REVIEW ARTICLE
https://doi.org/10.29289/2594539420220034

Hormone therapy in the treatment of breast cancer and main outcomes in sexuality

Eduarda Trevisan Cerigatto[1]*, Caroline Choptian Rodrigues Moreira[1], Diancarlos Pereira de Andrade[1], Priscila Nunes Silva Morosini[2], Alexandra Czepula[1]

ABSTRACT

Hormone-dependent breast cancer has growth factors that respond positively to the hormones estrogen and progesterone. Thus, adjuvant endocrine therapy causes decreased or undetectable serum levels of these hormones. However, this treatment can have side effects that compromise the sexual health of patients, such as dyspareunia, vaginal dryness and decreased libido. In this scenario, the objective of this work was to document the main outcomes in sexuality in women after treatment for hormone-positive breast cancer. Thus, this is an integrative literature review, in which the following databases were used: U.S. National Library of Medicine (PubMed), Virtual Health Library (BVS), SCOPUS and Scientific Electronic Library Online (SCIELO), using the descriptors: "sexuality", "antineoplastic agents, hormonal" and "breast neoplasms", joined by the Boolean operator "AND". Full articles published in the last 5 years (2017-2022) were included; written in Portuguese or English. Articles dealing with non-hormone-dependent or metastatic breast cancer, or with patients younger than 18 years, or articles that did not answer the research question were excluded. In total, 26 articles were identified, of which 7 comprised the final sample of this review. A total of 3,850 women participated in the included studies. The main sexual dysfunctions found were: dyspareunia, hot flashes, decreased libido, vaginal dryness, breast tenderness, self-image concerns and hair loss. The symptom vaginal dryness was the most prevalent, mentioned in 71.4% of the articles included. In view of the adverse effects listed in this review, there is a need to carry out more studies on this topic, since the diagnosis of this comorbidity brings clinical, psychological, emotional, sociocultural and economic outcomes for the patient. Thus, a multidisciplinary team must assertively address these complaints to improve the overall quality of life of these women.

KEYWORDS: sexuality; antineoplastic agents, hormonal; breast neoplasms.

INTRODUCTION

Breast cancer is the most prevalent cancer among women — with the exception of non-melanoma skin tumors[1]. Treatment may include surgery, radiotherapy, chemotherapy, immunotherapy and/or hormone therapy. The use of the latter as a treatment strategy is based on immunohistochemical findings of positivity for female hormone receptors[2].

In this context, pharmaceutical options for hormone therapy include selective estrogen receptor modulators (SERM) and aromatase inhibitors (AI). Tamoxifen, belonging to the SERM class, competitively inhibits estrogen binding to breast hormone receptors. On the other hand, AI decrease estradiol concentration by inhibiting aromatase, the enzyme that converts androstenedione into estrone in peripheral tissues[3].

Therefore, the result of these medications is a decrease in the action of estrogen in breast cancers that respond positively to this hormone. This fact can interfere with the homeostasis of sex hormones, causing sexual dysfunctions that simulate menopause, the most prevalent of which are: hot flashes, vaginal dryness and dyspareunia[4].

Thus, hot flashes appear as a sensation of intense heat, where approximately 83.3% of patients undergoing hormone therapy reported having this symptom, according to Daldoul et al.[5]. The presence of vaginal dryness, in turn, was present in up to 50% of the patients evaluated in the same article.

Bui et al. observed several symptoms in premenopausal women undergoing hormone-responsive breast cancer treatment, including: vaginal dryness, decreased sexual interest, and day and night

[1]Faculdades Pequeno Príncipe – Curitiba (PR), Brazil.
[2]Unidades de Alta Complexidade em Oncologia, Hospital São Vicente, Mastology – Curitiba (PR), Brazil.
***Corresponding author:** eduarda.t.10@hotmail.com
Conflict of interests: nothing to declare. **Funding:** none.
Received on: 11/01/2022. **Accepted on:** 02/23/2023

sweats, both for women with ovarian function suppression (OFS) and those on hormone therapy only. That is, the current literature shows that even in women only undergoing hormone therapy, there is already a considerable impact on their sexuality[6].

Symptoms of sexual dysfunction can occur with development of the cancer itself, but are more often associated with its treatment and follow-up. Thus, the study points out that sexual dysfunction is a common and a lasting complication for cancer survivors, affecting over 60% of women diagnosed with cancer[7].

Hormone therapy protocols recommend that patients receive 5 to 10 years of therapy. Thus, a significant number of patients discontinue treatment, which has a direct impact on mortality and relapses[8]. Therefore, sexual side effects can be significant in the quality of life and prognosis of these women[9].

