Cardiovascular pathology – a factor of the adverse course of diabetic polyneuropathy

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Diabetic polyneuropathy (DP) and angiopathy are interdependent processes, as disturbances in the microcirculatory system of peripheral nerves lead to increased axonal damage and is a kind of predictor of polyneuropathy progressing [6]. 80% of deaths from diabetes mellitus (DM) are associated with cardiovascular catastrophes, including coronary heart disease (CHD), stroke and peripheral artery disease [3].

The objective: to analyze the most common cardiovascular pathology (CVP) and show its impact on the course of DP in type I and II DM.

Materials and methods. Was clinically examined 101 patients with DP. The examined patients were divided into groups: with DP on the background of type 1 DM (group I) (n=54) and with DP on the background of type II DM (group II) (n=47), and also were divided into subgroups: DP on the background of type I and II DM and existing CVP (including diabetic angiopathy) 82 (82%) (subgroup A) and with the DP on the background of DM type I and II without CVP – 19 (19%) (subgroup B). Patients were examined to determine the neurological status, were performed laboratory and instrumental methods of examination. Static calculation was performed in MS Excel 2003 and in the programme STATISTICA 10.

Results. Regarding to the patients of subgroup A and B we noted the natural predominance of trophic disorders, changes in the reflex sphere and sensitivity in subgroup A. Patients of group II more often than in group I had pathology of the cardiovascular system. Hypertension (HT) and CHD in both cases were registered with a high frequency. In subgroup A there was a combination of several nosologies: from the respiratory, urinary, gastroenterological system (1%), urinary and gastroenterological (3%), gastroenterological and endocrine (2%), urinary and endocrine (1%). In subgroup B diseases of urinary and gastroenterological pathology were found in (5%), gastroenterological (3%), endocrine (11%). The examined patients from group I and with the concomitant CVP have lower linear velocity of blood flow (LVBF) on both tibial arteries, patients in group II – have marginally higher LVBF. Analysis of the results of duplex scanning of lower extremity arteries showed a high degree of stenosis, in particular the anterior tibial arteries (ATA) up to 30–40%, posterior tibial arteries (PTA) up to 40–50% and occlusion (PTA and femoral, popliteal, tibial segment) in individuals of group I.

Conclusions. In patients with DP on the background of type I and II DM and available CVP (subgroup A), the clinical manifestations of polyneuropathy were quite pronounced, especially in the field of trophic disorders, because CVP enhances the ischemia of the microsaceous channel of the peripheral nerves. In addition, persons with concomitant CVP have a wide range of another comorbid pathology, which accelerates the onset of DM complications.

Keywords: diabetic polyneuropathy, cardiovascular pathology, diabetic angiopathy, linear velocity of blood flow, transsyndromic comorbidity, echocardiography.
While to 60% of patients with a long-standing history of diabetes mellitus (DM) have diabetic neuropathy (DP), 7–10% of people with the first diagnosed DM have verified DP [1, 17, 19]. The incidence of DP is higher in people with type 2 DM (6.10 per 100,000 people per year) than in people with type 1 DM (2.80 per 100,000 people per year) [2, 11, 14, 15]. Opposite, the prevalence of DP is almost the same as in type 2 DM (8–51%) [7, 8, 13]) and type 1 DM (11–50%) [4, 7, 18]). It is important that the prevalence of DP is even higher when asymptomatic (subclinical) neuropathy is included, 45% in patients with type 2 DM and 54% in patients with type 1 DM [7].

Damage to the blood vessels of the lower extremities in DM is the main cause of amputations of the lower extremities, unrelated to physical traumas or road accidents [10].

Foot loss is an important problem in economic terms, especially if amputation is the end of long hospital treatment with the patient’s discharge home and the need to care for him. The cost of primary treatment is estimated at 7–10 thousand USD [12].

Increased lipid profile indicators in a patient with DM together with hypertension (HT), which predominates in middle-aged and elderly people, contributes to the formation of metabolic syndrome, which can lead to vascular accidents in the future [5].

DP and angiopathy are interdependent processes, as disturbances in the microcirculatory system of peripheral nerves lead to increased axonal damage, and the presence of trophic disorders in DP is accompanied by an inability of the vascular system to adequately deliver nutrients to nerve fibers, which contributes to chronic ischemia and is a kind of predictor of polyneuropathy progressing [6].

