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Sexual quality of life in hormonotherapy for breast cancer patients

Qualidade de vida sexual para pacientes com câncer de mama em hormonioterapia

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ABSTRACT

Objectives: To evaluate how hormonal therapy can impact breast cancer patients sexual quality of life and compare two widely used therapeutic agents: anastrozole and tamoxifen. Studies so far have evaluated the side effects of such therapy on patients general quality of life, but literature remains scarce regarding the impact it has on sexual aspects. We believe there is a demand for a detailed view of these aspects since most patients undergo these treatments for at least five years. **Material and Methods:** Transverse observational study evaluated in 2019, 41 women with a history of breast cancer, all of them undergoing hormonal therapy. Group presented a mean age of 55.4 years (35 to 77 years); those in menopause with a mean time of menopause of 10.92 years (2 to 28 years). Thirty-eight women lived maritally and/or were sexually active. The mean duration of treatment was 36.84 months. We analyzed data in pre-and postmenopausal women, evaluating the results of questionnaires with general parameters (age, treatment time, general quality of life, adaptation to therapy) as well as specific instruments for evaluation of sexual dysfunction (FSDS-R) and quality of life with specific aspects for breast cancer (FACT-B). The results were placed in 2x2 contingency tables comparing the group receiving tamoxifen versus anastrozole. **Results and Conclusion:** Tamoxifen compared to anastrozole is a drug with apparent less impact on most common sexual dysfunctions (orgasm, dyspareunia, and feeling good quality of sex life), following those already published in international literature. We found no impact on physical, socio-familiar, and emotional well-being. Finally, we conclude that the results of this study significantly contribute to the choice of adequate therapeutic agent and highlight the need to bring this topic during routine consults and to the decision with the patient for the best suited treatment option.

Keywords: Breast neoplasms; Antineoplastic agents, Hormonal; Sexual dysfunction, Physiological; Quality of life; Tamoxifen; Anastrozole.

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RESUMO

Objetivos: Avaliar como a terapia hormonal pode impactar na qualidade de vida sexual de pacientes com câncer de mama e comparar dois agentes terapêuticos amplamente utilizados: anastrozol e tamoxifeno. Os estudos até o momento avaliaram os efeitos colaterais dessa terapia na qualidade de vida geral dos pacientes, mas a literatura ainda é escassa quanto ao impacto que ela tem nos aspectos sexuais. Acreditamos que haja uma demanda por uma visão detalhada desses aspectos, pois a maioria dos pacientes faz esses tratamentos há pelo menos cinco anos. **Material e Métodos:** Estudo observacional transversal avaliou em 2019, 41 mulheres com histórico de câncer de mama, todas em terapia hormonal. Grupo apresentou média de idade de 55,4 anos (35 a 77 anos); aquelas na menopausa com tempo médio de menopausa de 10,92 anos (2 a 28 anos). Trinta e oito mulheres viviam conjugalmente e/ou eram sexualmente ativas. A duração média do tratamento foi de 36,84 meses. Analisamos dados em mulheres na pré e pós-menopausa, avaliando os resultados de questionários com parâmetros gerais (idade, tempo de tratamento, qualidade de vida geral, adaptação à terapia) e instrumentos específicos para avaliação de disfunção sexual (FSDS-R) e qualidade de vida com aspectos específicos para o câncer de mama (FACT-B). Os resultados foram colocados em tabelas de contingência 2x2 comparando o grupo que recebeu tamoxifeno versus anastrozol. **Resultados e Conclusão:** O tamoxifeno comparado ao anastrozol é um fármaco com aparente menor impacto nas disfunções sexuais mais comuns (orgasmo, dispareunia e sensação de boa qualidade de vida sexual), seguindo os já publicados na literatura internacional. Não encontramos impacto no bem-estar físico, sociofamiliar e emocional. Por fim, concluímos que os resultados deste estudo contribuem significativamente para a escolha do agente terapêutico adequado e evidenciam a necessidade de trazer este tema durante as consultas de rotina e para a decisão com o paciente sobre a opção de tratamento mais adequada.

