

Prevalence and comorbidity of pain and fatigue in women with breast cancer

PREVALÊNCIA E COMORBIDADE DE DOR E FADIGA EM MULHERES COM CÂNCER DE MAMA

PREVALENCIA Y COMORBILIDAD DE DOLOR Y FATIGA EN MUJERES CON CÁNCER DE MAMA

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ABSTRACT

This study analyzed the prevalence and comorbidity of pain and fatigue in women with breast cancer. This is a cross-sectional study using a non-probabilistic sample of 182 women following outpatient treatment for breast cancer, who were interviewed from July 2006 to March 2007. Fatigue was assessed using the Piper Fatigue Scale, and divided into two categories (scores 0.1-4.9 and $\geq 5-10$). Pain was assessed by the 0-10 scale, and categorized the same way as fatigue. Fatigue occurred in 94 women (51.6%), and was ≥ 5 in 44 (46.8%) of the women. Pain occurred in 86 women (47.2%), with scores ≥ 5 in 50 (58.1%). Fatigue and pain were correlated ($r=0.38$, $p=0.003$) and the comorbidity fatigue and pain was 38.3%. Intense pain increased fatigue ($p=0.089$) and intense fatigue increased pain ($p=0.016$). Both data are new in our area, and confirm the existence of a cluster of symptoms and the harms resulting from that comorbidity.

DESCRIPTORS

Breast neoplasms
Fatigue
Pain
Hospice care

RESUMO

O estudo analisou a prevalência e a comorbidade de dor e fadiga em mulheres com câncer de mama. Trata-se de estudo transversal, com amostra, não probabilística de 182 mulheres em tratamento ambulatorial para câncer de mama, entrevistadas no período de julho 2006 a março de 2007. Fadiga, avaliada pela Escala de Fadiga de Piper, foi dividida em duas categorias (escore 0,1-4,9 e $\geq 5-10$). Dor, avaliada pela escala de 0-10, foi categorizada do mesmo modo que fadiga. Fadiga ocorreu em 94 mulheres (51,6%), sendo ≥ 5 em 44 (46,8%) delas. Dor ocorreu em 86 mulheres (47,2%), sendo ≥ 5 em 50 (58,1%). Fadiga e dor correlacionaram-se ($r=0,38$, $p=0,003$) e a comorbidade fadiga e dor foi de 38,3%. Dor intensa acentuou a fadiga ($p=0,089$) e fadiga intensa acentuou a dor ($p=0,016$). Tais dados são inéditos em nosso meio, confirmam a existência de um cluster de sintoma e dos prejuízos decorrentes dessa comorbidade.

DESCRITORES

Neoplasias da mama
Fadiga
Dor
Cuidados paliativos

RESUMEN

Estudio analítico de análisis de prevalencia y comorbilidad de dolor y fatiga en mujeres con cáncer de mama. Investigación transversal, con muestra no probabilística de 182 mujeres en tratamiento ambulatorio de cáncer de mama, entrevistadas en período de julio 2006 a marzo 2007. Fatiga evaluada por Escala de Fatiga de Piper, fue dividida en dos categorías (puntaje 0,1-4,9 y $\geq 5-10$). Dolor evaluado por escala de 0-10, categorizado del mismo modo que fatiga. Existió fatiga en 94 mujeres (51,6%), siendo ≥ 5 en 44 (46,8%) de ellas. Existió dolor en 86 mujeres (47,2%), siendo ≥ 5 en 50 (58,1%). Se correlacionaron dolor/fatiga ($r=0,38$, $p=0,089$) y la comorbilidad fatiga/dolor fue de 38,3%. El dolor intenso agudizó la fatiga ($p=0,089$) y la fatiga intensa acentuó el dolor ($p=0,016$). Datos inéditos en nuestro medio, confirman la existencia de un cluster de síntomas y los perjuicios derivados de la comorbilidad.

