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Original Article

ANTIOXIDANTS CONSUMPTION DURING CHEMOTHERAPY TREATMENT

Consumo de antioxidantes durante tratamento quimioterápico

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SUMMARY - ***Background*** - The cancer is defined as chronic multifactorial disease, in which cells have uncontrolled growth. Several factors contribute to its development, one of them is inadequate diet. The stages of initiation, promotion and progression of carcinogenesis have often been related to oxidative stress. ***Aim*** - To assess the consumption of antioxidants in cancer patients during the different cycles of chemotherapy. ***Methods*** - A descriptive exploratory study, including patients undergoing outpatient chemotherapy. To investigate the consumption of antioxidants, was prepared a semi-quantitative food frequency questionnaire (sqFFQ) and an anamnesis clinic-nutrition chart. ***Results*** - The sample consisted of 30 patients with mean age of 56.4 ± 2.3 years. According to the daily consumption represented by cycles, there was an adequate intake of vitamin C, vitamin E and zinc and inadequate intake of vitamin A and selenium. By dividing the study in the four quartiles of intake of antioxidants, there was adequate intake of vitamin A with 25% and inadequate amounts of vitamin C, vitamin E, Zinc in 25% of the sample and also selenium in all quartiles. Among the studied food sources considered rich in antioxidants, the most used were carrot, spinach, papaya, orange, soybean oil, sunflower oil, red meat, cheese and chicken. ***Conclusion*** - The studied population reached the recommended daily intake for antioxidants when it was analyzed in cycles of treatment, but there was high percentage of inadequate intake when divided into quartiles. Thus, the nutritional advice is an indispensable factor to help prevent and control cancer.

HEADINGS - Antioxidants. Neoplams. Drug therapy.

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RESUMO - ***Racional*** - O câncer é definido como enfermidade multicausal crônica, em que as células possuem crescimento descontrolado. Resulta de vários fatores, sendo um dos principais, a dieta inadequada. As fases de iniciação, promoção e progressão de carcinogênese têm sido frequentemente relacionadas ao estresse oxidativo. ***Objetivo*** - Verificar o consumo de antioxidantes em pacientes com câncer durante os diferentes ciclos de quimioterapia. ***Métodos*** - Estudo descritivo exploratório, incluindo pacientes em tratamento quimioterápico em ambulatório de quimioterapia. Para investigar o consumo de antioxidantes foi elaborado um questionário de frequência alimentar semi-quantitativo (QFASQ) e uma ficha de anamnese clinica - nutricional. ***Resultados*** - Amostra foi composta por 30 pacientes com idade média de 56,4±2,3 anos. De acordo com o consumo diário representado pelos ciclos, houve adequado consumo de vitamina C, vitamina E e Zinco e inadequado consumo de vitamina A e Selênio. Ao dividir a tabela estudada segundo os quatro quartis de consumo diário de antioxidantes, houve consumo adequado de vitamina A em 25% da amostra e inadequado de vitamina C, vitamina E, zinco em 25% da amostra e de também selênio em todos os ciclos. Entre as fontes alimentares consideradas ricas nos antioxidantes estudados, as mais consumidas foram cenoura, espinafre, mamão, laranja, óleo de soja, óleo de girassol, carne vermelha, queijo e carne de frango. ***Conclusão*** - A população estudada atingiu o consumo diário recomendado para os antioxidantes analisados quando dividida nos ciclos do tratamento, mas houve porcentagem alta de consumo inadequado quando dividida nos quartis. Desta forma, a orientação nutricional é um fator indispensável para auxiliar na prevenção e controle do câncer.

DESCRITORES - Antioxidantes. Neoplasias. Quimioterapia.

INTRODUCTION

Cancer, a term used to represent more than 100 diseases, including malignant tumors from different locations, is defined as a chronic disease multifactorial, in which cells have uncontrolled growth[14,29].

The development of its various forms is the result of an interaction between endogenous and environmental factors. Currently the population is highly exposed to risk factors such as smoking, sedentary life, to carcinogenic substances in the workplace and community and inadequate diet, which is the most notable factor[8,14]. According to a report by the International Agency for Cancer Research - IAR / WHO, the global impact of cancer has doubled in 30 years.

Malignant neoplasms constitute the second cause of death in the population since 2003, representing approximately 17% of deaths of known cause, reported in 2007 in the Mortality Information System. In Brazil, the estimates for the year 2011, show 489,270 new cases to occur[14].

