Cost of the Disease in Patients with Breast Cancer Treated with Tamoxifen

Custo da Doença em Pacientes com Carcinoma Mamário Tratados com Tamoxifeno

Costo de la Enfermedad en Pacientes com Carcinoma Mamário Tratados com Tamoxifeno

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Abstract

Introduction: The estimate of the National Cancer Institute José Alencar Gomes da Silva, for each year of the 2018-2019 biennium in Brazil, was 59,700 new cases of breast cancer, with an estimated risk of 56.33 cases per 100,000 women. In 2014, public expenditures on cancer care were approximately R$ 2.5 billion. **Objective:** To evaluate the impact of direct medical costs on breast cancer patients treated with tamoxifen using the Unified Health System. **Method:** Prospective, quantitative, retrospective, cost-of-disease study with prevalence and bottom-up approach. Data collection was performed at the Oncology Outpatient Clinic of the Hospital São Vicente in Curitiba, Paraná. **Results:** The mean cost of the treatment was R$ 14,497.70 for neoadjuvant or adjuvant treatment and R$ 9,108.60 for palliative treatment. In relation to these variables, the cost of tamoxifen was the one that most impacted, in relation to the total cost of the treatment, representing more than 80% of this value. The mean annual cost of tamoxifen per patient was R$ 1,947.60. **Conclusion:** The average cost of treatment was high in relation to the Brazilian average salary of R$ 2,110.00 (IBGE-2017). The costs investigated in this study can help public health managers in strategies to rationalize expenditures, optimize capital and maintain patient care.
Key words: Breast Neoplasms/economics; Tamoxifen; Unified Health System.

Resumo

Introdução: A estimativa do Instituto Nacional de Câncer José Alencar Gomes da Silva para o Brasil, para cada ano do biênio 2018-2019, foi de 59.700 novos casos de câncer de mama, com um risco estimado de 56,33 casos a cada 100 mil mulheres. Em 2014, os gastos públicos com atenção oncológica foram de aproximadamente R$ 2,5 bilhões. **Objetivo:** Avaliar o impacto dos custos diretos médicos em pacientes com carcinoma mamário tratados com tamoxifeno pelo Sistema Único de Saúde. **Método:** Estudo exploratório de custo da doença, quantitativo, retrospectivo, com caráter de prevalência e de abordagem *bottom-up*. A coleta dos dados foi realizada no ambulatório de Oncologia do Hospital São Vicente em Curitiba, Paraná. **Resultados:** A média do custo do tratamento dos pacientes foi R$ 14.497,70 em tratamento neoadjuvante ou adjuvante e de R$ 9.108,60 em tratamento paliativo. Em relação a essas variáveis, o custo do tamoxifeno foi o que mais impactou em relação ao custo total do tratamento, representando mais de 80% deste valor. A média do custo anual gasto com tamoxifeno por paciente foi de R$ 1.947,60. **Conclusão:** O custo médio do tratamento demonstrou ser alto em relação à média salarial dos brasileiros de R$ 2.110.00 (IBGE-2017). Os custos levantados neste estudo podem auxiliar os gestores de saúde pública em estratégias para racionalização dos gastos, otimização do capital e manutenção do atendimento à população.
Palavras-chave: Neoplasias da Mama/economia; Tamoxifeno; Sistema Único de Saúde.

