International Journal of Research
ISSN: 2348-6848 Vol-5, Special Issue-18
2nd EduIndex® International Conference on Science Changes the World held on 28-29th June 2018 at **Edupedia Publications Pvt Ltd**, New Delhi in Association with www.tadqiqot.uz of the Republic of Uzbekistan

Type 2 Diabetes, Arterial Hypertension and Cardiac Complications

Shakhzod Samadov, Shakhzoda Mullaboeva, Otabek Nizomov

Tashkent Medical Academy, Tashkent, Uzbekistan. 100109

Abstract

Diabetes mellitus (DM) is one of the most common chronic diseases and represents a serious public health problem, as with diabetes, there is a decline in the quality of life, early disability and high mortality. Analysis of the results of the United Kingdom Prospective Diabetic Study (UKPDS) showed that increasing glycated hemoglobin levels by only 1% increases the risk of death associated with diabetes by 21%, myocardial infarction by 14%, peripheral vascular disease by 43%, microvascular complications - by 37%, development of cataracts - by 19%. The ONTARGET program, which examines the effects of blockade of RAAS using telmisartan on many components of the cardiovascular continuum, and which is expected to end in 2008, will provide new data on the results of treatment of patients with cardiovascular diseases and diabetes.

Keywords: diabetes mellitus; cardiovascular complications; arterial hypertension; glycosylated hemoglobin; lethality.

INTRODUCTION

Diabetes mellitus (DM) is one of the most common chronic diseases and represents a serious public health problem, as with diabetes, there is a decline in the quality of life, early disability and high mortality. In all countries there is an increase in the incidence of diabetes. The number of patients with diabetes mellitus is currently approaching 200 million people, with the majority (90%) of patients being patients with type 2 diabetes. According to forecasts, while maintaining such growth rates by 2010, the number of people with diabetes mellitus on the planet will reach 221 million people, and by 2025 the estimated diabetes mellitus will already be over 300 million people [1]. Diabetes mellitus type 2 is characterized by the development of severe disabling complications leading to complete loss of ability to work and premature mortality. According to the Study of Cost of Diabetes in Europe - Type 2 (CODE-2), who studied the prevalence of various diabetic complications in patients

with diabetes mellitus (mean age of the examined 67 years), 59% of patients had complications, 23% had 2, and 3% - 3 complications of type 2 diabetes mellitus. Cardiovascular pathology was detected in 43%, cerebrovascular disease in 12% of patients. It was found that with the existing type 2 diabetes mellitus, the risk of developing cardiovascular pathology is 3-4 times higher than in its absence. Patients with type 2 diabetes have the same degree of risk of premature death as patients who underwent myocardial infarction without the presence of diabetes mellitus. In most of the world's developed countries, diabetes mellitus occupies the third or fourth place in the overall mortality structure, is the leading cause of blindness and decreased vision in the adult population. Despite the success of medicine, diabetes remains one of the priority diseases, the social and medical significance of which is obvious. The main cause of mortality in diabetes mellitus are vascular complications, in the pathogenesis of which the main role belongs to hyperglycemia and its metabolic effects. The risk of macro- and microangiopathy in patients with type 2 diabetes directly depends on the level of glycemia [2].

Analysis of the results of the United Kingdom Prospective Diabetic Study (UKPDS) showed that increasing glycated hemoglobin levels by only 1% increases the risk of death associated with diabetes by 21%, myocardial infarction by 14%, peripheral vascular disease by 43%, microvascular complications - by 37%, development of cataracts - by 19% [3]. The incidence of any complications of diabetes, including death of patients, increases in proportion to the average level of glycated hemoglobin HbA1c. Mortality from cardiovascular diseases among patients with type 1 and type 2 diabetes is 35% and 75%, respectively. Life expectancy in patients with type 2 diabetes is less, and mortality (with age) is almost twice as high as in patients who do not have this disease. High cardiovascular risk with diabetes is due to several circumstances. First, many risk factors for cardiovascular disease (CVD) are present in patients already at the stage preceding diabetes (Figure 1). As is known, insulin resistance plays a leading role in the development of type 2 diabetes mellitus (IR). In modern interpretation, insulin resistance should be understood as the primary selective and specific violation of the biological action of insulin, accompanied by a decrease in glucose consumption by tissues (mainly skeletal muscles) and leading to chronic compensatory hyperinsulinemia. In conditions of insulin resistance, there is a decrease in the intake of glucose into insulin-dependent tissues (muscle, fat), increase in glucose production by the liver, which contribute to the development of hyperglycemia. With