The stages of initiation, promotion and progression of carcinogenesis have often been related to oxidative stress, characterized in circumstances where the excess of free radicals results in tissue damage or production of toxic or harmful to the tissues. A body found in oxidative stress occurs when an imbalance between the pro-oxidants and antioxidants, so that the former are predominant[9,19,25].

Antioxidants are defined as any substance which, when present in low concentrations in comparison to an oxidative substrate, significantly delays or inhibits its oxidation. Among the key enzymes responsible for the body's antioxidant defense are superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), which constitute the first defense of endogenous neutralization of reactive oxygen species (EROS). The cells try to keep low amounts of superoxide and hydrogen peroxide, thus preventing the formation of hydroxyl radical. The non-enzymatic defenses are composed mainly of antioxidants, eg glutathione (GSH), vitamin A, vitamin C, vitamin E, zinc and selenium[12].

Antioxidants act in three rows of organic defense against EROS. The first is the prevention, characterized by protection against the formation of aggressive substances. The second is the intercept, antioxidants intercept free radicals, which once formed begin their destructive activities. And the last is the repair that occurs when the first two lines were not completely effective and the products of destruction by EROS are continuously formed and can accumulate in the body[15].

Among the benefits of antioxidants, there is the capacity they have to increase the effects of anticancer drugs and, thereby, decrease the dose of these drugs without affecting the therapeutic effect, providing a reduction of side effects[15]. Such concomitant administration is also important because it appears to protect healthy cells from the action of drugs, particularly the tissues of a rapid cell proliferation. Another beneficial fact is that the antioxidants alone can control tumor growth without producing toxicity, but less efficiently than antiblastic drugs, but when administered together to obtain the desired effect. Studies of this association show the great importance of maintaining the levels of these nutrients for cancer patients to provide better quality of life and greater survival[16,23,27], requiring only the recommended intake as the RDA's and supplementation in cases of malnutrition .

The continued growth as well as the aging population, will significantly impact the cancer in the world, have become key strategies to prevent and control cancer[14]. The existence of sufficient antioxidants, both endogenous and exogenous, represent major difference between health and disease[20]. The interactions between antioxidants and anticancer drugs, result in decreased production of tumor cells with fewer side effects[23,27].

Thus, this study aimed to investigate the use of antioxidants in patients in cycles of chemotherapy.

METHODS

It is descriptive exploratory study of quantitative character, comprising adults of both genders with a diagnosis of cancer, undergoing chemotherapy. The sample was recruited in the outpatient chemotherapy at a hospital in Santa Maria, Brazil, with non-probability sampling.

Inclusion criteria were patients over 20 years, undergoing chemotherapy from the 2nd cycle. Exclusion criteria were patients who had less than 20 years, undergoing chemotherapy in the 1st cycle and had other diseases besides cancer.

Clinical-nutrition anamnesis was applied aiming to collect data such as identification, age, sex, type of cancer and chemotherapy treatment cycle.

Data collection was initiated after approval by the Ethics Research Center Franciscan University, under protocol number 090.2010.2, and patient consent, after signing the consent form, according to the guidelines and standards on research involving human subjects included in Resolution No. 196/96 of the National Health Ministry of Health (1996).

Food consumption

It was investigated using a food frequency questionnaire semi-quantitative (sqFFQ). It was divided into five groups: vitamin A, vitamin C, vitamin E, zinc and selenium. In each of the food groups, was determined food intake on a daily and weekly. The week was divided into a scale ranging from 0 to 4, where 0 does not consume anything, 1 less than once a week, 2 one to two times a week, 3 three or four times in a week, and 4 more than five times week.

The sqFFQ was prepared from dietary sources with reasonable amounts of these nutrients, often consumed by the population, in addition to foods containing these antioxidants characterized as major sources, based on food composition tables[21]. The sqFFQ was applied individually, once.

The weekly consumption was assessed by first selecting the most food sources rich in antioxidants[17]. Were considered dietary sources of vitamin A: liver, beat pudding, carrots, spinach. Sources of vitamin C were: pepper, orange, papaya, mango. The vitamin E were: sunflower oil, soybean oil, avocado, margarine. The zinc were: red meat, turkey, peanuts, cheese. The selenium were brown-and-stop, wheat germ, salmon, chicken.

