaluating adherence, such as self-reports, medical records, pill count, and population-based databases. There is a lack of agreement between distinct measures of adherence. In this study, we chose a method that could be easily applied in daily clinical practice and had not yet been used with patients on tamoxifen.

Higher scores on the EORTC QLQ-INFO25 indicate higher perceived levels of information received. The tool had never been used exclusively with women having this type of cancer, and we did not find other references of its application in a similar sample of women within the literature. In other groups of cancer patients, score averages have been reported to range from 22.0 to 68.0 among lymphoma patients, and from 19.0 to 64.6 among patients with metastasised colorectal cancer [11, 12].

It was noted that during application of the EORTC-INFO25 questionnaire the participants left many questions unanswered: the sum of unanswered questions for all women in the first application of the questionnaire was 60, and in the last 128 questions were left blank. The explanation for this could involve the complexity of the questionnaire and its extension. The high percentage of unanswered questions has reduced significantly the number of samples for statistical tests and may have affected the data analysis. We found no significant differences between adherent and non-adherent patients on all scales of the EORTC QLQ-INFO25 questionnaire.

Our study had limitations, such as the method used to determine adherence and the fact that the Morisky-Green test has not been validated for women with breast cancer receiving endocrine therapy. Another important limitation was the small sample size. Future studies should include a larger number of Brazilian breast cancer women to define levels of tamoxifen adherence in this population and information received.

Conclusions

A high prevalence of suboptimal tamoxifen adherence was observed. We found no significant differences among women with breast cancer concerning their perceptions of information received about breast cancer and its treatment. Tamoxifen adherence was lower than expected in a group of Brazilian women with breast cancer. Furthermore, adherent and non-adherent patients reported having received the same amount of information regarding treatment and disease.

We gratefully acknowledge the cooperation of the pharmacy staff and the patients of the Women's Hospital (CAISM) at the State University of Campinas (UNICAMP) for their support and collaboration during the research. The research group in clinical pharmacy and pharmaceutical care of the State University of Campinas (UNICAMP), Coordination for the Improvement of Higher Education Personnel (CAPES), from which the main researcher received a fellowship.

The authors declare no conflict of interest.

References

1. EBCTCG – Early Breast Cancer Trialists’ Collaborative Group (2011). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet, 2011; 378: 711-84.
2. Ziller V, Kalder M, Albert US, Holzhauer W, Ziller M, Wagner U, Hadji P. Adherence to adjuvant endocrine therapy in postmenopausal women with breast cancer. Ann Oncol, 2009; 20: 431-6.
3. McCowan C, Wang S, Thompson AM, Makubate B, Petrie DJ. The value of high adherence to tamoxifen in women with breast cancer: a community-based cohort study. Br J Cancer 2013; 109: 1172-80.
4. Hershman DL, Kushi LH, Shao T, et al. Early discontinuation and nonadherence to adjuvant hormonal therapy in a cohort of 8,769 early-stage breast cancer patients. J Clin Oncol 2010; 28: 4120-8.
5. Murphy CC, Bartholomew LK, Carpenter MY, Bluethmann SM, Vernon SW. Adherence to adjuvant hormonal therapy among breast cancer survivors in clinical practice: a systematic review. Breast Cancer Res Treat 2012; 134: 459-78.
6. Grunfeld EA, Hunter MS, Sikka P, Mittal S. Adherence beliefs among breast cancer patients taking tamoxifen. Patient Educ Couns 2005; 59: 97-102.
7. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986; 24: 67-74.
8. Arraras JI, Greimel E, Sezer O, et al. An international validation study of the EORTC QLQ-INFO25 questionnaire: an instrument to assess the information given to cancer patients. Eur J Cancer 2010; 46: 2726-38.
9. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Ins 1993; 85: 365-76.

Table 3. Comparison of INFO25 parameters between adherent and non-adherent patients

| Item                        | Mean (SD) | t   | P-value |
|-----------------------------|-----------|-----|---------|
| Adherent patients           |           |     |         |
| Information about the disease | 48.3 (35.7) | 0.376 | 0.710 |
| Information about medical tests | 58.3 (24.3) | 0.010 | 0.992 |
| Information about treatment | 57.2 (24.1) | 0.089 | 0.930 |
| Information on other health services | 46.9 (31.2) | 0.530 | 0.600 |
| Satisfaction with the amount of information received | 58.3 (29.5) | 0.514 | 0.611 |
| Helpfulness of information  | 66.7 (17.8) | 1.255 | 0.219 |
| Global score                | 55.0 (24.1) | 0.345 | 0.733 |
| Non-adherent patients       |           |     |         |
| Information about the disease | 52.5 (24.7) |     |         |
| Information about medical tests | 58.5 (29.5) |     |         |
| Information about treatment | 56.2 (28.3) |     |         |
| Information on other health services | 40.9 (25.9) |     |         |
| Satisfaction with the amount of information received | 63.8 (24.4) |     |         |
| Helpfulness of information  | 78.3 (23.8) |     |         |
| Global score                | 57.7 (17.6) |     |         |

SD – standard deviation.
10. Singer S, Engelberg PM, Weißflog G, Kuhnt S, Ernst J. Construct validity of the EORTC quality of life questionnaire information module. Qual Life Res 2013; 22: 123-9.

11. Husson O, Oerlemans S, Mols F, Smeets RE, Poortmans PM, van de Poll-Franse LV. Satisfaction with information provision is associated with baseline but not with follow-up quality of life among lymphoma patients: results from the PROFILES registry. Acta Oncol 2014; 53: 917-26.

12. Husson O, Thong MS, Mols F, Creemers GJ, van de Poll-Franse LV. Information provision and patient reported outcomes in patients with metastasized colorectal cancer: results from the PROFILES registry. J Palliat Med 2013; 16: 281-8.

Address for correspondence
Priscila Mazzola
Department of Pathology
State University of Campinas
São Paulo, Brazil
e-mail: pmazzola@fcf.unicamp.br

Submitted: 29.08.2017
Accepted: 22.11.2017