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## THE EFFECT OF THERAPY WITH OLMESARTAN OR TELMISARTAN IN PATIENTS WITH ARTERIAL HYPERTENSION COMBINED WITH OBESITY

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### ABSTRACT

**The aim:** To evaluate the hemodynamic and echocardiographic parameters, the level of adiponectin and IL-6 in such patients under the influence of therapy with sartans (telmisartan or olmesartan) and atorvastatin 12 weeks later

**Materials and methods:** Fifty patients with arterial hypertension of II stage and 2 level, who underwent elective in-patient treatment were examined. During the next 12 weeks, they took olmesartan (1st group) or telmisartan (2nd group) in combination with atorvastatin.

**Results:** The combined use of olmesartan or telmisartan in with atorvastatin for 12 weeks had a resulted in a significant decrease in systolic and diastolic blood pressure, heart rate and myocardial mass. After treatment with olmesartan in combination with atorvastatin, the adiponectin content in the blood increased by 41.6% ( $p < 0.05$ ). In the group of patients who receiving telmisartan, an increase adiponectin level was noted in 80.0% of patients and a had shown a significantly higher increase in adiponectin levels, namely for 59.4% after treatment ( $p < 0.01$ ). The level of IL-6 has significantly decreased, both with the administration of olmesartan (2.7 times) and telmisartan (2.6 times) ( $p < 0.01$ ).

**Conclusions:** Telmisartan, in comparison with olmesartan, significantly reduces the size of the left ventricular and left atrium myocardium, and decreased left ventricular mass index. Telmisartan improves the cardio-metabolic profile of obese and hypertensive patients by increase of adiponectin concentrations and decrease of IL-6 levels.

**KEY WORDS:** arterial hypertension, obesity, olmesartan, telmisartan, atorvastatin, adiponectin, IL-6

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### INTRODUCTION

Comorbidity, in particular, arterial hypertension (AH) in combination with obesity is a serious problem in internal medicine, which is associated with the early development of lesions of target organs.

Pathogenesis of hypertension in obese persons is accompanied by hyperactivity of the sympathetic and renin-angiotensin-aldosterone system, vasoconstriction, metabolic disorders and an increase of the volume of circulating blood [1]. On the background of such a combined pathology, endothelial dysfunction occurs, which contributes to the structural and functional re-arrangement of the left ventricular myocardium (LV) with the formation of hypertrophy, followed by myocardial dysfunction [2, 3].

Remodeling of LV damages the target organs in hypertension and is an independent risk factor for cardiovascular events such as heart failure, myocardial infarction, arrhythmias and sudden cardiac death [4].

Different cytokines are involved in the pathogenesis of this comorbidity, among which a great importance is given to pro-inflammatory interleukin 6 (IL-6) and protective cytokine – adiponectin.

Adiponectin is an important adipocytokine produced by white adipocytes and has anti-atherosclerotic and anti-inflammatory properties, also it improves insulin resistance

[4]. We had established that reduction of its level is associated with progression of hypertension and remodeling of the left heart [5].

It is currently known that in the remodeling of the cardiovascular system, an important role is played by immune-inflammatory processes.

On the other hand, IL-6 is a pro-inflammatory cytokine, which has the biggest damaging effect upon myocardium.

However, the role of these cytokines with myocardial restructuring is not entirely clear.

An important problem in treating patients with hypertension in combination with obesity is the selection of adequate therapy. Among the various groups of drugs used to treat this comorbidity, the focus is done on the antihypertensive properties of these drugs. Alongside, some of the sartans may increase the level of adiponectin, including olmesartan and telmisartan.

Olmесartan and telmisartan are antagonists of the angiotensin II receptor. They are effective both in lowering blood pressure (BP), helping to reduce the size of the hypertrophied left heart, and have a positive effect on the level of adiponectin [4, 6].

Nevertheless, there are no definitive findings on the effect of sartans on the level of BP, the level of adiponectin and IL-6, as well as the influence on the hypertrophy of the left parts of heart

## THE AIM

The aim of this work was to evaluate the hemodynamic and echocardiographic parameters, the level of adiponectin and IL-6 in patients with hypertension in combination with obesity under the influence of therapy with sartans (telmisartan or olmesartan) and atorvastatin 12 weeks later.

