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# The level of metabolic hormones in young people with arterial hypertension against the background of abdominal obesity

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## ABSTRACT

**Aim.** To study the level of metabolic hormones in young people with arterial hypertension (AH) against the background of abdominal obesity (AO).

**Materials and methods.** The study included 498 people who were divided into two groups. The experimental group encompassed 250 people with AH, of which – 159 people had AO, the average systolic pressure – 141.9 ± 13.9 mm Hg, diastolic pressure – 95.6 ± 7.5 mm Hg. The control group included 248 people comparable to the experimental group by gender and age, of whom 104 people had AO, the average systolic pressure – 118.5 ± 9.8 mm Hg, diastolic pressure – 77.8 ± 7.4 mm Hg. The levels of amylin, C-peptide, ghrelin, glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1), glucagon, insulin, pancreatic polypeptide (PP), and peptide YY (PYY) were determined by the multiplex analysis. The level of glucose was determined by the enzymatic method. Statistical processing of the results was carried out using the SPSS 13.0 software.

**Results.** Patients with AH had higher levels of amylin, C-peptide, and glucose and lower levels of PYY. There was no significant difference between the experimental group and the control group for the rest of the studied parameters. In the experimental group, the C-peptide, GLP-1, glucagon, and insulin levels were associated with AO. In the control group, the association of AO with the levels of C-peptide, insulin, and glucose was shown. The odds of AH in people under the age of 45 years were associated with a decrease in the level of PYY, a rise in the amylin levels, and an increase in waist circumference.

**Conclusion.** Of the studied metabolic hormones, an increased level of amylin and reduced PYY can serve as potential biomarkers indicating high odds of developing AH in people under 45 years of age. AO is a factor that contributes to the development of AH at a young age.

**Keywords:** abdominal obesity, metabolic markers, arterial hypertension

**Conflict of interest.** The authors declare the absence of obvious or potential conflict of interest related to the publication of this article.

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**Conformity with the principles of ethics.** All study participants signed an informed consent. The study was approved by the Ethics Committee at the Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences (Protocol No. 167 of 26.11.2019).

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# Уровень метаболических гормонов у молодых людей с артериальной гипертензией на фоне абдоминального ожирения

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**РЕЗЮМЕ**

**Цель:** исследовать уровень гормонов метаболизма у молодых людей с артериальной гипертензией (АГ) на фоне абдоминального ожирения (АО).

**Материалы и методы.** В исследовании приняли участие 498 человек, которые вошли в две группы. Основная группа – 250 человек с АГ, из них 159 с АО, среднее систолическое давление (СД) – 141,9 ± 13,9 мм рт. ст., диастолическое давление (ДД) – 95,6 ± 7,5 мм рт. ст. Группа контроля – 248 человек, сопоставимых с основной группой по полу и возрасту, с АО – 104 человека, средний уровень СД и ДД – 118,5 ± 9,8 и 77,8 ± 7,4 мм рт. ст. соответственно. Методом мультиплексного анализа определяли уровень амилина, С-пептида, грелина, глюкозо-зависимого инсулинотропного полипептида (ГИП), глюкагоноподобного пептида-1 (ГПП-1), глюкагона, инсулина, панкреатического полипептида (ППП), пептида YY. Уровень глюкозы определяли энзиматическим методом. Статистическая обработка результатов проводилась в программе SPSS 13.0.

**Результаты.** У пациентов с АГ отмечены более высокий уровень амилина, С-пептида, глюкозы и более низкий уровень пептида YY. Достоверной разницы между основной и контрольной группой по остальным изучаемым показателям не выявлено. В основной группе с АО были связаны показатели С-пептида, ГПП-1, глюкагона, инсулина. В контрольной группе была показана связь АО с уровнем С-пептида, инсулина и глюкозы. Относительный шанс наличия АГ у людей в возрасте до 45 лет был связан со снижением уровня пептида YY, с повышением уровня амилина и увеличением окружности талии.

**Заключение.** Из изученных нами гормонов метаболизма повышенный уровень амилина и сниженный показатель пептида YY могут служить в качестве потенциальных биомаркеров, указывающих на высокую вероятность развития АГ у людей до 45 лет. Абдоминальное ожирение является фактором, который способствует развитию АГ в молодом возрасте.