Statistical analysis

Daily intake was analyzed by comparing the average quantities consumed between cycles and the quartiles, using one-way ANOVA followed by Duncan's test to a variable of significance of 5%. The statistical test used to check the consumption of these foods, compared with the cycles was the test-T, followed by Duncan's test with significance level of 5%. Statistical analysis was performed in Statisct 6.0. Data were expressed as mean ± standard error (SE).

RESULTS

The sample consisted of 30 patients, 80% female (n = 24) and 20% male (n = 6), whose average age was 56.4 ± 2.3 years. There were patients from the 2nd to 6th cycle. As the 3rd and 5th numbers were lower than the other, they were grouped the 2nd and 4th cycles respectively.

By splitting the table in the four quartiles of intake of antioxidants was observed that the average daily intake of vitamin A was higher in the 6th cycle. However 25% of the sample reached the recommended daily intake according to the RDA's in every cycle since the 2nd cycle the sample was composed only by females. Was observed significant differences between the first and last quartile (Table 1). According to the cycles, the average daily intake of vitamin A showed inadequacy in all cycles (Figure 1).

The average daily intake of vitamin C in the sample was within the recommended RDA's for both genders in all cycles (Figure 2), but, according to quartile of intake showed that 25% of the sample (quartil1) had low intake of vitamin C. In the 2nd cycle was no statistical difference between quartile 1 and quartile 4 consumption.

TABLE 1 - Daily consumption of antioxidants in cycles according to the first and last quartiles

Cycles	Antioxidants	Quartile 1	Quartile 4	P
2nd Cycle	Vitamin A (g / d)	139,8±9,6	777,2±204,8	0,021*
	Vitamin C (mg / d)	13,8±4,35	234,5±48,6	0,0042*
	Vitamin E (mg / d)	11,33±0,33	109,5±80,11	0,34
	Zinc (mg / d)	1,6±0,46	19,08±11,7	0,18
	Selenium (mg / d)	3,05±0,5	9,8±1,1	0,0015*
4th Cycle	Vitamin A (g / d)	110,1±11,8	930,7±339	0,073
	Vitamin C (mg / d)	12,35±4,6	310,9±54,7	0,057
	Vitamin E (mg / d)	11±0	27,5±4,6	0,023*
	Zinc (mg / d)	1,44±0,04	37,7±16,9	0,19
	Selenium (mg / d)	3,12±0,6	47,3±17,7	0,067
6th Cycle	Vitamin A (g / d)	272,9±12,4	972,9±120,6	0,028*
	Vitamin C (mg / d)	17,13±1,5	187,82±89,3	0,007
	Vitamin E (mg / d)	11±0	32,4±1,4	0,004*
	Zinc (mg / d)	3,11±0,4	88,8±35,8	0,13
	Selenium (mg / d)	1,44±1,44	29,7±5,7	0,041*

Significance observed (P <0.05) between quartile 1 and quartile 4.

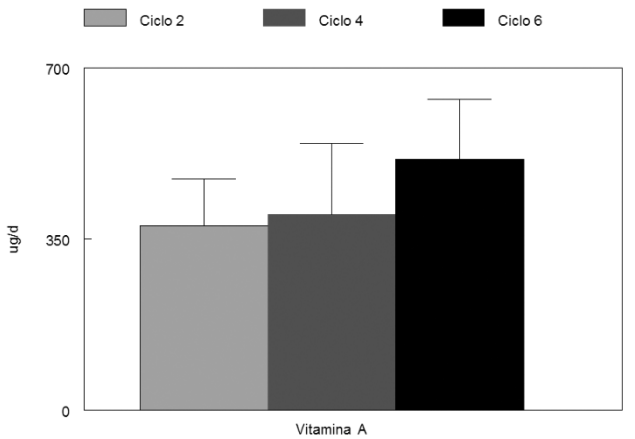
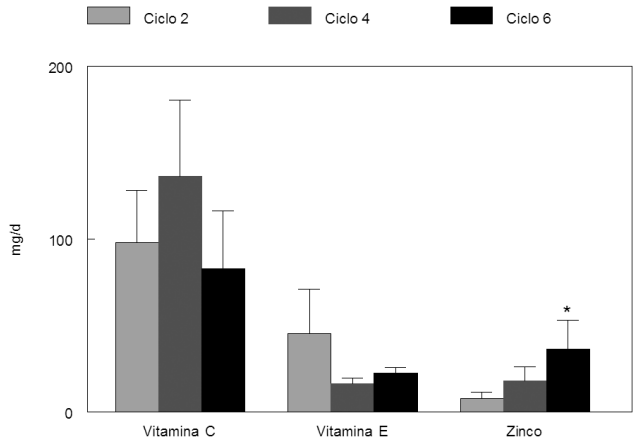


FIGURE 1 - Daily consumption of vitamin A and selenium in the different cycles of chemotherapy

Figure 2 shows average daily intake of vitamin E in all cycles, but according to quartiles of intake (Table 1), it can be seen that in the first quartile, ie 25% of the population, the use of vitamin E in all cycles was inappropriate.

