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PRECLINICAL ATHEROSCLEROSIS IN YOUNG MEN WITH METABOLIC SYNDROME AND THE POSSIBILITY OF ITS PRIMARY PREVENTION

Sharipova Elvina Midkhatovna
Bukhara State Medical Institute, Bukhara, Uzbekistan

Absract: *It is known that individuals with metabolic syndrome (MS), including abdominal obesity, impaired glucose tolerance(HTG), hyperinsulinemia, dyslipidemia (DLP), arterial hypertension (AH) and other manifestations, have a significantly higher risk of coronary heart disease, compared with healthy people. This implies the earliest detection and adequate primary prevention of atherosclerosis in this cohort of subjects. We attempted to assess the frequency and nature of preclinical manifestations of atherosclerosis in young men with MS, as well as to find out the possibilities of their correction by reducing body weight. 40 men aged 33-56 years (mean age 46 years) were examined and dynamically followed up, while 30 people made up the main and 10 – the control group.*

Keywords: *atherosclerosis, age, clinic, diagnosis.*

The inclusion criterion for the study was the presence of at least 3 of the following factorsTG (glucose fasting blood > 5,6 mmol/l), hypertension (BP > 130/85 mm Hg.St.), DLP (triglycerides [TG] ≥ 1,7 mmol/l or cholesterol, high density lipoprotein [KHS-HDL] ≤ 0,9 mmol/l), waist circumference (OT) > 94 cm, microalbuminuria (≤ 20 µg/min), and the absence of clear clinical signs of atherosclerosis (ischemic heart disease, cerebrovascular disease, obliterating atherosclerosis of lower limb arteries). In addition to measuring OT, the impedance method was used to assess body weight, adipose tissue fraction, visceral fat index, and basal metabolic rate. In order to identify preclinical manifestations of atherosclerosis, the parameters of the blood lipid spectrum, the presence of pain-free ST segment depression on the ECG during the treadmilltest or daily ECG monitoring, an increase in the thickness of the carotid intimamedia complex (according to USDG), and a decrease in myocardial perfusion (according to SPECT) were analyzed. In the study group, the subjects were given an individualized diet to eliminate the imbalance between energy intake and expenditure, and systematic physical training was recommended – a daily forty-minute walk at a fast pace. If the dietary intervention was ineffective, drugs that inhibit the absorption of fats in the intestine (xenical) were added to the treatment. Subjects from the control group underwent dynamic observation, However, if necessary, they were also prescribed antihypertensive or lipid-lowering therapy. The follow-up period was 12 months. The average body weight of men with MS at the time of inclusion was 100.3 kg, while the fat content exceeded 28%, and the visceral fat index-13.5%. The total cholesterol level (TC) was 6.1 mmol/l, TG – 2.2 mmol/L, HDL-C – 1.1 mmol/l. In total, we detected DLP in 65% of patients with MS. According to ultrasound examination of the head and neck vessels, the average value of the intima-media complex in the carotid arteries exceeded 1.35 mm. In half of the examined patients, pain-free ST-segment depression was detected on the ECG during the treadmilltest with submaximal physical activity. Thus, some preclinical manifestations of atherosclerosis were found in almost 90% of young men with MS. In the main group of

patients, a decrease in body weight from 100.3 to 98 kg (- 2.3%) occurred during 12 months of follow-up. The proportion of fat decreased more significantly (-3.4%), especially visceral fat (-9%). Waist circumference decreased by an average of 2.1%. Significant changes were also observed in the blood lipid spectrum. Thus, the level of TC decreased in the main group by 10.3%, the concentration of HDL-C increased by 4.5%. The concentration of blood glucose also decreased by 10%. The trend towards normalization of blood pressure figures was found – SBP decreased by 3.2%, DBP-by 2.5%. However, we noted more significant changes in the group where, in addition to diet, xenical was added to the treatment. Body weight decreased in this group by 4%, and the proportion of fat-by 5.4%, while the visceral fat index decreased by 21% ($p < 0.05$). In this group, the levels of TC (-11,5%) and glucose (-19,3%) in the blood decreased more significantly. It should be noted that all patients of the main group, despite a relatively small decrease in body weight, noted a significant improvement in the quality of life (increased mood and performance, improved exercise tolerance, etc.). As expected, no significant changes in body weight, as well as the state of lipid and carbohydrate metabolism were found in the control group. So, most men with MS have some preclinical manifestations of atherosclerosis, which implies the timely initiation of adequate preventive measures, the central place among which is occupied by weight loss. It is shown that even a relatively small reduction in body weight leads to a significant improvement in lipid and carbohydrate metabolism, normalization of blood pressure, and improvement of the quality of life.

