Stakhneva E. M., Kuzminykh N. A, Scherbakova L. V., Kashtanova E. V.,
Polonskaya Ya. V., Shramko V. S. Garbuzova (Stryukova) E. V., Sadovsky E. V., Ragino Yu. I.
Research Institute of Therapy and Preventive Medicine, Branch of the Federal Research
Center Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences, Novosibirsk, Russia

Metabolic Blood Hormones in Young People With Electrocardiographic Signs of Ischemic Myocardial Changes

Aim	To study changes in blood concentrations of metabolic hormones and adipocytokines in people aged 25–44 years with electrocardiographic (ECG) signs of ischemic changes in the myocardium.
Material and methods	This study was a part of a cross-sectional survey of a random sample of Novosibirsk population aged 25–44 years. The study included 1363 people divided into two groups: group 1, subjects with ECG signs of ischemic changes in the myocardium and group 2, subjects without ECG changes. Blood serum concentrations of adipocytokines and metabolic hormones were measured by multiplex assay on a Luminex MAGPIX flow-through fluorometer.
Results	The group with ECG signs of myocardial ischemia had higher blood concentrations of adiponectin, resistin, glucagon, and interleukin 6 (IL-6) than in the comparison group. A multivariate logistic regression analysis showed that the glucagon concentration was associated with the presence of ECG signs of myocardial ischemia (OR, 1.019; CI, 1.018–1.034; p=0.017).
Conclusion	In young people aged 25–44 years, higher blood concentrations of glucagon are associated with the presence of ECG signs of myocardial ischemia.
Keywords	Ischemic heart disease; blood adipokines; multiplex assay
For citations	Stakhneva E. M, Kuzminykh N. A, Scherbakova L. V., Kashtanova E. V., Polonskaya Ya. V., Shramko V. S. et al. Metabolic Blood Hormones in Young People With Electrocardiographic Signs of Ischemic Myocardial Changes. Kardiologiia. 2023;63(11):4–11. [Russian: Стахнёва Е. М., Кузьминых Н. А., Щербакова Л. В., Каштанова Е.В., Полонская Я. В., Шрамко В. С. и др. Метаболические гормоны крови у молодых людей с электрокардиографическими признаками ишемических изменений миокарда. Кардиология. 2023;63(11):4–11].
Corresponding author	Stakhneva E. M. E-mail: stahneva@yandex.ru

Introduction

Numerous biologically active substances called adipocytokines are produced by adipose tissue. These molecules influence a range of physiological and pathological processes, including vascular tone, inflammation, smooth muscle cell migration, and endothelial function. All adipocytokines produced by adipocytes and non-adipose cells (monocytes/macrophages, smooth muscle cells, endothelial cells, etc.) are a wide range of various biomolecules, such as metabolic hormones (adiponectin, resistin, leptin, insulin, glucagon, c-peptide, glucose-dependent insulinotropic peptide, glucagon-like peptide-1), and pro-inflammatory cytokines (interleukins (IL-1β, IL-6, IL-8), monocyte chemoattractant protein 1 (MCP-1); tumor necrosis factor alpha (TNF-α), lipocalin-2, molecules of the complement system (adipsin) and vascular hemostasis (plasminogen activator inhibitor 1 (PAI-1)) [1].