The average daily intake of zinc was adequate in all cycles, showing a statistical significant increase from 6th cycle in relationship to cycle 2 (Figure 2). However, observing quartiles of intake (Table 1) it can be seen inadequate intake in the 1st quartile and consumption that exceeded daily intake limits in 4th quartile in the 6th cycle of chemotherapy.

With regard to selenium, there is a low average



Data expressed as mean ± standard error. ANOVA followed by Duncan's test (p> 0.05). (*) Statistical difference (p = 0.035) compared to cycle 2

FIGURE 2 - Daily consumption of vitamin C, vitamin E and zinc in the cycles of chemotherapy

TABLE 2 - Mean and standard error of the weekly consumption of foods rich in antioxidants in the different cycles of chemotherapy

Antioxidants	Food	2nd Cycle	4th Cycle	6th Cycle
Vitamin A (mg / day)	Liver	0,77±0,20	0,70±0,30	0,42±0,20
	Sweet potato	0,92±0,34	1±0,42	1,42±0,42
	Carrot	2.38±0,36	3±0,39	2,14±0,14
	Spinach	1±0,32	2±0,51	1,85±0,34
Vitamin C (mg / d)	Pepper	1,30±0,38	0,60±0,40	0,85±0,40
	Orange	2±0,33	2,2±0,35	1,57±0,42
	Papaya	2,92±0,41	2±0,47	3,57±0,29*
	Mango	1,15±0,27	1±0,29	1,28±0,28
Vitamin E (mg / d)	Sunflower oil	1,23±0,53	2±0,66	2,28±0,80
	Soybean oil	2,77±0,53	2±0,66	1,71±0,80
	Avocado	0,61±0,24	1±0,25	0,71±0,18
	Margarine	2,23±0,48	1,70±0,49	1,14±0,59
Zinc (mg / d)	Red meat	3,15±0,19	3,10±0,27	3,28±0,56
	Turkey	0,30±0,13	0,70±0,33	0,28±0,18
	Peanut	0,92±0,30	1,40±0,45	1,77±0,48
	Cheese	3±0,25	3,2±0,32	3±0,48
Selenium (mg / day)	Brazil nut	0,53±0,26	1,20±0,55	1,14±0,34
	Wheat germ	0,61±0,24	0,20±0,13	0,42±0,29
	Salmon	0,30±0,13	0,1±0,1	0,57±0,36
	Chicken	2,30±0,17	2±0,25	2.85±0,34*

(*) Range from zero to four, where zero = do not consume, 1 = consumption less than once a week, 2 = use once or twice a week, 3 = consumption of three to four times a week, 4 = consumption of five or more vezes. Test-t followed by Duncan's test.
(*) Significance observed (P <0.05)

daily intake in all cycles (Figure 1). When establishing the daily intake according to quartiles, it was observed that there was also a low intake in all cycles, according to the RDA's.

Table 2 shows the weekly intake of food sources considered rich in antioxidants studied in this research.

The most consumed foods rich in vitamin A are carrots and spinach, being consumed more frequently in the 4th cycle of chemotherapy. The most consumed food sources of vitamin C were the papaya and orange, and papaya consumed significantly more in the 6th cycle of chemotherapy cycles compared to 2nd and 4th (p = 0.025). Vitamin E was the most consumed food sources, soybean oil, followed by sunflower oil, with a weekly average frequency of twice a week in all cycles. Zinc was more consumed per week through the red meat and cheese, with average weekly consumption of 3 to 4 times in all cycles. The main source weekly intake of selenium was chicken meat, and consumed significantly more in the 6th cycle of chemotherapy (p = 0.027).

DISCUSSION

The cancer results from interactions between endogenous and environmental factors, being the most prominent, diet[7,29]. Through epidemiological studies, it is possible to identify relevant associations that exist on dietary patterns and prevalence of cancer[2,4], and feeding has an important role in the stages of initiation, promotion and progression of disease[10].

