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Should antioxidant vitamin supplementation be applied in patients with metabolic syndrome? A case-control study

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Abstract

Introduction: All cells in the human body are exposed to reactive oxygen species (ROS), which disturb the metabolic reactions in the organism. The antioxidant system in the human body consists of enzymatic and non-enzymatic mechanisms, among which vitamins A, C, and E play a major role.

The aim of the study was to evaluate the supply of vitamins A, C, and E from daily food rations (DFR) in postmenopausal women with metabolic syndrome (MS) in relation to current nutrition standards.

Material and methods: The study involved 184 women with MS, aged 45-68 years (mean 57.38 ±8.17 years). The control group comprised 90 women, aged 41-65 years (mean 57.48 ±5.79 years) without MS. The food intake was assessed using 24-hour dietary recalls.

Results: The evaluation of intake of vitamins measured with daily food rations (DFR) demonstrated that the optimal level of 90-110% according to standards was achieved only in 3.62% of women with metabolic syndrome for vitamin A, in 8.88% for vitamin C, and in 11.41% for vitamin E, which was significantly less often found than in the control group ($p < 0.001$).

Conclusions: Women with MS are characterised by diversified intake of vitamins A, C and E, and a subgroup of this patients present low level of antioxidant vitamins intake. Supplementation with antioxidant vitamins should be prescribed individually to postmenopausal women with MS.

Key words: metabolic syndrome, antioxidant vitamins supplementation, diet, menopause.

Introduction

All cells in the human body are exposed to reactive oxygen species (ROS), which disrupt the metabolic processes in the mitochondria and disturb metabolic reactions in the organism. To protect against negative ROS effects, the organism developed defence mechanisms in the form of an antioxidant barrier, the efficient functioning of which is particularly important in the case of patients with metabolic syndrome (MS) in the pathogenesis of which oxidative stress plays a significant role.

Disorders related to MS increase the risk for developing type 2 diabetes and cardiovascular diseases, which have been the leading cause of death in Poland for years. The incidence of MS, regardless of the accepted diagnostic criteria, is increasing not only in developed but also in developing countries where the progress of civilisation is associated with overconsumption and lower level of physical activity [1, 2]. According to research studies, overconsumption is often not accompanied by increased intake of essential nutrients, including antioxidant vitamins, but above all, it is associated with an excess of consumed energy, resulting in positive energy balance leading to weight gain and obesity.

The antioxidant system in the human body consists of the enzymatic and non-enzymatic mechanisms, among which vitamins A, C, and E play a significant role. The level of antioxidant compounds in cells is supported by their appropriate intake in the diet or by *de novo* synthesis. There are results of large population studies indicating that subjects with MS are characterised by low consumption of vegetables, fruits, and products typical of the Mediterranean diet, rich in antioxidant ingredients, including vitamins A, C, and E [3]. On the other hand, as it has been shown in numerous studies that patients with MS are characterised by increased

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oxidative stress and weakened antioxidant barrier compared to those without MS [4]. Thus, a properly balanced diet determines not only the homeostasis of the internal environment of the body, but can also significantly contribute to strengthening the antioxidant barrier in patients with MS.

Aim of the study

The aim of the study was to evaluate the supply of vitamins A, C, and E from daily food rations (DFR) in patients with MS in relation to the estimated average requirement (EAR) for vitamins A and C and adequate intake (AI) of vitamin E.

Material and methods

Study population

The study involved 184 patients, aged 30-65 years (mean 57.4 ±8.3 years), including 84 women aged 30-65 years (mean 57.4 ±8.9 years) and 100 men aged 41-65 years (mean 57.4 ±7.6 years). All of them were non-smokers and in the last year they did not take any dietary supplements. The control group comprised 90 subjects, 55 men and 35 women, aged 41-65 years (mean 57.65 ±5.78 years), clinically healthy, without MS.