OBJECTIVE

To review the current scientific literature to document key outcomes in sexuality in women undergoing treatment for hormone-positive breast cancer.

METHODS

This was an integrative literature review, allowing the critical evaluation of different methodological approaches, gathering and synthesizing knowledge, as well as drawing conclusions based on scientific evidence, applying its discoveries in clinical practice[10]. Inclusion criteria were: retrospective studies published up to 5 years ago, in Portuguese or English, with no location restriction, available online in full and with full or partial content approach.

Phase 1 began with the elaboration of the guiding question, formulated through the definition of the participants (women undergoing treatment for hormone-dependent breast cancer); interventions to be evaluated (use of hormone therapy) and results to be measured (impact on sexuality). Thus, the following question was formulated: "What does the current literature say about the main negative sexuality outcomes of hormone therapy in women with hormone-positive breast cancer?"

In turn, Phase 2 involved an extensive literature search, including searching through databases and manually searching the references of selected studies. The databases used were: U.S. National Library of Medicine (PubMed), Virtual Health Library, SCOPUS and Scientific Electronic Library Online (SCIELO). The keywords previously consulted in the medical subject headings (MeSH) were included, with the descriptors "Sexuality", "Antineoplastic Agents, Hormonal" and "Breast Neoplasms", joined by the Boolean operator "AND". Table 1, below, represents the complete description of the search keywords and filters used in the electronic databases.

Articles dealing with non-hormone-dependent breast cancer and with patients under 18 years of age were excluded, as well as news, editorials, comments and letters of introduction — where content is not based on the scientific method.

Table 1. Search key and filers by electronic database.

Database	Search key
SCOPUS	((("SEXUALITY") AND ("ANTINEOPLASTIC AGENTS, HORMONAL")) AND ("BREAST NEOPLASMS") (LIMIT-TO (PUBYEAR, 2022), (LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017)) AND (LIMIT-TO (LANGUAGE, "English"))
SCIELO	((("SEXUALIDADE") AND ("ANTINEOPLÁSICOS HORMONAIS")) AND (NEOPLASIAS DE MAMA") Filters: Full text, English, Portuguese, 5 year
PUBMED	((SEXUALITY) AND (ANTINEOPLASTIC AGENTS, HORMONAL)) AND (BREAST NEOPLASMS)
BVS	((SEXUALITY) AND (ANTINEOPLASTIC AGENTS, HORMONAL)) AND (BREAST NEOPLASMS) (year cluster: [2017 TO 2022])

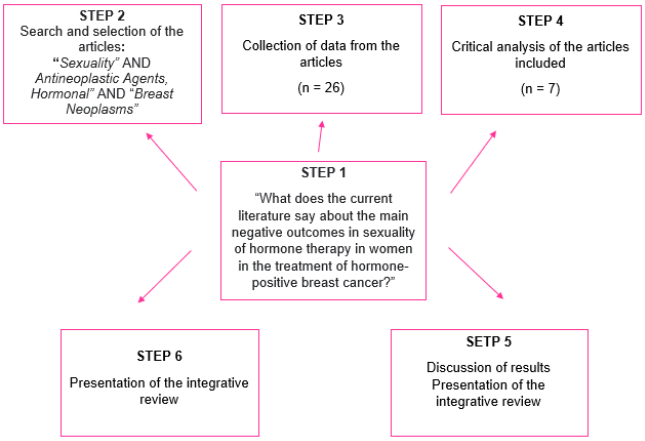
Therefore, the selection of articles was carried out in two stages: initially, with the reading of the titles, followed by the reading of the abstracts and, later, through the complete analysis of the studies. Screening was carried out independently by two researchers, inspired by predetermined criteria. A manual search was carried out in all references of the selected articles, having as eligibility criteria the articles most cited in the initial studies and that corroborate the primary objective of this work. Figure 1 shows the steps of the integrative review. In turn, Figure 2 illustrates the article selection flowchart.

In Phase 3, the following were removed from the articles: definition of subjects, methodology, sample size, measurement of variables, method of analysis and basic concepts employed. In step 4, a critical analysis of the included studies was therefore carried out, contemplating the information contained. Publication data were organized and synthesized to simplify the integration of findings, according to the following variables: database, title, journal, author, country/year and design/sample.

Finally, phases 5 and 6 were performed, corresponding to the discussion of results and presentation of the integrative review, respectively[11]. As for ethical aspects, all information extracted from the articles belongs to the public domain, and the ideas, concepts and definitions of the authors included in the review were respected.

RESULTS

In this study, 26 articles were identified. Of these, 1 article belongs to BVS, 20 to PUBMED and 5 to SCOPUS. Ten articles were excluded after reading the title. All articles selected by title were selected for reading in full, after reading the abstract. Of the 16 articles selected for reading in full, 4 were duplicates, resulting in 12 articles chosen for reading in full.



