

Dietary intake of antioxidants in patients with myelodysplastic syndrome



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ABSTRACT

Introduction: Changes in lifestyle, including eating habits, are determining factors in the possibility of protecting the body against the development of neoplastic tumors, including Myelodysplastic Syndrome (MDS). Objectives: To evaluate the usual intake of antioxidants in patients diagnosed with MDS. Methods: Cross-sectional study in a tertiary university hospital in Ceará. Participants were 102 patients with MDS and 102 healthy individuals, matched according to sex and age. Food consumption was evaluated through 2 24-hour recordings, and the nutritional orientation of the intake of antioxidant micronutrients (vitamins A, C and E and the minerals zinc, selenium and magnesium) was analyzed. Results: Most participants were female (62.7%). The mean age of patients with MDS was 72.07 years \pm 11.63 and of controls was 69.24 \pm 9.24 ($p = 0.066$). Among the MDS group, 77.5% were aged 65 years or older. The nutrients with the highest prevalence of inadequacy among patients with DMS were selenium (100.0%) and magnesium (98.0%). There was no difference in the prevalence of inadequate consumption of vitamin A, C, E, magnesium, selenium and zinc between the group with MDS and controls ($p > 0.05$). Patients with MDS older than 65 years had significantly lower consumption of vitamin C ($p = 0.037$) and selenium ($p = 0.004$) than



the group of young patients. Conclusion: The study showed a high prevalence of inadequate consumption of antioxidant vitamins and minerals among patients with MDS and a healthy population, with emphasis on the lower intake of vitamin C and

selenium associated with the group with MDS aged over 65 years.

Keywords: Food Consumption, Micronutrients, Antioxidants, Neoplasms, Leukemia Myeloid Acute, Carcinogenesis.

1 INTRODUCTION

Myelodysplastic syndrome (MDS) is a type of hematological cancer characterized by a set of disorders in the multiplication of hematopoietic stem cells that occurs in the process of hematopoiesis, with increased programmed cell death (apoptosis) and increased risk for the development of Acute Myeloid Leukemia (AML). Although it can happen in any age group, it is a more common syndrome in the elderly, usually diagnosed at 70 and the risk increases exponentially after 50 years^{1,2}.

The probability of neoplasms in a population is related to individual biological characteristics, socioeconomic, political and environmental conditions that surround them, in addition to risk and protective factors³. The possible association between MDS and nutritional aspects is still poorly studied. In a study conducted in Greece found that poor eating habits, such as excess red meat and alcohol, low intake of fruits and antioxidants were associated with increased risk in the emergence of this type of cancer⁴.

The imbalance between the production of Reactive Oxygen Species (ROS) and their elimination by antioxidants results in oxidative stress in cells and tissues. Consequently, becoming a chronic event, there is an etiological influence for chronic non-communicable diseases, including neoplasms. Since the generation of Free Radicals (RL) stimulates events related to carcinogenic processes⁵.

Nutritional aspects, including inadequate antioxidant intake, are associated with the emergence of neoplasms, including MDS. Food choices can potentiate or inhibit oxidative stress. Justified by the fact that oxidative stress can be stimulated by extrinsic and intrinsic factors, therefore, a balanced diet, with an adequate consumption of macro and micronutrients, including antioxidant elements, is a possible way to prevent metabolic disorders, including carcinogenic processes^{6,7,8}.

Antioxidants are substances capable of delaying or inhibiting the oxidation of a substrate. They play a role related to the protection of healthy cells against the oxidizing action of RL. Higher plasma concentrations of antioxidants may be associated with the prevention of cardiovascular diseases and cancers⁹.

Studies show that antioxidant substances can decrease oxidative damage in DNA playing a key role in the process of carcinogenesis, decreasing the risk of cancer. Thus, eating habits may play an important role in this process, increasing or not the state of metabolic stress¹⁰.

In this context, it is important to evaluate the relationship between the consumption of



antioxidants and neoplasms, especially myelodysplastic syndromes, since there is a scarcity of studies with this population. Thus, the aim of the study was to evaluate the habitual consumption of antioxidants (vitamins A, C and E, the minerals selenium, zinc and magnesium) in a patient diagnosed with MDS and to compare the amounts ingested to those recommended, evaluating the prevalence of inadequacy and the average consumption of antioxidant nutrients between the group of patients and healthy individuals.

