UDC: 616.379-008.64-06:616.13/.14]-092-073.7

Diabeetic angiopathies: urgent aspects of pathogenesis and diagnosis

T.P. Lysenko
Kharkiv Medical Academy of Postgraduate Education

The review deals with pathogenesis and diagnosis of diabetic angiopathies. It is shown that vascular lesions are based on common pathogenetic mechanisms. Early detection of vascular lesion markers is necessary for prevention and treatment of vitally dangerous complications. For this purpose, further development of ultrasonic methods of diagnosis is promising.
Key words*: diabetes mellitus, angiopathy, pathogenesis, ultrasonic diagnosis.*

Diabetes mellitus (DM) is regarded as one of the chief problems of the world health protection. Almost 6% of the global population suffer from DM, but its scope increases every year. By 2030 its prevalence is expected to rise by 54% (in developing countries from 2010 to 2030 by 69%), and most of all it concerns the age group from 40 to 60 years. In developed countries this increase will reach to 20% and will be mainly observed in people over 60 [32].

With an increase in the prevalence of DM the rate of its complications rises too, macro- and microangiopathies being the most significant of them. Macro- and microangiopathies in patients with DM are not uniform by their origin at all. Microvascular complications include retinopathy, nephropathy and neuropathy. Macroangiopathy generally affects the coronary and carotid arteries and those of the lower extremities. Detection of the most significant factor is of paramount importance for working out diagnostic and therapeutic strategies [24].

Diabetic angiopathies involve actually all organs because of changes in the conditions of their blood supply, lesions of different types of vessels resulting in a considerable deterioration in the course of the disease. The cardiovascular system is affected most of all. Today they even say about an epidemic of atherosclerotic complications in patients with type 2 DM. Eighty per cent of deaths in DM are related to cardiovascular incidents, which include coronary disease (CD), stroke and diseases of peripheral arteries [6].

Atherosclerotic lesions in DM are described as macroangiopathies, which are characterized by a rapid progress and multiple damages, including the coronary and carotid arteries and those of the lower extremities. Clinically such lesions manifest themselves in the form of CD, diabetic foot, ischaemic strokes and other diseases.

In DM patients before 55 the risk of development of stroke increases 10 times [29] and that of fatal CD 3.5 times [16]. DM cases have a considerably higher risk of development of heart failure [33], including patients who have survived myocardial infarction [18]. But DM is also an independent risk factor of the fatal outcome in heart failure [23].

Diabetic cardiomyopathy, which develops irrespective of the presence of CD or hypertension, is a common complication of DM. Its main peculiarity consists in unfavourable remodelling of the myocardium in the form of concentric myocardial hypertrophy in the left ventricle with diastolic dysfunction, which develops and precedes systolic myocardial dysfunction [11].

Lesions of peripheral vessels on the lower extremities, which are 2-4 times more common in patients with DM versus the general population, are not less significant. The rate and extent of peripheral angiopathies correlate with the duration and severity of DM [26]. Their development is also facilitated by the presence of hypertension, dyslipidaemia and central obesity, typical for DM [20]. Macroangiopathy most frequently involves the most distal vessels (the tibial and fibular arteries) and in combination with peripheral microangiopathy causes diffuse ischaemic lesions, where any organ-salvation surgical correction is not possible [3, 12, 20]. Besides, typical for DM are lesions of peripheral vessels of the Mцnckeberg's medial calcification type [14]. Such lesions are characterized by calcification of the medial layer of medium-sized and major arteries [2].

Peripheral angiopathies result in disability, caused by the necessity of incapacitating surgical interventions. Gangrene, in which amputation is actually inevitable, is the final stage of peripheral angiopathies. Amputations of extremities in patients with DM are made five times oftener than in patients without DM [26].

Diabetic nephropathy, which most commonly leads to the development of the terminal stage of renal failure, is another frequent complication of DM. This is detected by both the presence of persistent proteinuria and depression of the glomerular function without any infection of the urinary tracts and other renal diseases. Diabetic nephropathy is revealed in 35% of patients with type 1 DM and a bit less commonly in type 2 DM. Thickening of the basal membrane of glomeruli and thickening of the medial layer of the renal vessels are early morphological abnormalities in diabetic nephropathy. Later glomerular sclerosis and decelerated glomerular filtration develop [25]. Concomitant arterial hypertension is an important factor of the progression of nephropathy [28].

The severity of DM complications is evidence of the urgency of screening and early diagnosis of angiopathies. In this connection researches aimed at the detection of risk factors of the development of angiopathies are interesting. A lot of scientists carry out studies in this direction. For example, biomicroscopy and laser flowmetry helped to reveal reliable differences of blood flow intensity in patients with DM versus the control group of healthy patients. But at the same time the authors did not find any considerable differences in the group of patients with DM depending upon its duration. The authors drew a conclusion about the appearance of clinically significant angiopathic changes 10 and more years after the onset of DM [34].

According to other authors, who studied the thickness of the intima-media complex of the carotid artery in patients with type 2 DM, in cases with atherosclerotic events there are some relations between an increase of the above thickness and the patients' waist circumference as the marker of central obesity, the duration of diabetes, the presence of hypertension and concentration of glycated haemoglobin. But at the same time no relations with the patients' age, smoking and presence of dyslipidaemia were detected [15].

