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Original

Prevalence of Paresthesia, Fatigue, Edema and Pain After Treatment for Breast Cancer

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Abstract

Objective: To investigate the prevalence of chronic symptoms among patients who underwent breast cancer treatment, and to determine the factors that might be related to these symptoms. **Material and Methods:** A questionnaire was applied to 87 patients undergoing breast cancer follow-up. It evaluated the length of time since treatment, therapeutic procedure (type of surgery, chemotherapy, radiotherapy and/or endocrine therapy), use of analgesic medication, location and intensity of pain and presence of paresthesia, fatigue and upper-limb edema. **Results:** The patients' mean age was 54.46 years; the mean interval between locoregional treatment and the interview was 52.95 months. The prevalence of paresthesia symptoms was 65.5%; fatigue, 49.4%; edema, 31%; and pain, 31%. From multivariate analysis, we observed that fatigue was influenced by mastectomy (OR = 2.680; 95% CI = 1.127 - 6.373), radiotherapy (OR = 3.028; 95% CI = 1.142 - 8.030) and chemotherapy (OR = 5.271; 95% CI = 1.067 - 26.034), and was lower among patients who underwent endocrine therapy (OR = 0.407; 95% CI = 0.171 - 0.967). Paresthesia, edema and pain were not influenced by any of the therapeutic types. **Conclusions:** There was high prevalence of complaints among the patients who had undergone breast cancer treatment. Fatigue was the only symptom influenced by the different treatments.

Keywords: Breast Neoplasms,Fatigue,Pain Edema,Treatment outcome

Introduction

The prevalence of chronic complaints such as pain, fatigue, paresthesia and edema in the ipsilateral upper limb among patients who have undergone treatments for breast cancer may be high, ranging from 5 to 74%.[1-7] In many cases, such symptoms stop these women from returning to their previous daily routines, thereby causing a worsening of their quality of life.[8] It was expected that, in the year 2000 in Japan alone, around 42,016 patients who underwent breast cancer treatment would present some symptom.This number is expected to go up to 72,514 by the year 2020.[9]

These symptoms may interfere significantly in the patients' daily work and domestic activities, as well as affecting their exercise and recreation.[4] Nonetheless, within our setting, few studies have been conducted with the aim of investigating the frequency and importance of symptoms manifested following breast cancer treatment.[10] The data that are available show that many of these symptoms may be underestimated by doctors or by

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their patients, who try to accept them as normal or as irremediable consequences of the treatment.

Because of these uncertainties, we proposed to investigate the prevalence of pain and other symptoms (paresthesia, fatigue in the ipsilateral upper limb to disease and/or edema in the same limb) among patients who previously underwent treatments for breast cancer, and to determine the relationship between these symptoms and the therapy that was instituted.

Patients and Methods

This work has been approved by the research ethical committee of the Araújo Jorge Hospital of Goiás Anticancer Association. A questionnaire was applied to 87 patients undergoing breast cancer follow-up who consulted our Gynecology and Breast Service. The criteria for inclusion in the study were that the patients needed to present a diagnosis of breast cancer that had been made more than six months earlier, needed to be free from active disease and needed to be undergoing follow-up monitoring for possible recurrences and/or metastases. All patients gave informed consent to the study.

The questionnaire sought data on the following: age, length of time since the treatment (in months), type of surgery (mastectomy or quadrantectomy, both with full axillary clearance), whether radiotherapy was performed (only on the plastron, or whether it was also performed on the lymphatic drainage), whether chemotherapy was administered, whether endocrine therapy was performed, whether the patient used analgesic medication, the period of time (in months) for which it was used, the location of the pain and whether there was any paresthesia, fatigue and/or edema in an upper limb. The visual numerical pain scale (VNPS) was applied to verify the pain level: on this, zero signified absence of pain and ten, very intense pain.[11] Lastly, the patients were asked how much the symptoms were disturbing their lives, over a range from not at all to excessively (not at all, slightly, moderately, considerably and excessively).

We focused on the patients who complained of chronic pain (that had persisted for more than six months)[3] relating to the breast cancer treatment, without specifying the origin and type of pain. Therefore, chronic pain in the phantom breast was not distinguished from other types of pain.

Statistical Analysis

After checking the data, the prevalence of each of the symptoms was determined, calculated as the frequency of the symptoms divided by the total number of cases, multiplied by 100. For univariate analysis, Student's t test for measurable variables was used, while for nominal variables the X^2 test was used. To evaluate interrelations between factors that could contribute towards each symptom, logistic regression was used. Values were taken to be significant when $p < 0.05$.

Results

The patients' mean age was 54.46 years, with a standard deviation of ± 11.73 (ranging from 31 to 81 years). The mean length of time since the surgical treatment was 52.95 months, with a standard deviation of ± 46.90 (ranging from 6 to 240 months). The mean length of time for which analgesics had been used was 3.88 months (ranging from 0 to 90 months). The mean pain level on the VNPS was 1.15, ranging from 0 to 10.

Modified radical mastectomy was performed on 43 patients and quadrantectomy with axillary clearance associated with radiotherapy (breast conserving treatment) on 44 patients.

