Clinical and Diagnostic Significance of Measurement of Blood Activity of Endopeptidases and Their Inhibitors in Youths with Mitral Valve Prolapse

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Activity of leukocytic elastase in young male patients with mitral valve prolapse and high (group 1) and low (group 2) adaptive capacities was increased by 57.08 and 79.14%, respectively, compared to the control ($p<0.05$). The leukocytic elastase/α_1-proteinase inhibitor ratio in groups 1 and 2 surpassed the control value by 55.6% and by 2.16 times, respectively ($p<0.05$), this parameter can serve as a biochemical marker of adaptive capacity.

Key Words: *kinins; endopeptidases; mitral valve prolapse*

Proteolytic enzymes, or proteinases, play a unique role in functioning of the body. Cleaving one or more peptide bounds in the protein molecule proteinases can activate or modify protein properties, which can trigger various biochemical processes. Proteinases are involved in receptor-transmitter transduction, coordination, and realization of defense reaction of the body, including blood clotting, fibrinolysis, kinin production, and complement system activation.

Proteinase activity depends generally on the rate of their production from non-active precursors and inactivation by specific inhibitors in cells, tissues, and plasma comprising the so-called antiproteolytic potential [2]. A balance between proteolytic enzymes and their inhibitors can be shifted under certain pathological conditions, what leads to negative consequences for the organism up to critical states [4].

These properties and possible involvement of proteinases into processes of tissue destruction, inflammation, reparation, and manifestation of specific clinical symptoms in mitral valve prolapse (MVP) prompted us to study the role of serine proteinases in the development of various adaptive reactions in patients with MVP; to this end, total protein-esterase activity (TPEA) of leukocytic elastase (LE) and activity of inhibitors (α_1-proteinase inhibitor and α_2-macroglobulin) were measured in the serum.

MATERIALS AND METHODS

We examined 137 young male patients with grade I PMV without regurgitation (mean age 19.78±2.43 years). Control group included 30 individuals of the same age without history of cardiovascular diseases. Echocardioscopy and bicycle ergometry were performed using standard techniques [7,1]. Group 1 (N=64) with high adaptive capacities included patients with minimum complaints and exhibiting high tolerance to physical exercises. Group 2 (N=73) included patients with low adaptive capacity, maximum number of complaints, and moderate tolerance to physical load assessed by bicycle ergometry. Time on bicycle ergometer in group 1 did not differ significantly from the control (8.7±0.4 min), while in group 2 this parameter was significantly lower than in healthy people (by 22.5%, $p<0.05$) and was 6.9±0.5 min. Activities of proteinases and their inhibitor in blood was measured using standard techniques [3,5,6].

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TABLE 1. Activity of Proteinases and Their Inhibitors in Blood of Young Patients with Primary PMV and Adaptive Capacity of the Organism ($X \pm m$)

Parameter	Group		
	control (N=30)	1 (N=64)	2 (N=73)
TPEA, meu/ml	269.03±15.90	223.9±16.3*	285.0±21.2+
LE, meu/ml	195.52±12.76	307.13±13.85*	350.25±14.06*+
α_2-macroglobulin, U/ml	4.75±0.69	6.38±0.35*	6.99±0.38*
α_1-PI, U/ml	27.74±2.45	27.99±2.31	22.95±2.41
LE/α_1-PI	7.05±0.75	10.97±0.77*	15.26±0.73*+

Note. α_1-PI: α_1-protease inhibitor. p<0.05 compared to: *control, +group 1.

RESULTS

Increase in TPEA by 27.3% (p<0.05) was revealed in group 2 in comparison with group 1 (Table 1). In group 1, TPEA surpassed the control value by 16.78% (p<0.05), which indicated stability of the kinin system in patients with high adaptive capacity and was confirmed by clinical and experimental data. At the same time, there were no significant differences between group 2 and control.

LE producing the most deleterious effects on biological structures appears to be the main proteinase of azurophilic granules of polymorphonuclear leukocytes (EC 3.4.21.37). Activity of this enzyme significantly increased in groups 1 and 2 by 57.08 и 79.14%, respectively, in comparison with the control (p<0.05). It should be noted that LE activation was more pronounced in patients with reduced adaptive capacity compared to individuals with high adaptive capacity (by 14%; p<0.05).

The increase in LE activity in patients with PMV is probably a mechanism of collagen destruction, the marker of this process is increased content of free oxyproline fraction. Elastase activity in the organism is controlled by plasma and tissue proteinase inhibitors. Among them α_1-proteinase inhibitor has the highest molar concentration and plays the key role in endogenous regulation of LE activity. Moreover, it is one of main proteins of acute inflammation and provides about 80% plasma antiproteolytic potential. Normally, the released LE is rapidly bound by plasma inhibitors α_1-proteinase and partially α_2-macroglobulin. Our results showed that activity of α_1-proteinase inhibitor in patients with high and reduced adaptive capacity did not significantly differ from control values. This can be explained by the fact that in some cases α_1-proteinase inhibitor can be oxidized by reactive oxygen metabolites and its action on LE becomes inefficient. Then, low inhibitory potential results in uncontrolled elastase proteolysis and development of severe pathological states. Another elastase inhibitor α_2-macroglobulin is less effective. Our results suggest that activity of α_2-macroglobulin in groups 1 and 2 surpassed the control values by 34.32 and 47.16%, respectively (p<0.05). No significant differences between the groups were found. Thus, LE damages tissue and blood proteins despite inactivating action of its inhibitors. It can be assumed that the release of granulocyte elastase hydrolyzing various proteins, including numerous plasma proteins, impairs the regulatory mechanisms of plasma proteolytic systems responsible for adaptation and defense, when secreted into the circulation.

We believe that apart from individual measurement of activities of LE and α_1-proteinase inhibitor, the estimation of the ratio of these parameters can also be useful. We revealed an increase in this ratio in groups 1 and 2 by 55.6% and by 2.16 times, respectively, compared to the control (p<0.05). Thus, high value of LE/α_1-proteinase inhibitor ratio can serve as a biochemical marker of reduced adaptive capacity in young patients with PMV and indicate poor prognosis associated with destruction of many functional proteins.

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