2 METHODS

The study was of a cross-sectional type, carried out in the hematology outpatient clinic of a tertiary level university hospital in the state of Ceará, through voluntary agreement, with the signing of the free and informed consent term. Patients with MDS were evaluated and for comparative purposes, healthy individuals without the disease, paired according to sex and age. The research was submitted to and approved by the Research Ethics Committee of the institution, opinion n° 1.513.488.

Food consumption data were studied through the application and analysis of the 24-hour two-day recall, one of which was a weekend day. As a facilitating instrument, the photographic record with illustrations of household items and portions of food was used¹¹. The foods were recorded in homemade measurements, as well as the preparations contained in the recalls with the respective measurements transformed into weight measurements^{12,13} and recorded in the Dietwin Professional Plus® Nutritional Assessment Software, and a quantitative analysis of the participants' food consumption was performed, based on the Dietary Reference Intakes (DRIs)¹⁴. Nutritional adequacy was analyzed regarding the intake of antioxidant micronutrients (vitamins A, C and E and the minerals zinc, selenium and magnesium).

The evaluation of the qualitative adequacy of the consumption of antioxidant vitamins was based on *the RDA (Recommended Dietary Allowance)*, being considered as probably adequate intake the consumption equal to or above the RDA. The criteria for quantitative analysis of minerals were based on Otten, Hellwig and Meyers (2006)¹⁴.

To calculate the adequacy of the nutrients, a statistical analysis was used, which compared the average intake of the participants with the *Estimated Average Requirement (EAR)* of the nutrient. The calculation also took into account the CV (Coefficient of Variation) and the DP_{intr} (intrapersonal standard deviation estimate). A CV of 10% was considered for the micronutrients analyzed. As a result of the equation, a z-score was found, allowing the determination of the probability of adequacy of the intake of each nutrient. Intake was considered adequate when the probability of adequacy was equal to or greater than 85%, with $z=1.0515$.

The Statistical Productant Service Solutions - SPSS® (version 21) was used for the statistical analyses. The discrete variables, obtained by counting, were analyzed by frequency dispersion by the



chi-square test (χ^2). If the number of available information was lower than the minimum limit for χ^2 , Fisher's exact test was applied. The means were compared using the Student's t test (parametric) or Mann-Whitney test (non-parametric). The results were expressed as mean \pm standard deviation, with $p < 0.05$ defined as statistically significant.

3 FINDINGS

The study sample consisted of 102 patients with MDS and 102 healthy individuals. Most of the study participants, 62.7% (n=64), were female. The mean age of patients with MDS was 72.07 ± 11.63 years [38 - 96] and of the control group was 69.24 ± 9.24 years [40 - 92]. There was no significant difference between the age of the MDS and control groups ($p = 0.066$). According to the age among the MDS group, 77.5% (n= 79) of the patients were 65 years of age or older (Table 1).

Table 1 - Gender and age of patients with myelodysplastic syndrome (n= 102).

Variables	N	%
Gender		
Female	64	62,7
Male	38	37,3
Age		
< 65 years	23	22,5
≥ 65 years old	79	77,5

According to the association between the habitual intake of antioxidant vitamins and minerals, there was no significant difference in the average habitual intake of the following nutrients: vitamin A ($p = 0.489$), vitamin C ($p = 0.387$), vitamin E ($p = 0.423$), magnesium ($p = 0.285$), selenium ($p = 0.307$) and zinc ($p = 0.632$) between the MDS group and the control group (Table 2).



Table 2 - Comparison between the habitual food intake of patients with MDS and the control group.