Descritores: Neoplasias mamárias; Agentes antineoplásicos hormonais; Disfunção sexual fisiológica; Qualidade de vida; Tamoxifeno; Anastrozol.

INTRODUCTION

Breast cancer is one of the most common malignant neoplasms affecting women worldwide. In Brazil, there is an estimated risk of 61.61 new cases per 100,000 women for each year of the triennium 2020-2022.[1] Those carcinomas that express hormone receptors are candidates for antiestrogen therapy, and this population corresponds to 71.3% of Brazilian patients with breast carcinoma.[2,3] The use of hormone therapy (HT) for these patients has benefits described since the 1970s as adjuvant treatment or for metastatic disease (remissive or palliative).[4–9]

The most commonly used classes involve selective estrogen receptor modulators (SERM, the most common representative of which is Tamoxifen) and aromatase inhibitors (AI, such as anastrozole, letrozole, and exemestane). HT causes many side effects that, by blocking the antiestrogenic action, reproduce the physiological postmenopausal hypoestrogenism. This can have a great impact on all dimensions of the quality of life of these women. In Brazil, there are review articles on the subject, but, at least in our literature searches, there are few clinical studies directed mainly to the sexual health.[10–16]

This paper aims to evaluate and try to quantify impacts of HT on sexual activity and quality of life in patients with breast carcinoma, according to age, pre- and post-menopausal hormonal status, and type of hormone therapy used (Tamoxifen or Anastrozole).

METHODOLOGY

The study was approved by the Research Ethics Committee of the Faculdade de Ciências da Saúde da Pontifícia Universidade Católica de São Paulo (PUC-SP), in Sorocaba (SP), Brazil. This is a transverse observational study and the evaluation instruments were applied to patients with breast cancer who consented to participate after signing the Free and Informed Consent Form (Appendix I). All of them were on hormonal treatment with Tamoxifen (T) or Anastrozole (A) at the time of the interview, either in adjuvant mode or advanced disease, in the pre-or postmenopausal state, at the outpatient level, in the Clinical Oncology Service of the Conjunto Hospitalar de Sorocaba (Seconci-SP), convened with the PUC-SP School of Medicine. Patients with psychological disorders that would not allow them to understand the questionnaires and illiterate patients were excluded from the analysis.

The used instruments were: FACT-B (Functional Assesment of Cancer Therapy) (indicated for quality of life assessment for patients with breast carcinoma)[17] and the FSDS-R (Female Sexual Distress Scale Revised) in Portuguese.[18] Questions are presented in 5 Likert mode responses. For the FSDS-R the score level equal to or greater than 11 discriminates women with sexual dysfunction; this index was not used in the evaluations, observing only the descriptive answers. (Appendix II).

Both questionnaires were already validated to Portuguese: FACT-B at a study by LATORRE, Maria do Rosário Dias de Oliveira from Universidade de São Paulo - USP at 2012 and FSDS-R at a study by LIMA, Sonia Maria Rolim Rosa from Faculdade de Ciências Médicas Santa Casa de São Paulo at 2010.

For the making of contingency tables, the absolute numbers for the categories "Almost always or always" + "Most of the time" + "Sometimes" ("Favorable" group) versus "Few times" + "Almost never or never" ("Unfavorable" group) were grouped. The same was done for FACT-B, with the grouping "Not at all" + "A little" versus "More or less" + "A lot" + "Very much". Women who used (by crossover) both medications were included in the group with Anastrozole, because at the time of the evaluation all of them were on Anastrozole therapy.

The questions were given to the patient (Appendix II) and answered without any external assistance. None were required to answer all the questions – we aimed to provide participants privacy and no interference with the questionnaires. Therefore, some calculations present with smaller numbers because of the participants' lack of response to some questions.

Other parameters evaluated were age, time of menopause, marital status, and current sexual activity. The initial clinical stage, the current status of HT (adjuvant or remissive), and the time and type of previous treatment were collected from the patients' medical records and from questions asked by the researchers.