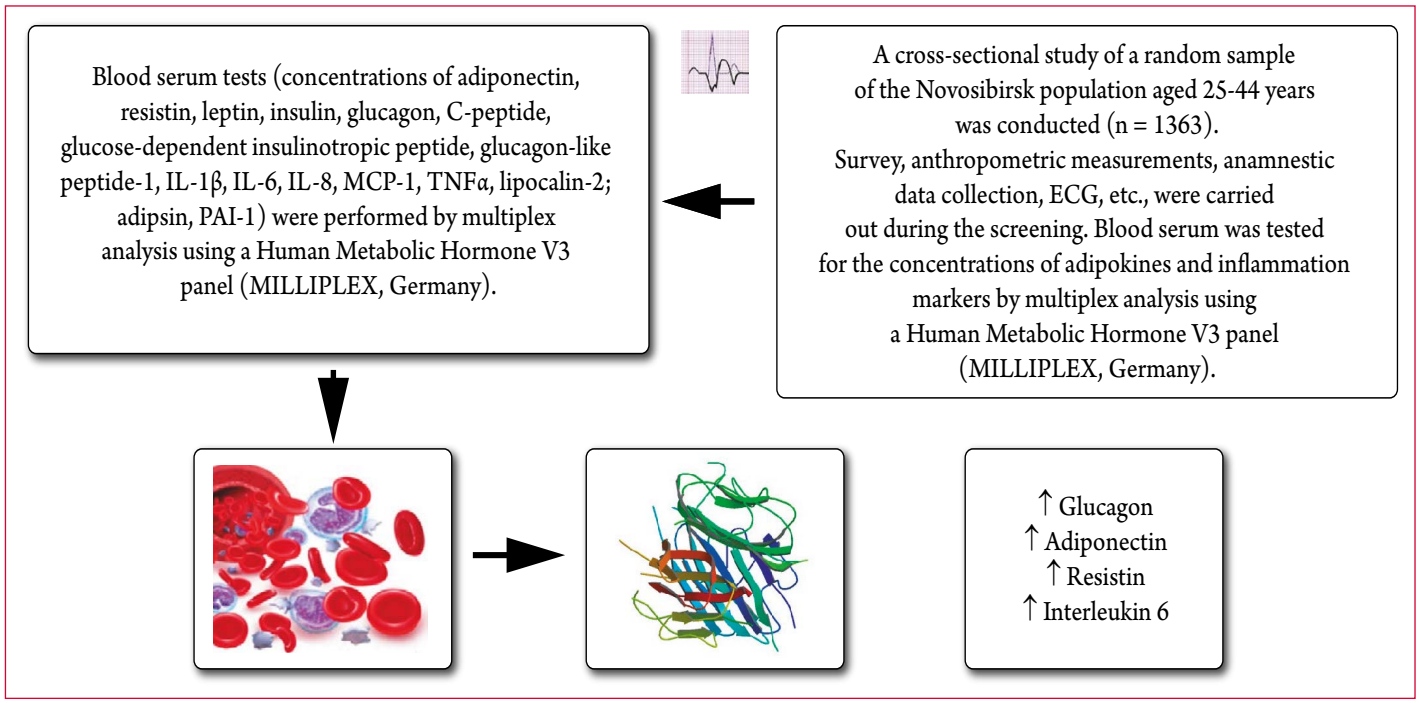
Being endogenous biologically active mediators of inflammation, adipocytokines regulate intercellular and intersystem interactions, determine cell survival, stimulation, or suppression of growth, as well as cell differentiation, functional activity, and apoptosis. These biomolucules coordinate the immune, endocrine and nervous systems in normal conditions and in response to pathological effects [2].

Investigation adipocytokines and their effects is an important area in modern medicine. Despite the high global prevalence of cardiovascular diseases (CVDs), the incidence of CVDs to increase in young people due to the increased prevalence of cardiovascular risk factors (smoking, obesity, diabetes mellitus, and arterial hypertension) compared to the elderly persons [3–5]. There is increasing evidence that adipocytokine imbalance is associated with the risk of cardiometabolic diseases and their complications. The role of adipocytokines as prognostic and diagnostic markers of cardiovascular diseases is also discussed [6–9].

The objective of this study was to examine changes in the blood levels of metabolic hormones and

ISSN 0022-9040. Kardiologiia. 2023;63(11). DOI: 10.18087/cardio.2023.11.n2492

Central illustration. Metabolic Blood Hormones in Young People With Electrocardiographic Signs of Ischemic Myocardial Changes



adipocytokines in young people aged 25–44 years with electrocardiographic (ECG) signs of myocardial ischemia.

Material and methods

A cross-sectional study of a random sample of the Novosibirsk population from 25 to 44 years old was conducted in the Research Institute for Internal and Preventive Medicine (a branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences). The sample was created using the base of the Territorial Fund of Compulsory Medical Insurance of 25–44-year-old individuals residing in a Novosibirsk district typical in terms of production, social, population and demographic, and transport structures, and degree of population migration. A random representative sample of 2,500 people was created using a random number generator; the response rate was 54%. The study included 1,363 people (654 males/709 females). The study was approved by the local ethics committee of the Research Institute for Internal and Preventive Medicine. All subjects signed the informed consent for the examination and processing of personal data.

The screening included a survey using a set of validated questionnaires, including the Rose Angina Questionnaire (RAQ); anthropometry (height, body weight, waist circumference (WC), and hip circumference (HC) with the calculation of the waist-to-hip ratio, body mass index; history taking; the standard 12-lead ECG interpreted according to the Minnesota code, ultrasonography, etc.

Epidemiological methods for identifying the main clinical manifestations of the disease were used during the screening. ECG signs of myocardial ischemia were determined according to the clinical and functional criteria (the Minnesota code) confirmed by the results of the survey based on the Rose Angina Questionnaire [10]. ECG signs of myocardial ischemia were the following: history of myocardial infarction (MI), major focal MI according to ECG, typical exertional angina (the Rose Angina Questionnaire), ischemic changes on the ECG without left ventricular hypertrophy, Q-QS waves in ECG at rest. Abdominal obesity (AO) was established with WC more than 80 cm in female patients and more than 94 cm in male patients.