Radiotherapy was performed on 61 patients (70.1%), chemotherapy on 76 (87.4%) and endocrine therapy with tamoxifen on 40 patients (46%). Among the 61 patients who underwent radiotherapy, 52 were irradiated only on the plastron and the other nine on both plastron and the lymphatic drainage.

Sixty-seven patients (88.5%) complained of at least one of the symptoms under analysis (pain, paresthesia, fatigue and edema). The most common complaint among the patients was paresthesia, mentioned by 57 patients (65.5%). Fatigue in the ipsilateral upper limb was the second most common complaint, among 43 patients (49.4%). Pain and edema were the least frequent complaints, mentioned by 27 patients (31%). Among the 27 patients who complained of pain, for 22 of them this symptom was in the breast that underwent surgery and for the other 5, it was in the ipsilateral upper limb.

Pain of mild intensity predominated, according to the VNPS (Table 1). When asked whether they had been using analgesics, 19 patients (21.8%) said that they had used this medication. This use was predominantly chronic (10 patients), as shown in Table 2.

It was observed that not all of the patients with

Table 1. Pain level according to the visual numerical pain scale applied to the patients.

Pain level*	Number of patients	Percentage (%)
0	60	68.9
1-2	11	12.6
3-4	8	9.2
5-6	5	5.7
7-8	1	1.1
9-10	2	2.3

* Among the 27 patients who reported pain, 19 of them classified the symptom as one of mild intensity (ranging from 1 to 4 on the visual numerical pain scale).

Table 2 - Length of time for which analgesics were used (in months).

Length of time for which analgesics were used months	Number of patients	Percentage (%)
Up to 1	7	8.0
1-6	2	2.3
6-12 *	5	5.7
12-24 *	1	1.1
More than 24 *	4	4.6

* Chronic use of analgesics

absence of pain (67.8%) responded "not at all" in relation to how much the symptoms were disturbing their lives (51.7%). This shows that, in 16.1% of the cases, the other chronic symptoms were the only ones that affected the patients in question (Table 3).

Table 4 shows the univariate analysis on each type of therapy and the symptoms that the patients

Table 3- Degree to which the symptoms disturbed the patient's daily routines, as reported by the patients themselves.

Degree to which the symptoms disturbed daily routines	Total	%
Not at all	45	51.7
Slightly	24	27.6
Moderately	10	11.5
Considerably	3	3.5
Excessively	5	5.7

complained about. Table 5 shows, by means of multivariate analysis, that there was significantly less fatigue among the patients who were using endocrine therapy. It was also observed that mastectomy, in comparison with quadrantectomy, not only involved the use of chemotherapy and radiotherapy but also was associated with a greater chance that the patient would present fatigue. The other variables, including paresthesia, edema and pain, were not influenced by any of the therapies studied.

Discussion

The stimulus for the present study came from the observation that patients were very frequently reporting symptoms that, until then, we had considered normal or expected and which we had not been valuing in our clinical practice.

Even though a long period had elapsed between the treatment and the interview, we observed that a large proportion of the patients presented symptoms, of which the most common were paresthesia and fatigue. On the other hand, pain and edema were less frequent. The prevalence of at least one of these chronic symptoms among the patients was surprisingly high (88.5%).

In our study, we observed that the patients who had undergone modified radical mastectomy presented a risk of presenting fatigue that was 2.6 times greater than the risk presented by the patients who underwent treatment with breast conservation. In contrast to our findings, Tasmuth et al.[5] observed in a similar study that the patients who underwent treatment with breast conservation presented more chronic symptoms than did the patients who underwent mastectomy. They showed that there was greater prevalence of pain and fatigue following conservative surgery. However, they found greater occurrence of edema among the patients who underwent mastectomy. The same research group subsequently observed greater prevalence of pain among the patients who underwent radiotherapy and chemotherapy. On applying the McGill questionnaire, 50% of the 569 patients said they had slight pain, which would interfere with their daily lives, while 25% presented moderate or severe pain.

Paresthesia and fatigue seem to be related to neuronal lesions resulting from the surgery. In particular, paresthesia seems to be a consequence from injury to the intercostobrachial nerve, thus causing changes to skin sensitivity in the proximal and posterointernal half of the arm.[12]

Among patients with malignant neoplasm, their pain may in 78% of the cases be caused by the cancer

Table 4. Analysis on each type of therapy and the symptoms that the patients complained about.

Variable	With paresthesia			With fatigue			With edema			With pain		
	N	(%)	p	N	(%)	p	N	(%)	p	N	(%)	p
Type of suger												
Mastectomy	29	(67.4)		16	(37.2)		12	(27.9)		11	(25.6)	
quadrantectomy	28	(63.6)	0.709	27	(61.4)	0.024	15	(34.1)	0.533	17	(38.6)	0.193
Radiheap												
No	19	(73.1)		8	(30.8)		7	(26.9)		6	(23.1)	
Yes	38	(62.3)	0.333	35	(57.4)	0.023	20	(32.8)	0.588	22	(36.1)	0.235
Chemotherapy												
No	8	(72.7)		2	(18.2)		2	(18.2)		2	(18.2)	
Yes	49	(64.5)	0.59	41	(53.9)	0.027	25	(32.9)	0.324	26	(34.2)	0.288
Hormone												
therapy	32	(68.1)		28	(59.6)		19	(40.4)		19	(40.4)	
No												
Yes	25	(62.5)	0.585	15	(37.5)	0.04	8	(20.0)	0.04	9	(22.5)	0.074

Table 5. Multivariate analysis on the relationship between each type of therapy and the symptoms that the patients complained about.