**Ключевые слова:** абдоминальное ожирение, маркеры метаболизма, артериальная гипертензия

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## INTRODUCTION

The prevalence of arterial hypertension (AH), which is the leading risk factor for cardiovascular diseases (CVDs), among the adult population reaches 45% [1, 2]. Obesity (primarily abdominal obesity (AO)) as a factor that causes an increase in AH is registered in the population, including young people, with increasing frequency [3, 4]. Both AO and AH contribute to CVDs, and their combination is associated with an even higher risk and a heavier course of AH. Some of the main causes of AH in obesity include hyperinsulinemia, insulin resistance, an imbalance of gastrointestinal hormones, such as ghrelin, amylin, YY peptide, glucagon-like peptide -1, and others, but the pathogenesis of AH in obese and non-obese people may differ. Despite improvements in the understanding of the pathogenetic mechanisms of AH and obesity, not all processes that underlie the comorbidity of obesity and AH have been studied, especially at a young age. Therefore, the aim of our research was to investigate the level of metabolic hormones in young people with AH and AO.

## MATERIALS AND METHODS

The study was carried out on the basis of a sample from the population screening of young residents (aged 25–44 years) of Novosibirsk, which was conducted at the Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences from 2013 to 2016. We selected 3,000 men and women aged 25–44 years from the database of the Territorial Compulsory Health Insurance Fund using a random number generator; 1,512 people responded to the invitation and took part in the screening. They filled out questionnaires, gave an informed consent to participate in the study, underwent anthropometric and instrumental examinations, and biological material was obtained from them.

The experimental group included all persons with newly diagnosed AH with systolic pressure greater than 140 mm Hg and / or diastolic pressure greater than 90 mm Hg, according to the clinical guidelines "Arterial hypertension in adults" approved by the Ministry of Health of Russia in 2020 [5]. The exclusion criterion was diabetes mellitus indicated in the questionnaire or fasting plasma glucose level greater than 7 mmol / l [6]. AO was recorded with a waist circumference of more than 80 cm in women and more than 94 cm in men [7]. Patients without AH, comparable in gender and age, were randomly recruited in the control group. The characteristics of the studied groups are shown in Figure.

In all patients, blood for the biochemistry test was taken in the morning on an empty stomach from the ulnar vein no earlier than 12 hours after the last meal. The levels of amylin, C-peptide, ghrelin, glucose-dependent insulinotropic polypeptide (GIP), glucagon–like peptide-1 (GLP-1), glucagon, insulin, pancreatic polypeptide (PP), and YY were determined by the multiplex analysis using the Human Metabolic Hormone V3 kit (EMD Millipore Corporation, Germany) on the Luminex 20 MAGPIX flow cytometer. Glucose was determined by the enzymatic method using the Thermo Fisher reagent kit (Finland) on the KONELAB Prime 30i biochemical analyzer (Finland).

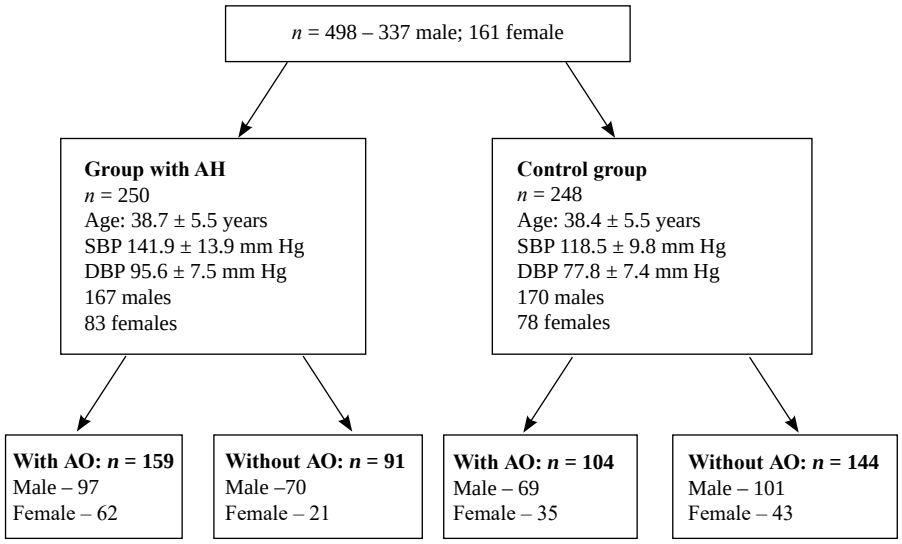


Figure.
Characteristics of the studied groups

Statistical processing of the results was carried out in the SPSS 13.0 software. The normality of data distribution was checked by the Kolmogorov – Smirnov test. Anamnestic data were presented as the mean and the standard deviation $M \pm SD$. Non-normally distributed quantitative variables were presented as the median and the interquartile range *Me* [*Q*25%; *Q*75%]. Normal distribution was seen only in two of the biochemical parameters studied by us; they were also presented as the median and the interquartile range *Me* [*Q*25%; *Q*75%]. The groups were compared using the nonparametric Mann – Whitney test. The correlation analysis was carried out using the Spearman's rank correlation coefficient. To identify the associations of the presence / absence of AH with the studied parameters, the multivariate logistic regression analysis was performed. The differences were statistically significant at $p < 0.05$.