an adequate ability of β-cells to compensate for the increase in glucose level by excessive production of insulin, the state of normoglycemia persists. However, subsequently, with an increase in the degree of insulin resistance, the insulin secretion ability of β-cells is depleted and they cease to cope with the increasing load of glucose. Initially, this manifests itself in the development of hyperglycemia in postprandial (after eating) period. An example of postprandial hyperglycemia is impaired glucose tolerance. With further progression of insulin secretion disorders by β-cells of the pancreas and persistent insulin resistance, impaired glucose tolerance passes into type 2 diabetes mellitus.

It is established that annually impaired glucose tolerance passes into type 2 diabetes in 4-9% of patients. Thus, macrovascular complications, which are manifestations of CVD, appear much earlier than the development of the complete picture of diabetes. Second, the decisive role in the development of complications of diabetes due to atherosclerosis, can also play factors such as obesity, arterial hypertension and dyslipidemia. Many patients with type 2 diabetes even before the diagnosis is diagnosed have several risk factors for cardiovascular disease, including, in addition to diabetes, hyperlipidemia, arterial hypertension and overweight. Thus, every second patient with diabetes mellitus is diagnosed with dyslipidemia, and almost all patients in this category have an overweight body. This "polygenic syndrome", which includes hypertriglyceridemia, a decrease in the level of high-density lipoproteins, abdominal obesity, arterial hypertension (AH), impaired fasting glycemia, as a separate concept was first introduced into scientific use under the names "metabolic trisinder", "abundance syndrome" , and later as a "metabolic syndrome".

Initially, a possible connection between the components of this syndrome was ignored by many, while in 1988 G.M. Reaven et al. did not put forward the hypothesis of insulin resistance as the primary cause of the development of the so-called metabolic syndrome. The great interest in the problem of the metabolic syndrome in the last decade is explained by its wide spread in the population (up to 20%), and by the fact that all its components belong to the established risk factors for cardiovascular diseases, including acute coronary syndrome and stroke. The increase in the total individual cardiovascular risk by several times with a combination of its factors causes a high medico-social significance of the metabolic syndrome [4]. Moreover, at present the presence of the metabolic syndrome is

considered as the main cause of high global cardiometabolic risk, which unites the risk of CVD and the risk of developing diabetes. The most common in patients with type 2 diabetes is arterial hypertension. Thus, the UKPDS study analyzed the cardiovascular diseases that already affected patients who had been diagnosed with diabetes for the first time. It was found that arterial hypertension occurred in almost 65% of patients, quite often patients already suffered in the past myocardial infarction (34%) or had changes on the ECG (33%). Diseases of peripheral vessels (macroangiopathy) were recorded in 46% of patients, and stroke - in 38% of patients. Arterial hypertension is observed in approximately 75-80% of patients with type 2 diabetes and causes the death of more than 50% of patients. The proven fact is that the association of diabetes mellitus and hypertension significantly increases the risk of adverse outcome in patients [5]. The combination of these diseases to a certain extent is natural. Arterial hypertension and diabetes mellitus are pathogenetically related. Their frequent coexistence is facilitated by the interaction of common hereditary and acquired factors. Among them, the most important are the following: genetic predisposition to increase blood pressure and diabetes; sodium retention in the body, as well as angiopathy and nephropathy, contributing to increased blood pressure and the development of diabetes mellitus; obesity, especially abdominal, which can cause or enhance the state of insulin resistance. Analyzing the causes and frequent coexistence of hypertension and diabetes, many researchers drew attention to possible common mechanisms for their development, namely, a similar complex of metabolic disorders.

