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CHANGE OF PROTEINASE INHIBITORS CONCENTRATION IN BLOOD SERUM IN PATIENTS WITH TYPE 2 DIABETES

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Lysosomal cysteine proteinases participate in many physiological and pathological processes: inflammation, atherosclerosis, immunogenesis, apoptosis [3]. Patients with type 2 diabetes mellitus (DM) are known to have an elevated activity cysteine proteinases [5]. The type 2 DM is also accompanied by rising of the cathepsines B+L and C activity in leucocytes of periphery blood [8]. Rising of activity proteinases is caused either by augmentation of their synthesis or, most probably, by an effect of decreasing of their endogenous inhibitors of the protein nature. Rising of lysosomal cysteine proteinases activity of patients with type 2 diabetes appears to be one of the reasons being responsible for the development of diabetic microvascular complications. Moreover, the increasing activity can reflect the reaction of enzymes to the disturbance of the lipid exchange leading to atherosclerosis being indispensable satellite of type 2 DM. At present it is beyond no doubts that inhibitors play a leading role in regulation of lysosomal cysteine proteinases activity [9]. It is known that the cathepsine B is weakly bound to inhibitors and its activity is easily restored with the decreasing of their concentrations [6], however even the small amount of inhibitors may steadily depress the cathepsine C activity [10].

The aim of the study was to elucidate the serum activity of a_1-proteinase inhibitor (a1-PI) and concentration cystatin C in patients with type 2 DM.

Materials and methods

Under observation there were 26 patients with type 2 DM at the age of 45 to 71. The DM was diagnosed on the basis of the anamnesis of disease, clinical picture and biochemical research according to the criteria of the WHO expert committee on diabetes mellitus. The duration of the disease varied from 1 to 23 years, on the average it has comprised 5.5 years.

Serum cystatin C was measured by ELISA-kit (KRKA, Slovenia). The activity of a_1-proteinase inhibitor was measured by a method based on ability of trypsin to split synthetic substrate of hydrochloride benzoyl-arginine-ethyl ether with formation of benzoyl-arginine [2].

Results and discussion

It is known that the activity serum cathepsin B is very low because of the high contents of proteinases inhibitors [4]. Due to the fact that other proteinases (serine) of blood can participate in degradation of substrate for cathepsin B, they usually mean a serum cathepsin-B-like activity. The research of serum proteolytic activity in patients with type 2 DM (n=14) has shown that the cathepsin B-like activity does not differ from that of healthy people. The α_1-PI refers to α-globulins and has large molecular mass (300-450 кDa). It is considered that it provides 90 % of antitrypsin activity of a serum blood [1]. Cystatin C is a proteiase inhibitor with a low molecular weigth (13 kDa). The serum activity of α_1-PI and serum concentration of cystatin C are shown in the table 1.

Activity of α_1-PI in patients DM was 57 % greater as compared with healthy individuals. The increased antitrypsin activity of blood plasma characterizes intensifying proteolytic processes in serum blood. However, serum cystatin C decreased in 1,8 times that is probably due to consumption of an inhibitor at rising activity of lysosomal enzymes of patients.

Table 1. Contents of serum α_1-proteinase inhibitor and cystatin C in patients with types 2 DM

Inhibitors	α_1-proteinase inhibitor	cystatin C
	IN	nmol/l
Patients, n=21	39,2 ± 8,64 *	38,7 ± 9,51 **
Control group, n=20	25,0 ± 2,64	67,8 ± 2,82
Significance level	p <0,05	p <0,01

Moreover the deficiency of cystatin C is probably the result of the loss of low molecular inhibitor with urine from depression of renal barrier to many proteins (albuminuria), including low-molecular proteins. Previously it was shown the significantly decreased serum - and increased urine apolipoprotein A-I (28 kDa) in patients with chronic glomerulonephritis [7].

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