Metabolic syndrome (definition)

The diagnosis of MS was established on the basis of International Diabetes Federation (IDF) criteria, stating the occurrence of abdominal obesity (waist circumference in women ≥ 80 cm, in men ≥ 94 cm) and at least two from the following risk factors: triglycerides ≥ 1.7 mmol/l or the treatment of this disorder, low HDL cholesterol level (in women < 1.3 mmol/l, in men < 1.0 mmol/l) or the treatment of this disorder, fasting glucose ≥ 6.1 mmol/l or treated type 2 diabetes, arterial blood pressure ≥ 130/85 mm Hg, or the treatment of hypertension [5].

Anthropometric analyses

Height was measured using a fixed stadiometer, and weight was taken with individuals wearing light clothes and no shoes on a digital scale with a capacity of 200 kg and accurate to the nearest 100 g. Body mass index (BMI) was calculated as weight (kilograms) divided by height in square metres. Waist circumference was measured at the midpoint between the bottom of the rib cage and above the top of the iliac crest during minimal respiration.

Nutritional evaluation

The food intake was assessed using 24-hour dietary recalls (24HR), in accordance with the guidelines of the National Food and Nutrition Institute of Warsaw [6, 7]. A total of 552 24-hour dietary recalls (three 24HR for each individual) were obtained from subjects with MS and 270 24-hour dietary recalls from subjects without MS by the interviewer, and the means of consumption were calculated for each nutrient. The "album of photographs of food products and dishes" of the National Food and Nutrition Institute of Warsaw was used to determine the normal size of the consumed portions [7].

The vitamin content in the DFR and the achievement of the standards were determined with "charts of nutritive values of products and foods" and "standards of human nutrition" using Diet 5.0 software (license No: 52/PD/2013), according to the National Food and Nutrition Institute of Warsaw [6, 8]. The program takes into account the loss of vitamins during technological and culinary food processing at the level of 25% for vitamin A, 55% for vitamin C, and 25% for vitamin E [6–8].

The evaluation of the intake of selected vitamins was made by calculating the degree of achieved standards at the level of: estimated average requirement (EAR) for vitamins A and C, and adequate intake (AI) for vitamin E. The desired level of standards was established at 90-110% [6]. The following parameters were analyzsed: MUFA – monounsaturated fatty acids; PUFA – polyunsaturated fatty acids; SFA – saturated fatty acids; cholesterol; proteins – animal proteins and plant proteins; carbohydrates – absorbable carbohydrates, sucrose, and fibre.

Statistical analyses

Statistical analysis was performed using Statistica 7.1 PL and Office 2010 software. The normal distribution was determined using the Shapiro-Wilk test. The Student's *t* test was used when variables were characterised by a normal distribution. The Mann-Whitney U test was used when at least one variable did not fit a normal distribution. In the case of the characteristics of nominal scales, the structure ratio displayed by percentage was calculated, and in comparison analysis the χ^2 test was used. Correlations were assessed by Spearman's coefficient (Rho). $p < 0.05$ was considered to be significant.

The study was approved by the Bioethics Committee of the Medical University of Lodz (No: RNN/556/10/KB). Written consent was obtained from all research participants.

Results

Clinical characteristics of studied women is shown in Table I. As expected, BMI, waist circumference, systolic and diastolic blood pressure, glucose, TG, and LDL cholesterol level were higher in MS patients, whereas HDL cholesterol level was lower in subjects with MS.

