EFFECT OF THE ANTIOXIDANT DIBUNOL ON THE COURSE OF NEUROTROPHIC DISTURBANCES IN THE RAT PANCREAS

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KEY WORDS: vagotomy; pancreas; dibunol; alkaline phosphatase; succinate dehydrogenase

The search for ways of correcting neurogenic dystrophies is dictated primarily by their widespread nature: they may be independent or accompanied by diseases, or arise in response to denervation undertaken therapeutically. Since it was discovered in the writers' laboratory that lipid peroxidation (LPO) is activated in organs whose innervation is disturbed [4], the use of antioxidants has appeared to be the most promising approach to the solution of this problem. The corrective effect of dibunol was studied in the present investigation for this purpose.

EXPERIMENTAL METHOD

The pancreas of 55 noninbred male rats weighing 180-220 g was used as the test object. There were four groups of animals: 1) intact, 2) intact, receiving dibunol for 14 days, 3) undergoing subdiaphragmatic vagotomy (7, 14, and 30 days previously), 4) receiving dibunol at the same times after vagotomy. Dibunol (ionol; 4-methyl-2,6-di-tert-butylphenol) was injected in a dose of 20 mg/kg into rats of groups 2 and 4 intraperitoneally, in a 3% solution of Tween-80, on alternate days starting with the 2nd day.

The morphological and physiological status of the pancreas was assessed by quantitative analysis of histochemical parameters. The state of the microcirculatory bed was studied by determining activity of the transport enzyme alkaline phosphatase (AlP) by Burstone's method.

The number of enzyme-positive capillaries was determined in a grid method, and their diameter measured with the MOV-1-15x ocular micrometer. To study the bioenergetics of the secretory apparatus of the pancreas, succinate dehydrogenase (SDH) activity was measured by Nachlas's densitometric method. The results were subjected to statistical analysis by means of Strelkov's tables.

EXPERIMENTAL RESULTS

Histochemical study of the pancreas of the control animals showed that the localization of AlP was limited to the blood vessels of the gland. Its activity was maximal in the microcirculatory bed, especially in the capillary walls. The number of enzyme-positive capillaries was 19.27 ± 0.19 conventional units and the diameter of their lumen was 20.05 ± 0.16 (Figs. 1 and 2). The enzyme SDH was intracellular in its localization and its activity was maximal in the cytoplasm of the pancreatic cells. The mean level of SDH activity was 325.4 ± 1.2 conventional units (Fig. 3), although in different cells it varied from strongly to weakly positive. These observations indicate the existence of physiological asynchronism of energy-providing processes in the secretory apparatus of the pancreas.

Injection of dibunol into the control animals (group 2) had no significant effect on the level of activity (AlP 18.93 ± 0.19, SDH 324.3 ± 2.1 conventional units), on the histo- and cytotopography of these two enzymes, or on morphological and physiological parameters of the capillary part of the microcirculation (19.8 ± 0.22 μ). All the parameters given differ significantly from the control ($p < 0.01$).

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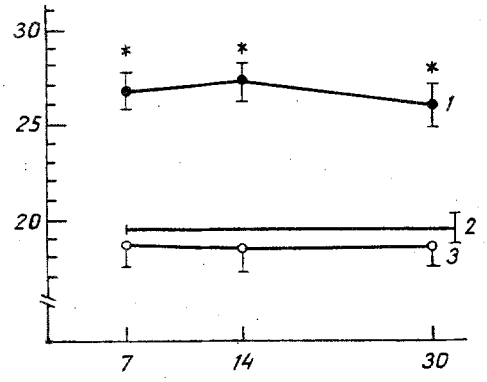

Fig. 1. Changes in number of enzyme-positive blood capillaries (relative to AlP) in pancreas of different groups of animals. Here and in Figs. 2 and 3: abscissa, time after subdiaphragmatic vagotomy, in days; 1) rats of group 3, 2) rats of group 1, 3) rats of group 4. Ordinate, number of blood capillaries per conventional unit of area. Asterisk indicates significant differences compared with control ($p < 0.01$).

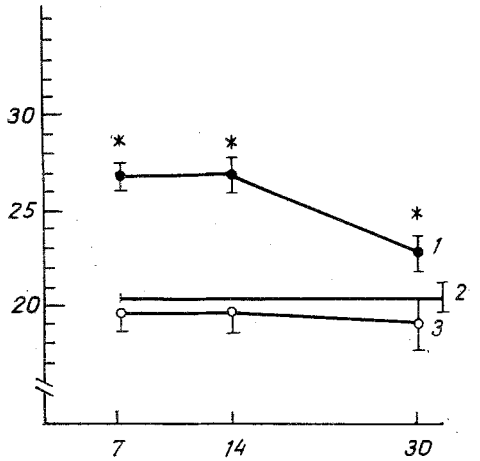

Fig. 2. Changes in size of lumen of enzyme-positive capillaries in pancreas of different groups of animals. Ordinate, diameter of capillary lumen, μ.

The results confirm the abundant data on the nontoxicity of dibunol [5-7]. It must be emphasized that the quantitative histochemical control used in this investigation enabled the adequacy of the pharmacological action of this compound on an organ such as the pancreas to be evaluated objectively.