## RESULTS AND DISCUSSION

In young patients with AH, we found an imbalance of metabolic markers compared to healthy controls. Against the background of AO, these shifts are most pronounced (Table).

Table

**The level of metabolic markers in young people with and without arterial hypertension, depending on the presence or absence of abdominal obesity**

| Parameter | | Control group | | Study group | | *p* |
|---|---|---|---|---|---|---|
| | | *Me* [$Q_{25\%}$; $Q_{75\%}$] | *p** | *Me* [$Q_{25\%}$; $Q_{75\%}$] | *p** | |
| Amylin, pg / ml | without AO | 44.7 [39.4; 48.8] | 0.551 | 71.9 [20.4; 73.2] | 0.16 | 0.0001 |
| | with AO | 44.7 [38.5; 55.7] | | 72.2 [26.5; 75.8] | | 0.0001 |
| C-Peptide, ng / ml | without AO | 0.86 [0.55; 1.95] | 0.003 | 0.86 [0.54; 2.01] | 0.0001 | 0.903 |
| | with AO | 1.48 [0.70; 2.78] | | 1.99 [0.89; 3.58] | | 0.036 |
| Ghrelin, pg / ml | without AO | 156.3 [94.5; 256.2] | 0.808 | 156.1 [107.8; 209.4] | 0.124 | 0.707 |
| | with AO | 156.6 [91.9; 302.7] | | 170.7 [116.3; 297.1] | | 0.422 |
| GIP, pg / ml | without AO | 77.0 [43.5; 121.1] | 0.456 | 78.6 [43.3; 117.9] | 0.573 | 0.931 |
| | with AO | 83.9 [40.8; 124.7] | | 83.1 [44.0; 133.0] | | 0.96 |
| GLP-1, pg / ml | without AO | 583.6 [330.5; 788.7] | 0.054 | 644.6 [299.1; 815.3] | 0.017 | 0.981 |
| | with AO | 643.7 [381.2; 940.1] | | 720.3 [374.9; 935.7] | | 0.571 |
| Glucagon, pg / ml | without AO | 43.6 [28.1; 58.7] | 0.695 | 45.2 [27.9; 57.9] | 0.043 | 0.941 |
| | with AO | 43.3 [28.9; 72.4] | | 48.8 [36.1; 67.5] | | 0.196 |
| Insulin, pg / ml | without AO | 1,934.6[ 406.9; 2,889.7] | 0.028 | 2,072.9[1,256.4; 2,776.3] | 0.048 | 0.366 |
| | with AO | 2,343.3 [931.0; 3,262.1] | | 2,365.1 [1,256.4; 3,282.3] | | 0.512 |
| PP, pg / ml | without AO | 125.9 [59.9; 185.3] | 0.468 | 90.0 [47.4; 185.1] | 0.23 | 0.343 |
| | with AO | 135.4 [59.4; 201.7] | | 122.9 [62.0; 198.3] | | 0.743 |
| YY, pg / ml | without AO | 310.4 [79.5; 372.5] | 0.936 | 208.5 [69.3; 303.4] | 0.636 | 0.011 |
| | with AO | 310.4 [48.2; 420.6] | | 208.5 [82.6; 303.4] | | 0.273 |
| Glucose, mmol / l | without AO | 5.6 [5.2; 5.9] | 0.002 | 5.9 [5.6; 6.1] | 0.505 | 0.0001 |
| | with AO | 5.8 [5.4; 6.2] | | 5.9 [5.5; 6.4] | | 0.116 |

The level of amylin, a multifunctional peptide hormone, that is produced by the pancreas along with insulin and participates in carbohydrate metabolism, in our study was 1.6 times higher ($p = 0.0001$) in patients with AH compared to the control group. The effect of AO on the level of amylin was not revealed. M.T. Kailasam et al. [8] also found an increase in plasma amylin in AH, but, unlike our results, body mass index in their study was a strong predictor of an increase in circulating amylin.

