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Relationship between physical activity practice and metabolic profile of postmenopausal women under treatment with aromatase inhibitors for breast cancer

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A B S T R A C T

Objective: To analyze the relationship between physical activity practice and metabolic profile of postmenopausal women under treatment with aromatase inhibitors (AIs) for the treatment of breast cancer.
Study design: Cross-sectional study, conducted with 101 postmenopausal women (aged 50–80 years). The sample was divided into two groups; group without cancer (GW; n = 65) and breast cancer group treated with AIs (GC; n = 36). Physical activity (PA) was evaluated by questionnaire. Correlations between physical activity and metabolic variables were made by Pearson's correlation coefficient and the magnitude of these relationships by linear regression.
Results: In GW, there were observed significant inverse correlations between physical activity and VLDL cholesterol ($\beta = -0.036$; 95% CI = −0.068; −0.004); triglycerides ($\beta = -0.036$; 95% CI = −0.015; −0.002); glycose ($\beta = -0.029$; 95% CI = −0.047; −0.012); and C-reactive protein ($\beta = -0.44$; 95% CI = −0.085; −0.003). However, for women under treatment of AIs there was no relationship between physical activity and metabolic variables.
Conclusion: The amount of physical activity practice is inversely related to lipid profile, glucose and C-reactive protein in women without breast cancer. This relation was not observed in the cancer survivors, suggesting that the use of aromatase inhibitors could influence or low intensity of physical activity.

Introduction

Cancer is a multifactorial disease that can be defined as abnormal and uncontrolled growth of cells of an organism [1,2] making it often invasive and metastatic, and can develop in any part of the body [3]. Breast cancer is the second most common type, accounting for 22% of women worldwide [4]. It is a common disease in industrialized and in developing countries. Recent studies show that this disease may be responsible for six million new cases in developed countries and 9.3 million in developing countries [5].

One of the most important risk factors for developing breast cancer is menopause, which is defined as cessation of menstrual cycle for at least one year [6]. Menopause has a major impact on the woman's body and promotes significant changes. Therefore, occurrence of breast cancer in postmenopausal women may be responsible for changes mainly in body composition, with greater weight gain and body fat, especially the fat trunk [7].

Moreover, the treatment of breast cancer is accomplished through aggressive procedures such as radiation, chemotherapy, immunotherapy and hormonal therapy or even surgical procedures such as mastectomy that can cause major physical, social and emotional changes [8]. Among these procedures, hormone therapy is the standard treatment for early breast cancer stage in women with hormone receptor positive (ER+) and it has been used for over

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two decades. Aromatase inhibitors (AIs), that is one type of hormone therapy, are substances that block aromatase enzyme responsible for converting androgens to estrogens in postmenopausal women. Thus, the pathway that transforms testosterone into estradiol, androstenedione into progesterone and modifies androstenedione (16OH) into estradiol are blocked [9].

Insufficient practice of physical activity has a major health impact and is associated with inadequate health conditions and development of several chronic diseases, especially metabolic syndrome, breast and colon cancer, and heart disease. This condition represents a significant public health problem [10,11]. According to scientific studies, physical activity has been recognize as an important strategy to assist in the physical and psychological rehabilitation of the patient [12].

Although the importance of physical activity practice to reverse the side effects of treatment for breast cancer, few studies in the literature correlate the physical activity practice with metabolic variables in women using aromatase inhibitors to treat breast cancer. Thus, the objective of this study is to analyze the relationship between the practice of physical activity and metabolic variables of postmenopausal women under treatment with aromatase inhibitors for the treatment of breast cancer.

Materials and methods

Sample

This is a cross-sectional study conducted from March 2015 to July 2015 in a city of southeastern Brazil. Women without breast cancer were invited through media (television and newspaper) and breast cancer survivors were recruited through a list of 348 patients provided by the clinical pharmacology department of oncology from the Public Regional Hospital in the city of Presidente Prudente, São Paulo state.