## MATERIALS AND METHODS

Fifty patients with AH of II stage and 2 level, who underwent elective in-patient treatment were examined. After initial examination, the patients were divided into 2 groups and treatment was prescribed: during the next 12 weeks, they took olmesartan (1st group) or telmisartan (2nd group) in combination with atorvastatin. Patients of the 1st group had telmisartan 20 mg and atorvastatin 20 mg once a day. Patients of the 2nd group took olmesartan 10 mg and atorvastatin 20 mg once a day. Clinical-hemodynamic and laboratory efficacy of these drugs were evaluated following 12 weeks of treatment. Therapy was considered effective if by the end of the observation period the target BP level was 130/85 mmHg and below. The metabolic efficacy of drugs was assessed by the dynamics of blood lipid levels, adiponectin, IL-6 and hemodynamic parameters.

Among the patients of the group with combined pathology (AH with obesity), there were 19 (38%) men, women – 31 (62%), average age was  $56.59 \pm 1.11$ .

Diagnosis of hypertension was established according to the standards of diagnosis and treatment in accordance with the recommendations of the Ukrainian Association of Cardiologists (2012), the European Society for Arterial Hypertension and the European Society of Cardiologists (ESH / ESC, 2013).

All patients underwent anthropometric, general-clinical, laboratory (lipid spectrum of blood), instrumental (electrocardiography, echocardiography, ultrasonography) examinations and immuno-enzymatic methods of study: «Adiponectin ELISA-09» kit by Mediagnost (Germany) and «Interleukin-6 IFA BEST» kit by Vector-Best (Russian Federation).

Patients were evaluated for height, body weight and body mass index according to the commonly accepted formulas.

The level of office BP was measured according to the standard of examination. The heart rate (HR) was determined after the 2nd measurement of the pressure.

The obtained results were statistically processed using Student's criterion, Pearson correlation analysis using MS Excel.

## RESULTS AND DISCUSSION

Patients included in the study had AH of stage II upon admission and 2nd level arterial hypertension, with moderate, high and very high risk.

The duration of AH varied from 5 to 25 years.

After 12 weeks, treatment with the combination of olmesartan or telmisartan with atorvastatin in patients of both groups showed a significant improvement in the general condition, which was manifested by the reduction of all

complaints, mostly backhead and frontal pain, cardiac discomfort heart and palpitation.

The results of the studies had showed that administration of olmesartan or telmisartan with atorvastatin in the corresponding doses had lead to a statistically significant decrease of systolic BP (SBP), diastolic BP (DBP) and heart rate on the background of improvement of the general condition of patients [7] (Table 1).

The results of ultrasound examination of the heart following 3 months of treatment showed a significant decrease in LV, left atrium (LA), LV Mass Index (LVMI) in patients receiving telmisartan, in contrast to the administration of olmesartan [5]. At the same time, there was a significant dynamics in the increase of ejection fraction and reduction of LV Mass (LVM) in the appointment of both sartans (Table 2).

After treatment with olmesartan in combination with atorvastatin, the adiponectin content in the blood increased by 41.6% ( $p < 0.05$ ). This may indicate on direct effect of olmesartan on the level of adiponectin, which, according to literature, has the ability to increase the concentration of this hormone in serum [8] (Table 3).

As well, in the 2nd group of patients receiving telmisartan, an increase in this fat hormone level was noted in 80.0% of patients and a had shown a significantly higher increase in adiponectin levels, namely for 59.4% after treatment ( $p < 0.01$ ).

The level of pro-inflammatory IL-6 has significantly decreased, both with the administration of olmesartan (2.7 times) and telmisartan (2.6 times)  $p < 0.01$ .

In patients with AH in combination with obesity, remodeling of the left heart departments is observed as the most common complication of AH. The mechanisms that bind obesity and the development of AH are not fully understood. Among the factors that can take part in the remodeling of the left heart departments, an important role is given to the relationship between the levels of adiponectin and IL-6.