Source: Adapted from Mendes et al.[18]

Figure 1. Steps of the integrative review.

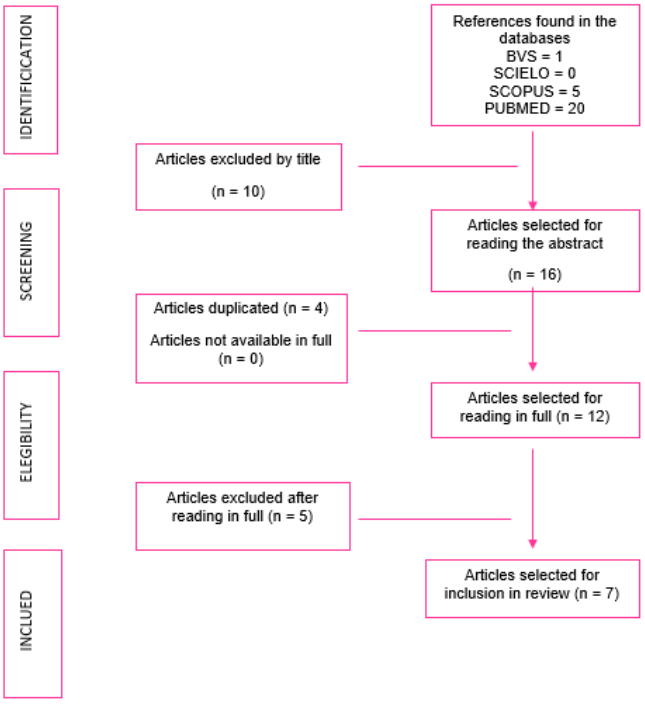


Figure 2. Flowchart of the selection process for articles included.

After the critical analysis of the pre-selected studies, 7 articles were listed as selected studies, since they presented aspects that answered the guiding question of this review. Regarding the year of publication of the articles included in this review, there were: 1 (14%) from 2017, 1 (14%) from 2018, 4 (57%) from 2019 and 1 (14%) from 2020.

Of the seven articles included, 2 (28%) were prospective studies, 1 (14%) randomized study, 1 (14%) a letter to the reader, 1 (14%) a cross-sectional observational study, 1 (14%) a case-control cohort study and 1 (14%) a multicenter prospective cohort study.

Still, regarding the countries of publication of the included articles: 1 (14%) was from the United Kingdom; 2 (28%) from England; 1 (14%) from Australia, 1 (14%) from New Zealand, 1 (14%) from the United States and 1 (14%) from Spain. Table 2 characterizes them using: number, title, total number of participants, main statistical results, main results and main limitations.

DISCUSSION

According to Table 2, a total of 3,850 women participated in the 7 studies included in this review. The main sexual dysfunctions found by these studies were: dyspareunia and hot flashes (discussed in 57% of the articles included); decreased libido (discussed in 28% of the articles included); vaginal dryness (discussed in 71% of the articles included); breast sensitivity (discussed in 28% of the articles included); concern with self-image (discussed in 42% of the articles included) and concern with hair loss (discussed in 14% of the articles included). Figure 3 shows in graphic form the main sexual dysfunctions found by the authors.

Dyspareunia

Dyspareunia is the term used to define pain during sexual intercourse whether due to lack of lubrication, vaginal irritation or vicinity diseases. Accordingly, Ribi et al.[12] evaluated the sexual dysfunctions and overall quality of life of 2287 women, divided into two distinct groups: 1260 in the SOFT trial and 1027 in the TEXT trial, over 6, 12 and 24 months. In SOFT (Suppression of Ovarian Function Trial), premenopausal women were randomly assigned to receive 5 years of tamoxifen; tamoxifen plus ovarian suppression or exemestane plus ovarian suppression. In turn, in the TEXT study (Tamoxifen and Exemestane Trial), women were also randomized to receive tamoxifen and exemestane, associated with ovarian suppression.

In that same study, participants were divided into five cohorts — cohort 1: tamoxifen alone; cohort 2: cytotoxic chemotherapy followed by tamoxifen alone; cohort 3: cytotoxic chemotherapy, followed by exemestane or tamoxifen combined with OFS; cohort 4: endocrine therapy alone, with exemestane or tamoxifen combined with OFS; and cohort 5: cytotoxic chemotherapy and OFS before the use of endocrine therapy. Thus, it was observed that the item "pain" or "discomfort during sexual intercourse" worsened over the first 6 months and remained constant until 24 months[12].