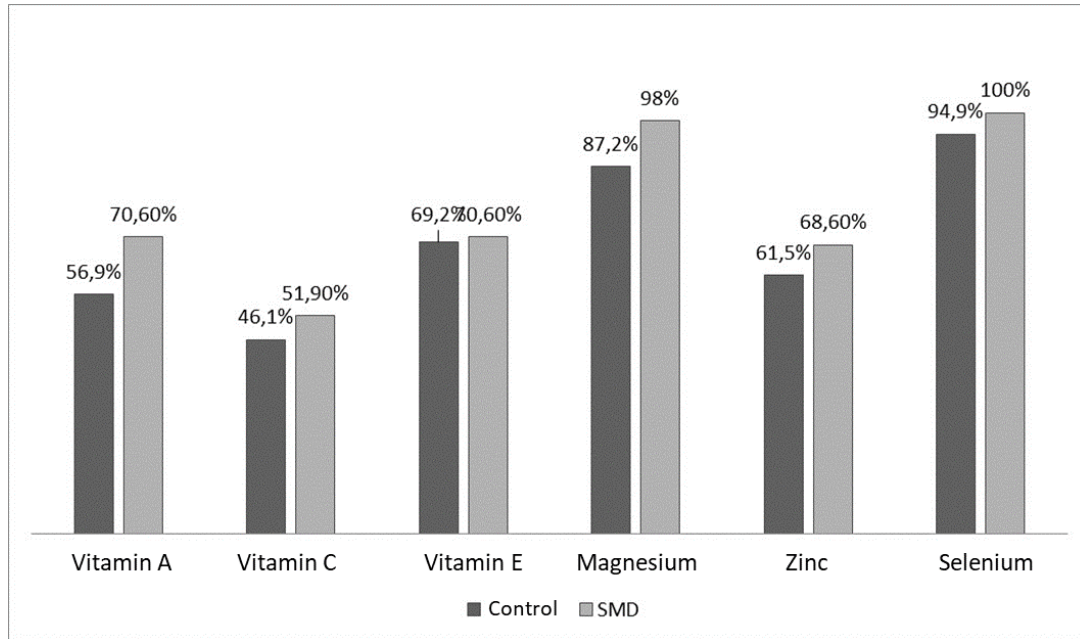
Antioxidant nutrients	SMD Group Mean +/- SD	Control group Mean +/- SD	p value
Vitamins			
Vitamin A ($\mu\text{g/day}$)	699,91 \pm 341,1	653,49 \pm 388,8	0,489 ¥
Vitamin C (mg/day)	161,43 \pm 65,04	287,67 \pm 99,9	0,387*
Vitamin E (mg/day)	10,42 \pm 3,75	9,76 \pm 5,68	0,423*
Minerals			
Magnesium (mg/day)	191,87 \pm 61,30	204,53 \pm 66,11	0,285*
Zinc (mg/day)	8,08 \pm 3,28	7,45 \pm 2,53	0,632*
Selenium ($\mu\text{g/day}$)	54.42 \pm 38.22	62.26 \pm 46.31	0,307 ¥

Legend: ¥ Tests by Mann-Whitney. * Student t tests.

The high prevalence of inadequate intake in both groups were: selenium and magnesium. For these micronutrients, prevalence rates of inadequate intake were around or above 87%. Selenium had an inadequate consumption of 100% for the group of patients with MDS. Regarding antioxidant vitamins, inadequate intake of vitamin A, vitamin C and vitamin E was between 51.9% and 70.6% for the MDS group, being higher than the control group (Graph 1).



Graph 1 - Prevalence of inadequate habitual consumption of antioxidant vitamins and minerals in the control group and patients with MDS.



When considering the mean value of dietary intake of nutrients, it was found that patients with MDS older than 65 years had significantly lower usual intake of vitamin C ($p= 0.037$) and selenium ($p= 0.004$) (Table 3).

TABLE 3. Comparison between the usual dietary intake of antioxidant vitamins and minerals of patients with MDS according to age.

Antioxidant nutrients	Age < 65 n = 23 (22.5%)	Age ≥ 65 n = 79 (77.5%)	p value
Vitamins			
Vitamin A (µg/day)	848,9 ± 133,0	984,8 ± 142,8	0,430
Vitamin C (mg/day)	291,1 ± 116,1	123,6 ± 31,4	0,037
Vitamin E (mg/day)	15,09 ± 8,49	13,96 ± 6,88	0,657
Minerals			
Zinc (mg/day)	7,51 ± 2,70	8,25 ± 3,43	0,246



Selenium ($\mu\text{g}/\text{day}$)	73.83 ± 36.34	48.77 ± 73.09	0,004
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4 DISCUSSION

Regarding the clinical characteristics of the patients in this study, the majority were female (62.7%). Regarding age, most participants were elderly aged ≥ 65 years. Patients with MDS had a mean age of 72.07 ± 11.63 years, while the control group was 69.24 ± 9.24 years ($p=0.066$).

