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Protein intake in women with breast cancer before, during, and after treatment

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Abstract

Objective: Breast cancer is the most frequently diagnosed cancer in women accounting for 16% of cancer diagnosis.It is the second cause of cancer related deaths among women. Medical treatments such as chemotherapy can negatively interfere with nutritional status. The objective of this study was to assess the intake of proteins before, during and after chemotherapy treatment in a cohort of women with non-metastatic breast cancer (stage I, II) treated at the Valencian Institute of Oncology.

Methods: A three-day anthropometric and nutritional assessment was carried out using the DIAL program and the nutritional intake was compared with the Reference Intake values provided by the European Food Safety Authority.

Results: After the treatment, a statistically significant reduction in the mean protein consumption was observed (p-value=0.006), although it continues to surpass the Reference Intake in more than 50%. The risk of consuming proteins in excess of what is recommended in patients with breast cancer (1.3g proteins/kg/day) increases significantly (p=0.031) during and after the treatment.

Conclusion: Protein consumption decreases in women with breast cancer during treatment, and even more after the end of treatment. However, before, during and after treatment, protein consumption exceeds the RI established for the general population. The risk of consuming proteins over the recommended amount in patients with breast cancer is increased during and after treatment. The usefulness and possible benefits of nutritional intervention in these patients should be considered in order to improve their nutritional status and overall general health.

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Introduction

Cancer is the second leading cause of death worldwide, after cardiovascular diseases, with some 8.8 million deaths/year [1]. Among the various types of cancer, breast cancer is the second most common cancer in the world and the most frequent in women, in both developed and developing countries [2,3]. The incidence of breast cancer has increased in recent years, in Spain around 26,000 new breast cancer cases are diagnosed each year and 1 in 8 women will have breast cancer throughout their lives [4].

In a patient with cancer there is a high risk of malnutrition due to the characteristics of the disease and the treatments applied [5,6]. Therefore, it is essential to investigate the relation of nutritional status and dietary behaviors that occur before, during and after treatment, in order to know and avoid the increase in morbidity and mortality of cancer patients [7].

Alterations in the nutritional status and dietary intake contributing to the development of malnutrition have been observed during antineoplastic/chemotherapeutic treatments. Such treatments do not only affect the malignant cells but also affect the healthy ones producing side effects such as: alterations in the perception of smell and taste, loss of appetite, nausea, vomiting, alterations in the mucosa of the mouth between others, acute enteritis, constipation and anorexia among others [8-10]. Therefore, oncological treatments can produce macro and micronutrient deficits and it becomes of vital importance to carry out adequate nutritional therapy to improve the quality of life of the oncological patient [11].

A protein intake above the Reference Intake (RI) values provided by the European Food Safety Authority (EFSA) has been associated with increased survival in women with breast cancer during and after treatment [12-14]. Currently, there is growing interest in the quality of proteins, in particular essential amino acids, and their effects on preserving muscle mass, muscle signaling, glycolysis, bone health and satiety [15,16]. In addition, the benefits produced by proteins on lean body mass could be improved with physical activity [17-19]. A recent study that links protein intake and survival to breast cancer states that there is a lower risk of death with a higher protein intake, although they did not find a clear mechanism for that relationship [20]. Despite this, this benefit is not obtained from the consumption of all types of proteins, different studies claim that the excessive consumption of proteins from red meat and/or processed meat before, during and after treatment produces the reverse effect due to its high content of fats, salt, nitrates, hormones and extra antibiotics [10, 21-27].

The objective of this study will be to assess the evolution of protein intake before, during and after antineoplastic treatment in women with breast cancer and to determine if it was necessary to carry out a nutritional intervention in this regard.

Material and methods

Sample

This study was carried out in a cohort of 55 women who attended outpatient clinics of the Valencian Institute of Oncology (IVO), were diagnosed with non-invasive breast cancer (type I, II) and who were going to receive treatment with chemotherapy. The study protocol was approved by the IVO Ethics Committee (2013/23).

All women who met the inclusion criteria: being diagnosed with breast cancer (stage I and II) and whose treatment was chemotherapy were offered participation in the study. Those that agreed to participate, signed an informed consent. The period of data collection was between the second semester of 2015 and the end of 2017.

100 women were offered the opportunity to participate, of which 70 accepted (Figure 1). A total of three nutritional evaluations were carried out on the 70 women who participated: the first one after being diagnosed but before the start of treatment, the second in the middle of treatment and the third after the end of treatment. For this study, only those women who completed the follow-up in the three assessment periods of the cohort were included, and finally 55 women were included in the study (Figure 1). The exclusion criterion in the study: not to having delivered any one of the three food surveys or incomplete information in any of the surveys. Anthropometric data on patients was also collected.