Resumen

Introducción: La estimación del Instituto Nacional del Cáncer José Alencar Gomes da Silva para Brasil, para cada año del bienio 2018-2019, fue de 59,700 casos nuevos de cáncer de mama, con un riesgo estimado de 56.33 casos por 100,000 mujeres. En 2014, los gastos públicos con atención oncológica fueron de aproximadamente R $ 2,5 mil millones. **Objetivo:** Evaluar el impacto de los costos directos médicos en pacientes con carcinoma mamario tratados con tamoxifeno por el Sistema Único de Salud. **Método:** Estudio exploratorio de costo de la enfermedad, cuantitativo, retrospectivo, con carácter de prevalencia y de enfoque bottom-up. La recolección de los datos fue realizada en el Ambulatorio de Oncología del Hospital São Vicente en Curitiba, Paraná. **Resultados:** El promedio del costo del tratamiento de los pacientes fue R$ 14.497,70 en tratamiento neoadyuvante o adyuvante y de R$ 9.108,60 en tratamiento paliativo. En relación a estas variables el costo del tamoxifeno fue el que más impactó en relación al costo total del tratamiento, representando más del 80% de este valor. El promedio del costo anual gastado con tamoxifeno por paciente fue de R$ 1.947,60. **Conclusión:** El costo promedio del tratamiento demostró ser alto en relación al promedio salarial de los brasileños de R $ 2.110.00 (IBGE-2017). Los costos levantados en este estudio pueden auxiliar a los gestores de salud pública en estrategias para racionalización de los gastos, optimización del capital y mantenimiento de la atención a la población.
Palabras clave: Neoplasias de la Mama/economía; Tamoxifeno; Sistema Único de Salud.

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INTRODUCTION

Mammary carcinoma or breast cancer is considered the second of major incidence in the whole world and of highest mortality in the female population. The estimate of "Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA) for Brazil, for each year of 2018-2019, was 59,700 new cases of breast cancer with an estimated risk of 56,33 cases at each 100 thousand women[1].

When the disease is early diagnosed, the treatment has more curative potential. According to INCA, in South America, particularly in Brazil, the survival in five years raised from 78% to 87% as result of the public policies adopted[2,3].

In 2014, according to data of the Ministry of Health, public expenditures with oncologic care were approximately R$ 2.5 billion. These figures correspond to the expenditures with surgeries, chemotherapy and radiotherapy. Between 2000 and 2014, these expenses had an increase of 375%[4].

Pursuant to the Breast Cancer Control Program, the treatment for breast cancer varies according to the disease staging in local (surgery and radiotherapy) and systemic (chemotherapy, hormone therapy and biologic therapy) treatment. Further, the biological characteristics and the conditions of the patient (age, menopause status, co-morbidities, etc.) also affect the therapeutic approach of choice[5].

Tamoxifen is widely prescribed for every disease staging in hormone treatment. According to the Ministry of Health Diagnosis and Therapeutic Guidelines of Breast Cancer, the use of tamoxifen is indicated in adjuvant, neoadjuvant and palliative therapies, where tumors have positive hormone receptors and for patients in pre and post menopause[4,6].

Tamoxifen is a selective modulator of the receptor of estrogen that inhibits the growth of breast cancer cells by competitive antagonism of estrogen. It is associated to bigger disease-free and global survival when utilized in adjuvant treatment, in addition to reduction of contralateral breast cancer[4,6].

Studies about cost-of-illness also known as burden of disease are among the first economic studies connected to health identified in the literature. The method is an empiric approach to estimate the social impact of diseases and injuries, which combines direct medical costs (professional fees, medication, complementary tests, hospital daily costs), direct non-medical costs (transportation, domicile adjustments, nourishment and clothes), indirect (loss of productivity) and intangible (changes of the quality of life, pain, suffering)[7-9].

The assessment of costs of illness can be carried out under different perspectives, from the angle of the patient, of the employer, of the health insurer, government or society. The present study evaluated the costs of treatment of breast cancer with tamoxifen under the perspective of the National Health System (SUS)[10,11].

Studies of the type cost-of-illness are important for public health because they manage to quantify the resources spent by the system. The goal of this study was to evaluate the impact of medical direct costs with breast cancer patients treated with tamoxifen by SUS and contribute as a supporting tool for decision-making ensuring the actual beneficial individual right to treatment and the right of universal access to SUS.

METHOD

Retrospective, quantitative, exploratory cost-of-illness study with prevalence and bottom-up approach.

Data collection was conducted at the Oncology Ward of Hospital São Vicente "*Ambulatório de Oncologia do Hospital São Vicente HSV-FUNEF*" in Curitiba, Paraná. The initial listing of the patients was obtained from a report of tamoxifen use per patient extracted from the system utilized by the hospital facility (MV®) from January 1, 2010 through January 31, 2016.

