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# ASSESS THE IMPACT OF DIABETIC NEPHROPATHY ON RENAL HEMODYNAMICS

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**Abstract:**

40 patients with type 2 diabetes mellitus (DM) without kidney damage (20 people) and with various stages of diabetic nephropathy caused by DM 2 (20 people) aged 37 to 54 years were examined, and the control group consisted of 20 healthy individuals. The duration of the disease ranged from 6 months to 20 years. We studied such indicators as the results of general blood and urine tests, lipid spectrum, glycemic profile, glycosylated hemoglobin, microalbuminuria, glomerular filtration rate (GFR) according to the CKD-EPI formula, and parameters of intrarenal hemodynamics - Doppler parameters PI, RI, Vmax. An analysis of the data obtained during the study suggests that in DM 2, the kidneys are actively involved in the pathological process already in the very debut of the disease. The appearance of MAU or normally elevated blood pressure in a patient with DM 2 indicates an already advanced pathological process in the kidneys in terms of the possibility of its reverse development.

**Keywords:** Diabetes mellitus, diabetic nephropathy, microalbuminuria, glomerular filtration rate, intrarenal hemodynamics, lipid spectrum, glycemic profile,

**INTRODUCTION.** Diabetes mellitus (DM) today is increasingly acquiring the features of a global epidemic [2,4]. According to the World Health Organization (WHO) worldwide in 2010, there were 192 million people suffering from diabetes. It is predicted that by 2045 this figure will be more than 650 million people [1,6,8]. Diabetic nephropathy (DN) is today the most common cause of end-stage renal disease - almost 35% of uremics [5,11]. The scale of renal involvement in DM has increased tremendously in recent years, bypassing, including in terms of costs, even such a disease as glomerulonephritis (GN) [3,7,9]. And if the number of cases of detection of DN in DM 1 in recent years either does not change [6,10], or tends to decrease, then in DM 2, the frequency of detection of nephropathy increased by 50% (3). To date, it is undeniable that in DN caused by type 2 diabetes, the so-called "preclinical" (latent) stage of development is clearly distinguished, in which there are no clinical symptoms of the disease and only functional and laboratory changes that characterize the functioning of the kidneys are revealed. It is also undeniable that only the early stages of DN are capable of reverse development [11, 12]. Insufficient knowledge of the functional state of the kidneys in the early stages of DN in DM 2, the lack of informative criteria for their diagnosis, as well as the undeveloped approaches to their effective correction determine the relevance of the chosen topic for study.

**THE AIM OF THE STUDY** was to study the features of the functional state of the kidneys in patients in the early stages of DN caused by type 2 diabetes.

**MATERIALS AND METHODS OF RESEARCH:** 40 patients with type 2 diabetes mellitus (DM) without kidney damage (20 people) and with various stages of diabetic nephropathy caused by DM 2 (20 people) aged 37 to 54 years were examined, and the control group consisted of 30 healthy persons. The duration of the disease ranged from 6 months to 20 years. We studied such indicators as the results of general blood and urine tests, lipid spectrum, glycemic profile, glycosylated hemoglobin, microalbuminuria, glomerular filtration rate (GFR) according to the CKD-EPI formula, the level of endothelin-1 in blood plasma and parameters of intrarenal hemodynamics - Doppler indicators PI, RI,Vmax.

**RESULTS:** Intraglomerular hypertension RI (0.5 (0.47 - 0.55), PI (0.72 (0.5 - 0.9), Vmax (0.95 (0.89 - 1.01). That is, the absence of a patient with DM 2 MAU does not at all indicate the absence of kidney problems.The algorithm for examining such a patient should certainly include the determination of GFR using the CKD-EPI formula.

In the 2nd group of patients with diabetic nephropathy, the level of blood endothelin-1 remained high (5.86 pg/ml, $p<0.05$), decreasing as diabetic

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nephropathy progressed, and at the 5th stage did not significantly differ from the control group (4.46±0.31 pg/ml, p>0.05). And also in the group of patients, it was possible to establish that with the appearance of MAU (33.0 (28.0-37.0)), GFR decreases and reaches the normal level (134.0 (122.0-143.0). However, at the same time, decrease in renal blood flow RI (0.6 (0.57-0.68), PI (1.36 (1.1-1.6), Vmax (0.77 (0.73-0.83) with an increase in peripheral vascular resistance characterizing endothelial dysfunction.

When assessing the state of lipid and carbohydrate metabolism, they are presented in Table 1. The examined did not reveal structural and organic damage to the kidneys. According to the characteristics of renal blood flow, renal normoperfusion was recorded, patients had no signs of kidney dysfunction (Table 1).