Diabetic angiopathies affect almost all organs due to impaired blood supply, and damage to various types of blood vessels leads to a significant deterioration in the course of the disease. The cardiovascular system is most affected. Today we are talking about an epidemic of atherosclerotic complications in patients with type II DM. 80% of deaths from DM are associated with cardiovascular catastrophes, including coronary heart disease (CHD), stroke and peripheral artery disease [3].

The objective: to analyze the most common cardiovascular pathology (CVP) and show its impact on the course of DP in type I and II DM.

MATERIALS AND METHODS

Was clinically examined 101 patient with DP, aged from 19 to 69 years (M±m; 50.94±1.34 years). Women predominated – 52 (52%) patients, men were 49 (49%). Type I DM was detected in 54 (54%), type II DM – in 47 (47%) patients.

The examined patients were divided into groups: with DP on the background of type I DM (group I) (n=54) and with DP on the background of type II DM (group II) (n=47). Depending on the presence of CVP, patients were divided into subgroups: DP on the background of type I and II DM and existing CVP (including diabetic angiopathy) 82 (82%) (subgroup A) and with the DP on the background of type DM I and II without CVP – 19 (19%) (subgroup B).

Patients were examined to determine the neurological status, were performed laboratory (general blood test, general urine test, biochemical blood test, glycated hemoglobin) and instrumental methods of examination (duplex scanning of the vessels of the lower extremities, electrocardiography (ECG), echocardiography (Echo), electroneuromyography (ENMG)). Static calculation was performed in MS Excel 2003 and in the programme for statistical analysis STATISTICA 10.

RESEARCH RESULTS AND DISCUSSION

In subgroup A type I DM was verified in 42 (51%) patients, type II – in 40 (49%), in subgroup B type I DM – in 12 (63%), type II – in 17 (37%). The average data on the age category of patients are shown in Fig. 1.

Among 101 examined patient we observed changes in the reflex sphere of the lower extremities in 86 (86%), namely: decreased knee reflexes – 64 (74%), loss – 9 (10%), decreased Achilles reflexes – 49 (57%), loss – 36 (42%), decreased plantar reflexes in 40 (47%), loss in 45 (52%).

There were disturbances in the reflex sphere of the upper extremities in 42 (42%) examined patients: decreased carpal reflex – 16 (38%), loss – 26 (62%), decreased biceps reflex – 26 (62%), loss – 16 (38%), decreased triceps reflex – 23 (55%), loss – 3 (7%).

Sensitivity disorders were found in 92 (92%) patients, of which 64 (70%) had hypoesthesia of the distal extremities, and 28 (30%) had hyperesthesia.

Regarding to the patients of subgroup A and B we noted the natural predominance of trophic disorders (Table 1), changes in the reflex sphere and sensitivity in subgroup A. Decrease in vibrational sensitivity is present in both subgroups, but in subgroup A the indicators are lower, in particular in the lower extremities (7.18±0.34 s).

In 1 patient of subgroup A was revealed a slight peripheral parasis of both hands, in subgroup B in 1 patient previous changes were combined with slight peripheral parasis of both feet. Manifestations
of «diabetic foot» were diagnosed in 12 (15%) patients of subgroup A, and in 6 (8%) amputation of fingers was performed, in subgroup B none of the patients had such complication of DM.

Patients of group II more often than in group I had pathology of the cardiovascular system (Fig. 2). HT and CHD in both cases were registered with a high frequency. In addition to CVP, disorders of the gastrointestinal tract in people with type II DM also dominate (Fig. 3). Gallstone disease (GD), chronic cholecystitis (CC), chronic pancreatitis (CP) and chronic hepatitis (CH) were more commonly diagnosed in both type I and type II DM.

In subgroup A there was a combination of several nosologies: from the respiratory, urinary, gastroenterological system (1%),