Our studies had proven that the administration of telmisartan and olmesartan resulted in a significant decrease in IL-6 on the background of a significant increase in adiponectin levels. As a result of anti-hypertensive therapy by both sartans, regression of the left heart departments was observed. However, telmisartan was more effective compared with olmesartan in decreasing LV, LA, and LVMI. On the whole, these representatives of the saratans family are effective in treating of AH in obese patients due to pronounced lowering of BP, decreasing echocardiographic parameters by positively influencing the adiponectin content and reducing IL-6.

## CONCLUSIONS

1. The administration of telmisartan and olmesartan resulted in a significant decrease in systolic, diastolic BP, heart rate and myocardial mass.
2. Telmisartan, in comparison with olmesartan, significantly reduces the size of the left atrium, left ventricular and decreased LV Mass Index.

**Table 1.** Dynamics of anthropometric and hemodynamic indices

Indexes	I group (olmesartan and atorvastatin)		II group (telmisartan and atorvastatin)	
	before treatment	after treatment	before treatment	after treatment
BMI, kg/m <sup>2</sup>	32,78±0,63	31,99±0,57	35,54±1,00	34,23±0,95
Waist volume, cm	90,00±2,15	89,08±2,01	92,72±1,99	91,00±1,96
Thigh volume, cm	92,44±0,71	91,04±0,71	91,40±0,83	90,16±0,82
SBP, mm Hg,	168,20±2,28	144,40±1,64*	169,80±1,94	138,60±1,72*
DBP, mm Hg,	107,20±0,66	81,80±0,64*	109,60±0,75	76,40±1,02*
HR, per 1 min	85,36±0,65	77,92±0,45*	86,48±0,69	74,88±0,40*

Note: \* p < 0.01 compared to pre-treatment rates.

**Table 2.** The data of ultrasonography of the heart in patients

Indexes	I group (olmesartan and atorvastatin)		II group (telmisartan and atorvastatin)	
	before treatment	after treatment	before treatment	after treatment
RV (0,9-2,6 cm)	2,38±0,05	2,41±0,05	2,34±0,06	2,31±0,06
IVS (0,6-1,1 cm)	1,09±0,04	1,11±0,04	1,04±0,04	1,03±0,03
LV (3,5-5,7 cm)	4,88±0,15	4,56±0,09	4,89±0,13	4,48±0,11**
Wall of LV (0,6-1,1 cm)	1,05±0,03	1,06±0,02	1,10±0,06	1,08±0,05
LA, cm	4,21±0,09	4,08±0,07	4,68±0,05	3,98±0,06*
AA, cm	3,22±0,07	3,19±0,06	3,10±0,07	3,12±0,06
EF (over 55 %)	57,28±1,24	61,20±0,70*	55,96±0,07	59,92±0,80*
MM (male 115-150 g, female 95-120 g)	213,68±14,33	173,23±12,85**	234,31±19,45	183,21±10,47**
MMI (male 71-94 g/m <sup>2</sup> , female 71-89 g/m <sup>2</sup> )	100,47±7,18	85,56±6,32	117,68±10,31	88,71±4,82**

Note: \* p < 0.01 – in comparison with the indicators before treatment; \*\* p < 0,05 – in comparison with the indicators before treatment; • – p < 0,05 probability of change under the influence of complex therapy with olmesartan or telmisartan.

**Table 3.** Dynamics of adiponectin and IL-6

Indexes	I group (olmesartan and atorvastatin)		II group (telmisartan and atorvastatin)	
	before treatment	after treatment	before treatment	after treatment
Adiponectin, (female – 11,7 µg/ml, male – 7,9 µg/ml)	15,75±1,03	22,30±1,58**	16,27±0,57	25,94±0,65*•
IL-6, (1,5 – 7 pg/ml)	8,68±1,08	3,12±0,41*	9,57±0,96	3,68±0,50*

Note: \* – p < 0.01 compared with the indicator before treatment, \*\* – p < 0,05 compared with the treatment; • – p < 0,05 probability of change under the influence of complex therapy with olmesartan or telmisartan.

3. Telmisartan improves the cardio-metabolic profile of obese and hypertensive patients by increase of adiponectin concentrations and decrease of IL-6 levels.

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**Conflicts of interest:**

*Authors declare no conflict of interest.*

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