Based in the total patients listed, the inclusion criteria defined were patients with breast cancer in hormone therapy with tamoxifen, above 18 years old attended by SUS. The exclusion criteria were pregnant women, HIV-infected (*human immunodeficiency virus*), using tamoxifen concomitant with chemotherapy or radiotherapy in treatment for less than six months without data or with incomplete data in the chart, and who did not sign the informed consent form (ICF) because of death or non-adherence to the study.

Charts provided the data of the research subjects and logged in a clinical form specifically designed for the study. Next, the data obtained from the clinical forms were compiled to Microsoft Office Excel® spreadsheets and Microsoft Office Word®.

Data about the characteristics of the patient (demography, date of the diagnosis of the disease, staging, co-morbidities and other treatment performed) of the disease (time from the diagnosis to the treatment, choice of treatment, regimen and dose, frequency, duration, side effects, interventions, suspension, changes, visits, diagnosis tests and admissions) and of the resources utilized (cost of the visits, tests, surgical procedures, medications) were collected.

Because it is a study under the perspective of SUS, only direct medical costs were included, according to the Methodological Guidelines for Economic Evaluation Studies of Health Technologies [11]. These costs consisted of the total sum of the costs of medical and non-medical visits

(multidisciplinary), lab tests, diagnosis tests, medications, surgical procedures, visits to emergency care unit, intensive care units and admissions.

It was utilized the Table of Procedures, Medications and orthosis, prosthetics and special materials of SUS (SIGTAP-DATASUS) with values referenced to October 2017. The value of each visit specified in this table was multiplied by the number of visits of each patient in the cut-off period adopted by the study.

The value of the diagnosis and lab tests were also sourced from SIGTAP table and the value of each test multiplied by the total number of tests performed by the patients in the period evaluated.

For the calculation of the values of admission and surgical procedures, it was utilized the Authorization of Hospital Admission issued for each patient during the period evaluated.

The table Brasíndice® was utilized for the analysis of the cost of the medication and other pharmacy inputs and the value of the mean cost obtained in the hospital system utilized by the institution (MV®).

The costs evaluated were separated in groups: medications, visits, tests, surgeries and admissions (Microsoft Office Excel®); comparison among patients that underwent some surgical procedure during the treatment (surgical and non-surgical) for evaluation of the cost differences; comparison between the types of treatment (adjuvant and palliative) to evaluate the cost differences.

Some variables were selected to correlate with the costs through the coefficient of correlation of Spearman's Rho. The data of the patients' profile and costs of the mammary carcinoma were analyzed by descriptive statistics and tests of association. The choice of the statistic tests was based in the distribution and normality of the variables with the test Kolmogorov-Smirnov. If the distribution was normal, the variables were presented as mean and standard deviation and it was applied the test t of Student. Whether non-normal distribution was found, the values were expressed as median and range, and the tests of Mann-Whitney and Kruskal-Wallis were applied. When pertinent, it was used the chi-square test for comparison. All the statistical analyzes were performed with statistic program SPSS v.17.0, and results with values of $p < 0.05$ were considered statistically significant.

The Institutional Review Board (IRB) of "Setor de Ciências da Saúde" of "Universidade Federal do Paraná", registry CEP/SD - PB: 1912874/ 2017-02 approved the study. All the patients included in the sample signed the informed consent form, met the inclusion criteria and failed to meet the exclusion criteria described in the study. The ICF was signed by 176 patients.

RESULTS

From the initial listing, 815 patients were submitted to hormone therapy with tamoxifen. Out of these, 639 were excluded because they failed to meet the inclusion criteria or for meeting some of the study exclusion criteria. The result was a sample with 176 patients.

The main exclusion criteria evidenced were the association of chemotherapy or radiotherapy to the treatment, modification of the treatment during the cut-off period of the study due to treatment switch because of the progression of the disease, those with incomplete charts or who did not sign the ICF.

The sociodemographic data were compiled in a sole table (Table 1) where it is possible to see that the majority of the patients were women in the mean age range of 65 years old.

