

## Hypotensive Effect of Moxonidin in Patients with Adiposity

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### ABSTRACT

Nowadays for treatment of arterial hypertension a set of hypotensive drugs are available, however in case of obesity they are less effective. The aim of our investigation was study of moxonidin effect on metabolic disorders and detection of advantages of moxonidin administration in case of obese patients with the purpose of arterial pressure correction. Total of 30 patients with various degree of obesity and moderate arterial hypertension accompanied by various metabolic disorders have been investigated. Has been stated that moxonidin is effective hypotensive drug that positively affects on metabolism and on the background of hypo-calorie diet decreases systolic and diastolic pressures significantly.

**KEYWORDS:** *hypertension, obesity, moxonidin*

Nowadays, obesity and arterial hypertension are the most important problems for population. Topicality of the above-mentioned pathologies is determined by widespread of risk factors leading to obesity and hypertensive disease, which is obvious and enrooted in population especially for the last decade. Mainly it concerns life-style and feeding type alterations. At modern technical progress, human's life-style is less mobile; moreover, daily ration includes high calorie fatty-reach products, which in turn, in the presence of genetic predisposition, supports development and manifestation of the mentioned pathologies.

Another reason, emphasizing topicality of the raised question is the presence of reason-result relations between excessive body weight and cardio-vascular pathology.

Nuses Health Study has shown that in individuals, above 18 years, risk for cardio-vascular pathology increases with each excess kilogram by 3,1%. According to the literary data, arterial hypertension in 17% of cases is determined by obesity.

It must be mentioned that in the presence of both, obesity and arterial hypertension, the risk for cardio-vascular complications (atherosclerosis, ischemic disease of heart, myocardial infarction, insult) increases much more.

Thus, coming from the afore-said, prevention and elaboration of effective treatment measures of obesity and arterial hypertension is of paramount importance.

Although, many anti-hypertensive drugs are available, most of them are less effective in the presence of obesity. Moreover, arterial hypertension, developed on the background of obesity, negatively affects on metabolic processes. That's why, at such instances, use of anti-hypertensive drugs that are able regulate both, arterial hypertension and metabolic processes are suggested.

It is well known that the central nervous system plays a major role in regulation of arterial pressure and arterial hypertension is the result of increased sympathetic nervous system tonus.

The same process is detected in case of obesity. Activation of sympathico-adrenal and renin-angiotensin-aldosterone systems displays.

These processes increase stroke volume and cardiac output, peripheral resistance, reabsorption of sodium and

water leading to increase in circulating blood volume - hypervolemia. Hypervolemia in turn increases peripheral resistance and develops arterial hypertension.

Noteworthy that sensitivity of cardiomyocytes and vascular smooth muscles' cells to vasopressive agents increases, the more so that in case of dyslipidemia synthesis of vasoconstrictors (endothelin-1 and thromboxan-A<sub>2</sub>) are increased and synthesis of vasodilators (nitric oxide and prostacyclin) is reduced. So, endothelial dysfunction displays.

In case of increased resistance to insulin and hyperglycemia increases glucose filtration resulting exaggerated reabsorption of glucose and sodium, which in turn supports development of hypervolemia, increased peripheral vascular resistance and arterial hypertension.

The aim of investigation - due to the leading role of hypersympathicotonia determining arterial hypertension in case of obesity, the aim of our investigation was to reduce sympathetic nervous system's activity via the influence on appropriate centers.

Evaluation of positive effects would reveal advantages of the suggested method compared to the traditional methods of anti-hypertensive treatment.

It is known that in the brain (retro-ventro-lateral region, hypothalamic ventromedian region and anteroventral nucleus of III ventricle) I<sub>1</sub> receptors for imidazole regulating sympathetic tonus and arterial pressure are detected.

We were aimed to study effect of moxonidin, agonist of imidazole receptors (I<sub>1</sub>) on arterial pressure and other metabolic indices in patients with various degree of obesity.

### MATERIAL AND METHOD

A total of 30 patients with moderate form of hypertensive disease (according to the classification of world health organization) were investigated. They applied to clinics with the diagnosis of obesity.

According to the classification of world health organization, of 30 patients 1 had excessive body weight (body mass index - BMI 26,4 kg/m<sup>2</sup>), 9 patient - I degree obesity (BMI 32,23±1,22 kg/m<sup>2</sup>), 8 patient - II degree obesity (BMI 36,95±1,16 kg/m<sup>2</sup>) and 12 patient - III degree obesity (BMI 47,76±5,20 kg/m<sup>2</sup>).

Has been investigated: blood lipid specter (triglycerides, cholesterol), factors of coagulation (prothrombin index, INR), glucose tolerance test, concentration of nitric oxide, body mass index, circumferences of the waist and hip, electrocardiography and echocardiography (left ventricular ejection fraction, thickness of ventricular septum, left atrial size), and arterial pressure, using the Korotckoff's method.

After primary clinical and laboratory investigations, patients were subjected to moxonidin therapy with the dose of 200 mcg once a day in the morning. During the treatment period patients were examined twice with the intervals of 2 weeks. Treatment procedures have been carried out on the background of hypo-calorie diet and calories were selected according to the degree of obesity.

Caloric value of the daily ration for patients with excessive body mass consisted 1000 kcal; for patients with I degree obesity - 600 kcal; for patients with II degree obesity - 800 kcal; for patients with III degree obesity - 1500 kcal.