Hypolipidemic drugs in the elderly demic therapy can have a negative impact on the quality of life, which is of paramount importance for elderly patients, especially those with limited life expectancy. In addition, potential patient adherence to treatment should be evaluated, which largely determines its success. Since all current guidelines for the treatment of hyperlipidemia in the elderly recommend only the use of statins, we will discuss in more detail the safety and efficacy of this pharmacological group.

Safety of statins in elderly patients and adherence to treatment Serious and fatal HP with statin use are rarely reported, but in general, side effects develop in about 10% of patients [13, 14]. The incidence of HP in large clinical trials did not differ between elderly and younger patients, but these studies practically did not involve people over 80 years of age with "fragility" and significant comorbidity [15]. The most common HP in both groups was dyspepsia. The greatest concern with statin treatment is caused by HP on the part of the muscles. The frequency of muscle pain and weakness in clinical studies was extremely variable, and in real practice it may differ significantly from that in clinical studies. In the large USAGE study (n=10138), 30% of participants experienced muscle pain [16]. In observational studies, the incidence of myalgia and statin withdrawal due to HP from muscle pain was significantly higher than in RCTs (an average of 2 times), and in elderly patients it was higher than in younger patients [17-20]. It is not clear whether this is due to age-related muscle mass loss, polypharmacy, drug interactions, impaired function of enzymes involved in drug metabolism, or a combination of these factors [21]. Rhabdomyolysis with statins develops at a rate of 1 10,000, which is about 400 times less common than bleeding with low-dose aspirin [22]. Muscle HP and related neuropathies are usually dose-dependent. The risk factors also include female gender, low rise/low body mass index, concomitant use of fibrates (gemfibrozil>the fenofibrate) and other drugs metabolized with the participation of cytochrome P450, application during surgical procedures, liver or kidney disease, fatty liver disease, hypothyroidism, diabetes and high alcohol consumption [23,38].

Other serious statindisorders requiring monitoring in elderly patients include confusion, renal failure, and hepatotoxicity [23,37]. A number of studies (TNT, SAGE, PROVE-IT TIMI 22) the use of high doses of statins was associated with a higher rate of increase of indicators of liver function tests in the elderly compared to younger people [24-26], but the abolition of statins due to asymptomatic increase in hepatic transaminases, according to the results of the meta-analysis of 14 RCTS for primary prevention of CVD

(n=46262), was observed in 0.4% more often in older than in younger individuals [27]. Available evidence suggests that statin use is associated with a moderate but statistically significant increase in the risk of new cases of diabetes mellitus [28, 29]. The increase in AR of their occurrence according to a meta-analysis of 14 primary prevention studies was 0.5% [95% confidence interval (CI) 0.1-1%; p=0.012], but the outcomes in patients with a newly reported increase in HbA1c levels during RCT did not differ from those in patients without diabetes [27,36]. It is assumed that the risk of developing myalgia, diabetes mellitus, and liver dysfunction is higher in women than in men, but this requires further research [30,33,34]. Data on the effects of statins on cognitive function and the risk of developing and progressing dementia are highly controversial. In some observational studies conducted in Europe, Asia, and North America, statin use was associated with a reduced risk of developing and/or progressing vascular dementia and/or Alzheimer's disease [31,32,33]. However, in a meta-analysis of 2 RCTs (26,340 participants aged 40-82 years, including 11,610 aged 70 years and older), good quality evidence was obtained that statins do not prevent the development of cognitive dysfunction or dementia in older individuals at risk of vascular disease [33]. Similar data were obtained in another systematic review [34]. On the contrary, according фармаконадзорато the US pharmacovigilance authorities, statin use is mainly associated with rare cases of cognitive impairment (memory loss and impairment, forgetfulness, amnesia, confusion) [35]. These disorders are usually mild in nature, are completely reversible after statin withdrawal, and do not lead to the progression of cognitive dysfunction. A causal link between statin use and an increased risk of diabetes and dementia has not been definitively proven, but in 2012

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