Tab. I. Clinical characteristics of studied women

Parameter	MS (n = 184)	Without MS (n = 90)	p-value
	Mean ±SD/% (n)	Mean ±SD/% (n)	
Age [years]	57.38 ±8.17	54.78 ±5.79	NS[a]
Sex [% women]	59.78 (110)	55.56 (50)	NS[a]
Type 2 diabetes [%]	47.28 (87)	27.78 (25)	< 0.001[c]
Hypertension [%]	80.43 (148)	55.56 (50)	0.0432[c]
Body mass index [kg/m^2]	34.35 ±5.31	27.61 ±2.72	< 0.0001[a]
Waist [cm]	114.21 ±12.16	97.31 ±9.94	< 0.0001[a]
Systolic blood pressure [mmHg]	144.17 ±15.22	129.03 ±12.31	< 0.0001[b]
Diastolic blood pressure [mmHg]	87.47 ±10.81	81.45 ±7.92	< 0.0001[b]
Plasma concentration			
Glucose [mmol/l]	8.13 ±3.05	5.56 ±0.54	< 0.0001[b]
Triglycerides [mmol/l]	1.91 ±0.92	1.43 ±0.32	< 0.0001[b]
Total cholesterol [mmol/l]	4.56 ±1.26	4.56 ±0.91	NS[a]
High-density lipoprotein [mmol/l]	1.09 ±0.24	1.27 ±0.24	< 0.0001[a]
Low-density lipoprotein [mmol/l]	2.97 ±0.97	2.91 ±0.81	< 0.0001[a]

[a]Student's t test; [b]Mann-Whitney U test; [c]χ^2 test
NS – not significant

There were no significant differences in total cholesterol level between the MS group and the controls. Diabetes and hypertension were more prevalent in patients with MS than in healthy subjects. Age was not different between groups.

The dietary characteristics of the studied women is shown in Table II. The consumption of energy, protein, fat, carbohydrates, fibre, PUFA, MUFA, SFA, as well as vitamin A, C, and E did not differ significantly between patients with MS and controls, except

Tab. II. Dietary characteristics of studied women

Parameter	Recommendations	MS (n = 184)	Without MS (n = 90)	p-value
		Mean ±SD	Mean ±SD	
Total energy [kcal/d]		2159.96 ±91.77	1995.47 ±99.24	NS[a]
Proteins [g]		101.67 ±44.72	90.52 ±29.13	NS[a]
Animal proteins [g]		69.66 ±33.98	31.16 ±11.7	0.0023[a]
Plant proteins [g]		32.01 ±14.65	59.36 ±21.8	0.0051[a]
Carbohydrates [g]		283.39 ±150.78	296.06 ±49.72	NS[a]
Absorbable carbohydrates [g]		259.43 ±145.19	264.82 ±39.42	NS[a]
Sucrose [g]		69.13 ±31.50	22.73 ±10.17	0.0027[a]
Fibre [g]	20–40	23.97 ±10.89	28.24 ±9.8	NS[a]
Fats [g]		78.25 ±30.50	71.94 ±9.27	NS[a]
Saturated fatty acids [g]		34.96 ±25.39	28.42 ±7.40	NS[a]
Monounsaturated fatty acids [g]		33.06 ±26.46	30.17 ±6.91	NS[a]
Polyunsaturated fatty acids [g]		10.14 ±7.69	13.08 ±3.42	NS[a]
n-6 [g]		10.13 ±6.59	10.18 ±2.49	NS[a]
n-3 [g]		1.01 ±0.99	3.91 ±0.96	0.0049[a]
Cholesterol [mg]	< 300	380.12 ±234.53	260.18 ±67.32	0.0002[a]
Vitamin A [µg of retinol equivalent]	500 (EAR)	1300.14 ±1043.86	1173.00 ±535.32	NS[a]
Vitamin C [mg]	60 (EAR)	103.99 ±139.14	93.30 ±127.95	NS[a]
Vitamin E [mg of α-tocopherol equivalent]	8 (AI)	8.85 ±5.59	9.33 ±5.09	NS[a]

[a]Mann-Whitney U test
F – female, M – male; NS – not significant; EAR – estimated average requirement; AI – adequate intake

for cholesterol and sucrose, a higher consumption of which was noted in MS patients. Furthermore, significant differences were demonstrated in the pattern of protein and PUFA intake; namely, MS patients were characterised by higher consumption of animal protein and lower consumption of n-3 fatty acids than subjects without MS.