A cohort study published by Li et al.[13] revealed that adjuvant chemotherapy did not influence the severity of vasomotor and sexual symptoms in women with cancer, except for the symptom of pain with sexual intercourse. The authors reported that one of the reasons why some studies identify high rates of dyspareunia in patients undergoing chemotherapy is due to differences in samples in terms of menopausal status and therapies used.

Daldoul et al.[14], gathered results of dyspareunia in about 60% of patients on hormone therapy who were evaluated. Thus, according to the sample size of 30 women, 12 had dyspareunia with sexual dysfunction, versus 6 women who also had dyspareunia but without sexual dysfunction. The study also demonstrated that this symptom has already been reported in patients because of fear of infertility and loss of sexual perception.

Table 2. Main sexual dysfunctions encountered.

Nº	Title	n total	Sexual dysfunctions	Statistical results	Main results	Main limitations
1	*Female Sexuality in Premenopausal Patients with Breast Cancer on Endocrine Therapy*	30	Dyspareunia	n=12	Sexual dysfunction was present in over 63.3% of patients. Endocrine therapy and most of its side effects were not associated with sexual dysfunction.	Sexual function was not assessed before endocrine therapy was started (the observed dysfunction may have been caused by the breast cancer itself or even preceded the disease).
			Hot flashes	n=18		
			Vaginal dryness	n=14		
			FSFI	63.3% of participants with score of sexual dysfunction		
2	*Treatment-induced symptoms, depression and age as predictors of sexual problems in premenopausal women with early breast cancer receiving adjuvant endocrine therapy*	2287 (1260 SOFT, 1027 TEXT)	Dyspareunia	6 months: n=409 12 months: n=416 24 months: n=402	Sexual problems increased at six months and persisted at that level. In general. Patients with the most severe worsening of vaginal dryness, sleep disturbances and bone or joint pain at 6 months reported a greater increase in sexual problems at all checkpoints.	The study did not discriminate between the sexual side effects of tamoxifen and exemestane. Some of the patients may not have continued with the long-term treatment, and this influences the results.
			Hot flashes	6 months: n=6 12 months: n=3 24 months: n=2		
			Vaginal dryness	6 months: n=13 12 months: n=12 24 months: n=9		
			Decreased libido	6 months: n=647 12 months: n=737 24 months: n=700		
3	*Identifying distinct trajectories of change in young breast cancer survivors' sexual functioning*	896	Concern with body image	RRR=2.52 SD=0.53	Five distinct trajectories of sexual function were identified: one asymptomatic, one minimally symptomatic, two moderately symptomatic and one severely symptomatic. 12% of women were asymptomatic during the entire follow-up. Most patients had stable mild symptoms (42%). 11% had stable severe symptoms that did not improve over time.	Possible pre-diagnosis sexual dysfunctions were not determined. The severely symptomatic line suggests that symptoms were prior to diagnosis. One of the questionnaires (CARES SCALE) did not have the "sexual desire" item, in addition to not obtaining information about recently sexually inactive women.
4	*Partner status moderates the relationships between sexual problems and selfefficacy for managing sexual problems and psychosocial quality-of-life for postmenopausal breast cancer survivors taking adjuvant endocrine therapy*	125	Decreased libido	n=64	Women who reported greater sexual problems and lower sexual self-efficacy had worse quality of life and lower sexual satisfaction. Women without partners had worse psychosocial quality of life when compared to women with steady partners.	The sample was mostly Caucasian, with advanced education and with older women, limiting the generalizability of these data. Patients' sexual partners were not accessed during the studies.
			Vaginal dryness	n=63		

Continue...

Table 2. Continuation.

Nº	Title	n total	Sexual dysfunctions	Statistical results	Main results	Main limitations
5	*Quality of life in elderly breast cancer patients with localized disease receiving endocrine treatment: a prospective study*	148	Sexual function	Tamoxifen: Mean: 6.1 SD: 13.5 Anastrozole: Mean: 10.1 SD: 16.4 EORTC QLQ-BR-23 SCORE: First visit: 5.4 Second visit: 5.2 Third visit: 9.3	Better quality of life scores were found in women after using endocrine therapy for three years, which shows good adaptation of patients to the treatment. Differences in quality of life impact between aromatase inhibitors and tamoxifen were irrelevant.	More comprehensive results were found regarding aromatase inhibitors, since more patients used aromatase inhibitors when compared to tamoxifen. There may have been a follow-up bias, as only 79% of participants answered the questionnaire on the second visit, which could have led to erroneously optimistic results.
			Sexual pleasure	Tamoxifen: Mean: 33.3 SD: 38.4 Anastrozole: Mean: 30.8 SD: 29.1 EORTC QLQ-BR-23 SCORE: First visit: 29.6; Second visit: 21.5; Third visit: 31.1		
			Active sexual life	Tamoxifen: Mean: 6.1 SD: 13.2 Anastrozole: Mean: 11.6 SD: 19.7 EORTC QLQ-BR-23 SCORE: First visit: 5.3 Second visit: 4.8 Third visit: 10.6		
			Hot flashes	Tamoxifen: Mean: 5.9 SD: 13.1 Anastrozole: Mean: 17.5 SD: 24.1 EORTC QLQ-BR-23 SCORE: First visit: 13.9 Second visit: 21.2 Third visit: 16.4		
			Sexual interest	Tamoxifen: Mean: 6.1 SD: 13.5 Anastrozole: Mean: 8.5 SD: 15.7 EORTC QLQ-BR-23 SCORE: First visit: 5.5 Second visit: 5.6 Third visit: 8		