DESCRIPTORES

Neoplasias de la mama
Fatiga
Dolor
Cuidados paliativos

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INTRODUCTION

Pain and fatigue are frequently reported, cause suffering and affect the quality of life of patients with different types of cancer, which prompts us to investigate how breast cancer is manifested. Pain in women with breast cancer occurs in 47% of cases⁽¹⁻²⁾ and increases as the disease develops. Moderate or intense pain occurs in 30% of patients receiving treatment and in 60% to 90% of those in the advanced stages. In addition to being frequent and intense, pain can manifest daily, in different sites, and last many hours per day⁽³⁾.

Pain may be related to the growth of a tumor, to a metastasis process or treatment; it can change according to mood, cognitive aspects such as expectations and beliefs and it seems it may also originate from other symptoms such as cachexia, anorexia and fatigue⁽³⁾.

Fatigue is a subjective and unpleasant sensation, with physical, psychological and emotional symptoms. It is a type of tiredness that is not relieved with the usual strategies used to restore energy⁽⁴⁾. It varies in duration and intensity and reduces, at different levels, the ability to perform daily activities⁽⁴⁾. It is a symptom with multiple factors and can impact various spheres of life, though the factors that compose it are little known. The prevalence of fatigue varies from 32% to 94%⁽⁵⁻⁶⁾ among women with breast cancer.

There is evidence in oncology that tumor hypermetabolism and its byproducts, factors of tumor necrosis, neurotoxins and the high-energy expenditure are the causes of

fatigue. Chemotherapy and radiotherapy are causal or classical aggravating factors of fatigue that result from cytotoxicity of chemotherapeutic agents and from tissue necrosis arising from radiotherapy⁽⁷⁾.

Fatigue in breast cancer is related to pain, depression, sleep disorders, menopause, age, immobility and dyspnea, though this issue is not totally clarified^(1-2,8-11). Fatigue and pain are frequent and seem to be related while their co-existence can be extremely deleterious to patients.

OBJECTIVES

To analyze the prevalence and comorbidity of pain and fatigue in women with breast cancer.

LITERATURE REVIEW

To analyze the literature on the theme of comorbidity in pain and fatigue in women with breast cancer, a bibliographic review was carried out in the PubMed, COCHRANE, CINAHL, EMBASE and LILACS databases without time of publication limitations using the descriptors *breast cancer* or *breast neoplasm AND fatigue AND pain*.

The search identified 1,122 studies and after reading the abstracts, 37 full texts were selected. Of the 37, 18 were repeated and nine did not address the relationship between fatigue and pain, which is the focus of this study. Hence, ten studies referred to the comorbidity of fatigue and pain and a summary is shown in Table 1.

Table 1 – Studies on the comorbidity of fatigue and pain in women with breast cancer - São Paulo, Brazil - 2008

Author and year	Sample and study design	Objectives	Instruments	Correlation and Comorbidity
Byar et al., 2006.	25 women in stages I or II of the disease. (longitudinal study)	To compare fatigue and other physical and psychological symptoms and their relationship with quality of life during chemotherapy and one year after treatment.	FATIGUE: Piper Fatigue Scale e Symptom Experience Scale. PAIN: Symptom Experience Scale.	Correlation of fatigue and pain one year after the first chemotherapy: (r=-0.57; p=0.008).
Reuter et al., 2006.	353 women recently diagnosed with breast cancer. (cross-sectional study)	To explore the contribution of coping strategies, depression, pain and age on fatigue in women with breast cancer.	FATIGUE Profile of Mood States Fatigue-inertia Scale. PAIN: Escala Visual Analógica.	Pain and fatigue displayed weak correlation: (r=0.22; p<0,001).
Badr et al., 2006.	23 women in stages I, II and III of the disease, post treatment. (cross-sectional study)	To identify the relationship between mood states and transitory physical symptoms.	FATIGUE: Brief Fatigue Inventory (0-10). PAIN: Brief Pain Inventory (0-10).	Pain and fatigue displayed weak correlation: (r=0.27; p=0,0001).
Gélinas, Filion et al., 2004.	103 women in stages I, II and III the disease, post treatment. (cross-sectional study).	To verify the predictive ability of stress on persistent fatigue after cancer treatment	FATIGUE: Multidimensional Fatigue Inventory. PAIN: Brief Pain Inventory.	Pain and fatigue displayed? weak correlation: (r=0.30; p<0.01).
Gaston-Johansson et al., 1999.	127 women in stages I, II and III the disease, post treatment. (cross-sectional study).	To determine the influence of fatigue, pain and depression on the health status of patients with breast cancer who completed adjuvant chemotherapy	FATIGUE: Piper Fatigue Scale e Fatigue Visual Analogue Scale. PAIN: Gaston-Johansson Pain-ometer.	Pain and fatigue displayed weak correlation: (r=0.34; p<0.001).