| Table 1 |
| --- |
| **Frequency of changes of the main parameters of the patients’ neurological status with DP subgroups A and B (absolute values)** |
| **Indicator** | **Subgroup A, n=82** | **Subgroup B, n=19** |
| --- | --- | --- |
| Trophic disorders of the lower extremities | | |
| Hypohidrosis | 32 | 11 |
| Hyperhidrosis | 27 | 2 |
| Hypertrichosis | 21 | 9 |
| Hypotrichosis | 32 | 3 |
| White dermographism | 49 | 10 |
| Red dermographism | 33 | 9 |
| Hyperkeratosis | 47 | 10 |
| Foot fissure | 42 | 6 |
| Trophic changes of the nails | 44 | 13 |
| Dry skin | 26 | 8 |
| Reflexes | | |
| Carpo radial loss | 25 | 1 |
| Carpo radial decreased | 12 | 4 |
| Biceps loss | 15 | 1 |
| Biceps decreased | 22 | 4 |
| Triceps loss | 3 | 0 |
| Triceps decreased | 21 | 2 |
| Knee loss | 8 | 1 |
| Knee decreased | 54 | 10 |
| Achilles loss | 34 | 2 |
| Achilles decreased | 38 | 11 |
| Plantar loss | 38 | 7 |
| Plantar decreased | 32 | 8 |
| Sensitivity | | |
| Hyperesthesia | 23 | 5 |
| Hypoesthesia | 53 | 11 |
| Average Indicator of vibrational sense on upper extremities, s | 11.23±0.47 | 13±1.01 |
| Average Indicator of vibrational sense on lower extremities, s | 7.18±0.34 | 7.73±0.56 |

Fig. 1. The average age of the patients in each of the groups and subgroups

Fig. 2. Distribution of CVP in DP on the background of type I and II DM

*Note. HT – hypertension, CHD – coronary heart disease, AF – atrial fibrillation, CgHD – congenital heart disease.
urinary and gastroenterological (3%), gastroenterological and endocrine (2%), urinary and endocrine (1%). Were diagnosed single lesions of the endocrine system (actually the thyroid gland) (15%), gastroenterological (5%), urinary (2%). Among this cohort of patients (5%) – varicose of the lower extremities, in (1%) – suffered acute thrombosis of the veins of the left lower extremity. In subgroup B diseases of urinary and gastroenterological pathology were found in (5%), gastroenterological (5%), endocrine (11%).

Among transsyndromal comorbidity dominate retinopathy, nephropathy and angiopathy of the lower extremities dominate (Fig. 4), which are more often present in subgroup A.

Lipid profile indicators (Fig. 5, 6) in patients of subgroup A and B are within normal values. In subgroup A the quantity of the scope for all parameters of lipid metabolism is higher, in particular for total cholesterol.

The average rate of glycated hemoglobin (Fig. 7) in patients of group II is significantly higher than in group I, in subgroup B is slightly higher than in A.

According to the results of the recorded ECG in subgroup A in 14 (17%) blockade of the legs of His bundle, 12 (15%) sinus
tachycardia, 7 (9%) early ventricular repolarization syndrome, 3 (4%) sinus bradycardia, 1 (1%) Q-T prolongation, in subgroup B – 3 (16%) early repolarization syndrome, 2 (11%) blockade of the legs of His bundle, 2 (11%) sinus tachycardia.

The results of the Echo, which was carried out in 17 patients, in the subgroup А demonstrated the following changes: diastolic left ventricular (LV) dysfunction (7%), LV concentric hypertrophy (5%), left atrial (LA) dilatation (4%), fibrocalcific aortic valve (AV) (4%), prolapse of the anterior mitral valve (MV) (3%), additional atypical LV chord (1%), aortic dilatation (1%), AV stenosis (1%), pulmonary hypertension (1%), dilatation of both atrias and LV (1%), LV systolic dysfunction (1%), hypokinesis of the posterior basal and posterior diaphragmatic LV (1%). In subgroup В - additional chord of LV 1 (5%), diastolic dysfunction of LV 1 (5%), prolapse of MV 1 (5%).

In 34 (34%) patients (21 from group I and 13 from group II), was performed duplex vascular scans of the lower extremities. Linear velocity of blood flow (LVBF) in the anterior (ATA) and posterior tibial (PTA) arteries was within normal range in all examined (table 2).

The examined patients from group I with the concomitant CVP have lower LVBF on both tibial arteries. The LVBF on the left ATA is quite low – 45.45±5.85 sm/s. Regarding to the patients in group II, we observed marginally higher LVBF rates in patients with concomitant CVP. This phenomenon was associated with compensatory acceleration of blood flow in stenosed vessels during the initial stages of atherosclerosis and a wide intake of antiplatelet agents by patients of this sample.

Analysis of the results of duplex scanning of lower extremity arteries (table 3) showed a high incidence of stenosis, in particular ATA up to 30–40%, PTA up to 40–50% and occlusion (PTA and femoral, popliteal, tibial segment) in individuals of group I. According to the literature [9, 16], despite hyperlipidemia, it has been proved that in the absence of circulating insulin, such changes in lipid metabolism do not lead to the emergence of a vascular lesion, but the need to increase the dose of insulin is a sensitive indicator of the development of macroangiopathy.