The mean time of treatment was 55 months (standard deviation ± 14 months). In relation to the therapeutic follow up of the patients, according to the classification BI-RADs® of diagnosis, 51.5% of the patients presented diagnosis of BI-RADs® 2, and 25% with BI-RADs® 0. The most relevant co-morbidity associated to the use of tamoxifen (26.1%) was hepatic steatosis, while systemic arterial hypertension (38.9%) and *diabetes mellitus* (13.9%) were the co-morbidities of highest occurrence non-associated to the use of tamoxifen. Among the patients with secondary metastasis, pulmonary and multiple organs metastasis, percentually equivalent (1.7%) were the most frequent.

The mean number of medical visits per patient during the period of treatment was 16 visits for patients in adjuvant treatment and 13 visits for patients in palliative care (Table 2).

It is observed a mean of medical visits of 3.5 visits/year for patients in adjuvant treatment and 2.8 visits/years for patients in palliative care. There was no significant difference in the mean of medical visits among the patients of different treatment groups. The medical specialization with highest number of ward visits was oncology with mean of 3.4 visits/year and standard deviation of ±2.2. This specialization represented 85.8% of the total number of medical visits. Among the others, are general clinic, dermatology, endocrinology and cardiology.

Only 26 patients (14.7%) patients had non-medical visits during the entire period of the study. The mean of these visits for these patients was 0.81 visits/year with standard deviation of ±0.59. Among the multidisciplinary professionals who attended the patients are: nutritionist, psychologist, social worker, pharmacist, physiotherapist and nursing team. It was identified sub-notification of multidisciplinary visits in

Table 1. Sociodemographic variables

Variable	n (%)
Gender	
Male	2 (1.1)
Female	174 (98.9)
Marital Status	
Married	65 (36.9)
Divorced	11 (6.3)
Not declared	2 (1.1)
Separated	1 (0.6)
Single	67 (38.1)
Widow/widower	30 (17.0)
Race	
Caucasian	171 (97.2)
Black	4 (2.3)
Brown	1 (0.6)
Education	
Complete elementary School	22 (12.5)
Incomplete Elementary School	6 (3.4)
Complete High School	18 (10.2)
Incomplete High School	8 (4.5)
Literate	1 (0.6)
Master degree	1 (0.6)
Not declared	120 (68.2)
Occupation	
Work	49 (27.8)
Does not work	125 (71.0)
Not declared	2 (1.1)
Location	
Capital	131 (74.4)
Metropolitan Region	27 (15.3)
Others	18 (10.3)

the charts and the. It was identified in the charts some sub-notification of multidisciplinary consultations and the non-reimbursement of the cost of the majority of physiotherapy and nursing visits. The pharmacy visit represented 79% of the total of non-medical visits conducted whose objective was the search for guidances about the use of the medication.

Fifty (50) patients (28.4%) had visits at emergency care units during the period of the study. The mean for these patients were 0.53 visits/year with standard deviation of ±0.4. The reason for these visits in its majority was for general clinic about treatment-unrelated co-morbidities.

The mean value of expenditures of medical visits for patients in palliative care similarly to adjuvant treatment corresponded to 1.5% of the total spent with the treatment and the mean expenditure with non-medical visits was lower than 0.1% of the total value of the treatment. The value paid for specialized care medical visit was R$ 10.00. The unitary value paid for the visit with university formation professionals (except physicians) in the specialized care ward was R$ 6.30. These values were described according to SIGTAP (october/2017). The mean value spent with visits at the emergency care unit either for patients in adjuvant treatment or palliative care was below 0.5% in relation to the total cost of the treatment.

The mean value spent with medical and non-medical visits was inferior to 2.0% of the total cost of the treatment both for patients who did submit to any surgical procedure or for those who did not. There was a significant difference of values spent with non-medical visits among those who underwent surgical procedure and those who did not (p<0.05).

The mean value spent with diagnosis tests by patients in adjuvant and palliative treatment corresponded to 3.78% and 4.34% of the mean value of the cost of the treatment, respectively. The patients who had surgery procedures presented a mean expense with diagnosis tests per year of R$ 117.27 tests/year with standard deviation of ±70.22. The mean with lab tests was R$ 10.43 tests/year with standard deviation of ± 9.13. The mean of the diagnosis and lab tests corresponded to a value ≤1.00 % of the mean of the treatment cost. No significant correlation between the lab and diagnosis tests was found among the patients who did submit to surgery and those who did not.