Age did not differentiate between groups. No significant differences were found in the intake of the tested vitamins between the MS patients and the controls. The mean intake of vitamin A in the MS group was 1300.14 ±1043.86 µg, and it was 260.03% of EAR. The mean intake of vitamin C in the MS group was 103.99 ±139.14 mg, and it was 173.32% of EAR. The mean intake of vitamin E in the MS group was 8.85 ±5.59 mg, and it was 110.63% of AI.

Vitamin A intake positively correlated with the intake of SFA (Rho = 0.55, $p < 0.001$), MUFA (Rho = 0.51, $p < 0.001$), PUFA (Rho = 0.32, $p < 0.001$), cholesterol (Rho = 0.58, $p < 0.001$), and fibre (Rho = 0.45, $p < 0.001$). Correlations were also found between vitamin E intake and the intake of SFA (Rho = 0.24, $p < 0.001$), MUFA (Rho = 0.40, $p < 0.001$), PUFA (Rho=0.84, p<0.001), cholesterol (Rho = 0.40, $p < 0.001$), and fibre (Rho = 0.56, $p < 0.001$). Vitamin C intake correlated only with the intake of fibre (Rho = 0.42, $p < 0.001$). Moreover, a correlation was demonstrated among the intakes of antioxidant vitamins. The intake of vitamin A correlated with the intake of vitamin E (Rho = 0.33, $p < 0.001$) and vitamin C (Rho = 0.26, $p < 0.001$), and the intake of vitamin C correlated with the intake of vitamin E (Rho = 0.38, $p < 0.001$).

The evaluation of intake of vitamins measured with daily food rations (DFR) demonstrated that the optimal level of 90-110% according to standards was achieved only in 3.62% of women with metabolic syndrome for vitamin A, in 8.88% for vitamin C, and in 11.41% for vitamin E, which was significantly less often found than in the control group ($p < 0.001$) (Figs. 1-3).

Insufficient intake of vitamin A measured with DFR was found in the case of 13.96% women with MS. The requirement determined by EAR exceeded 82.42% DFR. Insufficient intake of vitamin C measured with DFR was found in the case of 52.96% women with MS. The requirement determined by EAR exceeded 46.74% DFR. Insufficient intake of vitamin E measured with DFR was found in the case of 57.6% women with MS. The requirement determined by AI exceeded 30.98% DFR.

Discussion

Antioxidant vitamins play an important role in the prevention of metabolic and cardiovascular diseases. They are part of antioxidant barrier protecting the organism against ROS, therefore their supply in a diet should balance the demand determined by standards. Since the standards established by the National Food and Nutrition Institute concern the healthy population, it seems to be justified to advise patients with metabolic disorders, who are exposed to greater oxidative stress, to receive higher intake of vitamins A, C, and E in their diet or in their supplementation [9-12].

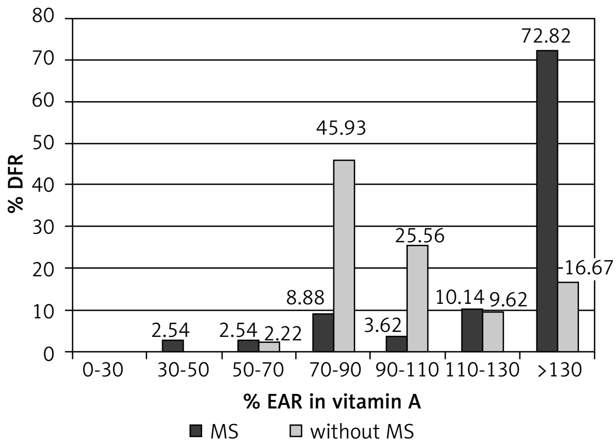

Fig. 1. The percentage of women who achieved ranges of DFR according to EAR in vitamin A