Table 1 – Studies on the comorbidity of fatigue and pain in women with breast cancer - São Paulo, Brazil – 2008 (continuation)

Author and year	Sample and study design	Objectives	Instruments	Correlation and Comorbidity
Jacobsen ET al., 1999.	54 patients in the beginning and during the first cycle of chemotherapy (longitudinal study)	To investigate the characteristics, course and correlations of fatigue in ? women with breast cancer receiving adjuvant chemotherapy.	Fatigue Scale from the Profile of Mood States. Fatigue Symptom Inventory. Memorial Symptom Assessment Scale.	Pain and fatigue displayed weak correlation: (r=0.37; p≤0.05).
Arndt et al., 2006.	314 women one year after the diagnosis (cross-sectional study)	To identify the predictive symptoms of limited quality of life in women after one year of the first cancer treatment.	Both symptoms were evaluated through the Quality of Life Questionnaire Core 30 Items and Breast Cancer Specific Module.	Pain and fatigue displayed moderate correlation: (r=0.68;p<0.001).
Ferrell et al., 1998.	298 women in different stages of the disease. (cross-sectional study)	To evaluate the quality of life of women with breast cancer.	FATIGUE: QOL-Breast Cancer Version. PAIN: QOL-Breast Cancer Version and Brief Pain Inventory.	Pain and fatigue displayed moderate correlation: (r=0.69; p≤0.05).
Nieboer et al., 2005.	430 women in chemotherapy. (longitudinal study)	To verify whether different chemotherapy schemes are related to fatigue, hemoglobin, mental health, pain, and menopause symptoms.	FATIGUE: Vitality Scale (score ≤ 46 was defined as fatigue). PAIN: Rotterdam Symptom Checklist.	Comorbidity among symptoms: of the patients with fatigue, 41% experienced pain.
Meeske et al., 2007	1183 female survivors of breast cancer. (longitudinal study)	To identify correlations of fatigue and evaluate the relationship between fatigue and health-related quality of life.	FATIGUE: Piper Fatigue Scale. PAIN: SF-36 Bodily Pain – subscale.	Comorbidity among symptoms: of the patients with fatigue, 46% experienced moderate to intense pain.

Table 1 reveals weak to moderate (0.27 to 0.69) correlation between fatigue and pain in seven of the selected studies, while symptoms displayed negative correlation in one of the studies (-0.57). Two studies analyzed the comorbidity of fatigue and pain: 41% and 46% respectively. There were no national studies addressing the subject.

METHOD

This is a quantitative and cross-sectional study.

Population and sample

The convenience sample was composed of 182 women with breast cancer in outpatient follow-up in any phase of the disease and treatment. Inclusion criteria were being 18 years old or older and having communication and comprehension capacity preserved.

Setting and period of time

Data were collected in three private oncologic services: a private oncologic clinic, the Brigadeiro Hospital and Santa Helena Hospital between July 2006 and March 2007.

Procedures and data collections instruments

The patients were approached after an outpatient medical visit or during chemotherapy sessions. Those who consented to participate in the study completed three instruments: Identification Form, Piper Fatigue Scale and Pain Intensity Scale.

The identification form was composed of questions addressing marital status, age, employment, schooling, type

of service in which the patient was being treated, the tumor stage and treatments.

The Piper Fatigue Scale is a self-report instrument composed of 22 items with a numerical scale (from 0 to 10). It evaluates the following dimensions: sensorial (five items), affective (five items), cognitive/mood (six items), behavior/intensity (six items). It was validated for the Portuguese language (reliability and factorial analysis) and displayed appropriate psychometric properties⁽¹²⁾. The numerical Pain Intensity Scale (from 0 to 10) was used to evaluate pain in the week prior to the interview (last seven days).

