EFFECT OF RESERPINE ON CHOLINESTERASE OF THE RAT BLOOD AND HEART

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UDC 615.214.22.015.43:[612.128+612.173.1]·577.153.9

Reserpine increases pseudocholinesterase activity in the blood but lowers it in the heart. Acetylcholinesterase activity is unchanged. Reserpine has no effect on cholinesterase in vitro.

The results of the study of the pharmacodynamics of reserpine have shown that it not only has a marked sympatholytic effect but also acts on certain stages of cholinergic processes [1-4, 8, 10, 11]. This paper describes an investigation of the action of reserpine on the cholinesterase activity of the blood and myocardium.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 130-160 g. Cholinesterase activity was determined by means of a Warburg apparatus by Ammon's method [7] and utilizing certain practical recommendations made by other workers [12-14]. The animals were decapitated. Cholinesterase activity was investigated in the blood plasma and in a suspension of erythrocytes prepared by Witter's method [13]. To prepare extracts from the heart tissues the organ was washed in isotonic sodium chloride solution, dried with filter paper, and the atrium and ventricles were then weighed separately and ground in a mortar with 25 mM sodium bicarbonate solution (6 ml for the atria and 10 ml for the ventricles). Extraction continued for 1 h and the extract was separated by centrifugation. The reaction mixture consisted of 1.5 ml extract and 0.5 ml substrate dissolved in 25 mM sodium bicarbonate. The substrates used were acetylcholine (AC), acetyl-β-methylcholine (MC), benzoylcholine (BeC), and butyrylcholine (BuC). The final concentrations of the substrates for determination of the blood cholinesterase were 6.7 mM and for determination of cholinesterase in the heart 2.2 mM. The cholinesterase activity was expressed in microliters carbon dioxide liberated during incubation for 30 min at 37°C per 0.1 ml plasma or erythrocyte suspension and per gram fresh weight of atria or ventricles. Deductions were made for spontaneous hydrolysis of the substrate and liberation of carbon dioxide from the erythrocytes. Reserpine (Rausedil, Hungary) was injected intraperitoneally in a single dose of 7.5 mg/kg. Cholinesterase activity was determined 8 h after the injection, when the effect of reserpine is adequately reflected [5, 9].

EXPERIMENTAL RESULTS

The results are given in Table 1. After a single injection of reserpine total cholinesterase activity of the heart (measured as the intensity of AC hydrolysis) was reduced. It was shown by the use of differential substrates (BeC and MC) that the observed changes in total activity were accounted for by pseudocholinesterase; acetylcholinesterase activity was unchanged. Under the influence of reserpine an increase in the total cholinesterase activity was observed, purely on account of pseudocholinesterase.

Department of Pathological Physiology, Ternopol' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 2, pp. 49-51, February, 1973. Original article submitted February 25, 1972.

TABLE 1. Action of Reserpine on Cholinesterase Activity of the Blood and Heart

Animals	Substrate	Statistical index	Blood		Heart	
			plasma	erythrocytes	atria	ventricles
Control animals	AC	*M*	28,5	21,8	3103	901
		±*m*	1,70	2,03	178,9	37,4
		n	11	12	12	12
	MC	*M*	9,8	10,2	723	185
		±*m*	0,30	1,34	119,9	29,1
		n	12	12	11	12
	BeC	*M*	6,0	2/12*	1304	525
		±*m*	0,62		126,7	25,3
		n	12		11	12
	BuC	*M*	16,6	18,0		
		±*m*	1,27	1,45		
		n	15	14		
Animals receiving reserpine	AC	*M*	33,4	32,0	2517	655
		±*m*	1,03	3,84	157,9	29,6
		n	11	12	13	14
		P	<0,05	<0,02	<0,001	<0,001
	MC	*M*	9,6	9,9	740	202
		±*m*	0,62	0,85	31,9	25,4
		n	6	6	14	14
		P	>0,5	>0,5	>0,5	>0,25
	BeC	*M*	7,9	8/9*	1104	373
		±*m*	0,41		89,5	32,1
		n	8		14	14
		P	<0,05	<0,01	<0,01	<0,001
	BuC	*M*	21,5	22,5		
		±*m*	1,94	1,03		
		n	11	11		
		P	<0,05	<0,05		

Note. Numerator gives number of cases in which enzyme activity could be determined; denominator gives number of experiments. Index of significance P in this case determined on the basis of the χ^2 criterion.

So far as the erythrocytes are concerned, hardly any hydrolysis of BeC was observed in the control animals although hydrolysis of AC and MC did take place. Only in two of the twelve animals was slight activity found (0.6 and 2.2). It was therefore decided to use BuC, which was hydrolyzed intensively by the erythrocytes. After injection of reserpine the intensity of MC hydrolysis remained unchanged. Hydrolysis of BuC was increased.

Hydrolysis of BeC was observed in most animals; in addition, the values of activity were higher (2.0-4.9) than in the control animals.

To ascertain whether reserpine acts directly or indirectly on enzymic hydrolysis of AC and related substrates experiments were carried out in vitro. They showed that reserpine, in a concentration of 0.01%, does not change the intensity of hydrolysis of AC and BeC by erythrocytes and blood plasma during incubation for 1 h.

Reserpine thus evidently acts indirectly through the regulatory systems of the body on the intensity of enzymic hydrolysis of AC. The results of these experiments, showing a decrease in cholinesterase activity of the heart after administration of reserpine, are in agreement with those obtained by Khripchenko et al. [6], who found a decrease in the brain cholinesterase activity in reserpinized rats.

According to Witter [13], the enzyme which hydrolyzes BuC in erythrocytes is insensitive to eserine and it evidently cannot be classed as a cholinesterase.

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