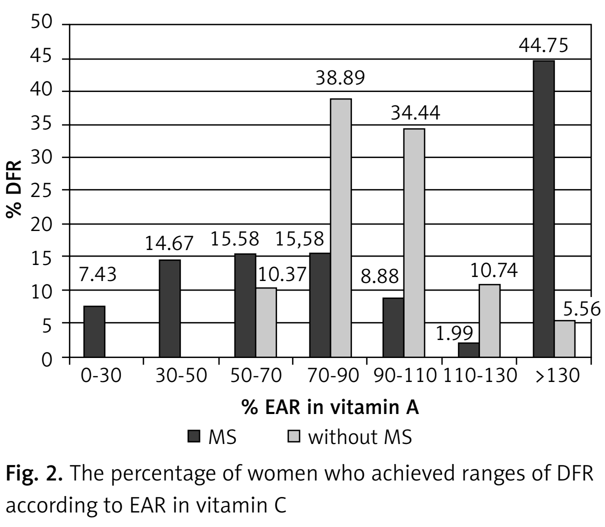

Fig. 2. The percentage of women who achieved ranges of DFR according to EAR in vitamin C

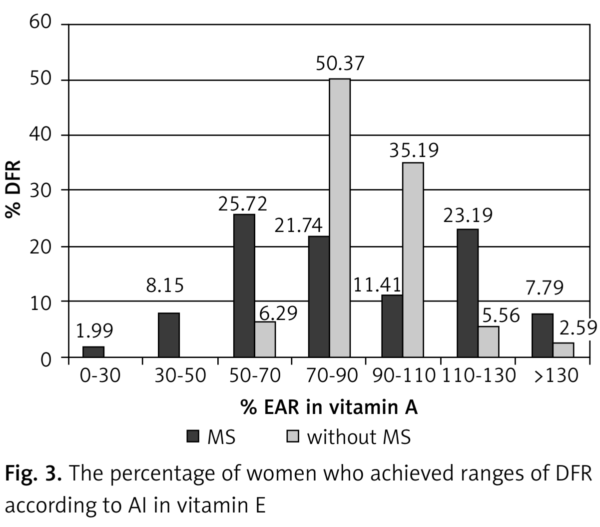

Fig. 3. The percentage of women who achieved ranges of DFR according to AI in vitamin E

In our study, we found out that the average intake of vitamin A and C displayed by DFR in postmenopausal women with MS was high, exceeding the standard of EAR. In turn, the average intake of vitamin E displayed by DFR did not differ from the standard of AI.

However, the analysis of the intake of these vitamins in patients with MS demonstrated that the desired level of 90-110% of the standard for vitamin A was achieved only in 3.62% of the patients, for vitamin C – in 8.88%, whereas for vitamin E – in 11.41%. On the other hand, in relation to vitamins A and C, a large group of patients with MS exceeded the average requirement for these vitamins specified by the standard. In the case of vitamin E, over 57% did not have a sufficient intake of the vitamin.

Ostrowska *et al*. obtained similar results. They found a high intake of vitamins A and C among obese men and women [13]. Also Bronkowska *et al.* observed a high intake of antioxidant vitamins A and C among perimenopausal women [14]. Terlikowska *et al*., examining women aged 40-73 years, with hypertension, obesity, and metabolic syndrome, found the intake of vitamin E at the level of 118% of EAR standard, whereas the intake of vitamins C and A did not deviate from the established standard [15]. Pachocka *et al*., examining patients with hypercholesterolaemia, found normal intake of antioxidant vitamins [16]. Stefańska *et al*., assessing the intake of vitamins in the diet by women with normal body weight, overweight, and obesity, observed higher intake of vitamins A, C, and E by obese women than by those with normal weight or overweight [17]. A high intake of antioxidant vitamins was also found in the diet of obese subjects with obstructive sleep apnoea [18].

In turn, the Multicentre Polish Population Health Status Study – WOBASZ – demonstrated normal content of vitamin C and E in the DFR [19]. Similar data were presented in the study evaluating the content of vitamins in the DFR of a selected Polish population [20]. However, Waszkiewicz-Robak *et al*. reported normal levels of intake of vitamins A and E in food rations of the Polish population and too low intake of vitamin C [21]. Troszczyńska *et al*., analysing the food rations of the Polish population, found that the content of fat-soluble vitamins was in accordance with the standard [22]. On the other hand, a study conducted by Nadolna *et al.* indicated too low intake of vitamins A and E by Polish adults [23].