All subjects with ECG signs of myocardial ischemia (n=46) were included to the study (treatment group); the remaining subjects made up the group without such signs (control group), n=1317 (Table 1).

The tests were performed on blood serum. Blood samples were taken from the ulnar vein on an empty stomach in the morning. Blood tests were performed by multiplex analysis using a Human Metabolic Hormone V3 panel (MILLIPLEX, Germany) in a Luminex MAGPIX system. The levels of adipokines and markers of inflammation were determined: adiponectin, adipsin, amylin, ghrelin, lipocalin-2, secretin, PAI-1, leptin, resistin, interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), monocyte chemoattractant protein-1

Table 1. Clinical characteristics of patients examined

Parameter	Control group, n=1317	Treatment group, n=46	p
Age, years	37.33 [31.83; 41.92]	39.08 [32.50; 43.12]	0.170
Male/female, %	48.3 / 51.7	39.1 / 60.9	0.222
Waist circumference (WC), cm	85.5 [76.0; 96.0]	84.0 [76.6; 95.0]	0.427
Body mass index (BMI), kg/m^2	25.15 [22.06; 28.96]	24.84 [22.34; 28.27]	0.763
Arterial hypertension (AH), %	18.8	23.9	0.381
Systolic blood pressure (SBP), mm Hg	119.5 [110.5; 129.5]	117.5 [104.9; 134.4]	0.572
Diastolic blood pressure (DBP), mm Hg	78.5 [71.5; 86.5]	78.2 [69.9; 85.6]	0.648
Diabetes mellitus (DM), %	2.4	2.2	0.703
Glycemia, mmol/L	5.73 [5.31; 6.04]	5.57 [5.10; 5.83]	0.046

Data are presented as a percentage (%) of cases of the total number of subjects per group, medians and interquartile ranges (Me [25 %; 75 %]).

(MCP-1), insulin, C-peptide, glucose-dependent insulinotropic peptide (GIP), glucagon-like peptide-1 (GLP-1), glucagon, pancreatic polypeptide (PP), polypeptide YY (PYY).

The data obtained were statistically processed using SPSS version 23.0. Clinical characteristics of patients examined, and test results are presented as the medians and interquartile ranges (Me [25th percentile; 75th percentile]). Samples were compared using the Mann-Whitney U-test. A multivariate logistic regression analysis was conducted, with the «presence of ECG signs of myocardial ischemia» being the dependent variable, in order to calculate the odds ratio (Exp B) and 95% confidence interval (CI). The differences were statistically significant with p value being less than 0.05.

Results

After comparing the two patient groups, we found that the young individuals in the treatment group had abnormal concentrations of certain adipokines and metabolic hormones compared to the control group (Table 2).

Subjects with ECG signs of myocardial ischemia had blood concentrations of adipokines, such as adiponectin, resistin, glucagon, and IL6, statistically significantly higher than subjects in the control group ($p<0.05$) (Table 2). There was a trend to higher blood levels of amylin in the treatment group ($p=0.054$).

Additionally, greater concentrations of lipocalin-2, ghrelin, pancreatic peptide (PP), glucose-dependent insulinotropic polypeptide (GIP), and glucagon-like peptide-1 (GLP-1), and lower concentrations of polypeptide YY (PYY) (by 16%) and secretin (by 7%) were shown in the treatment group. However, statistical significance was not achieved (Table 2).

Table 3 displays the findings of the multivariate logistic regression analysis (standardized by age and sex) examining the relationship between adipokines and the presence of ECG signs of myocardial ischemia.

Multivariate logistic analysis showed that the concentration of glucagon was associated with

