



# Effect of vitamin-mineral complexes on quality of life of patients with arterial hypertension

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## ABSTRACT

**Objective:** A considerable proportion of the population due to both economic reasons and traditions appear to be experiencing chronic deficit in micronutrients, which may be deteriorated on the background of drug therapy being performed. The purpose of our study was to optimize pharmacotherapy of patients with first-ever prescribed diuretic-containing combined therapy for arterial hypertension (AH) by means of adding a vitamin-mineral complex.

**Method:** To determine B-group vitamins (thiamine, riboflavin, pyridoxine) in blood plasma by means of high-performance liquid chromatography (HPLC) and, on achieving the target values of arterial pressure (AP), to analyse the patients' quality of life by means of such neuropsychological tests as the General Health Questionnaire – 36 (GHQ-36) and WAM (wellbeing, activity, mood) questionnaire.

**Results:** The group of patients receiving antihypertensive therapy alone demonstrated a decrease in blood plasma thiamine, riboflavin and pyridoxine from  $34.5 \pm 4.2$  to  $25.4 \pm 3.2$  ng/ml ( $p < 0.05$ ), from  $11.3 \pm 1.5$  to  $7.8 \pm 1.1$  ng/ml ( $p < 0.05$ ) and from  $13.4 \pm 1.5$  to  $9.1 \pm 1.3$  ng/ml, respectively. In patients receiving the vitamin-mineral complex additionally to drug therapy of AH, no significant alterations in the content of micronutrients in blood plasma were revealed. We noted more pronounced dynamics in the scores by the GHQ-36 and a more pronounced increase in the patients' activity by the WAM test, amounting to  $28.9 \Delta \%$  and  $15.51 \Delta \%$ , respectively ( $p < 0.05$ ).

**Conclusion:** Supplementing antihypertensive pharmacotherapy with a vitamin-mineral complex makes it possible not only to maintain the level of micronutrients at the level of the physiological requirements but to improve the patients' quality of life as assessed by neuropsychological scales.

**Keywords:** vitamins, arterial hypertension, pharmacotherapy, diuretics

## INTRODUCTION

A considerable proportion of the population due to both economic reasons and traditions of nutrition experience chronic deficit of micronutrients, receiving minimal amounts of vitamins sufficient for preventing the development of severe avitaminosis but insufficient for completely meeting the requirements of the body, optimal performance of all vitamin-related vital processes (1).

A leading role in the aetiology and pathogenesis of a series of diseases is played by disorders in neurohumoral regulation of metabolic processes closely related to imbalance of vitamins being component parts of coenzymes and participating in metabolism of carbohydrates, proteins, fat, in cell respiration and other processes. Vitamins in a non-coenzymatic form are capable of activating or inhibiting enzymes (2).

Danger of a hypovitaminosis background as a sociohygienic factor is made worse by its mass nature, lack of pronounced specific symptomatology, insufficient awareness of the population and medical personnel about the real prevalence of hypovitaminoses and their consequences for human health, by the absence of appropriate alertness in this matter (3).

On the one hand, vitamin deficiency is a background predisposing to the development of diseases. On the other hand, vitamin deficiency deteriorates the course of any disease, hampering successful treatment thereof (4) and leading to a decrease in quality of life (5). Drug therapy makes additional contribution to the formation of vitamin insufficiency.

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**Table 1:** Clinical and demographic characteristics of the groups of hypertensive patients

Parameters	AHT + VMC (group 1)	AHT (group 2)
Average age, years	50.1±2.6	51.3±5.6
Women/men, abs.	16/14	16/14
Degree II AH, abs. (%)	30 (100%)	30 (100%)
SAP	171.0±8.9	168.3±4.5
DAP	108.4±6.7	103.8±7.9
Not treated previously, abs. (%)	30 (100%)	30 (100%)
<b>AH type</b>	unknown	6 (20%)
	secondary	4 (13.2%)
	essential	20 (66.6%)
Family history of cardiovascular disease, abs. (%)	16 (52.8%)	20 (66.6%)
<b>Occupational qualification</b>	People of intellectual occupation and white-collar employees	20 (66.6%)
	People of qualified manual labour	6 (20%)
	People of non-qualified manual labour	4 (13.2%)