The inclusion criteria of the study for all women were: (i) age between 50 and 80 years; (ii) be postmenopausal (not have had a menstrual cycle for at least one year reported by the subjects) [13]; (iii) not be engaged on regular exercise for at least six months prior to evaluation; (iv) be free of muscle skeletal injuries; (v) be physically able to participate in physical training certificate by the medical doctor; (vi) have signed the consent form and formal clarification to participate in the research. Especially for breast cancer survivors, plus all the criteria mentioned above: use aromatase inhibitors and be in the stages I–III breast cancer. According to this, the study sample consisted of 101 postmenopausal women, being 65 without cancer and 36 cancer survivors treated with aromatase inhibitors.

The study was approved by the Research Ethics Committee of the Sao Paulo State University (number 6727715.1.0000.5402/2015).

Data collection

Anthropometry

Body mass was measured using a mechanical scale (Filizola) with a precision of 0.1 kg and a maximum capacity of 180 kg. Height was measured using a fixed stadiometer (Sanny), with precision of 0.1 cm and length of 2.20 m, according to the methodology proposed by Freitas Jr. et al. [17]. The values of weight and height were used to calculate body mass index (BMI).

Metabolic profile

Blood samples were collected and analyzed in a specialized laboratory, with 12 h of fasting for all variables. The collection was carried out in vacuum tube with gel separator without anticoagulant; after collection, the blood was centrifuged for 10 min at 3000 rpm to separate the serum from other components of the blood, and the serum was used for analysis.

For measurement of glucose was used a colorimetric enzymatic kit processed in a Autohumalyzer unit [14]. Abnormalities of glucose values were defined according to the reference value proposed by the American Diabetes Association [15].

It was evaluated the serum levels of triacylglycerol, total cholesterol, HDL-cholesterol and LDL-cholesterol by an automatic biochemical analyzer RAXT (Technicon, USA) C-reactive protein was measured using an enzymatic kit Elisa: Iimmulite 2000 analyzer (Siemens Healthcare Diagnostics) [16].

Physical activity

The Baecke Physical Activity Questionnaire was used to assess physical activity. This questionnaire assess physical activity in three different domains (physical activity at work, physical activity in leisure time and occupational physical activity). After the summation of the physical activities of these three areas, a dimensionless score that determines the practice of general physical activity was generated. This instrument has been validated for the Brazilian population by Florindo et al. [18]. This questionnaire has been also tested against the gold standard for physical activity evaluation (doubly labeled water) by Philippaerts et al. [19].

Statistics analysis

For statistical analysis, we performed the Kolmogorov-Smirnov normality test, which found that the sample had normal distribution, being expressed as mean and standard deviation. The sample characterization analysis was performed using the Student's *t*-test to display the variables stratified by women with and without the disease. The Pearson correlation coefficient was used to investigate the relationship between physical activity practice and metabolic variables. To verify the magnitude of these associations, linear regression (considering the total sample and also stratifying in women without cancer and women with cancer) was used in the unadjusted and adjusted (age, education level, marital status, type of job and time of menopause) models. All analysis were performed using a SPSS statistical software (version 15.0) with the level of significance set at 5%.

Results

The general characteristics of sample indicate that 25% of GC had high school while none of the women without cancer had done undergraduate degree ($p = 0.020$). There was no statistical difference in marital status, type of work and time of menopause between the groups.

In relation to age, weight, height, BMI and physical activity level, significant differences were not observed among women of both groups (Table 1).

Table 2 shows the relationship between physical activity practice and metabolic variables in total sample size and according to the groups. It is observed that higher amount of physical activity is inversely related to glucose in total sample size and VLDL, triglycerides, glycose and C-reactive protein in women of GW. However, this association was not observed in women of GC.

To check the magnitude of the relationship between physical activity practice and metabolic variables, a linear regression unadjusted and adjusted (age, education level, marital status, type of job and time of menopause) was performed. In unadjusted analysis, it was observed that higher physical activity practice was related to lower values of glucose in the total sample size and