Descriptive data were presented as absolute and relative numbers, and means; 2 x 2 contingency tables with chi-square by Fisher's exact test, and Yates' correction in the classical requirements, with the statistical significance level for $p<0.05$.

RESULTS

Forty-one women, with a mean age of 55.4 years (from 35 to 77 years) were evaluated in the year 2019. The menopausal women had a mean menopausal period of 10.92 years (from 2 to 28 years). 38 stated living maritally and/or being sexually active, and 3 did not respond. Mean time on hormone therapy was 36.84 months. For all those who had a crossover, its order was from Tamoxifen to Anastrozole, but the factors requiring the treatment changes or discontinuation were not documented. Table 1 shows the parameters of the study population.

Table 1. Characteristics of the population studied.

Type of treatment	Number	% of total
Adjuvant	33	80.49%
Remissive (palliative)	8	19.51%
TOTAL	41	100.00%
Only tamoxifen	19	46.35%
Only anastrozole	15	36.58%
Both	7	17.07%
TOTAL	41	100.0%
Before menopause	13	31.70%
After menopause	28	68.30%
TOTAL	41	100.0%
CANCER STAGING STAGE I	7	17.07%
STAGE II (IIA e IIB)	20	48.78%
STAGE IIIA	5	12.20%
STAGE IIIB	1	2.44%
STAGE IV or recurrent	8	19.51%
TOTAL	41	100.00%

Except for one patient (premenopausal), all responded that they understood the need for their hormone treatment, and none of them have suspended their treatment. If they could suspend it, 4/8 of premenopausal women and 4/26 of those in menopause said they would, which results in 8/34 women (23.52%). The main reason was because of side effects (7/40; 17.5%), and three patients pointed out specific situations: 2 for living too far from the treatment facilities and 1 for the need to change daily life schedule.

A cross-referencing of numbers in contingency tables determined no statistical correlation when considering the pre-and postmenopausal groups for the following conditions: impact of adverse effect vs. discontinuation of medication; impact on their life vs. impact of adverse effect; impact of adverse effect vs. discontinuation or change of medication.

The analyses regarding the FSDS-R instrument (Table 2) showed statistically significant numbers ($p< 0.05$) when comparing the groups with Tamoxifen (T) versus Anastrozole (A) in the following questions: question M. "In the past 4 weeks, how satisfied were you with your ability to achieve orgasm ("enjoy") during sexual activity or intercourse?", favoring the T group; questions Q and R regarding dyspareunia (pain at initial and after penetration, respectively) also favored the T group; question P, regarding overall sexual satisfaction, favored the group receiving tamoxifen, as well, wich coincids with question GS7 of the FACT-B Instrument additionally favoring the T group (see Table 3). For the other questions regarding orgasm, the comparisons between the T and A groups did not prove to be significant (questions K and L). The questions regarding sexual desire, activity and frequency of intercourse, sexual arousal and vaginal wetness found no differences between groups A and T, as well.

Table 2. FSDS-R instrument with its questions and levels of statistical significance for each of the questions.