Food and beverage records

To assess intake, the same three-day food questionnaire (24h/day) was used before, during and after treatment, which means a total of 165 food surveys were collected. The questionnaires were filled out by the patients without giving them previous dietary recommendations but having received instructions on how to fill out the questionnaire. To obtain information on protein intake, the DIAL computer program,which identifies the energy and the macro and micronutrients contained in the diet, was used [28].

Evaluation of misreporting

The nutritional intake of proteins was compared with the RI values established by the EFSA. The RI is calculated based on the estimated average needs of the population, and takes into account the current levels of physical activity and lifestyle of women in middle age. The RI used corresponds to moderately active women [29].

Statistical analysis

The mean and Standard Deviation (SD) of protein intake have been calculated in the three moments of the study and have been compared with the Analysis of Variance (ANOVA) test with Bonferroni correction. The percentage of the RI for protein consumed in each of the periods studied has been calculated and compared by the Chi-square test (X^2) with Bonferroni correction. The data are shown as means±standard deviations for continuous variables and as frequencies for discrete variables.A one-way ANOVAwas performed to determine the differences between the groups for continuous variables and the Chi-square test (X^2) with Bonferroni correction was used to determine the differences between the groups for continuous variables. The Hazard Ratio (HR) and its 95% Confidence Interval (95% CI) were calculated and the Trends Manteal-Haenzel test was applied.The protein intake taken as a reference level was the pre-treatment intake.All statistical analyzes were performed using the SPSS statistical package for social sciences version 22 for Windows, and statistically significant differences were considered in all comparisons with $p<0.05$.

Results

Table 1 shows the main characteristics of the cohort. A total of 55 women diagnosed with non-invasive breast cancer participated in the study.The age of women with breast cancer ranges from 30 to 79 years, with an average age being 51.49±11.17

years. The Body Mass Index (BMI) of the women is between 18.9 and 35.8; the average woman is within the overweight range with a BMI of 25.52±4.83 kg/m². The Physical Activity Level (PAL) of the women is between 1.20 and 1.64, the average women scores 1.48±0.19 for PAL meaning light physical activity.

Table 2 shows the values of protein intake in the different study stages.The average of proteins consumed by the patients in the different stages of the treatment is above the RI for general population in more than 50%. It can be observed that during treatment, protein intake is reduced in a statistically significant way (p-value=0.006), but even then remains higher than the RI.

Table 3 shows the number of women who have a lower and higher protein intake than the RI for patients with breast cancer, in each of the study moments. Protein consumption is greater than 1.3 g protein/kg/day in most patients [30,31]. In addition, the number of women who increase protein consumption is greater as the stages of treatment progress.

The risk of an intake higher than 1.3 g protein/kg/day is expressed with the Hazard Ratio (HR) and its Confidence Interval 95% (CI 95%), taking as a reference the intake prior to treatment. A pattern is observed in which the risk of consuming proteins above that recommended increased during treatment in a statistically significant way (p=0.031) and triples after treatment.

Discussion

In Spain, 30% of all female cancers correspond to breast cancer, and about 26,000 cases are diagnosed each year. According to the Spanish Association against Cancer (AECC), the majority of cases are diagnosed between 35 and 80 years old, with a maximum between 45 and 65 years which is similar to this study [4].

Although there are genetic risk factors related to breast cancer, it has been seen that only 5-10% of all cancers are attributed to genetic defects, while the remaining 90-95% are attributed to lifestyle and environment [32]. In this study, BMI and PAL were evaluated as influential factors in breast cancer. It is observed that the average woman diagnosed with breast cancer is overweight (BMI≥25), as defined by WHO and is sedentary or performslight physical activity (PAL=1.40-1.69), as defined by the Food and Agriculture Organization in 2001 [33]. In a study in which BMI is compared between patients with and without breast cancer, it is observed that BMI is higher in the case of women with breast cancer than without cancer [34]. Some studies affirm that there is a lower risk of breast cancer in women with normal weight and in women who practice physical activity [35-37]. Although genetic factors cannot be modified, lifestyle and environmental factors are potentially modifiable; therefore, they become a focus for a preventive strategy for breast cancer [32,38].