Continue...

Table 2. Continuation.

Nº	Title	n total	Sexual dysfunctions	Statistical results	Main results	Main limitations
5	*Quality of life in elderly breast cancer patients with localized disease receiving endocrine treatment: a prospective study*	148	Breast sensitivity	Tamoxifen: Mean: 11.7 SD: 9.3 Anastrozole: Mean: 9.3 SD: 12.2 EORTC QLQ-BR-23 SCORE: First visit: 13.6 Second visit: 12.5 Third visit: 9.6	Better quality of life scores were found in women after using endocrine therapy for three years, which shows good adaptation of patients to the treatment. Differences in quality of life impact between aromatase inhibitors and tamoxifen were irrelevant.	More comprehensive results were found regarding aromatase inhibitors, since more patients used aromatase inhibitors when compared to tamoxifen. There may have been a follow-up bias, as only 79% of participants answered the questionnaire on the second visit, which could have led to erroneously optimistic results.
			Concern with body image	Tamoxifen: Mean: 97.1 SD: 5.1 Anastrozole: Mean: 95.1 SD: 13.7 EORTC QLQ-BR-23 SCORE: First visit: 13.6 Second visit: 12.5 Third visit: 9.6		
			Concern about hair loss	EORTC QLQ-BR-23 SCORE: First visit: 24.2 Second visit: 20.2 Third visit: 18.7		
6	*Impact of chemotherapy on symptoms and symptom clusters in postmenopausal women with breast cancer prior to aromatase inhibitor therapy*	339	Dyspareunia	Mean: 0.731 - 11.1 (anastOnly - 228 women) 0.859 - 10.4 (***chemoanast*** - 111 women) TOTAL: 10.8 DP: 23.4 (anastOnly); 21.4 (***chemoanast***) TOTAL: 22.7	The most severe symptoms occurred in women on aromatase inhibitors. There were no differences in symptom severity between the two groups.	Other factors that may influence the symptomatology process of women undergoing treatment were not accounted for, such as broader demographic characteristics, personality, general health status, comorbidities, menopausal status and genetic differences, among others.
			Hot flashes	Anastrozole mean 20.9 (anastOnly) 23.2 (***chemoanast***) TOTAL: 21.7 General mean: 0.851 (anastOnly - 228 women) 0.833 (***chemoanast*** - 111 women) Anastrozole SD: 27.0 (anastOnly) 27.3 (***chemoanast***) TOTAL: 27.1		
			Vaginal dryness	Mean: 0.583 – 16.9 (anastOnly); 0.769 - 20.9 (***chemoanast***) TOTAL 18.2 SD: 23.5 (anastOnly); 28.5 (***chemoanast***) TOTAL 25.3		

Continue...

Table 2. Continuation.

Nº	Title	n total	Sexual dysfunctions	Statistical results	Main results	Main limitations
6	*Impact of chemotherapy on symptoms and symptom clusters in postmenopausal women with breast cancer prior to aromatase inhibitor therapy*	339	Breast sensitivity	Anastrozole mean: 37.1 (anastOnly); 23 (***chemoanast***) TOTAL: 32.5 Anastrozole SD: 30.2 (anastOnly) 27.6 (***chemoanast***) TOTAL: 30.1	The most severe symptoms occurred in women on aromatase inhibitors. There were no differences in symptom severity between the two groups.	Other factors that may influence the symptomatology process of women undergoing treatment were not accounted for, such as broader demographic characteristics, personality, general health status, comorbidities, menopausal status and genetic differences, among others.
			Concern with body image	Anastrozole mean 29.7 (anastOnly) 33.3 (***chemoanast***) TOTAL: 30.9 Anastrozole SD 28.7 (anastOnly) 31.1 (***chemoanast***) TOTAL: 29.5		
7	*The effects of fractional microablative CO 2 laser therapy on sexual function in postmenopausal women and women with a history of breast cancer treated with endocrine therapy* *FSFI SCORE improvement data	25	FSFI – Excitation IMPROVEMENT	0.52	There was a statistically significant improvement in all domains of FSFI, WBFS and FSDS-R when comparing baseline scores with the three post-treatment symptom scores for all patients.	Small sample size. Absence of control group. Because of the size of the groups, it was not possible to directly compare postmenopausal women with women treated with hormone therapy.
			FSFI – Sexual desire IMPROVEMENT	0.37		
			FSFI - Lubrification IMPROVEMENT	0.33		
			FSFI - Orgasms IMPROVEMENT	0.66		
			FSFI – Dyspareunia IMPROVEMENT	0.91		
		3850				