The food frequency questionnaire semi-quantitative (sqFFQ) was chosen as one of the best methodological tools for studies linking diet and disease; it quantifies the usual food intake of populations and has good reproducibility[3,22]. Its disadvantages are present a very extensive list of foods - staying too long and perhaps tedious to the respondent - and the possible loss of information on the consumption of some foods not included in the questionnaire[28].

Vitamin A was the first fat-soluble vitamin to be recognized and beta-carotene is the carotenoid with the highest power of formation of this vitamin found in nature, being able to confer protection against various types of tumors in animals[18]. According to the division of quartiles, this study showed a higher intake of vitamin A in the 6th cycle, being appropriate in different cycles, which, according to the RDA's, it is recommended 700µg for women and 900µg for men above 20 years old. Considering this vitamin, the mechanism involved in carcinogenesis is unclear, however, its action seems to be recognized by blocking the initial phase of mammary tumorigenesis, as well as acting in the regulation of cell differentiation, preventing increasing cells with malignant characteristics[26]. It is therefore considered important to recommend the food sources of antioxidant, such as carrots and spinach in this study, to act in the regulation of cell differentiation.

The daily intake of vitamin C has been shown adequate in all cycles, unlike a case-control study that showed dietary recall in three days, that 29% of cases and 3% of controls consumption had less than 50%[16] of the RDA. Based on the antioxidant, this vitamin has its possible mechanism of action as a blocker of carcinogenesis. Scientific studies are few and controversial, but a meta-analysis that assessed the risk of breast cancer, in publications from 1982 to 1997,

showed an inverse relationship between the relative risk of this type of cancer and consumption of vitamin C. In the study by Gandini et al.[6], 2000, vitamin C appears to be protective against breast cancer. According to the RDA's, the recommended intake of this vitamin is 75 mg for women and 90 mg for men over age 20.

Vitamin E has the task of preventing tumor cells continue the cell cycle, stopping them in G1 phase (longer period of cell growth) and leading to apoptosis[16]. This study revealed that in every cycle the daily recommendations were reached, but according to quartiles, 25% of the sample (quartile 1) did not reach the recommended intake. The RDA's are 15 mg for both sexes over 20 years. An inverse association between intake of vitamin E and breast cancer in Chinese women. This is one of the most important non-enzymatic lipophilic antioxidants, which act mainly against lipid peroxidation, removing peroxyl radical[6]. The more important is the alpha-tocopherol and is involved in the prevention of alopecia, one of the many physical and psychological stress caused by anticancer agents[13]. In a study that examined 1995 women with HPV infection - which is present in 94% of cases of cervical cancer - it was observed less infection in patients with higher concentrations of alpha-tocopherol[11].

The consumption of zinc, was found that the intake in the 6th cycle in quartile 4 exceeded the recommended limits, and an adequate intake quartile was not achieved in cycles, but when you compare the cycles, the intake was in accordance with the recommendations, which according to the RDA's is 8 mg for women and 11 mg for men over age 20. It is really important, because its deficiency results in a variety of immunological defects and symptoms as hypogeusia, delayed healing, various forms of alopecia and skin lesions[17].

Regarding the consumption of selenium may be noted that the sample did not reach the recommended daily intake according to the RDA's, which is 55 mg for both sexes over 20 years and was inadequate in all cycles. Selenium has great importance for humans, because their low levels in cells and tissues give lower concentrations of the antioxidant enzyme glutathione peroxidase; this results in greater susceptibility of cells and the organism to oxidative damage induced by free radicals[24]. Selenium deficiency is also an important factor predisposing the development of tumors. Epidemiological studies show an inverse relationship between selenium levels in plasma and incidence of cancer[5]. This lower energy consumption can be justified by the food on the list that are not part of the usual diet, except the chicken.

All patients received nutritional guidance, provided by the hospital nutritionist, every cycle, as recommended by the National Nutrition Oncology Consensus, 2009. The differences with existing studies can be justified by the 2009 Consensus permission of some foods, forbidden during chemotherapy. The inadequacies of daily intake of antioxidants occurred in this study may have happened by the existence of side effects of drugs, which were present in some cycles, causing a series of clinical symptoms, eg, nausea/vomiting, diarrhea or constipation, reported by some patients or, also, by the different nutritional guidance during treatment.

CONCLUSION

The population reached the recommended daily intake for antioxidants analyzed when divided into cycles of treatment, but there was high percentage of inadequate intake when divided into quartiles. Thus, the nutritional advice is an indispensable factor to help prevent and control cancer.

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