Studies confirm the higher incidence of MDS among the elderly. It is noteworthy that clinical characteristics of patients with MDS change according to geographic location, which can be justified by genetic, occupational, and lifestyle changes, including eating and economic habits^{16,17}. Unlike the findings of this study, most studies with MDS find a higher prevalence of the disease among men, which may be associated with greater occupational exposure and lifestyle^{17,18,19}. And the higher prevalence of females in our study may be related to the greater demand for health services by this group.

Mean ages lower than ours were found in other studies. A cohort study that evaluated 7012 patients in 11 different countries, used for the development of the IPSS-R, mean age was 71 years²¹. In another study with 476 participants with MDS from 12 treatment centers in Brazil, they were evaluated and 68.3 years was the mean age²⁰. Adding to the studies, a group of researchers evaluated 345 Brazilian patients and found an average of 65 ± 17 years²⁰. In a recent study in Ceará, 288 patients with MDS were evaluated and the mean age found was 69.3 ± 15.6 years²¹. On the other hand, in an American cohort of 54,953 patients, the mean age was 76 years¹⁹. However, in all the studies cited, we can observe that the pathological state is present in patients with a mean age above 60 years.

It is important to show the high prevalence of vitamin and mineral inadequacy between the two groups evaluated. The micronutrients analyzed have an anti-inflammatory role and act in the fight against ROS. Another study that evaluated the intake of antioxidant minerals, carried out in Brazil, with elderly over 60 years, showed insufficient intake of all the minerals analyzed, which were copper, zinc, manganese and selenium²². This study did not find significant differences between the values found in the prevalence of inadequate consumption of antioxidant vitamins and minerals between the two groups studied.

Previous studies, evaluating the general Brazilian population, have shown high rates of inadequate consumption of antioxidant vitamins and minerals. Another study found a higher percentage of inadequacy in the consumption of antioxidant vitamins compared to minerals²³. While in our study, the highest prevalence of inadequacy occurred in the consumption of antioxidant minerals.

For the consumption of vitamin C, the prevalence of inadequacy was approximately half of the individuals studied. Probably the low intake of vitamin C in the population is due to insufficient



consumption of food sources of this vitamin. Patients over 65 years of age, in our study, had significantly lower usual intake of vitamin C.

Vitamin C is water-soluble and antioxidant, reacts with simple oxygen, hydroxyl radical and superoxide radical and plays a role in the process of amino acid and collagen biosynthesis. Associating with this, it participates in the maintenance of thiol enzymes in their reduced states, sparing glutathione peroxidase. Studies have shown that the modulating effect of high doses of vitamin C and vitamin E on the clastogenic effect of doxorubicin on the bone marrow of animals showed a reduction in the total number of chromosomal aberrations and in the percentage of abnormal metaphases induced by doxorubicin. Thus, the concomitant administration of antioxidant and antineoplastic vitamins proved to be important, as it probably protects healthy cells from damage caused by drugs, especially tissue cells of rapid cell proliferation^{23,24}.

Meanwhile, vitamin E presented a high percentage of insufficient intake, approximately 70% for both groups. The most important form of vitamin E is α -tocopherol, another antioxidant of important role in human metabolic processes. It has a protective action of adipose tissues against the attack of RL, such as the formation of peroxide radicals by polyunsaturated fatty acids in the phospholipid membranes. It also has an important function of inhibiting the growth of malignant lymphoma and breast cancer cells in vitro. It prevents tumor cells from following the cell cycle, disrupting it in the G1 phase, leading to cell apoptosis. When deficiency occurs, the cellular damage caused by the production of RL by the tumor causes lipid peroxidation and cell destruction^{23,24}.

Vitamin A, the first fat-soluble vitamin to be recognized, being β -carotene. The carotenoid with greater power of vitamin A formation, has protective role against various types of tumors in animals. It has the ability to inhibit the oxidation of compounds by peroxides. It plays an important role in the immune process and in human vision. Its deficiency is associated with xerophthalmia and night blindness. Its consumption plays an important role in relation to the lower risk of the onset of chronic diseases^{23,24}.