TEXT: Tamoxifen and Exemestane Trial; n: sample number; RRR: relative risk; SD: standard deviation; M: mean; FSFI SCORE: score for questionnaire female sexual function index; EORTC QLQ-BR-23 SCORE: score for quality of life specific for breast cancer; chemoanast: women previously treated with chemotherapy in addition to anastrozole; anastOnly: women treated only with anastrozole.

Dyspareunia: pain and/or discomfort during penetrative sexual intercourse; hot flashes: feeling of intense warmth over the chest, neck and face, which can be accompanied by chills; SOFT: Suppression of Ovarian Function Trial,

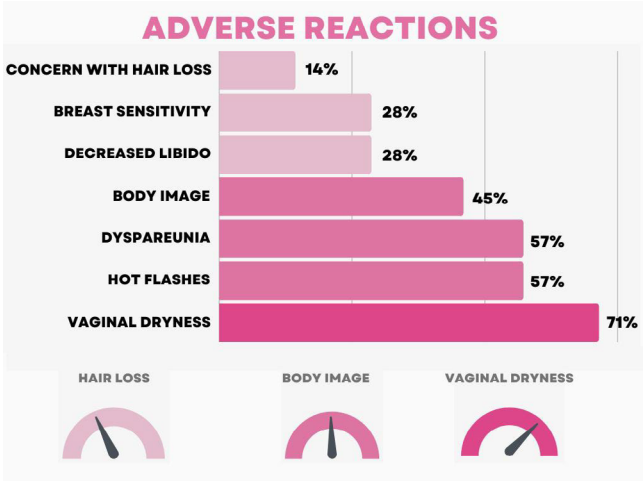


Figure 3. Main adverse effects found on sexuality.

Hot flashes

Hot flashes are defined as a feeling of intense heat in the chest, neck and face, and may be accompanied by chills, palpitations and anxiety attacks. Thus, women undergoing treatments that cause early menopause, such as endocrine therapy, may experience more severe and even longer hot flashes[15].

Among the articles read in full, Franzoi et al.[16] and Dos Santos et al.[17], 2021 are integrative reviews that discuss pharmacological and non-pharmacological interventions currently available to mitigate the negative side effects of adjuvant endocrine therapy.

Thus, they were not selected to be included in this review, as they did not directly answer the research question. Despite this, these studies are addressed in the present discussion to summarize these management options, since the authors consider

it essential to improve the sexual function of cancer patients to increase the quality of life of these women[16,17].

In the context of pharmacological interventions for this symptom, antidepressants such as SSRIs (selective serotonin reuptake inhibitors) and SNRIs (serotonin-noradrenaline reuptake inhibitors) can be used, especially venlafaxine combined with tamoxifen[14,15].

Randomized clinical trials have shown the effectiveness of the anticonvulsants gabapentin and pregabalin in controlling hot flashes[13]. The alpha-adrenergic antihypertensive drug clonidine has also been shown to be effective, but it is rarely prescribed because of its side effects, which include dry mouth, constipation and drowsiness[14,15].

Vaginal dryness

Dorfman et al.[9], in their cross-sectional study, state that up to 93% of breast cancer patients using hormone therapy experience sexual side effects, including vaginal dryness. According to the study, particularly among postmenopausal women, endocrine therapy can exacerbate menopausal symptoms, and vaginal dryness is highlighted as one of the main symptoms.

Daldoul et al.[14]. conducted a cross-sectional observational study that gathered a sample of 30 patients on hormone therapy. With this, the fear of these patients in relation to vaginal dryness was observed. In this scenario, the authors indicated that, among this same sample, 14 women reported vaginal dryness with sexual dysfunction, versus 5 without dysfunction.

Thus, in the context of lack of vaginal lubrication, some measures can be taken to improve this side effect. Cancer patients can receive local estrogen hormone therapies, such as intravaginal pills, rings, inserts and creams[17].