Certain therapeutic agents are antivitamin (6). Antivitamins possessing structural analogy with vitamins enter into competition with vitamins for the site of binding with proteins and displace vitamins. This leads to both formation of inactive complexes and enhanced excretion of vitamins from the body and the development of endogenous vitamin insufficiency. Widely-used trioxazine-series tranquilizers interfere with the synthesis of the co-enzymatic forms of riboflavin (7). Antibiotics and sulphanilamide drugs inhibit intestinal microflora, disturbing the endogenous synthesis of vitamin K, biotin and pantothenic acid. Antibiotics, sulphur-containing drugs and antacid agents may decrease the level of thiamine in the body (Nardone, 2013). Taking antihyperlipidaemic drugs is accompanied and followed by impaired absorption of folic acid. Thus, drug therapy may be an additional factor contributing to a decrease in the provision of the body with vitamins. The subject of the study was diuretic therapy which, according to the opinion of a series of authors, may lead to a decrease in the level of B-group vitamins. It is the B-group vitamins that are most commonly used in medical practice in order to decrease the degree of asthenia and to increase both mental (8) and physical performance (9).

We studied the effect of newly prescribed combined, diuretic-containing antihypertensive therapy on the level of thiamine, riboflavin and pyridoxine in blood serum of patients. Neuropsychological tests were used to assess the effect of taking a vitamin-mineral complex (VMC) as part of combined therapy on quality of life of hypertensive patients.

## MATERIALS AND METHODS

### Characteristics of Patients Included into the Study

The study included a total of 60 patients with degree II AH. Of these, 30 patients received antihypertensive therapy (AHT) + VMC (constituting the Study Group) and 30 patients received AHT alone (Control Group). The clinical and demographic characteristics of the patients participating in the study did not differ (**Table 1**).

All patients enrolled into the study were treatment-naïve, i.e. having previously received no antihypertensive therapy.

### Pharmacotherapy of Patients Participating in the Study

A combination of drugs – an angiotensin-converting enzyme inhibitor (ACEI) + hydrochlorothiazide at a dose of 25 mg was taken by 22 patients with AH. Of these, 10 (33.3%) patients (group 1) received AHT + VMC and 10 (33.3%) patients (group 2) received AHT alone.

A combination of drugs – an ACE inhibitor + hydrochlorothiazide at a dose of 25 mg was taken by also 22 patients, of whom 12 (40%) patients received AHT + CMC and 10 (33.3%) patients (group 3) received AHT alone.

A combination of drugs, consisting of an adrenoceptor-blocking agent + furosemide in the dose of 20 mg was taken by 4 patients: AHT + VMC by 2 (6.6%) patients; AHT alone (group 2) by 2 patients (6.6%).

Enap N was used for drug therapy in 14 patients with AH: AHT + VMC in 6 (20%) patients; AHT alone (group 2) in 8 (26.4%) patients.

### Composition of VMC and Dosage Regimen

Hypertensive patients of the first group along with antihypertensive therapy took a combined complex of vitamins – VMC at a dose of 1 tablet once daily. The VMC contained the following vitamins: vitamin A – 1.03 mg (3,000 IU), vitamin

E – 10 mg (10 IU), vitamin D3 – 5 µg (200 IU), vitamin C – 60 mg, vitamin B1 – 1.5 mg, vitamin B2 – 1.7 mg, vitamin B5 – 6 mg, vitamin B6 – 2 mg, vitamin Bc – 150 µg, vitamin B12 – 2 µg, vitamin PP – 15 mg, vitamin H – 15 µg.

### Method of Determining B-group Vitamins in Blood Plasma

Blood plasma B-group vitamins (thiamine, riboflavin, pyridoxine) were quantified by means of HPLC, using a chromatographic system manufactured by the "Shimadzy" company (LC-6A, detector SPD – 6A), column Diasorb 130-C16T (4 × 250 mm, 7 µm), metering loop volume 100 µl. Elution was carried out by an aqueous solution of methyl alcohol with various proportion of the components and by adding of ion-pair reagents. The flow rate was 1 ml per minute, with UV detection at a wavelength of 254 nm (10).

Blood samples for determining the content of endogenous level of vitamins B1, B2 and B6 were taken on an empty stomach at 08 hours 30 minutes. Blood was sampled in the amount of 5 ml from the ulnar vein.

To determine the concentration of B-group vitamins, blood samples were centrifuged, plasma removed, frozen and kept at a temperature of - 30° C until quantitative determination of vitamins.

The equilibrium concentration of vitamins in blood plasma of patients was studied prior to pharmacotherapy and at 2 weeks of treatment.

### Scales for Neuropsychological Testing

The 36-Item Short Form Survey (SF-36) is a nonspecific questionnaire for assessment of quality of life of the patient, reflecting general well-being and the degree of satisfaction of those sides of human life activity influenced by health status (11).