The most requested diagnosis tests were mammography, breast ultrasound, chest x-ray and full abdomen ultrasound. The evaluation of the number of mammographies per patient during the treatment indicates that there were 0.59 tests/patients/year, with standard deviation of ± 0.4. Therefore, the mean of the cost of mammography was R$ 26.77 tests/year with standard deviation of ± 18.05. The

Table 2. Comparison of the total number of visits and tests among treatment groups

VISITS AND TESTS	ADJUVANT			PALLIATIVE		
	Total	Mean	Median	Total	Mean	Median
Medical visits	2.673	16.10	16	125	12.5	15
Non-medical visits	81	10	0	14	11	0.5
Emergency Care visits	110	66	0	7	47	0
Diagnosis tests	1,696	322	10	91	318	7
Lab tests	1,739	39	5	52	24	0

unitary value paid for the test was R$ 45.00, according to SIGTAP table (October/2017).

The mean number of breast ultrasounds was 0.51 tests/patients/year with standard deviation of ±0.36. The mean of the value spent with breast ultrasound was R$ 1250 tests/year with standard deviation of ±8.62, which corresponds to an annual mean cost of R$ 10.28. The unitary value paid per test is R$ 24.20, according to the table SIGTAP (October/2017).

The mean number of chest x-ray requested was 0.73 tests/patients/year with standard deviation of ± 0.68. The mean of the value spent in chest x-ray was R$ 5.00 patient/year with standard deviation of ±4.65, which corresponds to a mean annual expense of R$ 3.95. The unitary value paid for chest x-ray, according to the table SIGTAP (October/2017) was R$ 6.88.

The mean value of ultrasounds of full abdomen was 0.59 tests/patient with standard deviation of ±0.48. The mean of the value spent during the treatment was R$ 82.37 ultrasounds/year, corresponding to a mean annual expenditure of R$ 21.40 patient/year, with standard deviation of ±18.09. The unitary value paid for the test according to the table SIGTAP (October/2017) was R$ 37.95.

The mean number of lab tests requested during the period of treatment was 10.27 tests with standard deviation of ±13.80. The mean number of lab tests was 2.24 tests/year. The most frequent lab test requested was blood count with mean of 0.05 tests/year requested, with standard deviation of ±0.05. The mean value spent per year was R$ 2.41, with standard deviation of ±2.5. The unitary value paid for the blood count according to the table of SIGTAP (October/2017) was R$ 4.11.

The mean value of the cost with surgical procedures for the patients who did any surgical procedure during the study period, despite the type of treatment was R$ 732.30 procedures/year with standard deviation of ±580.17. It was possible to demonstrate that the mean value of the cost with surgeries during the study period for the patients who had these procedures was 25.43% of the mean value

of the total cost of these patients treatment. There was significant statistical difference in the variables of cost of surgeries and total cost of the treatment of the patients who underwent surgical procedure. These variables are directly correlated (Table 3).

The mean of the cost with tamoxifen during the treatment period for patients of this study was R$ 8,924.66, with standard deviation of ±2,265.83. The mean of the annual cost with tamoxifen was R$ 1,947.60, regardless of the type of treatment or surgical procedure conducted.

Comparing the patients who did or did not submit to surgical procedure, it is possible to show that the mean of expenditure with tamoxifen of surgical patients was 14% bigger than the patients who did not submit to surgical procedure. This fact might be correlated to the cost of the treatment being higher in this group due to the added costs of the surgical procedures. For the patients who underwent some surgical procedure during treatment, the mean of the treatment cost with tamoxifen represented 68.71% of the mean of the total cost of the treatment and 94.06% for the patients who did not submit to any surgical procedure (Table 4). It was evidenced that the patients who did not submit to surgical treatment were elders in its majority and/or had metastasis.

For the other cost variables analyzed in this study, the cost of tamoxifen was the most impressive over the total cost of the treatment. The mean of the treatment cost with tamoxifen represented more than 80% of the mean value of the total treatment of the patients, except in the group that underwent some surgical procedure during the treatment.

