Imbalance in the Antioxidant Defense System as a Possible Cause of Decreased Compensatory and Adaptive Reserves in Youths with Mitral Valve Prolapse

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An imbalance in the first line of the antioxidant defence and hyperactivity of the glutathione-dependent system were revealed in 137 youths with mitral valve prolapse. Increased activities of superoxide dismutase and glutathione reductase (by 6 and 1.82-2.10 times, respectively) can serve as an additional diagnostic criterion of decreased compensatory reserves in patients with mitral valve prolapse.

Key Words: *mitral valve; glutathione reductase; catalase; superoxide dismutase*

Mitral valve prolapse (MVP) is considered as a variant of hereditary systemic connective tissue and psychovegetative deficiency. It manifests in increased sensitivity to somatogenic and psychogenic factors. It should be emphasized that MVP patients exhibit different reactions to external factors, which depends on their initial reactivity.

Here we evaluated the role of antioxidant (AO) defense system enzymes in the formation of various compensatory and adaptive reactions in youths with MVP, which determines adaptation of the organism.

MATERIALS AND METHODS

Clinical, instrumental, and biochemical studies involved 137 youths of military age (15-27 years, mean 17.78±2.43 years). Thirty male donors (16-26 years) without no cardiovascular disorders comprised the control group. The groups were age-matched.

Main clinical characteristics were evaluated. On the day of admission, MVP patients and healthy donors were subjected to echocardioscopy on a Sim 5000 plus device equipped with a 2-MHz pick-up. Activity of AO enzymes was measured in erythrocytes isolated from cubital vein blood. Hemolysate (20%) was prepared using bidistilled water.

Activities of catalase and glutathione reductase (GR) were measured by the calorimetric and spectrophotometric method, respectively.

RESULTS

According to clinical and functional characteristics, the patients were divided into 2 groups of subjects with high (group 1, n=64) and low compensatory and adaptive reserves of the organism (group 2, n=73) [4].

Study of the AO defense system showed that MVP patients significantly differ from healthy donors by activities of catalase, superoxide dismutase (SOD), and GR in erythrocytes (Table 1). In group 1 patients, catalase activity was lower (by 3.26 times), while SOD and GR activities were higher than in the control (by 3.99 and 2.03 times, respectively, p<0.05).

Group 2 patients had similar but more pronounced differences from the control. In group 1 patients catalase activity was lower (by 4.59 times), while

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TABLE 1. Activity of AO Enzymes in Erythrocytes from MVP Patients ($X \pm m$)

Parameter	Control	Group 1	Group 2
Catalase, mcat/g hemoglobin	5.650±0.141	1.73±0.18*	1.23±0.17*+
SOD, U/g hemoglobin	(1.66±0.271)×10^2	(6.53±0.38)×10^{2}*	(10.35±0.92)×10^{2}*+
GR, μmol/g hemoglobin	(2.52±0.166)×10^4	(5.12±0.18)×10^{4}*	(4.67±0.22)×10^{4}*

Note. $p<0.05$: *compared to the control; +compared to group 1.

TABLE 2. Correlations between Activity of AO Defense Enzymes in Erythrocytes and Cardiac and Hemodynamic Parameters

Parameter	Correlation coefficient		p
	Group 1	Group 2	
Catalase and stroke volume	0.406	0.455	<0.02
Catalase and cardiac output	0.563	0.567	<0.01
Catalase and cardiac index	-0.679	-0.728	<0.01
SOD and cardiac index	-0.511	-0.507	<0.01

SOD and GR activities were higher than in the control (by 6.23 and 1.85 times, respectively, $p<0.05$). Catalase activity in group 1 patients with MVP was higher than in group 2 by 40.6% ($p<0.05$), while SOD activity was 58.5% higher in group 2 compared to group 1 ($p<0.05$). No intergroup differences were found in GR activity. These data reflect discoordination of AO processes in MVP patients.

Thus, patients of both groups exhibit similar changes of different degree. These changes can be regarded as manifestations of oxidative stress, which in low doses has a training effect, but severe oxidative stress led to cell destruction. The observed changes in group 1 patients correspond to the stress response under normal conditions, which can be accompanied by short-term accumulation reactive oxygen species. It is associated with adaptive reaction to extreme conditions, when reactive oxygen species play a role of secondary messengers [2]. Group 2 patients were characterized by activation of free radical processes, decreased buffer capacity of AO defense system and its disturbed mobilization in response to activation of prooxidant systems, which is a manifestation of the pathological process.

GR activity increased most significantly in group 1 patients with MVP. These changes were directed towards the increase in the concentration of reduced glutathione and reflected activation of detoxification processes [3], which probably served as a compensatory mechanism in group 1 patients with MVP. Reduced glutathione is a natural electron acceptor under conditions of LPO initiation. The protective role of GR was less pronounced in group 2 patients, which reflects a deficiency of detoxification processes. Our results suggest that depletion of AO defense enzymes is the major molecular cause of exhaustion of compensatory and adaptive reserves in group 2 patients with MVP [1].

Activities of catalase and SOD in the blood significantly correlated with cardiohemodynamic signs for compensatory and adaptive reserves of the cardiovascular system (Table 2).

Our findings indicate that erythrocytes from group 2 patients with MVP are characterized by an imbalance in the first line of AO protection, which eliminates superoxide anion radical and H_2O_2. These changes are accompanied by hyperactivity of the glutathione-dependent system responsible for utilization of H_2O_2 under conditions of low catalase activity and led to supression of adaptive and compensatory mechanisms in group 2 patients with MVP. Taking into account increased activity of third-line of defense enzymes involved into H_2O_2 utilization and changes in GR function towards accumulation of reduced glutathione, we conclude that these parameters reflect an imbalance in free radical processes and AO defense system in MVP patients with low compensatory and adaptive reserves.

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