The WAM test is designed for rapid assessment of wellbeing, activity and mood (hence its abbreviated name by the first letters of these functional states). The respondents are asked to correlate their state with a series of signs by a multiple-stage scale (12).

## RESULTS

### Dynamics of the Level of B-group Vitamins in Blood Plasma of Patients

Patients with newly prescribed combined diuretic-containing antihypertensive therapy over the period of follow up during two weeks demonstrated a statistically significant decrease in blood plasma thiamine, riboflavin and pyridoxine from 34.5±4.2 to 25.4±3.2 ng/ml ( $p<0.05$ ), from 11.3±1.5 to 7.8±1.1 ng/ml ( $p<0.05$ ) and from 13.4±1.5 to 9.1±1.3 ng/ml, respectively.

Prior to pharmacotherapy, the provision below the physiological norm in this group of patients was revealed for thiamine in five (16.7%) patients, for riboflavin in four (13.4%) patients, and for pyridoxine in five (16.7%) patients, which corresponds to the average statistical data for the Moscow region (13)The findings of the follow-up examination at 2 weeks of pharmacotherapy revealed the vitamin provision below the physiological norm for thiamine in seven (23.3%) patients, for riboflavin in six (20.0%) patients and for pyridoxine in eight (26.7%) patients.

In patients receiving for the first time diuretic-containing combined antihypertensive therapy and simultaneously taking the VMC over the follow-up period during 2 weeks, no significant changes in the content of group B-group vitamins in blood plasma were revealed: the content of thiamine prior to therapy – 36.4 ±4.5 ng/ml, at 2 weeks – 36.9±5.1 ng/ml ( $p>0.05$ ), for riboflavin 11.8±1.9 and 10.1±2.1 ng/ml ( $p>0.05$ ), for pyridoxine 12.7±1.7 and 13.2±2.5 ( $p>0.05$ ), respectively. The number of patients with the vitamin provision below the physiological norm both prior to pharmacotherapy and at 2 weeks thereafter was as follows: for thiamine 4 (13.3%), for riboflavin – 4 (13.3%) and for pyridoxine – 6 (20.0%).

### Analysis of the Dynamics of the Patients' State by Neuropsychological Scales

The most pronounced dynamics according to the General Health Questionnaire – 36 (GHQ-36) was observed in hypertensive patients of all groups by the scale social dysfunction. Patients simultaneously taking AHT + VMC showed a statistically significant decrease in the scoring values by this scale from 11.6±2.4 points to 5.1±2.1 points ( $p<0.01$ ). Both groups of the examined patients demonstrated a statistically significant ( $p<0.05$ ) decrease in the total scoring value, with a maximum decrease in the first group (AHT + VMC) by 28.9 Δ% and a minimal decrease in the group of patients receiving AHT alone by 15.51 Δ% (**Table 2**).

The findings of the WAM test showed a statistically significant increase in the scoring for the well-being in patients of both groups ( $p<0.05$ ). The score for activity increased more considerably in patients simultaneously taking

**Table 2:** Dynamics of the patients' condition by the scale of general health on the background of the carried out therapy

Parameters	AHT + VMC		AHT AГT	
	At baseline	At 2 weeks of therapy	At baseline	At 2 weeks of therapy
<b>A (somatization)</b>	14.3±2.5	11.5±3.4	14.9±2.7	12.9±2.1
<b>B (anxiety)</b>	12.7±2.1	9.7±1.5	12.8±3.1	11.5±3.2
<b>C (depression)</b>	15.1± 2.8	12.5±1.8	15.2±2.7	12.5±1.8
<b>D (social dysfunction)</b>	11.6±2.4	5.1±2.1*	11.9±1.9	9.4±1.7
<b>Total score</b>	53.7±2.05	38.2±2.2*	54.8±2.6	46.3±2.2*

\* - statistically significant compared with the baseline value

**Table 3:** Dynamics of the WAM test parameters in patients on the background of therapy performed

Parameters	AHT + VMC		AHT	
	At baseline	At 2 weeks of therapy	At baseline	At 2 weeks of therapy
<b>Well-being (WAM scale score)</b>	1.9±0.23	2.5±0.24*	1.75±0.19	2.4±0.18*
<b>Activity (WAM scale score)</b>	1.83±0.2	2.47±0.23*	1.93±0.2	2.07±0.23
<b>Mood (WAM scale score)</b>	1.54±0.32	1.98±0.41	1.6±0.19	2.1±0.20

antihypertensive therapy and the vitamin-mineral complex from 1.77±0.12 to 2.2±0.18 points ( $p < 0.05$ ). The group of patients receiving antihypertensive therapy alone demonstrated an inconsiderable increase in the activity from 1.93±0.2 to 2.07±0.23 points, which, however was not statistically significant. In both groups of patients there was statistically insignificant dynamics for the mood scoring towards elevation (**Table 3**).

