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# HYPOMAGNESEMIA AS A PREDICTOR OF EARLY REMODELING OF BLOOD VESSELS IN YOUNG MEN WITH ESSENTIAL HYPERTENSION

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***Abstract***

*The article highlights the features of changes in the level of magnesium in the serum, the elasticity of the vascular wall and shows their relationship in young men with essential hypertension and abdominal obesity. The indices of magnesemia, the markers of the arterial wall elasticity (the augmentation index, the arterial stiffness index and the pulse wave velocity), and the thickness of the perivascular adipose tissue (extra-media of carotid arteries) were evaluated.*

*Clinical manifestations of magnesium deficiency were identified in more than half of the cases and the risk of its development was found in a third of patients with essential hypertension and obesity, it correlated with the results of laboratory studies of serum magnesium levels. Besides, the severity of hypomagnesemia was inversely proportional to the blood pressure (r=-0.58, p=0,022).Evaluation of vascular wall stiffness markers in patients with essential hypertension and obesity showed their significant increase not only in comparison with the similar indicators of practically healthy individuals but also with the parameters of patients with essential hypertension without obesity. The correlation analysis revealed that the magnesium level in the serum of such patients had a strong negative relationship with both the augmentation index (r =-0.68, p =0.023) and the arterial stiffness index (r=-0.55, p=0,042).The extra media index in patients with essential hypertension and obesity was twice as high as one in practically healthy individuals. It was also revealed that the extra-media indicator in these patients was positively related to the level of blood pressure (r=+0.68, p=0.033), the augmentation index (r =+0.48, p=0.018), and negatively related to magnesium content in serum (r= +0.61, p=0.023).*

*It was concluded that young men with essential hypertension and abdominal obesity have clinical signs of hypomagnesemia. The identified correlations between the serum magnesium content, the increase in arterial wall stiffness and the level of the blood pressure in such patients make it possible to consider hypomagnesemia as a predictor of early vascular remodeling.*

***Keywords:*** *hypomagnesemia, essential hypertension, obesity, vascular remodeling, young age.*

## Introduction

Essential hypertension (EHT) is the most widespread cardiovascular disease (CVD), which is the main cause of early disability and morbidity all around the world. It is diagnosed in more than 30% of the world's population among the individuals who are over 25 years old [*Egan B et al., 2010; WHO 2013*]. EHT appears quite often in adolescence, it is regarded as a dysfunction of the autonomic nervous system and that is why one pays not enough attention to it. The number of children and adolescents with high blood pressure is said to have been increasing in recent years. It has a significant impact on the development of fatal cardiovascular events [*Flynn J et al., 2017; Tagiyeva A, 2017*]. The labile hypertension identified in adolescence and regarded as a vegetative dysfunction transforms often into EHT. It has been shown that increased personal anxiety in individuals of young age is associated with a change in the reactivity of

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the vascular endothelium with the subsequent development of endothelial dysfunction of the "areactive vascular wall" type. It may contribute to the formation of the early vascular stiffness and the increased vegetative lability due to the sympathetic link against the background of the chronic stress provoking the onset and subsequently aggravating the course of cardiovascular diseases [*Bulgakov M et al., 2015; Treumova S et al., 2017*]. Both genetic predisposition [*Shih P, O'Connor S, 2008; Ivanytska T et al., 2018*] and a combination of a number of external factors (among which. much attention has been lately paid to hypomagnesemia [*Belovol A et al., 2013*]) play an important role in the mechanisms of progression of EHT.

Some studies have shown that a fruit and vegetable diet with a high content of potassium, magnesium and calcium is associated with lower morbidity and mortality from cardiovascular diseases [*He K et al., 2006*]. In addition, there is an inverse relationship between the level of magnesium in the serum and a damage of the cardiovascular system. [*DiNicolantonio J et al., 2018*]. It is noted that in patients with arterial hypertension, compared to those without the high blood pressure, there is a decrease in the level of the intracellular magnesium concentration with the elevated concentrations of sodium and calcium [*Cunha A et al., 2012*]. Magnesium is known to be the second intracellular cation which is involved in various biochemical processes [*Barbagallo M et al., 2003*]. Magnesium affects blood pressure by modulating vascular tone. The changes in the extracellular level of magnesium are also able to modulate changes in vascular tone due to the changes in calcium-dependent processes of production and release of nitric oxide [*DiNicolantonio J et al., 2018*]. An increase in the level of extracellular magnesium inhibits calcium influx, and, conversely, a decrease in the level of magnesium is accompanied by the activation of calcium influx through the calcium channels. At the same time, an increase in the intracellular level of magnesium leads to a decrease in the intracellular level of free calcium and contributes to vasodilation [*Houston M et al., 2011; Cunha AR et al., 2012*]. It should be emphasized that magnesium deficiency as a macroelement is associated with oxidative stress, pro-inflammatory readiness, endothelial dysfunction, the increased platelet aggregation, insulin resistance and hyperglycemia [*Mazur A et al,. 2007; Sontia B, Touyz R, 2007*].