In the pathogenesis of arterial hypertension against the background of insulin resistance in patients with type 2 diabetes, several factors are involved. Normally, insulin causes vasodilation, which is not accompanied by a change in blood pressure in healthy individuals against the background of increased sympathetic activity, also caused by the action of insulin. In patients with insulin resistance, the vasodilating effect of insulin is blocked, and the development of hyperinsulinemia activates a number of mechanisms that increase the tonic stress of the vascular wall. Insulin resistance is accompanied by activation of the sympathetic nervous system. Activation of the sympathetic system leads to increased contractility of cardiomyocytes and smooth muscle cells of the vessels. This is accompanied by an increase in cardiac output, an increase in total peripheral vascular resistance (OPSS), and a level of blood pressure. In conditions of the effects of the baroreceptor apparatus of large vessels. But, perhaps, the central link in the pathogenesis of

hypertension with diabetes is a high activity of the renin-angiotensin-aldosterone system (RAAS) [6]. The daily profile of blood pressure in patients with diabetes mellitus has its own characteristics and differs from the daily profile of patients with arterial hypertension without metabolic disturbances. So, against the background of metabolic disorders, a higher average level of both systolic and diastolic blood pressure is detected per day, day and night. In a significantly larger number of patients, there is an insufficient decrease in blood pressure at night and nighttime hypertension. Another feature of the daily profile of blood pressure in patients on the background of diabetes is an increase in the variability of systolic and diastolic blood pressure during daytime and nighttime hours. For patients with type 2 diabetes and arterial hypertension is also characterized by a large magnitude and rate of morning rise in blood pressure. Regardless of the average level of blood pressure, excess BP variability and a higher rate of morning BP rise correlate with a more severe total lesion of target organs and is considered as a factor of unfavorable prognosis in patients with arterial hypertension. On the other hand, it is shown that diabetes mellitus (regardless of arterial hypertension and obesity) is combined with myocardial hypertrophy of the left ventricle of the heart (LVH) and increased arterial stiffness. The frequent coexistence of arterial hypertension and diabetes mellitus, associated with a high risk of cardiovascular events, dictates the need to determine the principles of management of patients with hypertension and diabetes 2. Many studies have shown that the importance for preventing cardiovascular complications in patients with diabetes has a hard control of blood pressure.

The importance of effective control of blood pressure to prevent cardiovascular complications in diabetic patients has been proved in many completed studies. According to a multicenter, randomized UKPDS study involving patients with type 2 diabetes mellitus and high blood pressure, strict glycemic control significantly reduces the incidence of microvascular complications, and a strict BP control (less than 144/82 mm Hg) significantly and reliably reduces the risk of any clinical complications associated with diabetes by 24%; mortality associated with diabetes by 32%; stroke by 44%, diabetic retinopathy and renal failure by 37%, reduction of visual acuity by 47%. One of the most important conclusions of this study is that the risk of mortality, development of micro- and macrovascular complications of DM significantly decreased with a rigid control of blood pressure in comparison with the control of blood glucose level [10, 12]. The HOT (Hypertension Optimal Treatment) study showed that achieving a lower target BP

(diastolic blood pressure less than 80 mmHg) in patients with diabetes mellitus was associated with an additional 51% reduction in cardiovascular risk [7]. No less impressive results were obtained in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation) study. The results of the ADVANCE study showed that intensive antihypertensive therapy reduced overall mortality by 14% and a 18% risk of cardiovascular mortality. In addition, the probability of cardiovascular complications decreases by 14% and by 21% of renal complications [8].

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