Question	Statistical significance favoring tamoxifen or anastrozole group
A. In the past 4 weeks how often have you felt sexual desire or interest?	NS
B. In the past 4 weeks how do you rate your degree of sexual desire or interest?	NS
C. In the past 4 weeks, how often have you felt sexually aroused during sexual activity or intercourse?	NS
D. In the past 4 weeks, how would you rate your degree of sexual arousal during sexual activity or sexual act?	NS
E. In the past 4 weeks, how would you rate your degree of safety to become sexually aroused during sexual activity or sexual act?	NS
F. In the past 4 weeks, how often were you satisfied with your sexual arousal during sexual activity or sexual act?	NS
G. In the past 4 weeks, how often (how many times) did you have vaginal lubrication (got "wet vagina") during sexual activity or intercourse?	NS
H. In the past 4 weeks, how do you difficulty in having vaginal lubrication (getting "wet rate your vagina") during sexual intercourse or sexual activities?	NS
I. In the past 4 weeks, how often (how many times) did you maintain vaginal lubrication (get a "wet vagina") until the end of sexual activity or intercourse?	NS
J. In the past 4 weeks, how difficult was it for you to maintain vaginal lubrication ("wet vagina") until the end of the sexual activity or act?	NS
K. In the past 4 weeks, when you had sexual stimulation or sexual act, how often (how many times) did you reach orgasm ("came")?	NS
L. In the past 4 weeks, when you had sexual stimulation or sexual intercourse, how difficult was it for you to reach orgasm ("climaxed/joyed")?	NS
M. In the past 4 weeks, how satisfied were you with your ability to reach orgasm ("enjoy") during sexual activity or intercourse?	Favorable to tamoxifen (p<0.001)
N. In the past 4 weeks, how satisfied were you with the emotional closeness between you and your partner during sexual activity?	NS
O. In the past 4 weeks, how satisfied were you with the sexual relationship between you and your partner?	NS
P. In the past 4 weeks, how satisfied were you with your overall sex life?	Favorable to tamoxifen (p<0.02)
Q. In the past 4 weeks, how often did you experience discomfort or pain at the beginning of vaginal penetration?	Favorable to tamoxifen (p=0.02)
R. In the past 4 weeks, how often did you feel discomfort or pain after vaginal penetration?	Favorable to tamoxifen (p=0.001)
S. In the past 4 weeks, how would you rate your degree of discomfort or pain during or after vaginal penetration?	NS

Legend: NS = No statistical significance. Statistical analysis based on chi-square by Fisher's exact test, and Yates' correction in the classical requirements, with the statistical significance level for p<0.05.

Table 3. FACT-B instrument with its questions and statistical significance levels for each of them.
FAVORABLE/UNFAVORABLE QUESTION SIGNIFICANCE
(NS = Not significant)

FACT-B divided by its' question groups	Statistical significance favoring tamoxifen or anastrozole group
Physical well-being group (GP)	
I am without energy	NS
I am nauseous	NS
Because of my physical condition I have trouble meeting family needs	NS
I am in pain	NS
I am bothered by side effects of treatment	NS
I feel sick	NS
I feel forced to spend time lying down	NS
Social/family well-being group (GS)	
I feel I have a good relationship with friends	NS
I get emotional support from my family	NS
I get support from my friends	NS
My family is accepting of my illness	NS
I am satisfied with the way my family talks about my illness	NS
I feel close to my partner - or the person who is most supportive	NS
I am satisfied with my sex life	Favorable to tamoxifen (p<0.01)
Emotional well-being group (EG)	
I feel sad	NS
I am satisfied with the way I am coping with my disease	NS
I am losing hope in the fight against my disease	NS
I feel nervous	NS
I am worried that my condition will get worse	NS
Functional well-being group (FG)	
I am able to work (including at home)	NS
I feel fulfilled with my work (including at home)	NS
I am able to feel pleasure in living	NS
I accept my illness	NS
I sleep well	NS
I like the things I normally do for fun	NS
I am satisfied with the quality of my life right now	NS
Additional worries group (B)	
I feel short of breath	NS
I feel insecure about the way I dress	NS
I have swelling or pain in one or both arms	NS
I feel sexually attractive	Favorable to tamoxifen (p<0.01)
I am bothered by hair loss	NS
I get worried that other members of my family will one day have the same disease as me	NS
I am worried about the effect of "stress" on my disease	NS
I am bothered by weight change	NS
I can feel like a woman	NS
I feel pain in some areas of my body	NS

Legend: NS = No statistical significance. Statistical analysis based on chi-square by Fisher's exact test, and Yates' correction in the classical requirements, with the statistical significance level for p<0.05.