**CONCLUSIONS**

1. In patients with DP on the background of type I and II DM and available CVP (subgroup А), the clinical manifestations of polyneuropathy were quite pronounced, especially in the field of trophic disorders. Hyperkeratosis, changes in the nail plate, cracks, hypotrichosis, hypohydrosis prevail, because CVP enhances the ischemia of the microsaceous channel of the peripheral nerves. The spread of white dermographism indicates initial lesions of the vegetative link of the nervous system.

2. In the examined patients with DP on the background of type I and II DM and the existing CVP (subgroup А), despite the lower level of glycated hemoglobin (8.88±0.18%) than in subgroup В (8.99±0.52%), was diagnosed a significant number of patients with a «diabetic foot». In addition, persons with concomitant CVP have a wide range of another comorbid pathology (from the gastroenterological, urinary, respiratory system), which accelerates the onset of DM complications.

3. Patients with DP and type I DM (group I) show with greater frequency the presence of lower extremity arterial stenoses of varying degrees, although the overall LVBF in the group is higher, with the exception of ATA on the right, than in the comparison group.

4. CVP creates an unfavorable background for restorative processes in the distal parts of nerve fibers, which are exposed to the devastating effects of hyperglycemia earliest and fastest.
1. Abbott A. et al. Prevalence and Characteristics of Painful Diabetic Neuropathy in a Large Community-Based Diabetic Population in the U.K. Diabetes Care, 2011, Oct. 34(10):2220-4.
2. Ang L., Jaiswal M., Martin C. & Pop-Busui R. Glucose control and diabetic neuropathy: lessons from recent large clinical trials. Curr. Diab. Rep. 14, 2014;1(25):36-46.
3. Beckman JA, Creager MA, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology, and management. JAMA. 2002; 287(25):?–61.
4. Boulton A, Knight G, Drury J & Ward J.D. The prevalence of symmetrical diabetic neuropathy in an insulin-treated population. Diabetes Care, 1985; 8:125-8.
5. Chupryna GM, Dubynetska VM, Vashenyuk OL, Vashenyuk NO. Features of clinical and paracrine parameters and comorbidity in patients with diabetic polyneuropathy. Health of Society, 2019;8(5):174-8.
6. Dubynetska VM., Chupryna GM. Diabetic polyneuropathy: a look at the problem through the prism of comorbidity, East European Jornal of Neurology, 2019;8(5):174-8.
7. Dyck PJ et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. Neurology, 1993; 43: 817-24.
8. Franklin GM, Kahn LB, Baxter J, Marchand JA & Hamman RF. Sensory neuropathy, retinopathy, and nephropathy in diabetes mellitus. N. Engl. J. Med.; 2005:352, 341-50.
9. Janka HU, Standl E. Hyperinsulinemia as a possible risk factor of macrovascular disease in diabetes mellitus. An overview. Diabetes Metab, 1987 Jul;13(Suppl 2):279-83.
10. Kaminskiy AV, Kovalenko AN. Diabetes mellitus and obesity: a clinical guide to diagnosis and treatment. K.: Lira; 2010. 256 p.
11. Martin CL, Albers JW & Pop-Busui R. Neuropathy and related findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. Diabetes Care; 2014;37:31-8.
12. Mota M, Vasile A, Mitroy N. Risk Factors Leading to Amputation in Patients with Diabetes Mellitus. Maria Mota, Andriana Vasile, Nikoletta Mitroy and others. International Journal of Endocrinology; 2005;01:9-24.
13. Partanen J. et al. Natural history of peripheral neuropathy in patients with non-insulin-dependent diabetes mellitus. N. Engl. J. Med.; 1995; 333, 89-94.
14. Pop-Busui R et al. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care; 2017; 40:136-54.
15. Pop-Busui R et al. Impact of glycemic control strategies on the progression of diabetic peripheral neuropathy in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Cohort. Diabetes Care;2013:36:3208-15.
16. Stout RW. Hormones and Atherosclerosis: M.: Medicine, 1985:240.
17. Tesfaye S, Andrew JM, Boulton, Peter J Dyck, Roy Freeman et al. diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2010 Oct; 33(10):2265-93.
18. Tesfaye S et al. Vascular risk factors and diabetic neuropathy. N. Engl. J. Med.; 2005:352, 341-50.
19. Tracy JA et al. The Spectrum of Diabetic Neuropathies. Physical Medicine and Rehabilitation Clinics N Am. 2008 Feb; 19(1):1-26. 1-v.