According to the statistical analyzes conducted with the variables, those who had a strong correlation with the treatment cost, the object of this study, were time of the treatment, cost of the surgeries and cost of tamoxifen as shown in Table 5.

Comparing the costs according to the type of treatment, it was noticed that treatment type 1 was bigger than 2 in relation to cost of tamoxifen and total treatment.

Table 3. Comparison of the costs of patients submitted to surgical procedures versus patients not submitted to surgical procedures

Cost (R$)	WITH SURGERY		WITHOUT SURGERY		p-value
	Mean* (±SD)	Median (25-75)	Mean* (±SD)	Median (25-75)	
Diagnosis Tests	146.00 (75)	14.000 (90-200)	331.60 (283)	255.40 (114-462)	0.17
Lab tests	2.90 (7)	0 (0-0)	20.40 (32)	3.50 (0-31)	0.59
Cost of the treatment	14,497.70 (3,196)	13,417.80 (12,198-15,433)	9,108.6 (2,452.96)	9,9378.80 (10.328)	0.00

Caption: SD = standard deviation.
Notes: Significant correlation in p -value <0.05 (Wilcox-Mann-Whitney®); * of the complete treatment.

Table 4. Cost of the treatment with tamoxifen in relation to the patients who underwent any surgical procedure

Cost (R$)	WITH SURGERY		WITHOUT SURGERY		p-value
	Mean* (±SD)	Median (25-75)	Mean* (±SD)	Median (25-75)	
Costs of tamoxifen	9,961.60 (1,452)	9,738.00 (9,738-9,738)	8,568.40 (2,387)	9,575.70 (7,953-9,738)	0.00
Cost of the treatment	14,497.70 (3,196)	13,417.80 (12,198-15,433)	9,108.6 (2,452.96)	9,9378.80 (10,328)	0.00

Caption: SD = standard deviation.
Notes: Significant correlation in p-value <0.05 (Wilcox-Mann-Whitney®); * of the complete treatment.

Table 5. Statistical Correlations among variables (Spearman's Rho)

	Time of treatment	BI-RADS®	Cost of medical visits	Cost of non-medical visits	Cost of diagnosis tests	Cost of lab tests	Cost of surgeries	Cost of emergency care units	Total cost of tamoxifen	Total cost of the treatment
Time of treatment (months)										
BI-RADS®	0.066									
Cost of medical visits	-0.363**	0.038								
Cost of non-medical visits	0.069	0.007	0.025							
Diagnosis tests	0.266**	0.193*	-0.040	0.041						
Lab tests	0.365**	0.147	-0.081	0.017	0.422**					
Cost of surgeries	0.405**	0.126	-0.101	0.027	0.373**	0.367**				
Cost of emergency care unit	0.079	0.005	-0.142	0.059	0.210**	0.246**	0.197**			
Total cost of tamoxifen	1.000**	0.066	-0.363**	0.069	0.266**	0.365**	0.405**	0.079		
Total cost of the treatment	0.815**	0.150*	-0.198**	0.050	0.557**	0.478**	0.743**	0.204**	0.815**	

Notes: Correlation of Spearman (Rho); * p-value<0.05; ** p-value<0.001. In the correlation, sig indicates the p-value and the coefficient of correlation indicates the power of the correlation between the variables. The signal of this correlation indicates whether the correlation is positive (both variables raise in the same direction) or negative (when one of the variables raises and the other drops). P-value <0.05 is significant and the interpretation of the coefficient of correlation is: 0.00 to 0.19 – correlation well weak; 0.20 to 0.39 – correlation weak; 0.40 to 0.69 – correlation moderate; 0.70 to 0.89 – correlation strong; 0.90 to 1.00 – correlation very strong.

DISCUSSION

The variable time of treatment had a strong correlation in relation to the total cost of treatment (Rho 0.815). These two variables had a directly proportional correlation, whereas the fact that the longer the treatment, higher is the cost. The mean time of study treatment was 55 months. The values are close to the described in the studies of Guedes et al.[12], Brito et al.[13] and Oliveira et al.[14].