Data analysis

Collected data were input in the statistical program SPSS version 14.0 for descriptive and inferential analysis. The qualitative variables were presented in absolute numbers and in percentages and the quantitative variables were expressed in averages, standard deviation (SD), medians, and minimum and maximum values.

Fatigue and pain were graduated in three categories: Fatigue – 0 = absence; between 0.1 and 4.9 = mild; between 5 and 10 = moderate or intense; and Pain – 0 = absence; between 1 and 4 = mild; between 5 and 10 = moderate or intense.

The prevalence of comorbidity for fatigue and pain was computed with confidence intervals at 95% (CI 95%). After verification of normality for the scores of fatigue and pain by the Shapiro-Wilk non-parametric test, Pearson's parametric tests were used between these two variables and the ANOVA test was used to compare the averages. Bonferroni's test was used for multiple comparisons to identify the group(s) distinct from the others. The level of significant was set at 5%.

Ethical aspects

The project was approved by the Research Ethics Committee at the University of São Paulo at Ribeirão Preto, College of Nursing (Process No. 511/2005/CEP-EEUSP) and Research Ethics Committees of the institutions where data were collected. All the participants were informed of the study's objectives, were ensured confidentiality, freedom to participate in or withdraw from the study at any time. Those who consented signed two copies of free and informed consent forms.

RESULTS

Most of the women in the studied sample were younger than 52 years old, had more than 13 years of schooling, were married, were being cared for in a private institution (78.0%) and were under cancer treatment (70.3%). Among those (n=129) whose stage of the disease was recorded in a medical file, 39.5% were in stage II (Table 2).

Table 2 – Characterization of women with breast cancer - São Paulo, Brazil - 2008

Age(years)	Average (DP) Median (Minimum-Maximum)	52.8 (10.5) 52.0 (29 - 81)		
Escolaridade (em anos)	Average(DP) Median (Minimum-Maximum)	12.4 (4.6) 13.0 (0 - 25)		
			N	%
Married			96	52.7
Employed			62	34.1
Type of service - private			142	78.0
stage*	I		32	17.6
	II		51	28.1
	III		19	10.4
	IV		27	14.8
	Ignored		53	29.1
Current treatment	Chemotherapy/ Radiotherapy		73	40.1
	Others		55	30.2
	No treatment		54	29.7

TNM staging system, according to the patient's chart.

A total of 62 (34.1%) studied women did not present pain or fatigue (Table 3). However, comorbidity of pain and fatigue was observed in 60 patients (Prevalence 33.0%

[CI95%: 20.2-40.3]). Among these, 23 (38.3%) displayed moderate and intense fatigue and pain.

Table 3 – Comorbidity of pain and fatigue in women with breast cancer – São Paulo, Brazil – 2008

Fatigue	Pain							
	Absent		Mild ³		Moderate/intense ⁴		Total	
	N	%	N	%	N	%	N	%
Absent	62	64.6	12	33.3	14	28.0	88	48.4
Mild ¹	22	22.9	15	41.7	13	26.0	50	27.5
Moderate/intense ²	12	12.5	9	25.0	23*	46.0	44	24.2
Total	96	100	36	100	50	100	182	100

*Moderate/intense comorbidity of fatigue and pain; ¹ Score of fatigue between 0.1 and 4.9; ² Score of fatigue between 5.0 and 10; ³ Score of pain between 1 and 4; ⁴ Score of pain between 5 and 10.

The analysis of those with pain (n=86) and/or fatigue (n=94) revealed the average score of pain was 4.9 (SD=1.9) and that of fatigue was 4.7 (SD=2.0).

To explore the relationship between pain and fatigue, the averages of fatigue were compared to the categories of pain and the averages of pain were compared to the cat-

egories of fatigue. The existence of correlation among symptoms was also investigated.

Table 4 shows that the average scores of pain were not equal according to the level of fatigue (p=0.019). Women with moderate or intense fatigue displayed a greater level of pain when compared to those with mild fatigue (p=0.016) (Table 4).