Quality of life was assessed by the FACT-B instrument, and Table 3 summarizes these data for the questions that achieved statistical significance. No significance was found for any question in the GP (physical well-being), emotional well-being (EG), functional well-being (FG) groups, all questions in the Social/family well-being (GS), and additional worries (B) groups. The only exception was for one question referring to satisfaction with sex life (GS) and feeling sexually attractive (B), both favoring the Tamoxifen group.

A direct question about the impact of hormone treatment on their quality of life showed thar 4/8 of premenopausal and 4/24 menopausal women reported a decrease in it after starting hormone therapy, exactly 8/34 women, or 23.52%.

DISCUSSION

The main side effects of HT for patients with breast cancer are already known, being coincident with the physiological postmenopausal hypoestrogenism. An observation study of up to 2 years of adjuvant treatment with aromatase inhibitors showed a significant rate of sexual dysfunction - 93% using the Female Sexual Function Index, with 75% of the women concerned about their sexual health. In the group that had maintained sexual activity, 79% developed new sexual problems in these 2 years.[19]

Tamoxifen was the gold standard for treating hormone-sensitive breast cancer in postmenopausal women, but the development of aromatase inhibitors, with its' mechanism of action more appropriate for postmenopausal women, made them the first choice for this group. With its increasing use among postmenopausal women, new toxicities such as arthralgias, bone loss, and cognitive dysfunction were described. Interestingly, these effects are poorly represented in older quality of life assessment instruments.[20–22] Other options of treatment to the group of high-risk HR-positive/ HER2 negative patients includes: ovarian suppression or ablation in premenopausal patients, leading to a menopausal state; and most recently, it has been shown efficacy in the combination of endocrine therapy with 2 years of adjuvant Abemaciclib (an CDK4/6 inhibitor). But this last treatment was not represented in our study since none of our patients had access to this medication.

Most papers in the literature focus on postmenopausal patients and more systemic complications with apparent less interest in genital and sexual aspects[23–26] which reflects in daily clinical practice. The Female Sexual Distress Scale- Revised (FSDS-R) is one of the assessments instruments created to assess the stress associated with female sexual dysfunction,[27] but there is no standard to these assessments and, not surprisingly, this may be due to the complexity regarding the study of sexual dysfunctions.[16,28] This makes medical practice and research on the subject quite challenging.

A study evaluated 83 patients 3 years after the diagnosis of breast cancer and concluded that 77% presented sexual dysfunction.[10] A longitudinal evaluation evaluating more than 760 patients with a medium interval of 6.3 years detected that while the physical and emotional functionalities progressively improved during HT, the complaints of reduced sexual activity, reduction of vaginal lubrication and urinary incontinence remained significant.[29] We have found other non-Brazilian studies that also reported similar results regarding general and sexual quality of life, also pointing that sexual quality of life remains as one of the most affected life domains among postmenopausal breast cancer patients undergoing HT.[30–34] An Iranian study also noted the unmet need for assessment of the impact on the quality of life in this group of women.[31] Three Brazilian literature reviews have also outlined these aspects, but mainly focusing on the general quality of life.[13–15] In our results, the observation of the number of women in the anastrozole group – and therefore mainly postmenopausal and more elderly women, who did not answer the question about orgasm (question M), may suggest that these menopausal women may feel embarrassed or uncomfortable about this issue in their sexual lives.

The ATAC study (anastrozole and tamoxifen alone or in cross-over, for adjuvant therapy)[35] evaluated, in two studies, quality of life (including FACT-B) and some sexual aspects.[36] No significant impacts on quality of life were observed, but the study did observe worsening vaginal dryness, dyspareunia and reduced libido in the groups with Anastrozole. This matches with our study observations.

Between 20 to 40% of patients on HT will present sexual complaints[28], and more specifically, 30% to 40% of patients under Tamoxifen[37] and more than 50% among those on aromatase inhibitors[29]. In the study conducted by Baumgart et al, women on Tamoxifen or Anastrozole were compared with women not on hormone therapy: 73.9% of patients on Anastrozole reported reduced vaginal lubrication, versus 40% of those on Tamoxifen; dyspareunia was reported in 56.5% of those in Anastrozole group versus 31.3% in the Tamoxifen group; 42.4% of patients reported dissatisfaction with their sex lives on Anastrozole versus 18% on Tamoxifen.[37] Our conclusions coincide with this and suggests Tamoxifen as a drug with less impact on these common sexual dysfunctions, providing a better quality of sexual life when compared to Anastrozole.