According to the Clinical Protocols and Therapeutic Guidelines in Oncology, the recommended time of treatment with tamoxifen is five years (60 months), but the current evidences suggest a protocol of ten years (120 months). Of the patients who initiated the treatment during the period of this study, 49.4% completed the five years treatment as determined[14]. The mean time of the treatment of this study was 4.6 years.

The advantages of hormone therapy, including increase of survival, are clinically evident and the free access to the drug in SUS contributes to this good prognosis. Studies ensure that the reduction of the mortality rates and the relapse of the disease are effective in fully fulfilling the

time of treatment. However, the results, many times, are not reached because of falling short from the total time of treatment. One of the main causes mentioned is the prolonged time of the therapy associated to the absence of tumor and/or symptoms[12,14].

In relation to the time of treatment, the mean of the total cost of the treatment for patients with time of treatment ≥55 months was R$ 2.316,13 treatment/year with standard deviation of ±506.60. This value is 6.55% greater than the mean of the cost of the treatment for patients with time of treatment <55 months, which was of R$ 2.143,66 treatment/year with standard deviation of ±126.60.

Age was one of the main risk factors for breast cancer with risk of death increased in tumors diagnosed after 50 years old[2,4,15]. The mean age-range obtained in this study differs from the studies of Leite et al.[6] and of Aguiar et al.[16], where the mean age was between 40 and 60 years. However, it is equivalent to the study of Haddad et al.[17], where the age range of the majority of the population was from 50 to 69 years. In this study, the minimum age was 25 years and the maximum, 95 years.

The category BI-RADs® 2 is indicative of benign findings whose conduct is the routine control of solid nodes and stable benign characteristics for more than two years, intramammary lymph nodes, implants, postoperatory architectural alterations. These characteristics are evidenced in the patients in adjuvant and palliative treatment of this study[18]. The results obtained herein in categories BI-RADs® are close to the data obtained in the study of Rocha[19].

In relation to co-morbidities associated to the use of tamoxifen, hepatic steatosis was shown to be the most relevant. This data is quite close to what was mentioned in the study of El-Beshbishy, 30%. The occurrence of hepatic alterations is described in the literature in more than 30% of the patients in tamoxifen. Among these changes, toxic hepatitis, non-alcoholic hepatic steatosis and necrosis are included. Despite its antiestrogenic action, tamoxifen has agonist actions to estrogen in liver receptors and in the lipid metabolism, which would provoke the hepatic alterations described[20,21].

The variables time of treatment and cost of the medical visits had a weak correlation and inversely proportional (Rho 0,363). In this case, it is not possible to affirm that the use of the medication for an extended time of treatment would reduce the number of visits, since the protocol and the necessity to renew the Authorizations for High Complexity Procedures at the Municipal Health Secretary to approve tamoxifen recommend visits at least at each four months. There is no consensus in literature about the frequency of the number of required visits to follow up patients in hormone therapy. The Oncology Consensus and Therapeutic Guidelines and Protocols recommend an average of at least three to six months of follow up for the majority of the cases. Limiting factors of this study as the case of the patients who were followed up by other professionals of complementary or private health system may have contributed for this correlation[4,8].

Detailed descriptions about the cost of medical and non-medical visits were not encountered in the literature for patients with mammary carcinoma in exclusive hormone therapy treatment, which hampered the comparative cost analysis.

It was possible to evidence the strong correlation between the cost of surgical procedures and the total cost of treatment (Rho 0.743). The correlation between these two variables is directly proportional, the patients who underwent any surgical procedure had a higher total treatment cost than the patients who had no surgical treatment according to data previously analyzed.

The data of this study differ from the data obtained by Kaliks et al.[22], where the mean cost per patient spent with mammography + setorectomy was R$ 12.125,00. However, the study encompassed patients in several disease staging and did not adopt the same criteria for our population, which hampered the comparative analysis. Studies that related the cost of surgical procedures in patients in hormone therapy exclusively were not encountered[22].

The number of mammographies per patient during the study was 0.59 tests/patient/year, with standard deviation of ±0.4. It was evidenced that the majority of the patients had a therapeutic follow up with annual request of mammography and biannual request[6] for those with metastasis.