Table 4 – Average scores (standard deviation) of pain according to the intensity of fatigue in women with breast cancer- São Paulo, Brazil - 2008

Fatigue	Pain							
	Absent		Mild ³		Moderate/intense ⁴		Total	
	N	%	N	%	N	%	N	%
Absent	62	64.6	12	33.3	14	28.0	88	48.4
Mild ¹	22	22.9	15	41.7	13	26.0	50	27.5
Moderate/intense ²	12	12.5	9	25.0	23*	46.0	44	24.2
Total	96	100	36	100	50	100	182	100

Bonferroni test 1x2:p=0.290; 1x3:p=0.858; 2x3:p=0.016

The average scores of fatigue differed according to the level of pain ($p=0.014$) as shown in Table 5. Women with moderate or intense pain presented a higher level of fatigue when compared to those without pain ($p=0.014$) (Table 5). Fatigue and pain mutually affect each other.

Table 5 – Average scores (standard deviation) of fatigue according to intensity of pain in women with breast cancer – São Paulo, Brazil – 2008

PAIN	FATIGUE AVERAGE (SD)	p-value
Absent ¹	4.2 (2.3)	0.014
Mild ²	4.4 (1.5)	
Moderate/intense ³	5.5 (1.9)	

Bonferroni test 1x2:p=0.290; 1x3:p=0.858; 2x3:p=0.016

A weak linear ($r=0.38$) relationship between fatigue and pain with statistical significance ($p=0.003$) was observed in 60 patients, indicating that an increase in one score implies an increase in the score of the other morbidity.

DISCUSSION

Fatigue and pain can contribute to the onset or worsening of other symptoms such as sleep and mood disorders, constipation, and consequently affect quality of life. More than half (51.6%) of this study's sample reported some level of fatigue with a high prevalence (44/94, 46.8%) of moderate and intense fatigue. Pain occurred in 47.2% ($n=86$) of the women and was described as moderate and intense by (50/86) 58.1%.

In other studies, the prevalence of fatigue varied from 20% to 97%^(1,6,8,13-15) and the prevalence of pain varied from 20% and 97%^(1,13-14,16). The great variability found is possibly due to differences in the adopted samples, instruments and cutoff points. The use of different instruments to measure the phenomena hinders comparison among studies given the difference of categories, domains and final score of each instrument. Table 1 shows the variation of instruments used to evaluate fatigue and pain in women with breast cancer. Nonetheless, the studies' results are useful despite limitations in comparing samples evaluated with different instruments because they enable the identification of trends.

Pain and fatigue vary according to the severity of the oncologic disease, the individuals' emotional and socio-demographic characteristics, type and phase of treatment,

among other factors. Fatigue and pain are more frequent in the advanced stage of the disease (metastasis) and fatigue also worsens during chemotherapy, radiotherapy and after bone marrow transplantation^(1,6,8-10,13-14,16-19).

The intensity of fatigue and pain observed in this study draws attention because about one third of women qualified fatigue and pain as moderate or intense, that is, between 5 and 10 (Table •3). The average of pain intensity was 4.9 (SD=1.9) and fatigue 4.7 (SD=1.9), according to Table 4. A similar result was observed by Ardnt *et al* (2006), who identified one third of complaints of fatigue and pain as having a magnitude above 50 (scale 0 to 100). Other studies addressing women with breast cancer report an average intensity of fatigue varying from 2.8 to 9.6^(1,6,8,16-19) and an average intensity of pain between 1.2 and 8.4^(1,16-19).

Fatigue and pain are reported as being constant, frequent or persistent; the sensation occurs several times a day and has a prolonged duration. Living with these symptoms leads patients and caregivers to bear significant physical and emotional exhaustion because these symptoms hinder deambulation, hygiene and feeding; they change mood, concentration, and affect relationships with significant others. Relatives become overwhelmed with the limitations of the patient and suffer from witnessing one dear to them suffering.