A Brazilian study assessed quality of life in 58 breast cancer women undergoing HT either on tamoxifen or anastrozole. Findings suggest quality of life was not different between these two groups, but interestingly, only 44% of the women were completely adherent to treatment in that study.[38]

Regarding adherence to hormone treatment, the CANTO cohort, published in 2018, studied self-reported adherence to Tamoxifen in women on adjuvant HT for breast cancer and prospectively assessed serum tamoxifen concentration. 87.7% of the patients reported maintaining Tamoxifen, and 12.3% admitted stopping treatment, discontinuing, or switching to an aromatase inhibitor.[39]

The fact that Tamoxifen was used in premenopausal women may account for the maintenance of orgasmic capacity, less dyspareunia, and the reported feeling of being sexually attractive seem in T group. On the other hand, in the A group, the side effects on sexual health were significant both in adjuvant and remissive modality. In spite of all this we could question: aren't we being condescending to such impactful adverse events when prescribing HT?[40]

The intimacy related to sexual health presents a challenge for these evaluations. A published thesis suggests a method to approach sexuality with patients undergoing HT, beginning with permission from the patient to start a discussion and gradually evolving until specific complaints and proper therapy.[41] Our observation, as mentioned early, found that a significant number of women in the postmenopausal group undergoing HT in the A group did not answer questions regarding orgasm (question M from FSDS-R). This points to the need for better methods for approaching sexual health-related discussions with HT patients, which should consider not only organic issues such as vaginal dryness but also psychic aspects such as depression, self-image, and counseling.[42–48]

Our study had limitations such as small number of patients (41 in total); bigger amostrage in Tamoxifen group (46,35%); the majority of patients were postmenopausal (68%) which could enhance the impact on sexual life as we have seen in some studies cited above; and almost 20% of patients were at a stage IV or recurrent disease, which could lead to a bigger impact not only in sexual quality but also in general quality of life, leading to misunderstanding results.

CONCLUSION

Hormonal treatment for breast cancer in women has an important impact on quality of life in general physical, social, family, and emotional well-being, leading to a reduced overall quality of life and sometimes to discontinuation of treatment (CANTO STUDY CITED ABOVE). But beyond those, there is also a significant impact is observed specifically on sexual health, which might be more present at younger patients and be different between the two class of drugs most widely used (SERMS vs. aromatase inhibitors).

Since these effects on sexual health does not seem life threatening or be more discrete than systemic or acute ones (such as thrombosis, osteoporosis etc) or even be more difficult to access with the patients in normal daily practice, maybe physicians are not paying the attention that it needs and sexual quality of life is being neglected. And even the patient might neglect it, maybe because of the stigma and fear of breast cancer and its possible recurrence, or even underestimating the impact these issues bring to daily life.

Our study suggested a major impact in general sexual well-being and orgasmic capacity in the A group; and although we had a 100% adherence rate, more than 20% of patients admitted that they would abandon treatment if they could. We had few patients who had a crossover, all of them from Tamoxifen to Anastrozole, the reasons were not documented, but maybe they have had undesirable side effects and tried another drug because of that.

Unfortunately, the number of Brazilian observations is scarce, and among those few, the majority relayed data from foreign populations. Hence, we believe our work can bring novel and reliable data to support clinical decisions during hormonal therapy for breast cancer patients in Brazil and abroad.

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AUTHORS' CONTRIBUTIONS

PPPSF: Collection and assembly of data, Conception and design, Data analysis and interpretation, Final approval of manuscript, Manuscript writing, Provision of study materials or patient.

ACSC: Collection and assembly of data, Data analysis and interpretation.