The American NHANES study reported that the intake of vitamins A, C, and E was in accordance with the recommended standard, both in the group of healthy subjects and in those with MS [9]. A study performed among the inhabitants of Alaska gave similar results to those presented in the NHANES study [24]. In the study of Li *et al.* the intake of vitamin A and E was consistent with the standard and did not differ significantly between patients with MS and healthy controls, whereas the intake of vitamin C in the group with MS was lower compared to healthy subjects [25]. In the study by Singh *et al*. the intake of vitamins A, C, and E in patients with coronary heart disease did not differ from the standard and it was insignificantly lower compared to healthy subjects [26]. In a large French population study the intake of vitamins C and E was found to be in accordance with the standard [27]. Sohn *et al*., examining the Korean population, reported the intake of vitamin A and C to be in accordance with the standard [28]. However, Al-Daghri *et al*. reported in their study significantly lower intake of vitamins A, C, and E in patients with MS compared to healthy subjects, and moreover, a significant percentage of the respondents did not receive the recommended nutrition standards (respectively, 37.5%, 42.5%, 98.7%) [29].

The research carried out in Poland and other countries demonstrate that the intake of antioxidant vitamins is differentiated in subjects with intensified oxidative stress. Some researchers showed their normal intake, often even exceeding the requirements, while others demonstrated their too low supply in the diet. Thus, the issue of the introduction of antioxidant vitamins supplementation in patients with MS requires further research studies. The results of studies on the effect of the administered vitamin supplements on cardiovascular complications are controversial. Some authors demonstrated reduced oxidative stress, decreased risk for cardiovascular diseases, as well as reduced death rate after application of antioxidant vitamins supplementation [30-32]. Other authors did not demonstrate the efficacy of vitamin supplementation in the reduction of oxidative stress in these patients [31, 32]. There are also results of studies indicating the existence of factors disturbing and changing the effect of vitamin supplements that should be taken into account when planning the use of vitamin supplementation in patients with cardiovascular diseases. They include, among others, smoking and exposure to environmental chemical agents [33, 34].

To date, no optimal dose has been established of the supplements, as well as their composition, which, in the light of the available data, seems to be the key issue. In the case of individuals who consume insufficient amounts of antioxidant vitamins, changes in their eating habits and possible supplementation are justified. However, it should be determined whether the introduction of supplementation is justified in patients whose intake of antioxidant vitamins is in accordance with the instructions and even exceeds them several times, but which is not accompanied by their balanced serum levels. This was shown in our previous studies and confirmed by the results of other studies [33, 35, 36]. Excessive intake of antioxidant vitamins from the diet or vitamin preparations, especially in patients with a balanced deficiency, may increase oxidative stress and thus may lead to an increased risk of cardiovascular complications. In particular, this type of undesirable effect is attributed to vitamins C and E [30-32]. Moreover, in our study we have shown that patients with MS demonstrated a variety of nutritional standards related to the intake of vitamins A, C, and E, whereas in the group of healthy individuals the intake of the tested vitamins was fairly balanced and the percentage of those who were characterised by too high or too low intake was much lower than in the group of patients with MS. Perhaps the rationalisation of dietary intake of vitamins, not differing significantly from the recommendations, would normalise their plasma levels and would improve the antioxidant barrier in these patients without the need of vitamin supplementation.

However, in the case when the dietary supplementation of vitamins A, C, and E is necessary, a very important issue seems to be the determination of the dose accompanied by an assessment of their dietary intake and plasma concentration individually for each patient.

Conclusions

Women with MS are characterised by diversified intake of vitamins A, C, and E, and a subgroup of this patients present low levels of antioxidant vitamins intake. Supplementation with antioxidant vitamins should be prescribed individually to postmenopausal women with MS.

Disclosure

Authors report no conflict of interest.

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