Table 2. Blood concentration of adipokines/metabolic hormones

Parameters	Control group, n=1317	Treatment group, n=46	p
Adiponectin, μg/mL	37,0 [25,5; 114,1]	109,0 [39,5; 136,7]	0,015
Adipsin, μg/mL	11,6 [7,5; 14,0]	12,1 [8,4; 14,1]	0,649
Lipocalin-2, ng/mL	384,1 [198,0; 1150,4]	461,4 [276,8; 1100,2]	0,485
Plasminogen activator inhibitor-1, ng/mL	21,4 [13,0; 31,7]	21,1 [14,5; 25,9]	0,557
Resistin, ng/mL	163,4 [25,4; 597,5]	509,8 [157,7; 753,1]	0,033
Amylin, pg/mL	6,2 [3,5; 14,2]	10,4 [5,6; 16,3]	0,054
Ghrelin, pg/mL	34,1 [18,6; 88,4]	66,8 [23,6; 105,5]	0,123
Interleukin-6, pg/mL	1,2 [0,6; 2,3]	1,9 [0,9; 6,9]	0,013
TNF-α, pg/mL	4,6 [2,9; 7,2]	4,1 [2,7; 6,8]	0,534
MCP-1, pg/mL	236,8 [161,3; 318,5]	231,3 [145,3; 321,4]	0,862
Insulin, pg/mL	463,9 [296,0; 700,6]	463,9 [382,5; 619,1]	0,629
C-peptide, ng/mL	0,8 [0,3; 1,2]	0,7 [0,4; 1,6]	0,299
Leptin, ng/mL	4,2 [1,6; 7,9]	4,8 [1,6; 11,0]	0,881
Pancreatic polypeptide, pg/mL	39,8 [23,0; 77,9]	55,1 [24,4; 108,6]	0,338
Polypeptide YY, pg/mL	57,0 [38,6; 77,7]	48,2 [28,3; 65,2]	0,118
Secretin, pg/mL	22,0 [15,0; 66,4]	20,5 [18,7; 59,7]	0,700
Glucose-dependent insulinotropic polypeptide, pg/mL	26,3 [16,2; 51,5]	29,3 [18,5; 56,6]	0,552
Glucagon-like peptide-1, pg/mL	280,8 [173,1; 488,8]	400,8 [176,0; 547,3]	0,326
Glucagon, pg/mL	11,4 [6,8; 21,7]	16,4 [12,0; 36,4]	0,021

The data are presented as the medians and interquartile ranges (Me [25 %; 75 %]).

ISSN 0022-9040. Kardiologiia. 2023;63(11). DOI: 10.18087/cardio.2023.11.n2492

the presence of ECG signs of myocardial ischemia (Exp (B) =1.019; 95% CI 1.018–1.034; p=0.017).

Discussion

Comparing the results between the two groups, we observed a difference in the blood concentrations of certain adipocytokines and metabolic hormones in young people with ECG signs of myocardial ischemia compared to the control group.

Adiponectin is one of the main adipose tissue cytokines. It is involved in various molecular and cellular processes, including lipid metabolism, energy regulation, immune response and inflammation, and increases insulin sensitivity. Low levels of adiponectin and high levels of leptin, as well as leptin/adiponectin ratio, are traditionally considered as markers of CVDs [11, 12]. Moreover, adiponectin levels are negatively correlated with cancer, CVDs, and diabetes [13]. Although reduced adiponectin is a biomarker used for the prediction of cardiovascular outcomes, there is a paradox of high levels of both leptin and adiponectin in the CVD pathogenesis [14]. The meta-analysis showed that elevated baseline plasma adiponectin levels were significantly associated with an increased risk of all-cause and cardiovascular death in patients with CVDs [7]. The blood levels of adiponectin were 11% higher in patients with coronary artery disease (CAD) (without diabetes) than in the control group. At the same time, the blood concentration of resistin was 1.9 times higher and the level of leptin was 2.7 times lower than in the control group [9]. Thus, the role of adiponectin in the pathogenesis of CVDs is controversial.

In our study, subjects with myocardial ischemia were found to have high serum levels of adiponectin, but the regression analysis showed no association of this adipocytokine with ECG signs of myocardial ischemia.

Well-known adipocytokine leptin is an important link between obesity and the development of CVDs. The associations have been explored earlier between the blood levels of leptin and stroke, chronic heart failure, acute myocardial infarction (MI), CAD [15]. It was shown in a prospective study that the incidence of CVDs was directly associated in male patients with the blood levels of leptin and adiponectin and the leptin/adiponectin ratio. At the same time, the leptin/adiponectin ratio is the preferred marker of a new-onset cardiovascular event [11]. We did not observe differences in blood concentrations of leptin between the groups.

Most studies show resistin as a potential factor for insulin resistance and diabetes [16, 17]. Specific nucleotide polymorphisms of the RETN gene encoding resistin synthesis were shown to be associated with obesity, insulin resistance, and diabetes mellitus [18, 19]. A positive correlation was also shown between resistin levels and adipose tissue mass, as well as higher serum levels of resistin in obese patients [17]. The involvement of resistin is also explored in various pathological processes leading to CVDs, including inflammation, endothelial dysfunction, thrombosis, angiogenesis, and smooth muscle cell dysfunction [9, 20]. Elevated resistin levels may be a marker of ischemia and myocardial damage in acute coronary syndrome [21].

In our study, subjects with signs of myocardial ischemia had blood concentrations of resistin 3 times as high as in the control group (Table 2), which confirms the negative role of resistin in the development of CAD.

