Short Reports

THE ROLE OF IMMUNE INFLAMMATION IN PROGRESS OF DIABETIC NEFPHOPATHY

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Pancreatic diabetes is a serious medical-social problem, it is dependent by its wide spread, a trend to increase in sickness rate, high disability rate of the sick of capable age. We should outline that diabetic nephropathy (DN) is one of the most frequent and prognostic – infavourable complications of pancreatic diabetes (PD). During the latest year DN occupies leading positions among the causes of terminal renal insufficiency. We should underline that uraemia is the most frequent, after heart-vascular catastrophes, cause of death of patients with PD of the 2nd type. Unsatisfactory results of DN treatment are linked to the difficulty of pathogenesis, a continual asymptomatic flow, late diagnostic [1].

According to modern views, the leading part in forming DN is played by hyperglycemia and the linked disruptions in metabolism [4]. During the last decade participation of immune-inflammatory mechanisms in development of diabetic kidney damage is discussed. Regardless of numerous studies, many mechanisms of DN formation require specification. Particularly, study of role of immune inflammation in forming cardio-nephral continuum proves to be possible. Development of these problems can provide for an optimization of approaches towards prevention and therapy of this pathology.

Research objectives: studying serum concentration and urinal excretion of monocytic chemoattractant protein-1 that transforms growth factor β1 (TFR- β1), interleukin (IL) – β1, contents molecules of inter-cell adhesion SVCAM-1 in blood serum among patients with DN.

Methods and materials. 85 patients with PD of the 2nd type, including 40 men and 45 women at age of 40–55 were studied. Disease continuity up to 5 years was registered for 40 patients, for 45 patients continuity of diabetic anamnesis equaled 6–10 years. An average level of HbA1 among the studied equaled 9,5 ± 2,9 %. All patients received capsuled sugar-decreasing medications. Patients' distribution was carried out depending on the stage of DN, according to classification of I.I. Dedov and M.V. Shestakova (2000). All patients were randomized into two groups: the1st group – 35 patients with albumin stage of DN, the 2nd group – 50 patients with proteinuric stage of diabetic nephropathy.

Study of TFR–β1, MCP-1, SVCAM-1, IL-6, IL-1β in urine and blood serum was carried out via method of immune-ferment analysis. Blood samples of 20 healthy donors served as a control of laboratory research.

Research results and discussions. Arterial hypertension (AH) was revealed among all patients with microalbuminuria. We should outline that for only 5 patients with normal excretion of albumin with urine an increase in arterial pressure was registered. The study of contents of SVCAM-1 and IL-6 in blood serum of patients with Pd showed its increase up to 368,3 ± 92,4 ng/ml ($p < 0,05$) and 144,3 ± 8,3 ng/ml ($p < 0,01$) correspondingly, compared to the control (265,3 ± 48,9 and 13,6 ± 0,2 ng/ml correspondingly). A strengthen in expression of SVCAM-1 and IL-6 with the progress of nephropathy, a reliably higher content of SVCAM-1 and IL-6 in blood serum was registered in the group of patients with proteinuria and AH (SVCAM-1 – 403,5 ± 101,2 ng/ml, $p < 0,05$, and IL-6 – 184,4 ± 5,2 pg/ml, $p < 0,01$, correspondingly). An increase in excretion of SVCAM-1 and IL-6 with a progress of nephropathy, reliably higher contents of SVCAM-1 and IL-6 in blood serum was registered among patients with proteinuria and AH (SVCAM-1 – 403,5 ± 101,2 ng/ml, $p < 0,05$, and IL-6 – 184,4 ± 5,2 pg/ml, $p < 0,01$, correspondingly). An increased level of SVCAM-1 in blood serum of patients with DN is dependent by hyperexpression of SVCAM-1 and IL-6 – modified cells of endothelium, and reflects both degree of inflammatory reaction in artery walls and a progression in endothelium dysfunction. An increased expression of SVCAM-1 can play an important part in developing nephrosclerosis, providing for migration of inflammatory cells into clews and intersticium. IL-6 regulates the activity of inhibitors of matrix metalloproteinases. Their level defines the contents of extracellular matrix in artery walls. An important characteristic of IL-6 is its impact over pro-agulant blood activity that provides for a formation of later complications of SD [3].

The results of defining initial serum content of IL-1β and MCP-1 has shown us a reliable increase in their concentration among patients with albuminuric stage of diabetic nephropathy, compared to the control group (36,1 ± 6,3 pg/ml and 112,4 ± 2,3 pg/ml, correspondingly). Higher levels of IL-1β (89,2 ± 4,2 pg/ml, $p < 0,05$) and MCP-1 (202,2 ± 5,9 pg/ml, $p < 0,05$) have been established in blood serum of patients with DN at proteinutic stage of the disease. Definition of urinal excretion volume of IL-1β and MCP-1 has shown the following results. An increase in urinal excretion of IL-1β among patients with PD of the 2nd type along with an increase in DN expression was es-

tablished. Among patients with proteinuria contents of IL-1β in urine was 2,8 ± 0,2 times ($p < 0,05$) higher than that of the control and 1,4 ± 0,2 times higher than that of patients with albuminuria. An increase in discharge of IL-1β with urine under PD provides for the support of activity of immune inflammation, an increase in expression of adhesion molecules, chemokins. Fibrogenic effects of IL-1β in kidney are also known [2]. An increase in MCP-1 concentration in urine among patients with PD (20,4 ± 6,2 pg/mmole), compared to the control (5,3 ± 1,2 pg/mmole) has been registered. We have established a reliable trend to increase in urinal excretion of MCP-1 along with the progress of nephropathy, a higher level of MCP-1 was registered among patients with DN with proteinuria (58,3 ± 12,4 pg/mmole, $p < 0,05$). It is known that endothelium cells represent molecules of VCAM-1, MCP-1 at surface that provide for attraction and transmission of monocytes, activation and generalization of the inflammation in vascular wall. Microphages that migrate into kidney intersticium play an important part in forming tubulointerstitial fibrosis, as they serve as a source of fibrogenic growth factors, particularly TFR-β1 [2].

Evaluation of urinal excretion of TFR-β1 has revealed its increase among patients with PD with a progress of nephropathy. The highest content of TFR-β1 in urine was established among patients with SD with proteinuria протеинурией (16,4 ± 4,2 pg/ml, $p < 0,05$). Study if TFR-β1 in blood serum of patients with PD of the 2nd type has shown its increase, compared to the control (43,6 ± 4,3 pg/ml) by 1,4 ± 0,3 ($p < 0,05$). Among patients with proteinuric stage of DN its highest serum concentration has been registered (86,4 ± 4,2 pg/ml, $p < 0,05$). Our correlation analysis has shown that level of TFR-β1correlated directly with albuminuria ($r = 0,59$, $p < 0,05$) and inversely – with glomerular filtration ($r = –0,33$, $p < 0,05$). It is known that TFR-β1 is studied as a key mediator of forming nephron sclerosis. Pathogenetic part of TFR-β1 is linked to an activation of synthesis of collagen and other components of matrix in kidney [1]. We should outline that an increase in TFR-β1 production under DN is generally defined by a disturbance in kidney regulation of TFR-β1 levels, as under DN kidney is its major supplier [4].

The received data testify the pathologic part of immune-inflammatory mechanisms in formation of diabetic nephropathy.

References

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