Similar data were got by Dahlйn et al. too (2013), who revealed the prognosticating value of such anthropometric data as sagittal abdominal diameter and, to a less extent, waist circumference with respect to a higher arterial stiffness in patients with DM [30], while the Japanese authors have demonstrated

that diabetes, which is especially associated with a higher level of triglycerides and high-density lipoproteins, considerably increases the arterial stiffness and risk of development of atherosclerosis [5]. At the same time, during the study of the prognosticating significance of the glycated haemoglobin level in DM this level did not show any essential influence on the value of the ankle brachial index and, respectively, on the risk of development of peripheral angiopathy [19].

On the whole, we can state that a lot of factors take part in the development of diabetic angiopathies, including morphological changes in the basement endothelial membrane of capillaries, their higher permeability and a lower diffusion of oxygen through them, rheological changes caused by a structural change of blood flow, etc. In order to study microcirculation the following techniques are used: plethysmography, laser Doppler flowmetry, capillaroscopy, and others [31].

Measurement of the carotid artery intima-media complex thickness is one of informative methods. An increased value of this index is regarded as a sign of early atherosclerosis [8]. Moreover it has been shown that the intima-media thickness is a strong predictor of cardiovascular events in future [27].

Study of the intima-media complex thickness of the common carotid or internal carotid artery with help of ultrasound is recommended as a noninvasive, but informative test for revealing subclinical forms of cardiovascular pathology and risks of their development [1, 8, 27]. Dynamic studies of this index are also used for controlling the efficacy of hypolipidaemic therapy [7; 10].

Estimation of the ankle brachial index is widely used for early detection of peripheral angiopathy and recommended as a screening test in high-risk patients [4]. Early revealing of signs of peripheral angiopathy and, respectively, opportune drug correction increase the efficacy of treatment of DM and make it possible to prevent severe incapacitating complications.

Researches in the direction of increasing informativity of diagnostic programmes in DM go on. In particular, it is suggested to study muscular microcirculation using ultrasonic examination with contrast enhancement, which makes it possible to assess the intensity of diabetic angiopathy [9]. Ultrasonic examination of vessels with contrast enhancement helped to show that patients with DM revealed changes in the adventitia membrane of their carotid arteries (lesions of the vasa vasorum) [22].

Besides assessment of the extent of stenosis there is an increasing interest to the estimation of characteristics of atherosclerotic plaques. Detection of their instability is a new criterion for identifying patients with a high risk of vascular complications, particularly stroke. For this purpose MRI, positron emission tomography and other modern methods of examination are used side by side with ultrasonic investigation [35].

Promising for early diagnosis of angiopathies are the techniques aimed at detection of endothelial dysfunction. The latter is the first manifestation of the atherosclerotic process, facilitates development of arterial wall stiffness and underlies the further evolution of atherosclerosis. Endothelial dysfunction has been shown to act a predictor of cardiovascular pathology [21]. It has been revealed that disturbances in glucose metabolism are some of important causes for endothelial dysfunction and an increase of arterial wall stiffness [13], DM complications being endothelium-dependent [6].

In order to study endothelial dysfunction ultrasonic technique is used. It has been suggested to assess the extent of arterial dilatation, which was induced by different methods, nitrates in particular, to measure the velocity of pulse waves and analyse them [21]. These techniques are already used in clinical practice, including such a purpose as assessment of the efficacy of angiotropic treatment. But the results of these researches are highly variable and the method requires further study and improvement.

Hence, diabetic angiopathies are a very common event in patients with DM. Especially dangerous is the presence of combination of micro- and macroangiopathic lesions, which considerably increase the severity of DM course. Only early diagnosis of these complications or their initial manifestations will make it possible to decrease disability and mortality of patients with DM. This can be facilitated by introduction of informative noninvasive and low-cost techniques of medical visualization, particularly ultrasonic methods of examination.

CONCLUSIONS

1. Despite a variety of vascular complications of DM these are based on common pathogenetic mechanisms, which differ only by the prevailing lesion of the microcirculation territory or arterial territory.

2. Detection of vascular lesion markers in some regions of blood supply can be useful for diagnosing the main kinds of angiopathies; in this connection it is reasonable to search for such markers, which are available for surveillance studies in the course of the disease.

3. Ultrasonic examination, as the least invasive and costly, is the most promising one in this aspect.

Диабетические ангиопатии: актуальные аспекты патогенеза и диагностики

Т.П. Лысенко

Обзор посвящен патогенезу и диагностике диабетических ангиопатий. Показано, что в основе сосудистых осложнений лежат единые патогенетические механизмы. Раннее выявление маркеров сосудистых поражений необходимо для профилактики и лечения опасных для жизни осложнений. С этой целью перспективно дальнейшее развитие ультразвуковых методов диагностики.

Ключевые слова: *сахарный диабет, ангиопатия, патогенез, ультразвуковая диагностика.*

Діабетичні ангіопатії: актуальні аспекти патогенезу та діагностики

Т.П. Лисенко

Огляд присвячено патогенезу та діагностиці діабетичних ангіопатій. Показано, що в основі судинних ускладнень лежать єдині патогенетичні механізми. Раннє виявлення маркерів судинних уражень необхідне для профілактики і лікування життєво небезпечних ускладнень. З цією метою перспективний подальший розвиток ультразвукових методів діагностики.

Ключові слова: *цукровий діабет, ангіопатія, патогенез, ультразвукова діагностика.*

Список литературы находится в редакции

Статья поступила в редакцию 06.06.2014