Adipsin (factor D of the complement system) is mainly produced by adipocytes, monocytes, and macrophages. Its pathophysiological role in the development of CVDs is not well understood. However, in a study including 370 patients with coronary atherosclerosis, it was found that serum levels of adipsin were directly associated with the adverse prognosis (death and re-hospitalization) for patients with CAD [22]. In our study, we did not find differences in the concentrations of this adipocytokine in the study groups.

Glucagon is a hormone produced by pancreatic α cells and some intestinal cells. It is traditionally seen as a major contributor to glucose homeostasis. Glucagon increases glucose production in the liver and is an anti-insulin hormone. Glucagon is known to participate in the pathophysiology of heart failure due to inhibition of cAMP formation and G-protein signaling [23]. Due to the fact that glucagon can have a pleiotropic effect on various cell types and organs through interaction with

Table 3. Logistic regression analysis of the associations of adipokines and metabolic hormones with the odds of having ECG signs of myocardial ischemia

Parameters	B	Exp B	95 % CI for Exp (B)	p
Age	0,094	1,099	0,984–1,227	0,093
Sex, male vs. female	-0,107	0,899	0,281–2,878	0,858
Adiponectin	0,001	1,001	0,998–1,004	0,563
Resistin	0,000	1,000	0,999–1,001	0,955
Glucagon	0,018	1,019	1,018–1,034	0,017
IL-6	-0,001	0,999	0,949–1,050	0,957

B, the non-standardized regression coefficient;
Exp B, the odds ratio for a variable; CI, confidence interval.

its receptor, its action includes a direct effect on the cardiovascular system [24]. In a randomized trial aimed at investigating the effect of glucagon on CAD, diabetes mellitus, and relevant risk factors, glucagon was positively associated with CAD (odds ratio 1.03; 95% CI 1,0003–1,0500), that is with each increase in the standard deviation of glucagon level, the probability of developing CAD increased by 3%. Moreover, glucagon was not associated with most cardiovascular risk factors [25]. Adela et al. [8] showed that blood level of glucagon was 11% lower in patients with CAD (without diabetes) than in the control group. In a study of mouse model of atherosclerosis (ApoE−/−), high-dose glucagon infusion significantly reduced the area and volume of aortic plaque in animals with both indicators being inversely proportional to and correlated with plasma levels of glucagon. Thus, glucagon has a pronounced atheroprotective effect due to its anti-inflammatory properties [24]. Thus, the association of glucagon with CAD is not well understood and the available data are contradictory.

In our study, glucagon concentration was 30% higher in subjects with ECG signs of myocardial ischemia than the rest of the subjects, and the fasting blood levels of glucose and insulin did not differ significantly between the groups. Moreover, multivariate logistic analysis showed that the concentration of glucagon was associated with the presence of ECG signs of myocardial ischemia. Thus, it is possible that pathological changes in the myocardium trigger the compensatory mechanisms of the body, including increasing the blood levels of glucagon irrespective of glucose concentration.

Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are the major human incretin hormones involved in glucose homeostasis. GIP is produced by duodenal and proximal jejunal cells [26]. Glucagon-like peptide 1 is a glucoregulatory hormone secreted by intestinal enteroendocrine L-cells in response to food intake. Activation of the GLP-1 receptor on beta cells induces glucose-dependent insulin secretion, thereby improving the glucose sensitivity of beta cells. Moreover, GLP-1 has a glucagonostatic effect due to glucose-dependent inhibition of glucagon release, contributing to the effect of reducing plasma levels of glucose [27]. Multiple GLP-1 receptor agonists are used in clinical practice to treat obesity and type 2 diabetes mellitus, which use the effects of GLP-1 on lowering plasma levels of glucose and reducing body weight [28–30]. GLP-1 receptor agonists also help reduce atherosclerosis and CVDs by lowering blood pressure and blood lipid levels. GLP-1R is expressed in many cell types, such as monocytes/macrophages, smooth muscle cells, endothelial cells, and cardiomyocytes. Some studies showed that protective properties against endothelial dysfunction, anti-inflammatory effects on macrophages, and antiproliferative effects on smooth muscle cells can contribute to atheroprotection through GLP-1R signaling [31]. When the effects of the GLP-1 receptor agonist were examined in 96 patients with myocardial infarction and without diabetes mellitus, it was found that the administration of the GLP-1 receptor agonist 30 minutes before stenting and for 7 days after the intervention reduces the area of infarction and improves the myocardial salvage index calculated as the difference between the estimated risk zone for necrosis and the ultimate area of infarction [32]. But the exact mechanisms of the GLP-1 receptor effects are still debated [27].

In our study, blood concentrations of the GLP-1 and GIP hormones were elevated 1.4-fold and 1.1-fold, respectively, in subjects with ischemic myocardial disorders, but statistical significance was not achieved.