Patients with AH also had higher levels of C-peptide, which is a fragment of endogenously produced proinsulin, and glucose (by 1.5 ($p = 0.003$) and 1.1 ($p = 0.0001$) times, respectively). In the study by S.I. Safronova et al. [9], the level of C-peptide was also higher in hypertensive patients compared to normotonic ones.

The level of the YY peptide in AH patients was 1.6 times lower (p = 0.006) compared to the control group, which is not consistent with the data obtained by E. Haj-Yehia et al. [10], where AH was more common in patients with high YY levels due to the direct vasoconstrictive effect of the peptide (in the authors' view). The difference can be explained by the fact that E. Haj-Yehia et al. studied patients with acute myocardial infarction.

There was no significant difference between the experimental and control groups in the rest of the studied parameters. Since the groups differed in waist circumference ($p = 0.0001$), further, in order to

consider the influence of AO, we analyzed the studied parameters depending on the presence / absence of AO. The results obtained in the study of serum metabolic markers are presented in Table.

In the control group, the level of statistical significance of differences $p < 0.05$ for C-peptide, insulin, and glucose was found between the subgroups with and without AO. The level of C-peptide was 1.7 times higher, and the level of insulin was 1.3 times higher in the subgroup with AO. The glucose concentration in this subgroup was 4% higher. Also, in the control group, there was a trend toward an increase ($p = 0.054$) in GPP-1 in patients with AO.

For the AH group, the differences between the subgroups were in the levels of C-peptide, insulin, GLP-1, and glucagon. C-peptide was 2.3 times higher in the subgroup with AO and AH, GLP-1 was 12% higher in patients, glucagon was 8% higher, and insulin was 15% higher compared to patients with AH but without AO. The remaining parameters in the AH group also did not depend on the presence of AO. The level of C-peptide was the highest in the subgroup with AO and AH.

When conducting the correlation analysis to assess the relationship of the studied biomarkers with the parameters characterizing AH, a weak correlation of systolic pressure parameters with amylin ($r = 0.224$; $p = 0.0001$), C-peptide ($r = 0.156$; $p = 0.001$), and glucose ($r = 0.23$; $p = 0.0001$) was revealed. Diastolic pressure was correlated with the same parameters: with amylin ($r = 0.260$; $p = 0.0001$), C-peptide ($r = 0.175$; $p = 0.0001$), and glucose ($r = 0.224$; $p = 0.0001$). There was no correlation with age for the studied markers.

To assess the odds of AH at a young age, the multivariate logistic regression analysis was performed, where the dichotomous parameter of the presence / absence of early AH was taken as a dependent variable, and the studied biomolecules and waist circumference were taken as independent variables. The relative chance of early AH was associated with a decrease in the level of YY (Exp(B) = 0.99; $p = 0.0001$; confidence interval (CI): 0.988–0.994), an increase in amylin levels (Exp(B) = 1.04; $p = 0.0001$; CI: 1.032–1.059), and an increase in waist circumference (Exp(B) = 1.05; $p = 0.0001$; CI: 1.019–1.062). Thus, with a decrease in the concentration of YY by 1 pg / ml and an increase in amylin by 1 pg / ml, the odds of having AH at a young age increase by 1 and 4%, respectively. With an increase in waist circumference by one centimeter, the odds of having AH in people under 45 years increase by 5%.

## CONCLUSION

Of the studied metabolic markers, an increased level of amylin and a reduced level of YY can serve as potential biomarkers indicating high odds of AH in people under 45 years, and AO is a modifiable factor that contributes to the development of AH at a young age.

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## Authors' contribution

Polonskaya Ya.V. – conception and design, statistical processing and interpretation of the results, drafting of the article. Kashtanova E.V. – conception and design, significant contribution to the interpretation of the data. Stakhneva E.M. – conception and design, editing of the manuscript. Shramko V.S. – carrying out of clinical and biochemical studies, editing of the manuscript to increase its scientific value. Sadovski E.V. – carrying out of clinical and biochemical studies, editing of the manuscript. Ledovskikh S.R. – compilation of the database, carrying out of the clinical and biochemical studies, editing of the manuscript. Shcherbakova L.V. – statistical processing and analysis of the data. Garbuzova E.V. – editing of the manuscript to increase its scientific value. Khudyakova A.D. – significant editing of the manuscript. Ragino Yu.I. – significant contribution to conception and design of the study, significant editing of the manuscript to increase its scientific value.

All authors approved the final version of the manuscript for publication and agreed to bear responsibility for all aspects of the work associated with proper study and solution of issues related to the accuracy and honesty of any section of the article.

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