In patients with breast cancer, periods of prolonged fasting after chemotherapy sessions are common, but if this lasts>48h, loss of muscle mass can be promoted, increasing the deterioration of the patient's nutritional status. A study shows that, after 6 months of antineoplastic treatment, a decrease in bone mineral density and an increase in body weight occurs, due to an increase in fat mass and a decrease in muscle mass and strength, a phenomenon known as Sarcopenic Obesity (SO) [39,40]. A study conducted in Mexican women showed that premenopausal women increase their BMI, body weight and muscle weakness during chemotherapy compared to postmenopausal women [6]. This weight gain may be due to factors such as decreased physical activity, ovarian failure, increased caloric intake and decreased basal metabolism [29]. The decrease in physical activity that occurs in 96% of patients due to the effects of constant fatigue and lack of energy produced by chemotherapy may also contribute to weight gain and muscle weakness [30,31]. SO increases the number and severity of complications in patients with breast cancer [41-45]. Despite being multifactorial, it could be prevented with a protein intake of 1.2 - 1.5g/kg/day [31,40].

Proteins are important for the human body as they are involved in the regulation of various physiological functions and tissue formation. Therefore, they are essential for the growth and development of the body, as well as for the transport of substances and the supply of biological energy. A protein deficit can produce many diseases such as stunted growth and development, fatigue, nutritional edema and even death [46,47].

The purpose of the nutritional assessment in the present study has been to identify the protein imbalance and observe its evolution during and at the end of the chemotherapy treatment. There is a statistically significant reduction in protein consumption with antineoplastic treatment. A similar study evaluated the intake of macronutrients before and during treatment with chemotherapy and was compared with intake in women without breast cancer. The main source of protein intake was meat, bread, milk and dairy products. In the same way as in our study, during the chemotherapy, the protein intake was significantly lower. Symptoms such as decreased appetite, dry mouth, loss of taste and smell perception, nausea, vomiting, and difficulty chewing [8-10], induced by antineoplastic treatment are associated with lower dietary intake and manifest themselves by a lower intake of specific food groups [34].

Although with chemotherapeutic treatment protein consumption is reduced in a statistically significant way, the results show an excessive protein intake above the IR for the population in general, during all the phases of the study. In the same way it is observed that the risk of consuming proteins above the recommended values for women with breast cancer also increases during and after treatment.

Currently, the younger population consumes more protein, progressively moving away from the patterns of the Mediterranean Diet (MD) [48]. Different cohort studies show a beneficial relationship between high adherence to MD and the risk of breast cancer [49-51]. One specifically, states that 32.4% of stage I breast cancers and 2.3% of all stage II breast cancers could be avoided if the population had a higher adherence to MD [52]. These benefits are mainly due to an increased intake of fruits, vegetables, whole grains and extra virgin olive oil [53,54]. Several biological mechanisms can explain this beneficial effect of MD; it has the capacity to reduce inflammation by decreasing C-reactive protein, interleukin-6, homocysteine and fibrinogen levels, as well as other biomarkers of inflammation [55].

There is evidence that moderately higher protein intakes to RI can decrease muscle loss and help maintain or improve physical function with age [56]. A high protein diet in patients with breast cancer has been associated with a reduction in mortality [12-14]. But this benefit is not seen with the consumption of all types of proteins. Different studies show inconsistently that the consumption of red and/or processed meats during adolescence is associated with a risk of breast cancer, while its replacement by other sources of proteins such as legumes, soy, skimmed milk, poultry, nuts, fish and proteins of

vegetable origin during adolescence could reduce breast cancer incidence [57-62]. Although the mechanisms involved require further investigation, several mechanisms have been important in explaining the association between the intake of red and/or processed meat and the risk of breast cancer. High-temperature cooking of red meat results in carcinogenic byproducts, such as heterocyclic amines and polycyclic aromatic hydrocarbons, thus increasing the risk of breast cancer [63,64]. Fat, heme iron, and N-glycineuraminic acid found in red meat can promote inflammation, oxidative stress, and tumor formation [58,65,66]. On the other hand, the use of exogenous hormones to stimulate the growth of animals can leave residues in the meat, thus being a risk factor for breast cancer [67]. Another study suggests that low protein intakes during middle age followed by moderate to high protein intake in adults can optimize lifespan and health [68].

Patients with breast cancer have expressed the need for dietary support during antineoplastic treatment to improve their nutritional status, health and prognosis [69], since care for unmet needs increases during treatment with chemotherapy [70]. The Spanish Society of Basic and Applied Nutrition, together with the Society of Oncology and Palliative and Professional Health Care of Nutrition and Cancer, have established the correction of nutritional deficiencies, prevention of premature death associated with malnutrition and improvement of the quality of life of patients with breast cancer and tolerance to cancer treatment as targets to promote a rapid nutritional intervention and prevent the worsening of nutritional status. However, this algorithm moves away from a personalized nutritional intervention (since it lacks specificity in the calculation of nutrients, compliance with daily dietary requirements and personalized dietary suggestions according to taste, tolerance, socioeconomic status, cultural beliefs and the schedule of each patient) and objective (since there are no specific recommendations for the intake of macro and micronutrients in these patients). Due to the lack of nutritional guidelines for patients with breast cancer, the American Cancer Society suggests a nutritional approach that considers the nutritional guidelines published in 2007 by the National Institute of Health in the United States, which establish a decrease of the consumption of fat and sugars (<30% of the total energy), a strong base of fruits and vegetables (5-9 servings/day), in addition to suggesting meat, eggs and low-fat dairy as a source of animal protein (1-2 times/week each), preferring low-fat fish, poultry, turkey and pork loin and promoting physical activity [71-73].