Conclusion

It is obvious that adipocytokine imbalance is associated with the risk of cardiometabolic diseases and their complications. The major risk factors for CVDs are arterial hypertension, obesity, and diabetes mellitus, all of which are strongly associated with adipocytokine imbalance. Increasing prevalence of these factors is observed in young people worldwide [3–5]. Our study in a young population of 25–44 years old in Novosibirsk, we found higher blood concentrations of the metabolic hormone glucagon in subjects with ECG signs of myocardial ischemia. Moreover, logistic analysis showed that the concentration of glucagon was associated with the presence of ECG signs of myocardial ischemia (Exp (B) =1.019; 95% CI 1.018–1.034; p=0.017). The study was limited to a small number of subjects with ECG signs of myocardial ischemia, since it was conducted in the young population. These findings should be examined in detail in large study groups to confirm the predictive significance of glucagon and its association with CAD.

Funding

The study was performed as a part of a budget project under the State Assignment # 122031700094-5 and as a part of the Russian Science Foundation grant # 21-15-00022.

No conflict of interest is reported.

The article was received on 21/04/2023

ISSN 0022-9040. Kardiologiia. 2023;63(11). DOI: 10.18087/cardio.2023.11.n2492

АТТЕНТО®

амлодипин + олмесартана медоксомил

Фиксированная комбинация:

- Эффективное снижение АД[1,2]
- Кардио- и ангиопротективный эффект[3]*

* Олмесартан продемонстрировал способность предотвращать или замедлять темпы прогрессирования поражения органов-мишеней
АД – артериальное давление

Показания к применению[4]:
эссенциальная гипертензия (при неэффективности монотерапии олмесартана медоксомилом или амлодипином).

Способ применения и дозы[4]
Препарат Аттенто® принимают внутрь 1 раз в сутки, в одно и то же время, независимо от времени приема пищи, не разжевывая, запивая достаточным количеством жидкости (например, стаканом воды).
Максимальная суточная доза амлодипина составляет 10 мг; олмесартана медоксомила – 40 мг.

Информация для специалистов здравоохранения. Отпускается по рецепту. RU-ATT-03-2023-V01-print. Дата утверждения 16.10.2023

1.Redon J., Fabia MJ. J Renin Angiotensin Aldosterone Syst. 2009 Sep; 10(3): 147-56
2. Chrysant SG et al. Clin Ther. 2008;30(4):587-604.
3. De la Sierra A, Volpe M. J.Hypertens. 2013Mar; 31 Suppl 1: S13-7
4. Ознакомтесь с полной информацией о лекарственном препарате Аттенто используя QR-код

Ознакомьтесь с полной информацией о лекарственном препарате Аттенто®, **используя QR-код**

БЕРЛИН-ХЕМИ МЕНАРИНИ

ООО «Берлин-Хеми/А.Менарини»,
123112, Москва, Пресненская набережная, дом 10,
БЦ «Башня на Набережной», блок Б.
Тел.: (495)785-01-00, факс: (495) 785-01-01, http://www.berlin-chemie.ru

