GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Effect of Antioxidant Therapy on Glutathione System of Erythrocytes in Chronic Brain Ischemia

E. A. Antipenko, A. V. Gustov, K. S. Davydova*, and E. V. Krylova*

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We studied the effect of antioxidant therapy on the state of glutathione system in erythrocytes in patients with stage 1, 2, and 3 circulatory encephalopathy treated with antioxidant cytoflavin against the background of basic therapy (kavinton and pyracetam). It was demonstrated that the response of the erythrocyte glutathione system to antioxidant therapy was quantitatively and qualitatively different at different stages of cerebrovascular failure, which was related to changes in the glutathione system during the development of chronic cerebral ischemia. Endogenous reserve of the antioxidant defense system should be taken into account when prescribing antioxidant therapy; the glutathione system can be a marker of this reserve.

Key Words: *antioxidant system; erythrocyte glutathione system*

Antioxidant therapy is widely used in chronic brain ischemia [1-4]. Endogenous antioxidant systems, including the glutathione (GT) system have limited buffer capacity. Their antioxidant potential can be exhausted, after which these systems start to produce the prooxidant effect [5]. Glutathione is present in cells in reduced (GSH) and oxidized (GSSG) forms. Normally, the content of reduced GT more than 100-fold surpasses the content of oxidized form, but during LPO activation this proportion changes. Sufficient amount of reduced GT is essential for efficient antioxidant defense.

Here we studied the state of antioxidant therapy on GT system depending on the severity of brain ischemia.

Department of Neurology, Neurosyrgery, and Psychiatry, Nizhnii Novgorod State Medical Academy; *Department of Human and Animal Physiology and Biochemistry, N. I. Lobachevskii State University, Nizhnii Novgorod, Russia

MATERIALS AND METHODS

A total of 45 patients (30 women and 15 men) with chronic cerebrovascular insufficiency (CCVI) were examined: they had stage I (n=15), II (n=15), and III (n=15) dyscirculatory encephalopathy (DE). Patient's age varied from 38 to 55 years (mean age 48.6±5.1 years). The content of total, oxidized, and reduced GT in peripheral blood erythrocytes was determined by the method of Woodwort and Fray. The dynamics of total GT and the GSH/GSSG ratio were analyzed during the therapy. The basic therapeutic complex included kavinton (intravenous drip infusion, 2 ml per 200 ml physiological saline No. 5) and pyracetam (intravenous infusion, 5 ml per 5 ml physiological saline No. 5). Patents of the main group received also antioxidant cytoflavin against the background of basic therapy (intravenous drip infusion, 10 ml per 200 ml 5% glucose No. 10). Reference group consisted of 45 patients receiving only basic complex. The groups were

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TABLE 1. Dynamics of Total GT (mg%) during Therapy ($M\pm\sigma$)

DE stage	Total GT, mg%			
	main group		reference group	
	before treatment	after treatment	before treatment	after treatment
I	103.5±47.58	84.7±41.5	108±47.64	173.9±46.66*↑ (p=0.14)
II	95.07±30.91	79.12±27.8*↓ (p=0.05)	95.0±32.45	133.4±41.99*↑ (p=0.05)
III	77.06±20.4	92.02±20.5	75.06±29.7	106.6±40.3

Note. Here and in Table 2: *compared to the level before therapy. Arrows show changes in the studied parameter.

TABLE 2. Dynamics of Reduced (GSH) to Oxidized (GSSG) GT Ratio during Therapy

DE stage	GSH/GSSG			
	main group		reference group	
	before treatment	after treatment	before treatment	after treatment
I	1.6	0.9*↓ (p=0.25)	1.7	3.08*↑ (p=0.33)
II	5.4	2.7*↓ (p=0.24)	5.3	2.07*↑ (p=0.24)
III	1.1	1.8*↑ (p=0.05)	1.18	1.1

comparable by sex, age, and clinical manifestations of the disease. The data were processed statistically using paired Student test (BIOSTAT software).

RESULTS

The initial state of GT system depended on the stage of DE. In all patients with DE, the content of total GT was below the control (147.8± 45.4), but this decrease was most pronounced in patients with stage III DE (Table 1). The GSH/GSSG ratio also differed in patients with different stages of CCVI: 1.6 in stage I, 5.4 in stage II, and 1.1 in stage III. The effect of therapy on the dynamics of GT system parameters is presented in Tables 1 and 2. The use of basic complex considerably increased the content of total GT in patients with stages I and II DE, but the GSH/GSSG ratio increased in patients with stage I DE, but decreased in individuals with stage II DE. Addition of cytoflavin to the treatment complex considerably reduced the content of total GT in patients with stage II DE, the GSH/GSSG ratio considerably decreased in patients with stages I and II DE, but increased in patients with stage III GE.

Thus, the content of total, reduced, and oxidized GT in erythrocytes changed with progression of CCVI, which reflects the level of adaptation of the antioxidant system in cerebral ischemia. The response of the GT system to antioxidant therapy was different at different stages of DE. The initial level of GT as a marker of adaptation reserve of the antioxidant system should be taken into account, when prescribing antioxidant therapy.

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