Figure

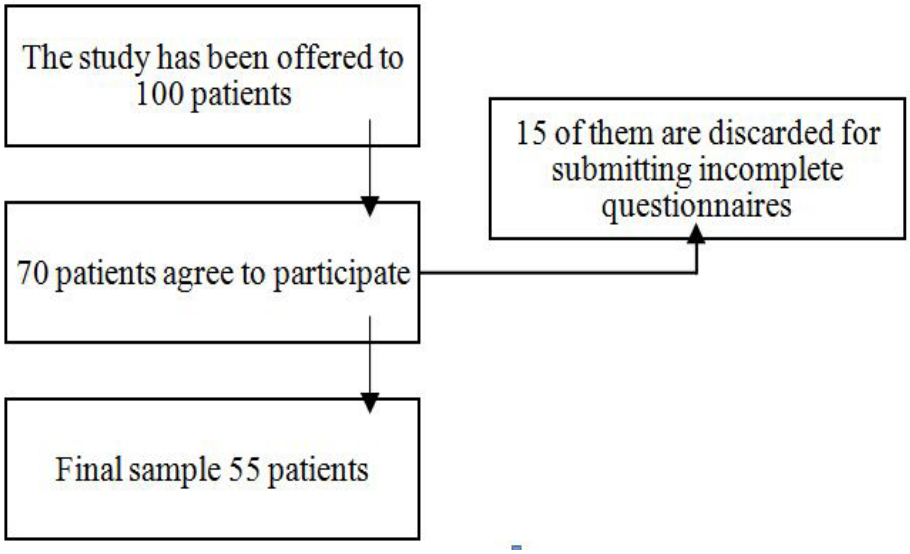

Figure 1: Flow chart selection of women with breast cancer participating in the study.

Tables

Table 1: Main characteristics of the cohort (n=55).

	Mean ± SD	Minimum	Maximum
Age	51,49 ± 11.17	30	79
BMI (kg/m²)	25,52 ± 4,83	18,9	35,8
PAL	1,48 ± 0,19	1,2	1,64

BMI: Body mass index; PAL: Physical Activity Level; SD: Standard deviation

Table 2: Protein intake in the three stages of the study.

	Mean±SD (Min– Max)	p-value	RI	% RI (Min – Max)	p-value
Before	86.19 ± 19.25 (54.90 – 143.00)			172.39 ± 38.50 (109.80 – 286.00)	
During	81.21 ± 17.22 (52.40 – 116.00)	0.006	50 g	162.40 ± 34.43 (104.80 – 232.00)	0.006
After	73.47 ± 13.97 (47.70 – 101.00)			146.94 ± 27.95 (95.40 – 202.00)	

Table 3: Relative risk according to the consumption of proteins in the three stages of study.

	<1.3g proteins/kg/day	>1.3g proteins/kg/day	HRc (CI 95%)	P-value trend	OR trend
Before	19 (51.35%)	18 (48.65%)	1 (Ref.)		
During	16 (43.24%)	21 (56.76%)	1.39 (0.55-3.46)	0.031	2.07 (1.07-4.02)
After	9 (24.32%)	28 (75.67%)	3.28 (1.22-8.84)		

EAR: Estimated Average Requirements; OR: Odds Ratio; CI: Confidence Interval; HRc: Hazard Ratio

Conclusion

Protein consumption decreases in women with breast cancer during treatment, and even more after the end of treatment. However, before, during and after treatment, protein consumption exceeds the RI established for the general population. The risk of consuming proteins over the recommended amount in patients with breast cancer is increased during and after treatment.

The study is limited to focusing only on protein intake and not on the consumption of energy, macro and micronutrients, in different foods or food groups. Therefore, it would be necessary to evaluate the intake of energy, macro and micronutrients and food groups before and during treatment with chemotherapy, in order to determine the association between the experience of specific symptoms and the intake of energy and macronutrients. In the same way, it would be necessary to determine if the protein consumption that is evaluated comes from the consumption of meat, fish or vegetables. It would also be necessary to determine the relation between the evolution of the breast cancer and the dietary sources of proteins.The results should be confirmed by additional studies such as larger prospective cohorts and randomized controlled trials.

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