REFERENCES

1. Ragino YI, Stakhneva EM, Polonskaya YV, Kashtanova EV. The Role of Secretory Activity Molecules of Visceral Adipocytes in Abdominal Obesity in the Development of Cardiovascular Disease: A Review. Biomolecules. 2020;10(3):374. DOI: 10.3390/biom10030374
2. Francisco V, Pino J, Gonzalez-Gay MA, Mera A, Lago F, Gómez R et al. Adipokines and inflammation: is it a question of weight? British Journal of Pharmacology. 2018;175(10):1569–79. DOI: 10.1111/bph.14181
3. Andreenko E.Yu., Yavelov I.S., Loukianov M.M., Vernohaeva A.N., Drapkina O.M., Boytsov S.A. Ischemic Heart Disease in Subjects of Young Age: Current State of the Problem: Prevalence and Cardio-Vascular Risk Factors. Kardiologiia. 2018;58(10):53–8. [Russian: Андреенко Е.Ю., Явелов И.С., Лукьянов М.М., Вернохаева А.Н., Драпкина О.М., Бойцов С.А. Ишемическая болезнь сердца у лиц молодого возраста: распространенность и сердечно-сосудистые факторы риска. Кардиология. 2018;58(10):53-8]. DOI: 10.18087/cardio.2018.10.10184
4. Neeland IJ, Ross R, Després J-P, Matsuzawa Y, Yamashita S, Shai I et al. Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. The Lancet Diabetes & Endocrinology. 2019;7(9):715–25. DOI: 10.1016/S2213-8587(19)30084-1
5. Otelea MR, Streinu-Cercel A, Băicus C, Maria Nitescu M. The Adipokine Profile and the Cardiometabolic Risk in Non-Obese Young Adults. Balkan Medical Journal. 2019;36(3):155–61. DOI: 10.4274/balkanmedj.galenos.2018.2018.0789
6. Carbone S, Canada JM, Billingsley HE, Siddiqui MS, Elagizi A, Lavie CJ. Obesity paradox in cardiovascular disease: where do we stand? Vascular Health and Risk Management. 2019;15:89–100. DOI: 10.2147/VHRM.S168946
7. Wu Z-J, Cheng Y-J, Gu W-J, Aung LHH. Adiponectin is associated with increased mortality in patients with already established cardiovascular disease: A systematic review and meta-analysis. Metabolism. 2014;63(9):1157–66. DOI: 10.1016/j.metabol.2014.05.001
8. Adela R, Reddy PNC, Ghosh TS, Aggarwal S, Yadav AK, Das B et al. Serum protein signature of coronary artery disease in type 2 diabetes mellitus. Journal of Translational Medicine. 2019;17(1):17. DOI: 10.1186/s12967-018-1755-5
9. Yuxiang L, Fujiu K. Human Resistin and Cardiovascular Disease. International Heart Journal. 2020;61(3):421–3. DOI: 10.1536/ihj.20-221
10. Kalinina A.M., Shalnova S.A., Gambaryan M.G., Eganyan R.A., Muromtseva G.A., Bochkareva E.V. et al. Epidemiological methods for identifying the main chronic non-communicable diseases and risk factors during mass population surveys. Methodical guide. Edited by Prof. Boytsov S.A. - M.: GNICPM; 2015. - 96p. Av. at: https://gnicpm.ru/wp-content/uploads/2020/01/metodposobie_epid_metody_viyavleniya_hniz_pri_massovih_obsledovaniyah.pdf. [Russian: Калинина А.М., Шальнова С.А., Гамбарян М.Г., Еганян Р.А., Муромцева Г.А., Бочкарева Е.В., Ким И.В. Эпидемиологические методы выявления основных хронических неинфекционных заболеваний и факторов риска при массовых обследованиях населения. Методическое пособие. Под ред. проф. Бойцова С.А. - М.: ГНИЦПМ; 2015. - 96с. Доступно на: https://gnicpm.ru/wp-content/uploads/2020/01/metodposobie_epid_metody_viyavleniya_hniz_pri_massovih_obsledovaniyah.pdf]
11. Kappelle PJWH, Dullaart RPF, van Beek AP, Hillege HL, Wolffenbuttel BHR. The plasma leptin/adiponectin ratio predicts first cardiovascular event in men: A prospective nested case–control study. European Journal of Internal Medicine. 2012;23(8):755–9. DOI: 10.1016/j.ejim.2012.06.013
12. Sierra-Johnson J, Romero-Corral A, Lopez-Jimenez F, Gami AS, Sert Kuniyoshi FH, Wolk R et al. Relation of Increased Leptin Concentrations to History of Myocardial Infarction and Stroke in the United States Population. The American Journal of Cardiology. 2007;100(2):234–9. DOI: 10.1016/j.amjcard.2007.02.088
13. Khoramipour K, Chamari K, Hekmatikar AA, Ziyaiyan A, Taherkhani S, Elguindy NM et al. Adiponectin: Structure, Physiological Functions, Role in Diseases, and Effects of Nutrition. Nutrients. 2021;13(4):1180. DOI: 10.3390/nu13041180
14. Zhao S, Kusminski CM, Scherer PE. Adiponectin, Leptin and Cardiovascular Disorders. Circulation Research. 2021;128(1):136–49. DOI: 10.1161/CIRCRESAHA.120.314458
15. Singh M, Bedi US, Singh PP, Arora R, Khosla S. Leptin and the clinical cardiovascular risk. International Journal of Cardiology. 2010;140(3):266–71. DOI: 10.1016/j.ijcard.2009.07.019