*To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world*

It is known that the elasticity of the vascular wall has a significant impact on the formation of arterial hypertension and the risk of cardiovascular diseases. There are data which demonstrate the relationship between the blood plasma magnesium level, endothelial function, arterial stiffness and the thickness of the carotid intima-media complex [*Almoznino-Sarafian D et al., 2009; Cunha A et al., 2012*]. In the aspect of the described problem, it is also necessary to note the significance of the influence of the perivascular adipose tissue (the extra media index determined by the ultrasonographic method [*Druzhilov M et al., 2016; Wesley K et al., 2017*]) on the elasticity of the vascular wall, especially since there are indications of its redundancy in patients with EHT, as well as its influence on the nature and rate of progression of the disease [*Renna N et al., 2013*].

It should be noted that such issues as an imbalance of magnesium and features of vascular remodeling in the presence of obesity in patients with EHT are not sufficiently covered; it was a prerequisite for this work.

The aim of the study is to study the characteristics of changes in the level of magnesium in the blood serum, the elasticity of the vascular wall and to determine their possible relationship in young men with essential hypertension in the presence of abdominal obesity.

### *Materials and Methods*

The study included 86 male patients who were 22-35 years old (the mean age was 28.6±3.5 years) with EHT, (the I and II degrees, 74 and 26%, accordingly) which lasted 4.4±1.3 years (the diagno-

sis of EHT was established on the basis of the standard criteria [*Williams B et al., 2018*], the burdened family history by EHT was noted in 26.9% of the cases and by early cardiovascular events in 15.85% of cases. The body mass index (BMI) in the examined patients was 27.9 ± 0.5 *kg/m²* (BMI ≥25 and <30 *kg/m²* were considered as the overweight criterion, BMI ≥30 *kg/m²* as the criterion for obesity, abdominal obesity - girth waist > 102 *cm*). Abdominal obesity was diagnosed in 27 examined patients (31.55% of cases), who became the first study group (EHT with obesity), patients with EHT without the signs of abdominal obesity (59 patients, or 68.45% of patients) made up the second study group (EHT without obesity).The patients with EHT Grade III, symptomatic hypertension, endocrine pathology, the patients with cardiac arrhythmias, and those who need to use two or more antihypertensive drugs were not included in this study. The reference indices were obtained in 20 practically healthy individuals (the control group). They and the examined patients were of the same sex and age.

All the patients underwent the standard clinical, biochemical, and instrumental studies: a clinical blood test, determination of blood glucose, urea, creatinine, transaminases, total protein and protein fractions, potassium, calcium, sodium, magnesium, uric acid, C-reactive protein, lipidogram, urinalysis, electrocardiography in 12 standard leads, ultrasonographic examination of the abdominal cavity and retroperitoneal space. The elasticity of the arterial wall and its changes were assessed according to ultrasonography ("RADMIR ULTIMA Expert") in a semi-automatic mode, we analyzed the augmentation index, arterial stiffness index and the pulse wave velocity. The thickness of the perivascular adipose tissue was determined by the extra-media index of the carotid arteries (high resolution ultrasonic linear sensor), the distance between the inner surface of the posterior wall of the internal jugular vein and the outer surface of the intima-media complex of the anterior wall of the common carotid artery was measured at a distance of 1.0-1.5 *cm* proximal to the common carotid artery bifurcation. The thickness of the extra-media of the carotid artery included the wall of the internal jugular vein, perivascular adipose tissue and adventitia of the common carotid artery. [*Skilton M et al, 2009*].

A test, developed and approved by the UNESCO Center for Micronutrients [*Gromova A, Limanova O, 2014*], was used for screening diagnostics of magnesium deficiency. The peculiarities of the emotional state, the physiological manifestations of hypomagnesemia, the presence of conditions and diseases associated with the low magnesium level, dietary habits and taking medications with the potential for the formation of hypomagnesemia are taken into account in this test. The results were evaluated as the following ones: 38-54 points - pronounced magnesium deficiency, 28-37 - magnesium deficiency, 18-27 - moderate magnesium deficiency, 8-17 - risk group for magnesium deficiency, 0-7 - no magnesium deficiency. The serum magnesium level was determined by means of an automated biochemical analyzer (Cobas 6000; Roche Diagnostics).

The statistical calculation was done by using the license software packages: the Microsoft Excel editor and the statistical analysis program StatPlus Pro 6.2. Statistical significance is accepted at the level $p<0.05$.

