sharp decrease in TPR. Meanwhile, the cardiac component of the hemodynamics may be the dominant factor in the mechanism of death: either rapidly progressive bradycardia or a combination of myocardial damage of ischemic character with a fall of TPR.

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ACTIVATION OF LIPID PEROXIDATION IN CHRONIC ISCHEMIC HEART DISEASE

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KEY WORDS: lipid peroxidation products; blood plasma; vitamins E and C; ischemic heart disease.

In the modern view lipid peroxidation (LPO) is a continuous physiological process which, on intensification, participates in the development of a number of pathological conditions. It has been shown, in particular, that activation of LPO accompanies ischemic heart damage in experimental animals and is one of the key causes of disturbance of the functioning of heart muscle cells during ischemic injury [6]. It has also been shown that the level of primary products of LPO, namely lipid hydroperoxides, in the plasma rises significantly in chronic ischemic heart disease (CIHD) [3].

Experimental data also have been obtained to show that a combination of bioantioxidants (α-tocopherol + ascorbate + rutin + glutamate) significantly lowers the levels of LPO, cholesterol, and atherogenic lipoproteins in patients with CIHD [1]. Treatment with α-tocopherol reduced pain in the heart region, and positive changes in the ECG were observed in patients with ischemic heart disease (IHD) [2]. The investigations listed above indicate that it is possible to use the intensity of LPO in the clinical diagnosis of IHD and to assess the effectiveness of treatment. A direct investigation of the intensity of LPO processes in human heart muscle is naturally impossible.

The aim of this investigation was to study concentrations of LPO products in the blood plasma of patients with CIHD and the possibility of using vitamin E as a natural inhibitor of free radical processes in the treatment of ischemic heart disease.

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EXPERIMENTAL METHOD

A 5-ml blood sample was taken from the cubital vein of patients 10-11 h after the last meal, and centrifuged by the ordinary clinical method to separate the blood cells. To prevent development of LPO reactions in the blood plasma after taking the samples, ionol (2,6-di-tert-butyl-N-methylphenol) in alcoholic solution was then added to the plasma to give a final ethanol concentration of not more than 1% and a final ionol concentration of 0.1 mM.

Total blood lipids were extracted with a chloroform-methanol mixture [5].

The concentration of LPO products in the blood plasma was measured by two methods: accumulation of primary LPO products (hydroperoxides with conjugated double bonds) and of end-products (fluorescent compounds formed as a result of interaction of primary LPO products with proteins of biological membranes) [8]. The concentration of hydroperoxides was estimated spectrophotometrically, by measuring the ratio between absorbents of alcoholic solutions of total plasma lipids at 232 and 215 nm (A_{232}/A_{215}) on a Perkin-Elmer 555 differential spectrophotometer (Sweden).

The concentration of fluorescent LPO products in alcoholic solutions of total plasma lipids were measured on a Hitachi 850 spectrofluorometer (Japan), as the intensity of fluorescence with excitation wavelengths of 360 nm and emission wavelengths of 440 nm, expressed as a ratio of the total lipid concentration. The spectral width of the monochromator slits was 5 nm.

The ionol used in the experiments was provided by Professor E. B. Burlakova and the vitamins E and C were of Soviet manufacture. Organic solvents of Soviet manufacture were used without additional purification.

Subjects of the control group and patients with CIHD were chosen at the clinic of the Andizhan Medical Institute. Levels of LPO products were measured with the assistance of L. L. Prilipko and A. I. Erin, on the staff of the Laboratory of Clinical Biochemistry, All-Union Mental Health Research Center, Academy of Medical Sciences of the USSR.

EXPERIMENTAL RESULTS

Comparison of plasma levels of LPO products in healthy subjects and patients with CIHD showed a significant increase in the latter. This increase was particularly marked in the case of analysis of fluorescent LPO products. The increase in the plasma hydroperoxide concentration in patients with CIHD did not exceed 30% compared with normal, whereas the concentration of fluorescent products was increased almost threefold.

Since vitamin E is well known as an LPO inhibitor in biological membranes [4, 9], the study of its therapeutic effect in CIHD, a disease associated with elevation of the plasma level of LPO products, would seem to be justified. The data in Figs. 1 and 2* show that treatment with vitamin E was able to reduce concentrations of LPO products actually below the control level. Traditional treatment (papaverine, platyphylline, polysaponin) lowers the plasma level of LPO products by a lesser degree, bringing it close to the control level.

The total concentration of primary LPO products in the blood plasma of the control group, consisting of persons chosen in the Andizhan Region, incidentally, was rather higher than the corresponding parameter for the European part of the USSR, and this can evidently be attributed to differences of diet.

The results of the present investigation confirmed the view that the development of LPO processes plays an essential role in the course of CIHD. Accordingly the use of vitamin E in the treatment of CIHD appears to be very promising, especially in conjunction with vitamin C. This conclusion is based on the fact that ascorbic acid reduces oxidized forms of tocopherols [7]. Combined administration of vitamins E and C thus evidently potentiates the therapeutic effect of vitamin E in treatment of CIHD.

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