16. Markova T.N., Mishchenko N.K., Petina D.V. Adipocytokines: modern definition, classification and physiological role. Problems of Endocrinology. 2022;68(1):73–80. [Russian: Маркова Т.Н., Мищенко Н.К., Петина Д.В. Адипоцитокины: современный взгляд на дефиницию, классификацию и роль в организме. Проблемы Эндокринологии. 2022;68(1):73-80]. DOI: 10.14341/probl12805
17. Acquarone E, Monacelli F, Borghi R, Nencioni A, Odetti P. Resistin: A reappraisal. Mechanisms of Ageing and Development. 2019;178:46–63. DOI: 10.1016/j.mad.2019.01.004
18. Hivert M-F, Manning AK, McAteer JB, Dupuis J, Fox CS, Cupples LA et al. Association of Variants in RETN With Plasma Resistin Levels and Diabetes-Related Traits in the Framingham Offspring Study. Diabetes. 2009;58(3):750–6. DOI: 10.2337/db08-1339
19. Elkhattabi L, Morjane I, Charoute H, Amghar S, Bouafi H, Elkarhat Z et al. In Silico Analysis of Coding/Noncoding SNPs of Human RETN Gene and Characterization of Their Impact on Resistin Stability and Structure. Journal of Diabetes Research. 2019;2019:4951627. DOI: 10.1155/2019/4951627
20. Jamaluddin MS, Weakley SM, Yao Q, Chen C. Resistin: functional roles and therapeutic considerations for cardiovascular disease. British Journal of Pharmacology. 2012;165(3):622–32. DOI: 10.1111/j.1476-5381.2011.01369.x
21. Chu S, Ding W, Li K, Pang Y, Tang C. Plasma Resistin Associated With Myocardium Injury in Patients With Acute Coronary Syndrome. Circulation Journal. 2008;72(8):1249–53. DOI: 10.1253/circj.72.1249
22. Ohtsuki T, Satoh K, Shimizu T, Ikeda S, Kikuchi N, Satoh T et al. Identification of Adipsin as a Novel Prognostic Biomarker in Patients With Coronary Artery Disease. Journal of the American Heart Association. 2019;8(23):e013716. DOI: 10.1161/JAHA.119.013716
23. Petersen KM, Bøgevig S, Holst JJ, Knop FK, Christensen MB. Hemodynamic Effects of Glucagon: A Literature Review. The Journal of Clinical Endocrinology & Metabolism. 2018;103(5):1804–12. DOI: 10.1210/jc.2018-00050
24. Osaka N, Kushima H, Mori Y, Saito T, Hiromura M, Terasaki M et al. Anti-inflammatory and atheroprotective properties of glucagon. Diabetes and Vascular Disease Research. 2020;17(5):147916412096518. DOI: 10.1177/1479164120965183
25. Ng JCM, Schooling CM. Effect of Glucagon on Ischemic Heart Disease and Its Risk Factors: A Mendelian Randomization Study. The Journal of Clinical Endocrinology & Metabolism. 2020;105(8):dgaa259. DOI: 10.1210/clinem/dgaa259
26. Meier JJ. The role of incretin-based therapies in the management of type 2 diabetes mellitus: perspectives on the past, present and future. Diabetes mellitus. 2020;22(5):461–6. DOI: 10.14341/DM11493
27. Andreasen CR, Andersen A, Knop FK, Vilsbøll T. How glucagon-like peptide 1 receptor agonists work. Endocrine Connections. 2021;10(7):R200–12. DOI: 10.1530/EC-21-0130
28. Alkhezi OS, Alahmed AA, Alfayez OM, Alzuman OA, Almutairi AR, Almohammed OA. Comparative effectiveness of glucagon-like peptide-1 receptor agonists for the management of obesity in adults without diabetes: A network meta-analysis of randomized clinical trials. Obesity Reviews. 2023;24(3):e13543. DOI: 10.1111/obr.13543
29. Htike ZZ, Zaccardi F, Papamargaritis D, Webb DR, Khunti K, Davies MJ. Efficacy and safety of glucagon-like peptide-1 receptor agonists in type 2 diabetes: A systematic review and mixed-treatment comparison analysis. Diabetes, Obesity and Metabolism. 2017;19(4):524–36. DOI: 10.1111/dom.12849

ISSN 0022-9040. Kardiologiia. 2023;63(11). DOI: 10.18087/cardio.2023.11.n2492

30. Pedrosa MR, Franco DR, Gieremek HW, Vidal CM, Bronzeri F, De Cassia Rocha A et al. GLP-1 Agonist to Treat Obesity and Prevent Cardiovascular Disease: What Have We Achieved so Far? Current Atherosclerosis Reports. 2022;24(11):867–84. DOI: 10.1007/s11883-022-01062-2
31. Ma X, Liu Z, Ilyas I, Little PJ, Kamato D, Sahebka A et al. GLP-1 receptor agonists (GLP-1RAs): cardiovascular actions and therapeutic potential. International Journal of Biological Sciences. 2021;17(8):2050–68. DOI: 10.7150/ijbs.59965
32. Chen WR, Chen YD, Tian F, Yang N, Cheng LQ, Hu SY et al. Effects of Liraglutide on Reperfusion Injury in Patients With ST-Segment–Elevation Myocardial Infarction. Circulation: Cardiovascular Imaging. 2016;9(12):e005146. DOI: 10.1161/CIRCIMAGING.116.005146