Pain and fatigue are related, occur simultaneously and one aggravates the other. A positive and moderate correlation ($r=0.38$; $p=0.003$), was found in this study, that is, the highest scores of fatigue corresponded to the highest scores of pain. Such findings are similar to those observed in seven studies that describe a positive correlation between fatigue and pain varying from 0.22 and 0.69^(1,6,14,16-19) as shown in Table 1. Opposite results were found by another study reporting a negative correlation between pain and fatigue⁽⁹⁾: while one symptom worsens the other improves. Apparently, there is not a physiopathological explanation for such results.

Comorbidity of fatigue and pain was found in 32.9% of this study's sample. It is worth highlighting that in 38.3% of the cases, both symptoms displayed clinically important intensity, between moderate and intense (Table 3). Such comorbidity was reported only in two other studies^(13,20), 41% ($n=430$) and 46% ($n=1,183$) of the samples, respectively.

Comorbidity between symptoms, currently a phenomenon called clustering of symptoms, and which was observed in this study, can be extremely deleterious to patients. Pain and fatigue *per se* are described as causes of suffering and distress, and in comorbidity they can be even more incapacitating. In physical, emotional and social terms, they can compromise adherence to treatment and cause more suffering to the women and her family. Few international studies analyzed such a correlation and the comorbidity between fatigue and pain in women with breast cancer and at the national level. This is the first such study.

One result of this study that deserves attention is that pain aggravated fatigue and fatigue aggravated pain. Such a relationship has been mentioned but few studies evidence its existence. The comparison of averages of pain (Table 4) among patients with mild (4.1 ± 1.5) fatigue with those with moderate/intense (5.5 ± 1.8) fatigue, revealed that the more intense the pain the more intense the fatigue ($p=0.016$). Oddly, the averages of pain did not differ in the comparison between absence of fatigue and moderate/intense fatigue ($p=0.858$). No studies showing worsened pain in situations of intense fatigue were found.

The comparison of averages of fatigue (Table 5) among patients without pain (4.2 ± 2.3) with those with moderate/intense pain (5.5 ± 1.9) revealed that the more intense the fatigue the more intense the pain ($p=0.020$), as shown in Table 5. Worsened fatigue when there is muscle and joint pain was observed in a study of women with breast cancer⁽¹³⁾. Another study conducted with survivors of breast cancer two years after diagnosis revealed that the averages of fatigue were also higher when there was intense pain⁽²⁰⁾.

This study's findings indicating that pain aggravates fatigue and vice-versa suggest that relieving one of the symptoms improves the other. Additionally, they confirm the concept of the clustering of symptoms that proposes that some symptoms occur concomitantly in oncologic disease and one can worsen the other because they present overlapping physiopatological mechanisms⁽²¹⁾. Little is known

about treating fatigue in oncologic diseases and most of the times it is not relieved. However, treatment for pain is known and effective and its appropriate implementation can improve both symptoms, a hypothesis that deserves to be tested in future studies. Additionally, the use of self-report instruments validated for Portuguese can contribute to better evaluate fatigue in patients with cancer in nurses' clinical practice^(12,22).

One of the study's limitations is its non-probabilistic sample, which impedes the generalization of results. Women in outpatient care were evaluated, most of whom were in stages I and II, though this information was ignored in about 30% of the cases, which represents another limitation.

Identifying the prevalence, intensity of symptoms and comorbidity of fatigue and pain in women with breast cancer allows professionals to plan preventative actions and treatment of symptoms. Verifying that intense pain is associated with more intense fatigue and *vice-versa* allows professionals and patients to attempt to relieve one of the symptoms, aware that doing so can also relieve the other symptom.

CONCLUSION

Fatigue and pain were frequent in women with breast cancer with significant magnitude. The comorbidity of pain and fatigue was high (32.9%) and in 38.3% of the cases, moderate and intense fatigue and pain were observed. A positive moderate and statistically significant correlation was found between pain and fatigue and one symptom worsened the other, confirming the concept of the clustering of symptoms.

The correlation and comorbidity observed between fatigue and pain indicate that relief of fatigue may be promoted through the appropriate management of pain, which is very important since actions to control fatigue are not well known but actions to control pain are well developed.

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