Another important highlight is that all patients with MDS showed inadequate selenium consumption. Studies highlight its association with the reduction of cardiovascular risk and the appearance of some tumors^{25,26}. A study cited above showed the consumption of selenium with greater inadequacy (98%) for patients with MDS and 87.2% for the control group²². In addition to its antioxidant role, because it is associated with the enzyme glutathione peroxidase, participating in the detoxification of hydrogen peroxide and other organic peroxides, it plays an important role in the metabolic process of thyroid hormones, highlighting that the syndromes caused by iodine deficiency were more severe in patients who were also selenium deficient²⁷.

The inadequate consumption of selenium may be associated with the type of habitual diet of the population studied and the variation of the amount of the mineral in food, since its concentration



may vary even according to the availability of soil²². The result presented reinforces the need for interventions, since the amount of selenium can be reached only with the consumption of two nuts per day. Another important observation is that the highest concentrations of selenium are in animal foods. It is observed that, due to the low levels of selenium in foods consumed in Brazil, the amount of food needed to reach the recommendation would be incompatible with the food intake capacity of an adult, which may also explain the inadequacy of this mineral in the studied group²⁷.

Zinc, despite having presented slightly lower rates of inadequacy when compared to selenium, magnesium and vitamin A, still has a high prevalence of consumption in both groups, the patients with MDS (68.6%) and the control group (61.5%). The inadequacy of zinc consumption can be associated by the high consumption of foods rich in carbohydrates, by the general population, and little consumption of meat in general, common among the elderly due to social and even physiological condition, with observation for total or partial edentulism, making it difficult to chew such foods, in addition, it should be remembered the conditions of difficulty in preparing the food, with advancing age²⁸.

Magnesium was another antioxidant mineral analyzed that presented the second highest rate of inadequacy of its consumption among patients with MDS (98%). It is present in our bones, soft tissues, muscles and body fluids, playing an important role in acting as a cofactor in enzymatic processes, role in bone metabolism and antioxidant²⁴.

In a study conducted with the elderly population in Brazil, from the Household Budget Survey 2008-2009, data similar to our study were found, where the inadequacy of the micronutrient intake was above 80%. It also presents high rates of inadequacy of other antioxidant micronutrients such as vitamins D, E, C and A, in addition to selenium and zinc, which corroborates the data found in this study²⁹.

In a study with 442 leukemia patients found an association between the intake of dietary nutrients, including vitamin C, carotenoids, in addition to dietary fiber, vitamins B1, B2, niacin and folate showed relevance in decreasing the risk of leukemia in adults, when compared to those who did not consume it³⁰.

Additionally, it is observed that food consumption in Brazil is rich in foods of high caloric density and low nutrient content, characterizing a diet with a higher probability of nutritional deficits. Thus, the importance of changes in the eating habits of Brazilians, including the elderly population, is reinforced, with the transition from the consumption of foods of high caloric density and poor in nutrients to more nutritious foods rich in antioxidants, such as fruits, vegetables, legumes, milks and their derivatives, grains and whole grains, oilseeds, lean meats and fish³¹.

One of the limitations of the present study was the methodology used regarding the collection of data on food consumption, because this method depends on the memory of a near past and as the



majority of the sample was formed by the elderly, this may make it difficult to retrieve information regarding food intake. In addition, there is considerable dependence on this instrument regarding the perception of the interviewees of the portions consumed.

Despite the limitations, this was the first local study that evaluated the dietary intake of antioxidant vitamins and minerals of MDS patients treated by SUS. The findings may support future scientific research with this specific Brazilian population, considering that the investigation of this type of study should always be explored in order to describe a national and regional diet pattern that may be associated with the risk of disease. Thus, increasing survival and improving the quality of life of the patient, and also assisting the professional nutritionist in his nutritional intervention, adopting preventive strategies.

5 CONCLUSION

It can be concluded, therefore, that the intake of antioxidant vitamins and minerals between the two populations was below the recommended values. Being magnesium and selenium, the antioxidant minerals that obtained the highest percentages of inadequacy in food consumption. It is worth mentioning the intake of vitamin C and selenium presented the lowest intake found in patients with MDS aged over 65 years. The high prevalence of inadequate intake of antioxidants seems to be related to the aging process, the disease itself and a diet with a low variety of foods that make up the sample diet.

In view of the data presented, the importance of monitoring these patients with guidance on a healthy diet balanced in vitamins and minerals, especially antioxidants, for the prevention and treatment of these patients is highlighted.



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