### *Results and Discussion*

In the course of screening diagnostics for the detection of clinical signs of magnesium deficiency, it was established that in the EHT with obesity group, moderate magnesium deficiency (22.5±3.8 points) was observed in half of the cases (15 patients), the risk of its development (14.8±2.7 points) was noted in 9 patients, and the signs of magnesium deficiency (5.5±1.5 points) were absent only in 3 individuals. Patients in this group with moderate magnesium deficiency received the highest scores on the scales of the emotional state, physiological manifestations of hypomagnesia and the presence of conditions and diseases associated with low magnesium level. In group II (the patients with EHT), moderate magnesium deficiency was observed in 3 individuals, the risk of developing magnesium deficiency was in 19 individuals (15%), the signs of magnesium deficiency were absent in 37 patients (45%), besides, the highest scores were given according to emotional state

scales and features of nutrition. As for practically healthy individuals, the risk of magnesium deficiency was observed only in 4 persons, the other individuals had no symptoms of magnesium deficiency. Thus, as for the majority of young patients with EHT, the clinical signs of magnesium deficiency of varying severity were found, the differences were statistically significant ($p<0.05$) in comparison with the control group.

In the patients suffering from EHT with obesity, hypomagnesemia (0.7±0.09 *mmol/l*) was detected in almost 2/3 of the cases (17 patients), the values of serum magnesium were within the reference values (0.98±0.12 *mmol/l*) in other studied. In the group of the patients with EHT without obesity, hypomagnesemia (0.73±0.06) was found in a third of the patients, other patients had normal serum levels of this macroelement (1.01±0.16 *mmol/l*).These data were close to the screening test results (Figure 1).

The correlation analysis revealed a negative relationship between serum magnesium levels and indicators of the scale of physiological manifestations of hypomagnesemia (r=-0.52, p=0.031) in the patients with EHT with obesity. A strong negative relationship between the level of arterial hypertension and the serum magnesium content (r=-0.58, p=0.022) and a strong positive relationship between the level of arterial hypertension and total screening tests for magnesium deficiency (r= +0.66, p=0.031) were established in these patients.

Interesting data were obtained during an ultrasound study of the carotid artery. So, in the patients of the first group (EHT with obesity), higher rates of augmentation index were observed in comparison with the patients of the second group — EHT without obesity (1.58±0.18 and 1.3±0.13, accordingly, p=0.018), and the control group (0.85±0.1; p=0.036); the same tendency was also noted in relation of the arterial stiffness index (9.54±1.37 and 7.25±1.55 accordingly, p=0.023; in the control group 5.5±1.12; p=0.040), and the pulse wave velocity (7.25±0.84 *m/s* and 6.11±0.42 *m/s*; p=0.043; in the control group 5.15±0.25*m/s*; p=0.034. The correlation analysis revealed that the magnesium level in the serum of patients with EHT had a strong negative relationship with both the augmentation index (r =-0.68, p=0.023) and the arterial stiffness index (r=-0.55, p=0.042).

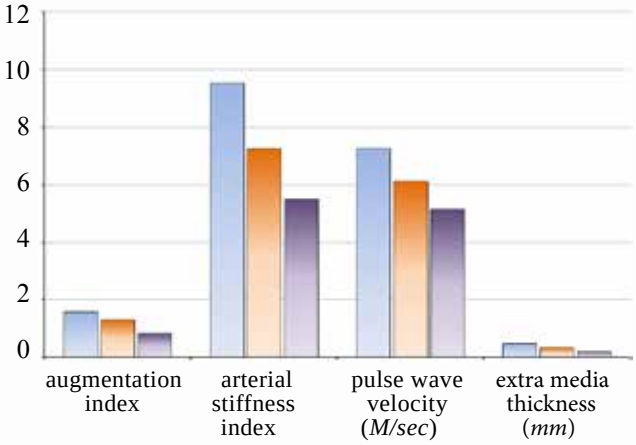


***Figure 1*** *Vascular wall elasticity indexes*
***Notes:*** *EH with (■) and without (■) obesity, control group (■)*

Extra-media thickness in patients of group I was 0.48±0.14, and was higher compared to the patients with EHT without obesity (0.34±0.18; p=0.014) and the control group (0.22±0.07; p=0.011). It was revealed that extra-media thickness in patients with EHT with obesity had strong correlations with the level of arterial hypertension (r= +0.68, p=0.033), the level of serum magnesium (r=-0.61, p=0.023), as well as with the augmentation index (r= +0.48, p=0.018) and low density lipoproteins (r= +0.69, p=0.002); comparing lipidograms between studied groups 1st and 2nd no statistically significant differences were found.

Thus, the conducted study allows us to make the following conclusions.

Young men with EHT and abdominal obesity are characterized by the presence of hypomagnesemia, which has clinically defined manifestations. The revealed correlations between the severity of hypomagnesemia, the increase in the arterial stiffness index, extra-media thickness and the intima-media complex, and blood pressure parameters in such patients allow us to consider it as a predictor of early vascular remodeling. The foregoing suggests finding possible ways to correct magnesium deficiency in young patients with EHT and taking into account its effectiveness as a preventive factor in the development of arterial stiffness.

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