**Table 1.** Biochemical parameters of blood in the examined patients.

| Parametrs | Control group | Group DM 2 types without | DN DM 2 types with DN |
|---|---|---|---|
| Fasting blood glucose, mmol/l | 5,5±0,8* | 7.2±0,7 | 8,6±0,7 |
| HbAk, % | 5,2±2,8* | 6,8±3,2 | 7,2±3,2 |
| Total cholesterol, mmol/l | 5,2±1,1* | 5,2±2,9 | 5,7±1,2 |
| Triglycerides, mmol/l | 2,0±1,1* | 2,06±0,8 | 2,36±1,2 |
| HDL cholesterol, mmol/l | 1,4±0,3 | 1,34±1,3 | 1,3±0,3 |
| LDL cholesterol, mmol/l | 3,2±1,1* | 3,33±1,8 | 3,6±1,1 |
| VLDL cholesterol, mmol/l | 0,87±0,7* | 1,1±0,4 | 1,2±0,6 |

***Note:*** ** - differences between groups are significant at p<0.05.*

When studying the functional state of the kidneys, it was found that the relative density of urine in the morning portion, which characterizes the concentration ability of the kidneys, was significantly lower in patients with type 2 diabetes with DN than in the control group (Tab. 2).

**Table 2.** The functional state of the kidneys in the examined patients.

| Parametrs | Control group | Group DM 2 types without | DN DM 2 types with DN |
|---|---|---|---|
| Relative density of urine in the morning portion, c.u. | 1018±0,9* | 1014±1,9* | 1016±1,2 |
| PU, mg/l | 264,8±19,4* | 351,1±19,8 | 280,1±17,8 |
| Blood creatinine, μmol/l | 88±13,4 | 108±16,7 | 92±12,6 |
| eGFR (SKE-EPI) | 68,9±11,6 | 60,5±12,9 | 64,5±14,2 |
| GFR (SKE-EPI) < 60 | 33,5* | 44 | 38,7 |

***Note:*** ** - differences between groups are significant at p<0.05*

When evaluating the parameters of renal hemodynamics in the study groups, lower values of Ved PA were found in patients of group 1. Patients of group 1 also showed a significantly higher RI MA compared to group 2, reflecting the resistance to blood flow in the distal regions (Table 3).

**Table 3.** Parameters of renal hemodynamics in patients of groups 1 and 2

| Parametrs | Group1 (n=20) | Group 2 (n=20) |
|---|---|---|
| RI MA | 0,71 (0,69; 0,77) | 0,67 (0,65; 0,73) |
| Ved ПА, м/с | 0,13 (0,10; 0,13) | 0,15 (0,12; 0,17) |

To assess the clinical significance of the differences obtained, a correlation analysis of renal function parameters and renal blood flow indices was performed (Table 4). A direct relationship was found between GFR and Ved PA (r=0.33, p<0.001). In addition, GFR had an inverse relationship with RI MA and Ved MA. It is also important

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to identify a direct relationship between the albumin/creatinine ratio and RI MA, as well as an inverse relationship between the level of creatinine and PI MA.

**Table 4.** Correlation analysis of parameters of kidney function and indices of renal blood flow

| Parametrs | R | P |
|---|---|---|
| GFR : Vps MA | -0,25 | 0,03 |
| GFR : RI MA | -0,28 | 0,02 |
| GFR : Ved PA | 0,33 | <0,001 |
| GFR : RI PA | -0,42 | <0,001 |
| albumin/creatinine : RI MA | 0,29 | 0,01 |
| creatinine level : PI MA | -0,26 | 0,03 |

The revealed features of the Doppler pattern in group 2 (decrease in Ved PA and increase in RI MA), as well as the obtained correlations between these parameters and kidney function, allow us to speak in favor of the hypothesis about the effect of changes in the characteristics of renal blood flow as manifestations of nephroangiopathy on the development of DN. These parameters (Ved PA and RI MA) can be considered as ultrasound markers of DN.

Thus, already at the initial stages of the disease, significant damage and involvement in the cascade of pathological processes of the vascular endothelium occurs, which is the initiating factor in the development of nephropathy.[12] At the 5th stage of diabetic nephropathy, the leading role of endothelin-1 in the pathogenesis of the disease is lost, and hemodynamic and homeostatic changes come to the fore. The proportion of certain progression factors in damage to the vascular endothelium depends on the stage of the disease. At the initial stages, the predominant effect of hyperglycemia was noted, and with the development of proteinuric and uremic stages of diabetic nephropathy, the role of hemodynamic and metabolic changes increased. [1,2,8]

In understanding the pathogenetic mechanisms of the formation of nephrosclerosis in diabetic nephropathy, the analysis of correlations between certain factors is of great importance. In the later stages of the process, damage to the glomerular filter comes to the fore, manifested by an increase in its permeability and a deterioration in the excretory function of the kidneys, which is confirmed by a direct correlation with the level of proteinuria, creatinine and blood urea.

**CONCLUSION:** So, the analysis of the data obtained during the study allows us to say that in DM 2, the kidneys are actively involved in the pathological process already in the very debut of the disease. The appearance of MAU or normally elevated blood pressure in a patient with DM 2 indicates an already advanced pathological process in the kidneys in terms of the possibility of its reverse development. Changes in the functional state of the kidneys take place already in the microalbuminuric stage of the development of DN,

Only such an approach to kidney problems in DM 2, in our opinion, will stop the epidemic of DN in the world today, only in this way can we achieve a reduction in the economic costs experienced by the budgets of developed countries, unsuccessfully trying to treat patients with advanced stages of DN.

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