## DISCUSSION

Monitoring of vitamin provision in various groups of adult population (by the content of vitamins in blood plasma) over the period from 1987 to 2009 showed that insufficiency of B-group vitamins in adult population is currently encountered considerably more frequently than insufficiency of vitamins C, A and E. The revealed deficits, irrespective of the residential area and occupational qualifications of the population, as a rule, touch upon not a single vitamin but have a pattern of combined insufficiency of B-group vitamins, and may be accompanied by insufficiency of other vitamins, as well (14).

In patients with cardiovascular diseases (CVDs) the vitamin status (thiamine, riboflavin) is characterized by a decreased content of vitamins in blood plasma (15) A decrease in blood plasma vitamins is associated not so much with alterations in metabolism in CVDs (16) but rather with the deficit appearing due to a low content of vitamins in the diet (17, 18) Deficit of one of the B-group vitamins (for example, that of B6) may be caused by deficit of another vitamin (B2) which is associated with impaired synthesis of co-enzymatic forms of pyridoxine in riboflavin deficiency (19) The risk of thiamine deficit is increased in patients taking diuretics (20) Diuretics may interfere with reabsorption of thiamine in the kidneys and elevate its urinary excretion (21) Enhanced excretion of thiamine with urine while administering furosemide and other diuretics was previously demonstrated in an experimental study on laboratory animals (22).

Authors of a series of works studied thiamine balance in patients with chronic heart failure) during drug therapy with loop diuretics (23) No similar studies in hypertensive patients have been conducted. We measured the content of thiamine, riboflavin and pyridoxine in patients prior to newly prescribed diuretic-containing antihypertensive combined therapy and at 2 weeks thereafter. The obtained results showed that in the group of patients not taking the VMC, a decrease in the level of vitamins in blood plasma amounted to 26.4 Δ %, 30.97 Δ % and 32.08 Δ % for thiamine, riboflavin and pyridoxine, respectively. Also in this group was an increase in the number of patients in whom vitamin provision was below the physiological norm. In the group of the patients receiving simultaneously AHT + VMC over the two-week period of follow up there were no significant changes either in the content of B-group vitamins or in the number of patients with vitamin provision below the physiological norm.

Deficit of B-group vitamins manifests itself as dysfunction of the digestive and nervous systems, increased nervousness, depression, sleep disorders, decreased daily activity, thus leading to deterioration of quality of life (24) Comparing the subjective assessment of the well-being of patients by the scales of the neuropsychological tests in two groups on the background of achieving the target values of AP demonstrated that patients additionally receiving the VMC were found to have more pronounced positive dynamics by the General Health Questionnaire (GHQ- 36) on the scale Social Dysfunction and by the WAM test activity scale. The obtained findings are in accord with the literature-published results of effective use of B-group vitamins with the purpose to relieve symptoms of asthenia (25) and to increase physical activity (26).

## CONCLUSION

All examined patients on the background of taking AHT demonstrated pronounced positive dynamics consisting in normalization of the AP values. However, in spite of comparable results for AP values, the patients whose combined therapy was supplemented with the VMC subjectively reported higher quality of life.

The results of the WAM test («Well-being, Activity, Mood») demonstrated a statistically significant increase in the activity of patients taking the VMC simultaneously with antihypertensive therapy. Analysing the findings of the neuropsychological testing by the 36-Item Short Form Survey (SF-36) for quality of life, showed that more pronounced positive dynamics by the «social dysfunction» scale was also observed in patients taking the VMC.

Patients with first-ever prescribed combined antihypertensive therapy containing a diuretic component during two-week follow up period were found to have a statistically significant decrease in the level of blood plasma B-group vitamins: thiamine, riboflavin, and pyridoxine. In the group of patients taking the VMC along with AHT, the level of B-group vitamins (thiamin, riboflavin and pyridoxine) during the period of follow up did not change significantly.

Thus, supplementing combined antihypertensive therapy with the VMC makes it possible not only to maintain the level of micronutrients within the limits of the physiological norm but to improve the patients' quality of life.

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