**RESULTS AND DISCUSSION**

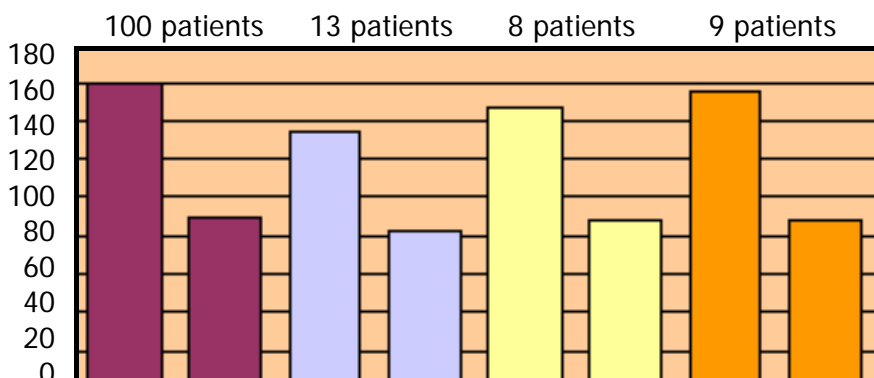
Initial systolic arterial pressure was  $60 \pm 9,94$  mm.Hg and diastolic -  $90 \pm 8,99$  mmHg; Heart rate -  $78,5 \pm 17,7$  per minute; Index of waist/hip circumferences -  $0,91 \pm 0,096$ ;

Blood test results: Triglycerides -  $216,8 \pm 52,23$  mg/dl; Cholesterol  $243,3 \pm 29,89$  mg/dl; Index of prothrombin  $103 \pm 12,49\%$ ; INR -  $0,96 \pm 0,18$ ; Glucose -  $94,5 \pm 17,32$  mg/dl, Ventricular ejection fraction -  $64 \pm 5,07\%$ , Thickness of ventricular septum -  $10 \pm 1,97$  mm; Left atrial size -  $39 \pm 4,32$  mm.

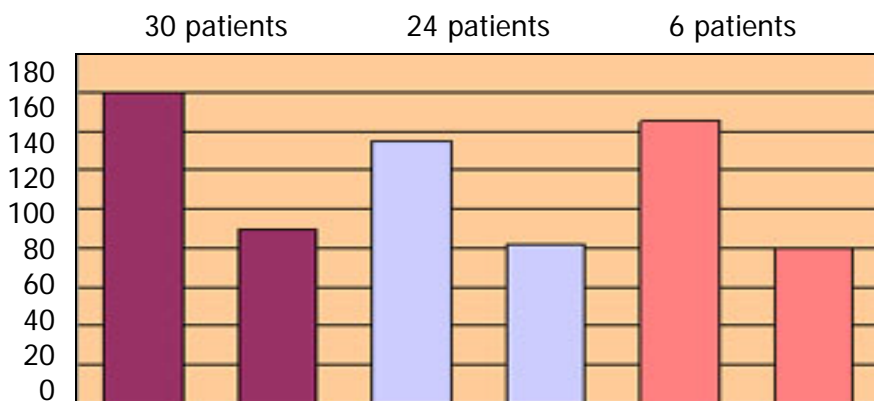
After 2 weeks of treatment with moxonidin arterial pressure was normalized in 13 patients (43,3%), in 8 patient arterial pressure was reduced by 10 mmHg (26,7%), and in 9 patient - lesser than 10 mmHg (30%). According to the obtained results, moxonidin dose was increased in 17 patients (400 mcg, twice a day). Heartbeat was not changed obviously.

After 4 weeks of treatment, patients underwent to repeated laboratory, electrocardiographic and echocardiographic examinations. Examinations have shown decreased level of triglycerides and cholesterol, improved indices of rheology, disorders of tolerance to glucose were not revealed.

According to the electrocardiographic data, disorders of heart rhythm, automatism and conductivity were not detected. Echocardiographic data were not changed as well.



**Fig.1** Indices of arterial pressure after 2 weeks of treatment.



**Fig.2** Indices of arterial pressure at the end of investigation.

	Left atrial size	Ventricular septal thickness	Ejection fraction
Before treatment	39±4,32 mm	10±1,97 mm	64±5,07%
After treatment	39±3,67 mm	10±1,78 mm	62±4,31%

**Tab.1** Results of investigation

	TG mg/dl	Ch mg/dl	PI %	INR	PTG mg/dl
Before treatment	216,8±52,2	243,3±29,89	103±12,49	0,96±0,18	94,5±17,3
After treatment	191± 45,32	214,3±25,2	96±5,93	1,2±0,11	96±4,9

**Tab.2** Indices of arterial pressure.**CONCLUSION**

Moxonidin is the effective antihypertensive drug positively effecting on metabolism in patients with obesity.

On the background of hypo-calorie diet it decreases systolic and diastolic pressures significantly.

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## Гипотензивная эффективность моксонидина в группе больных ожирением

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### Р Е З Ю М Е

Для терапии артериальной гипертензии существует множество препаратов, однако во время ожирения их эффективность снижается. Цель исследования - изучить влияние моксонидина на метаболические нарушения и его преимущества при лечении больных с ожирением с целью коррекции артериального давления. Обследовали 30 пациентов с различной степенью ожирения и умеренной артериальной гипертензией (по классификации ВОЗ) с сопутствующими разнообразными метаболическими нарушениями. Установлено, что моксонидин является эффективным гипотензивным средством, который положительно влияет на метаболический обмен и на фоне гипокалорийной диеты в виде монотерапии в дозе 200-400 мкг вызывает достоверное снижение как систолического, так и диастолического артериального давления.

**Ключевые слова:** артериальная гипертензия, ожирение, моноксидин