KLOTHO PROTEIN IN THE BLOOD OF MEN WITH TYPE 2 DIABETES

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Abstract: The Klotho protein content in men with diabetes was significantly lower than in individuals without diabetes (374 [117; 500] and 515 [315; 1009] pg/ml, respectively, $p < 0.0001$). In men with diabetes, in whom the glomerular filtration rate is less than 60 ml/min/1.73 cm2, the Klotho protein concentration was 4 times lower than in the comparison group (104 [93; 118] and 413 [147; 535] pg/ml, respectively, $p = 0.014$). In the presence of diabetes, an inverse correlation was observed between Klotho protein content and abdominal obesity (waist to hip ratio) (−0.329; $p = 0.047$), but multivariate analysis only revealed a tendency toward a negative association of these parameters (−0.385, $p = 0.078$).

Keywords: Klotho protein, diabetes mellitus, cardiovascular diseases, risk factors.

INTRODUCTION

Type 2 diabetes mellitus (DM) is a global health problem associated with a wide range of vascular complications that cause high morbidity and mortality. According to WHO, the incidence of diabetes has been steadily increasing over the past decades. Thus, the global prevalence of DM among people over 18 years of age increased from 4.7% in 1980 to 8.5% in 2023. About 20 years ago, scientists discovered the Klotho protein, a hormone secreted by brain and kidney cells known for its ability to slow down the aging process of the body [1]. Some studies have described that the Klotho protein can be considered an important humoral factor in systemic glucose metabolism in vitro and in vivo [2]. Although the molecular mechanisms of these physiological processes have not been fully determined, animal experiments have shown that the Klotho gene and protein are expressed in the islets of the pancreas. The Klotho protein inhibits insulin activity, including by influencing adipocyte receptors, and causes cell resistance to glucose [3].

MATERIALS AND METHODS

In the period from 2021 to 2023, we examined 37 men with type 2 diabetes (mean age 62.9 ± 10.3 years) and 141 men in the control group who did not suffer from diabetes (mean age 66.7 ± 13.5 years). The subjects were divided into age subgroups: 50-65 years and over 80 years. Exclusion criteria from the study: age under 50 years and from 66 to 79 years; female gender; the presence of severe concomitant pathology in the acute stage (chronic infectious and inflammatory diseases, respiratory failure, liver failure, chronic heart failure III-IV functional class), active oncological diseases, pathology of the parathyroid and thyroid glands; glomerular filtration rate (SFR) less than 30 ml / min; taking vitamin D, glucocorticosteroids, calcium supplements.

RESULTS AND DISCUSSION

The examination was performed according to a single protocol, according to which anamnestic and demographic data were collected, information on the family history of CVD development at a young age (<55 years for men and <65 years for women), alcohol consumption and smoking, drug treatment, a physical examination, a clinical and instrumental examination were performed, and blood was taken in the morning on an empty stomach. Regular physical activity in the questionnaire implied moderate activity of at least 150 min/week (30 min/day, 5 days/week) or intense activity of at least 75 min/week (15 min/day, 5 days/week). Anthropometric parameters were measured, the ratio of waist circumference (WC) to hip circumference (HC) and body mass index (BMI) were calculated. Abdominal obesity was diagnosed at WC > 94 cm and/or WC/HR > 0.94, obesity – at BMI ≥ 30 kg/m2. Systolic and diastolic blood pressure (BP) and heart rate were measured three times with the average value recorded. Lipid parameters (serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C), triglycerides (TG)), glucose, and creatinine were determined; the atherogenicity coefficient (AC) and SCF were calculated. The concentration of Klotho protein in the blood serum was measured using an enzyme immunoassay using monoclonal antibodies to the circulating form of human Klotho protein according to the manufacturer's instructions.

In the comparison group, in individuals without regular physical activity, the concentration of Klotho protein was lower than in men who did (428 [244; 626] and 978 [587; 1502] pg/ml, p = 0.0001), as well as in subjects with obesity (401 [122; 716] pg/ml with BMI≥30 kg/m2 and 540 [354; 1077] pg/ml with BMI<30 kg/m2, p = 0.021) and normal CA (501 [290; 775] pg/ml with CA less than 3.5 and 676 [358; 1300] pg/ml with CA 3.5 and more, p = 0.044). No other significant changes in the Klotho protein concentration dependent on CVD risk factors (smoking, alcohol consumption, abdominal obesity, lipid disorders, hypertension and reduced SCF) were found in the comparison group. A negative correlation was established between the Klotho protein content and WC/HC in the group of men with diabetes (−0.329; p = 0.047). In individuals without diabetes, a positive correlation was found between the concentration of Klotho protein and the presence of regular physical activity (0.429; p = 0.0001), TG level (0.209; p = 0.014) and VLDL-C (0.211; p = 0.013), as well as an inverse relationship between the level of Klotho protein and BMI ≥ 30 kg/m2 (−0.195; p = 0.020), WC/HR (−0.186; p = 0.027).

CONCLUSION

Thus, our results demonstrate that Klotho protein levels are associated with the presence of diabetes, obesity and renal function. Further studies, including those identifying molecular interactions, are needed to determine the effects of Klotho protein on these processes.

Klotho protein levels are significantly reduced in men with diabetes, especially in middle-aged men and in individuals with a SCF of less than 60 ml/min/1.73 cm2. In men with diabetes, Klotho protein concentrations are negatively correlated with the presence of abdominal obesity; multivariate analysis only suggests a tendency for such an association.

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