In the study of Kaliks et al.[22], the mean cost per patient with chest radiography and abdomen ultrasound was R$ 651,00. In the study of cost-effectiveness of Peregrino et al.[23], the cost of the mammographies varied between R$ 29.69 (natural history of the disease as of 40 years old) until R$ 146,60 (annual screening mammography as of 40 years old and biannual from 50-69 years).

The correlation between the variables total cost of the treatment and cost of tamoxifen has shown to be strong (Rho 0.815) and directly proportional. The longer the time of treatment with tamoxifen, higher is its cost and impact over the total cost of the treatment. The recommended treatment with tamoxifen according to the document The Oncology Consensus and Therapeutic Guidelines and Protocols, is five years (60 months) with possibility of extension to 10 years (120 months) according to recent studies. Pursuant to previous analysis, the mean time of treatment of this study was 55.0 months or 4.6 years[5,8.]

The correlation between the time of the treatment and the cost of tamoxifen was very strong (Rho 1.00). The patients with time of treatment ≥60 months were those who presented the highest means of value in relation to the cost of tamoxifen and, consequently, of the total cost of the treatment. As formerly analyzed, the mean of the cost of tamoxifen represented more than 80% of the total cost of the treatment for patients of this study. Studies demonstrated that the longer the time of the treatment, highest is the long term survival rate and improved quality of life of the patients[12,13].

In the study of Kaliks et al.[22], the annual cost of the treatment with tamoxifen was R$ 1.095,00 per patient. In the study of Sasse et al.[3], the semiannual cost of tamoxifen for SUS patients (including the drug, tests and adverse events) would be R$ 563.67. The values utilized by the authors correspond to the tables similarly adopted in the current study, but for 2005[3,22].

It was not possible to model the linear regression for the costs because they failed to represent normal distribution and this is one of the conditions to run the test.

The main limitation of this study was the lack of description of chart information. Several patients were excluded from the sample due to lack of data that proved the diagnosis, as, for example, result of the tests and absence of data as staging, that hampered the comparative analysis with other bibliographic references.

Another limiting factor and which excluded several patients were the charts of patients attended in the ward who obtained the tamoxifen at the SUS Oncology Ward Pharmacy but were followed up by other professionals in other complementary or particular healthcare system.

The results of the present study reflect the data of a Brazilian philanthropic institution, but caution is mandatory if these data are extrapolated to a national scenario.

It were utilized the costs of Brasíndice® for tamoxifen because of the variation of prices of the quotes requested by the institution after negotiations and/or contracts. The results of this cost may vary among institutions.

The non-existence of publications, which chose the same variables adopted herein somewhat hampered the comparative analyzes of the results obtained as it was mentioned throughout the text.

CONCLUSION

The present study of cost-of-illness designed the clinical and pharmacotherapeutic profiles and stratified the direct medical costs related to the treatment during the study period and the influence of factors connected to the profile of the patient that could impact the direct medical costs as age, gender, co-morbidities non-associated to the use of tamoxifen, among others.

The economic evaluations of the health economics have the objective of helping the health managers in decision-taking in relation to the incorporation of health technologies as drugs, equipment and technical procedures, organizational, educational and information systems and support to social programs and protocols through which hygiene care is provided to the population[24].

Therefore, the managers can use the results obtained in the present study analyzed under the perspective of SUS a support tool for decision-taking for the incorporation of health technologies, ensuring either the individual right to the actually beneficial treatment or to the universal right of access to SUS.

CONTRIBUTIONS

Mariangela Adriane Seroiska contributed substantially for the conception, planning, collection, analysis and interpretation of the data, wording and final approval of the version published. Luana Lenzi contributed for the analysis and interpretation of data, critical review and final approval of the version published. Astrid Wiens contributed for the conception, planning, analysis and interpretation of the data, critical review and final approval of the version published.

ACKNOWLEDGEMENTS

DECLARATION OF CONFLICT OF INTERESTS
There are no conflicts of interest to declare.

FUNDING SOURCES
None.

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