EFFECT OF α-TOCOPHEROL ON α-TOCOPHERYLQUINONE CONCENTRATION IN HUMAN BLOOD LIPIDS

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UDC 616.123-06:577.161.3]-08

KEY WORDS: electron paramagnetic resonance; lipids; α-tocopherol; α-tocopherylquinone; ischemic heart disease.

Investigations [9, 10] have shown that interaction of α-tocopherol (TP) with peroxide radicals *in vitro* leads to the formation of α-tocopherylquinone (TPQ). Some workers [1, 5, 15] consider that a similar mechanism also operates *in vivo*.

The present writer [7] found TPQ in human blood lipids by the electron paramagnetic resonance method. A fall in the TPQ concentration in plasma and erythrocyte lipids has been observed in patients with ischemic heart disease (IHD) compared with healthy blood donors [6, 8].

The aim of this investigation was to study the effect of TP on the TPQ concentration in human blood lipids.

EXPERIMENTAL METHOD

TPQ was determined by the EPR method in human plasma and erythrocyte lipids as described previously [7]. The TPQ concentration was calculated in relative units as the ratio of the amplitude of the signal from the recorded sample and the amplitude of the side standard.

Patients with IHD were divided into two groups: patients of group 1 received TP in a dose of 2.0 ml intramuscularly twice a day for 3 days; patients of group 2, who were almost identical in age, and with the same diagnosis, received the same treatment and diet but no injections of TP. Blood was taken for analysis in the morning before breakfast, twice (before the investigation and 3 days after it began). A 30% oily solution of vitamin E, from the "Oktyabr'" Leningrad Pharmaceutical Chemical Combine, was used.

EXPERIMENTAL RESULTS

An increase in the TPQ concentration in plasma lipids was found after administration of TP for 3 days ($P < 0.05$; Table 1). The fall in the TPQ level observed in plasma and erythrocyte lipids of patients with IHD was perhaps connected with a fall in the blood TP concentration. This fact has been observed by a number of workers [2, 4].

TPQ is evidently not only an indicator of interaction of lipid peroxides with vitamin E. It was suggested previously [3] that TPQ participates actively in biochemical processes in the body, and it has actually been claimed that this compound is an "active" compound of the vitamin E group. Other workers [6, 12, 14] also have described the effect of TPQ on the bio-

TABLE 1. TPQ Concentration (in relative units) in Plasma and Erythrocyte Lipids of Patients with IHD before and after Administration of TP for 3 Days (M ± m)

Group of patients	Plasma lipids		Erythrocyte lipids	
	background	three days later	background	three days later
1- (n=13)	2,27±0,45	3,96±0,47*	3,58±0,51	4,31±0,50
2- (n=13)	2,58±0,50	2,63±0,55	3,50±0,46	3,23±0,50

Department of Internal Medicine, Irkutsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR K. R. Sedov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 296-297, September, 1985. Original article submitted October 27, 1984.

0007-4888/85/0009-1195$09.50

logical activity of cells and tissues. It was stated in [11] that the mean life span of nematodes, usually 35 days, was increased to 46 days if TP or TPQ was added to the medium in high concentrations.

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LOCATION OF THE BINDING SITE FOR QUATERNARY AJMALINE DERIVATIVES IN THE SODIUM CHANNEL OF THE EXCITABLE MEMBRANE

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UDC 615.22:547.994].033.127-018.1

KEY WOPDS: ajmaline, sodium channel, cumulative block, axoplasm.

It was shown previously that blockade of sodium channels by the antiarrhythmic N-propylajmaline (NPA; Neogiluritmal) in the nerve fiber [1, 5, 8] and in myocardial cells [2] accumulates during rhythmic membrane depolarization. After the end of stimulation sodium currents (I_{Na}) in response to infrequent testing stimuli are gradually restored, in the course of 15-20 min, to their original level.

NPA is a permanently charged quaternary ammonium compound which can penetrate into the lipid matrix of the membrane because of the hydrophobicity of its C_3H_7 radical, near the charged nitrogen atom. In view of existing ideas on the mechanism of action of quaternary derivatives of local anesthetics on sodium channels [7], the writers postulated that NPA, if applied externally to the membrane, passes through its lipid layer into the cytoplasm, from which it enters the sodium channel when it opens during depolarization [5]. On binding with the receptor site of the inner mouth of the channel, NPA blocks movement of penetrating cations.

To test this hypothesis, in the investigation described below the action of another quaternary derivative of ajmaline, namely N-methylajmaline (NMA), which is less hydrophobic than NPA, on I_{Na} was investigated (see the Scheme, below).

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(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 9, pp. 297-299, September, 1985. Original article submitted September 19, 1983.

0007-4888/85/0009-1196$09.50