As non-hormonal options, there are aqueous compresses of 4% lidocaine in the vulvar vestibule (between the glans of the clitoris and the beginning of the perineum). Vaginal CO_2 or erbium laser therapy has been shown to be effective in improving the symptoms of vaginal dryness, dyspareunia and itching and/or vaginal redness in these patients[11]. However, as it is a recent therapy on the market, the lack of well-designed safety studies, in addition to its high cost, limits its recommendation[16].

Decreased libido

In the study by Dorfman et al.[9], almost 70% of postmenopausal patients diagnosed with hormone-positive breast cancer who received endocrine therapy reported at least one sexual problem. Of these, more than half declared a decreased libido and/or vaginal dryness, and 40.2% of women said they avoided intimacy with their partners.

Ribi et al.[12] comment in their discussion that many studies have reported an association between depressive symptoms and sexual problems related to sexual inactivity or hypoactive sexual desire disorder in breast cancer survivors. However, in contrast to the hypothesis of this study, depression was associated with sexual problems in the first six months, but no longer influenced sexual dysfunction in the following two years, indicating that the analyzed decreased libido may be involved in factors that are no longer psychological, but to physical factors such as fatigue, joint and musculoskeletal pain and genitourinary symptoms.

When comparing the two main drugs of endocrine therapy, Arraras et al.[15] commented that patients using AI had a greater reduction in libido compared to patients on tamoxifen, during 3 years of treatment. Accordingly, it is stated that the discontinuation of endocrine therapy is associated with a worse doctor-patient relationship, in addition to the side effects of the treatment.

Breast sensitivity

With regard to breast sensitivity, von Hippel et al.[18], studied the trajectory of groups undergoing therapy with aromatase inhibitors alone and in combination with chemotherapy. In this sense, the authors state that the impact of breast pain was greater in younger women and in the group with endocrine therapy alone. In addition, this study affirmed the controversy in the current literature about the influence of chemotherapy on sexual symptoms, as well as the difficulty in differentiating the symptoms of physiological menopause from those caused by hormone therapy.

Also, Li et al.[13], when comparing a group of women using only anastrozole and a group that received chemotherapy combined with an AI, greater breast sensitivity was observed in the group being treated only with AI. The authors provide in their discussion a meta-analysis in which breast pain is related to younger women, in agreement with Li and collaborators, in which women using only anastrozole were younger than women undergoing chemotherapy combined with AI.

When analyzing patients using quality of life questionnaires, Arraras et al.[15], comment in their results that symptoms of breast sensitivity and having an active sex life improved on the third visit, 3 years after starting treatment, compared to the first two visits. Depending on the study, the authors reported that other studies, involving radiotherapy, show improvement in breast tenderness after 2 years of treatment.

Limitations

In addition to the limitations already mentioned in Table 2, the importance of continued research in this area of oncology is highlighted, especially in underdeveloped and developing countries. In addition, it is difficult to detail the impact of hormone therapy on sexuality alone, since most of the analyzed studies have a set of oncological therapies involving cancer surgery and/or cytotoxic therapy, in addition to the psychological and emotional impact of cancer diagnosis and treatment. The clinical relevance of a varied population sample is also highlighted, for a better generalization of the adverse reactions found.

CONCLUSIONS

Vaginal dryness was found to be the most prevalent symptom, and other symptoms were also found, such as dyspareunia,

decreased libido, hot flashes, concern with body image, breast pain or tenderness and concern with hair loss.

There is a need to carry out more studies on this topic, since the diagnosis of this comorbidity affects clinical, psychological, emotional, sociocultural and economic outcomes for the patient. Thus, a multidisciplinary team must assertively address these complaints to improve the overall quality of life of these women.

AUTHORS' CONTRIBUTION

ETC: Conceptualization, Investigation, Methodology, Project Administration, Visualization, Writing – review & editing. CCRM: Conceptualization, Investigation, Methodology, Visualization, Writing – review & editing. DPA: Data curation, Formal Analysis. PNSM: Visualization, Review. ASIC: Investigation, Data curation, Methodology, Visualization, Supervision, Writing –original draft.