CFH: Collection and assembly of data, Data analysis and interpretation, Provision of study materials or patient.

LAS: Collection and assembly of data, Conception and design, Data analysis and interpretation, Provision of study materials or patient.

MVM: Manuscript writing.

NYH: Collection and assembly of data, Data analysis and interpretation.

LAP: Conception and design.

GLD: Conception and design.

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Appendix I. TCLE - free and informed consent form.

Title of Research: "Sexual aspects associated with women with breast cancer using hormone therapy".

Nature of the research: you are being invited to participate in this research, which aims to evaluate the main complaints related to quality of life, mainly involving sexuality alterations and genital atrophy, resulting from the use of Tamoxifen and Aromatase Inhibitor for the treatment of Breast Cancer. About the research and participants: The study will be conducted through the application of questionnaires attached to this term, which will address issues related to quality of life, sexuality and genital discomfort in patients who underwent treatment with Tamoxifen and Aromatase Inhibitor. This questionnaire will be given to the patients who use this therapy.

Involvement in the research: You are free to refuse to participate and to refuse to continue participating in any phase of the research, without any prejudice to you. Whenever you wish, you may request further information about the research by calling the person responsible for the project and, if necessary, by calling the Ethics in Research Committee of the School of Medical and Health Sciences of the PUC/SP, Rua Joubert Wey 290, Jardim Vergueiro, Sorocaba/SP, phone number (15)32129896.

Risks and discomfort: the participation in this research does not bring legal complications. The procedures adopted in this research obey the Ethics Criteria for Research with Human Beings, according to the Resolution no. 196/96 from the National Health Council. None of the procedures used offer risks to your dignity. Confidentiality: all the information collected in this study is strictly confidential, only the researchers and the counselors will have knowledge of the data. At the end of the study, the results of the completed questionnaires will be disclosed, safeguarding the confidentiality of the patients. Benefits: By participating in this research you will not have any direct benefit. However, we hope that this study will bring important information about the main complaints of patients taking Tamoxifen and Aromatase Inhibitor, so that the knowledge built from this research can help in the follow-up of patients, with more attention to the main symptoms and better management of them. Payment: you will have no expenses of any kind to participate in this research, as well as nothing will be paid for your participation.After these explanations, we request your free and informed consent to participate in this research. Therefore, please fill out the following items.

Obs: Do not sign this form if you still have doubts about it.

Free and Informed Consent:In view of the items presented above, I, freely and informedly, express my consent to participate in the research. I declare that I have received a copy of this consent form, and I authorize the research to be carried out and the disclosure of the data obtained in this study.

- Name of Research Participant and date.
- Signature of Research Participant.
- Researcher's Signature.
- Signature of Supervisor.

Patient Identification:

- Date: Medical record no:
- Age:
- Marital life status:
- No current or past partner;
- No current partner, but have had previous relationships;
- With current partner living with husbands;
- With current partner, but not living maritally.

*** Place for doctors! No need to answer the next questions.

- PS
- Early clinical stage:
- Current Status:
- Adjuvant Hormone Therapy.
- Remissive Hormone Therapy.
- Timing of hormone treatment for breast cancer:
- Hormonal and prior treatment (include time of each):
- Time of menopause:

Appendix II. Questionnaires.

FACT – B (Functional Assesment of Cancer Therapy – Breast).

FSDS- R (Female Sexual Distress Scale Revised).

Cost-effectiveness' aspects of treatment with hormone therapy:

1. Do you think your treatment is really important?

YES ( ) NO ( )

2. If you could suspend your treatment, would you suspend it?

YES ( ) NO ( )

If the answer is YES, please answer: For what reason would you suspend the treatment?

Because of the side effects it causes ( )

Because it is difficult to take the medication daily ( )

Because it disturbs your daily routine ( )

Another: _____

3. Are the effects evaluated in the questionnaire causing problems in your life?

YES ( ) NO ( )

If the answer is YES, please rate the severity:

Major ( )

Minor ( )

Not important ( )