	Paresthesia		Fatigue		Pain		Edema	
	OR (CI)	P	OR (CI)	P	OR (CI)	p	OR (CI)	p
Type of surgery*	0.845 (0.349-2.048)	0.709	2.680 (1.127-6.373)	0.026	1.832 (0.734-4.574)	0.195	1.336 (0.536-3.328)	0.495
RT	0.609 (0.222-1.671)	0.335	3.028 (1.142-8.030)	0.026	1.880 (0.657-5.380)	0.239	1.324 (0.478-3.665)	0.471
CT	0.681 (0.167-2.781)	0.592	5.271 (1.067-26.034)	0.041	2.340 (0.471-11.634)	0.299	2.206 (0.443-10.983)	0.365
HT	0.781 (0.322-1.896)	0.585	0.407 (0.171-0.967)	0.0422	0.428 (0.167-1.099)	0.078	0.368 (0.140-1.971)	0.482

OR: Odds Ratio, CI: confidence interval, RT: radiotherapy; CT: chemotherapy; hormone teherapy. * mastectomy versus quadrantectomy and axillary clearance.

itself, though primary direct tumor infiltration or invasion, or through metastasis.[13] In 19% of the cases, the pain is related to the treatment for the disease and, for the other 3%, its causes are unrelated to those previously mentioned.[14]

Chronic pain is more frequent among patients who have undergone breast conserving therapy than among those who have undergone mastectomy,[6] and is found either in the scar or in the ipsilateral upper limb.[3,5-6] Postoperative complications, along with cases of young patients or presentation of voluminous primary tumors, are other factors that may be associated with chronic pain.[5]

It has been reported that treatment with breast conservation may generate greater prevalence of chronic pain than radical treatment does, possibly because of the association with radiotherapy.[6] However, there is no consensus regarding this observation, given that this association was not found in another study.[15] In the present study, although this association was not found, there was a tendency for patients who had undergone radiotherapy to present greater prevalence of pain (2.5 times greater). This result possibly did not reach statistical significance because of the small sample size.

In our study, the prevalence of pain was moderate

(31%). When pain was reported, it was classified as mild by 70.3% of the patients (19/27). On the other hand, in the eight other cases, pain of great intensity was reported. Ten patients reported that they were making chronic use of analgesics, of whom six had been using them for more than six months.

When asked about how the symptoms were disturbing their lives, practically half of the patients (48%) complained of having some limitation. For 20% of them, this limitation was manifested more intensely, which confirmed what we had been observing in daily practice.

To our surprise, the patients who had made use of endocrine therapy with tamoxifen presented lower prevalence of fatigue, edema and pain. We were unable to explain this finding. This association was not found in the series of Tasmuth et al.[16] The fact that endocrine therapy with tamoxifen reduced the symptoms supports the need for prospective studies, so that the real link between this drug and the symptoms from the treatment can be understood. This finding also becomes a further point to consider in choosing between tamoxifen and aromatase inhibitors, and this confirmation is also necessary in other studies.

Since pain and other uncontrolled symptoms are the main causes of anxiety, depression and suicide among patients with cancer,[11] there is a need for greater monitoring of such patients during follow-up of their treatment. If possible, prophylactic measures should be developed for implementation during the period of oncological treatment. There is data suggesting that these women receive insufficient treatment and generally obtain little relief from these symptoms.[1]

The symptoms, and especially chronic pain, seem not to be merely a chance occurrence. They may be reduced through taking certain precautions such as preservation of the intercostobrachial nerve [17] and good application of analgesia during the operation,[18] together with use of COX-2 inhibitors on the days following the surgery.[19] Furthermore, there is the possibility of performing biopsies on sentinel lymph nodes, compared with axillary lymphadenectomy.[20]

Although retrospective, our study provides important information on the symptoms frequently presented by patients who are treated for breast cancer. As we foresaw, the high prevalence of complaints showed that they are underestimated in clinical practice, and these complaints interfered in some way in the lives of 48% of our patients.

Concordant with this hypothesis, two recently published papers have shown the importance of chronic symptoms following treatments and their interference in patients' quality of life.[21-22] In a prospective study that included 1,183 patients, Meeske et al.,[21] observed that chronic fatigue significantly impaired the quality of life among breast cancer survivors. Moreover, in relation to pain, a study conducted by Paim et al.,[22] in Minas Gerais, showed that pain and chronic dysfunction of the shoulder on the side that underwent surgery also significantly interfered with the patients' quality of life.

Therefore, we believe that because of the high prevalence of post-treatment symptoms reported here, and their interference in patients' lives, prospective studies should be conducted to seek ways to reduce the sequelae among breast cancer survivors and provide treatment for them.

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