REFERENCES

1. Instituto Nacional do Câncer. Tipos de câncer/câncer de mama. 2022 [cited on Feb 10, 2020]. Available from: https://www.inca.gov.br/tipos-de-cancer/cancer-de-mama.
2. World Health Organization. Breast tumours, WHO classification of tumours. 5th ed. Lyon: WHO Classification Editorial Board; 2019. [cited on Feb 12, 2020]. Available from: https://www.iarc.who.int/news-events/who-classification-of-tumours-5thedition-volume-2-breast-tumours/
3. Brunton LL, Hilal-Dandan R, Björn C, Knollmann BC. As bases farmacológicas da terapêutica de Goodman e Gilman. 12th ed. Rio de Janeiro: McGraw-Hill, 2012.
4. Gandhi C, Butler E, Pesek S, Kwait R, Edmonson D, Raker C, et al. Sexual Dysfunction in Breast Cancer Survivors: Is it Surgical Modality or Adjuvant Therapy? Am J Clin Oncol. 2019;42(6):500-6. https://doi.org/10.1097/COC.0000000000000552
5. Daldoul A, Ben Ahmed K, Tlili G, Krir MW, Gharbi O, Ben Ahmed S. Female sexuality in premenopausal patients with breast cancer on endocrine therapy. Breast J. 2017;23(4):489-91. https://doi.org/10.1111/tbj.12778
6. Bui KT, Willson ML, Goel S, Beith J, Goodwin A. Ovarian suppression for adjuvant treatment of hormone receptor-positive early breast cancer. Cochrane Database Syst Rev. 2020;3(3):CD013538. https://doi.org/10.1002/14651858
7. Valpey R, Kucherer S, Nguyen J. Sexual dysfunction in female cancer survivors: A narrative review. Gen Hosp Psychiatry. 2019;60:141-7. https://doi.org/10.1016/j.genhosppsych.2019.04.003
8. Peddie N, Agnew S, Crawford M, Dixon D, MacPherson I, Fleming L. The impact of medication side effects on adherence and persistence to hormone therapy in breast cancer survivors: a qualitative systematic review and thematic synthesis. Breast. 2021;58:147-59. https://doi.org/10.1016/j.breast.2021.05.005
9. Dorfman CS, Arthur SS, Kimmick GG, Westbrook KW, Marcom PK, Corbett C, et al. Partner status moderates the relationships between sexual problems and self-efficacy for managing sexual problems and psychosocial quality-of-life for postmenopausal breast cancer survivors taking adjuvant endocrine therapy. Menopause. 2019;26(8):823-32. https://doi.org/10.1097/gme.0000000000001337
10. Souza MT, Silva MD, Carvalho R. Revisão integrativa: o que é e como fazer. einstein (São Paulo). 2010;8(1):102-6. https://doi.org/10.1590/s1679-45082010rw1134
11. Mendes KDS, Pereira Silveira RCC, Galvão CM. Use of the bibliographic reference manager in the selection of primary studies in integrative reviews. Texto Contexto - Enferm. 2019;28:1-13. https://doi. org/10.1590/1980-265X-TCE-2017-0204
12. Ribi K, Luo W, Walley BA, Burstein HJ, Chirgwin J, Ansari RH, et al. Treatment-induced symptoms, depression and age as predictors of sexual problems in premenopausal women with early breast cancer receiving adjuvant endocrine therapy. Breast Cancer Res Treat. 2020;181(2):347-59. https://doi.org/10.1007/s10549-020-05622-5
13. Li H, Sereika SM, Marsland AL, Conley YP, Bender CM. Impact of chemotherapy on symptoms and symptom clusters in postmenopausal women with breast cancer prior to aromatase inhibitor therapy. J Clin Nurs. 2019;28(23–24):4560-71. https://doi.org/10.1111/jocn.15047
14. Daldoul A, Ben Ahmed K, Tlili G, Krir MW, Gharbi O, Ben Ahmed S. Female sexuality in premenopausal patients with breast cancer on endocrine therapy. Breast J. 2017;23(4):489-91. https://doi.org/10.1111/tbj.12778
15. Arraras JI, Illarramendi JJ, Manterola A, Asin G, Salgado E, Arrondo P, et al. Quality of life in elderly breast cancer patients with localized disease receiving endocrine treatment: a prospective study. Clin Transl Oncol. 2019;21(9):1231-9. https://doi.org/10.1007/s12094-019-02048-4
16. Franzoi MA, Agostinetto E, Perachino M, Del Mastro L, Azambuja E, Vaz-Luis I, et al. Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. Lancet Oncol. 2021;22(7):e303-13. https://doi.org/10.1016/s1470-2045(20)30666-5
17. Dos Santos BS, Bordignon C, Rosa DD. Managing common estrogen deprivation side effects in HR+ breast cancer: an evidence-based review. Curr Oncol Rep. 2021;23(6):63. https://doi.org/10.1007/s11912-021-01055-5
18. von Hippel C, Rosenberg SM, Austin SB, Sprunck-Harrild K, Ruddy KJ, Schapira L, et al. Identifying distinct trajectories of change in young breast cancer survivors' sexual functioning. Psychooncology. 2019;28(5):1033-40. https://doi.org/10.1002/pon.5047