After vagotomy (group 3), at all times of the experiment, considerable changes were found in the exchange portion of the microcirculation in the pancreas: a significant increase in the number of enzyme-positive capillaries (Fig. 1) and widening of their lumen (Fig. 2). Disturbance of the hemodynamics in the system maintaining the nutrition of the gland was accompanied by a decrease of SDH activity (except on the 30th day — Fig. 3) and by disappearance of its asynchronism in different secretory cells. The time course of the

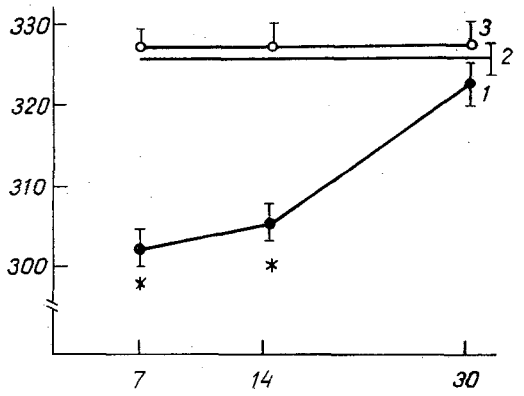

Fig. 3. Photometric parameters of SDH content in exocrine pancreatic cells in different groups of animals. Ordinate, conventional units of uptake.

quantitative parameters after vagotomy showed a similar trend for all parameters: the critical times were the 7th and 14th days, but by the 30th day of denervation there was a tendency for these parameters to return to normal (Figs. 1 and 2), or they actually did so (Fig. 3). The kinetics thus revealed coincides precisely with the phase structure of the course of the neurotrophic disturbance in organs of the digestive system, where during the first 2 weeks the predominant feature was the destructive component, to be succeeded in this role by compensatory and adaptive processes [3].

The results support the view that the leading role in the development of the destructive phase of this process is played by the vascular factor and the phenomena of hypoxia, activation of LPO, and disturbance of metabolism, and in particular, the bioenergetics of the denervated structures, accompanying it [3, 4, 8].

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Injection of dibunol into the animals after vagotomy (group 4) abolished the vascular disturbances in the gland and led to normalization of the histochemical parameters at all times of study (Figs. 1-3). The positive effect of the antioxidant indirectly confirms the activation of LPO in the pancreas in response to vagotomy. Dibunol, an acceptor of free radicals [1, 2], under these conditions probably depresses LPO activity to the optimal physiological level. By stabilizing the cellular membranes in this way, it evidently restores their cardinal characteristics: in particular, the mode of working of the enzyme systems and the balance between transport processes, which in turn maintains the adequacy of function of the blood-cell barriers.

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MYOCARDIAL ENERGY AND PLASTIC METABOLISM AFTER IRRADIATION OF THE RABBIT THYROID GLAND WITH DECIMETER WAVES

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Application of decimeter electromagnetic fields to the region of the thyroid gland is used to stimulate repair processes in various organs and tissues [3]. Since it has been shown that during the action of decimeter waves (DMW) on the thyroid region some degree of activation of the hormone-forming functions of the gland takes place [2], the question arises of the dosage of this agent, so as not to give rise to pathological changes either in the gland itself undergoing irradiation (the thyroid gland) and in the target organs for its hormones. From this standpoint, particular attention must be paid to the state of the heart muscle, for if thyroid function is intensified and, in particular in the presence of thyrotoxicosis, the energy metabolism of the myocardium and its supply of plastic materials are affected [4].

The aim of the present investigation was to assess the functional state of the mitochondria (MCH) of the myocardium and the glycogen and nucleic acid content of this tissue, in relation to the intensity of action of DMW on the thyroid gland, with the aim of choosing the conditions of irradiation which would not cause damage to the systems studied. A morphological study also was made of the state of the myocardial capillary network and on the

TABLE 1. Parameters of Respiratory and Phosphorylating Activity of Myocardial MCH during Irradiation of Thyroid Gland with DMW of Varied Intensity (oxidation substrate was a 5 mM solution of α-ketoglutarate, M ± m)

Time of investigation	Velocity of oxidation, nA O_2/min/mg protein				ADP/O	ADP/T
	V_c	V_{ADP}	V_4	V_{DNP}		
			DMW, 10 mW/cm^2			
After course	7,2±1,2	14,2±2,2	5,0±0,6	15,6±2,0	3,6±0,2	5,1±0,5*
After-period	7,0±1,3	14,5±2,5	6,2±1,3	20,2±2,6	3,1±0,3	5,0±0,55*
			DMW, 120 mW/cm^2			
After course	12,3±2,3*	21,5±3,1*	10,2±1,7*	24,2±3,7	2,6±0,15*	4,86±0,5
After-period	8,0±2,2	15,4±1,7	7,8±1,2**	22,2±1,5	2,7±0,3	4,2±0,6
			DMW, 240 mW/cm^2			
After course	15,6±1,5***	27,2±2,8***	17,7±3,1***	27,0±3,3***	2,4±0,2***	2,2±0,6***
After-period	12,3±1,0***	20,1±1,7	15,3±1,2***	22,3±2,1	2,5±0,2***	3,1±0,2
			Control			
	6,9±1,1	13,9±2,7	6,5±1,0	20,8±3,1	3,2±0,2	3,85±0,3

Legend. Isolation medium contained 0.3 M sucrose and 0.01 M versene; incubation medium contained 0.3 M sucrose, 10 mM KCl, 10 mM KH_2PO_4, 0.5 mM versene. *) Significance of differences compared with control, $p < 0.05$-0.01; **) significance of differences compared with course of DMW with PFD of 10 mW/cm^2, $p < 0.05$-0.01

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