

EFFECT OF 16-ACETYLGITOXIN ON CATECHOLAMINE CONCENTRATION IN HEART MUSCLE IN EXPERIMENTAL COARCTATION OF THE AORTA

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The effect of the glycoside 16-acetylgitoxin on the concentrations of adrenalin and noradrenalin in the myocardium of the left ventricle and in the adrenals was studied in rats with experimental coarctation of the aorta. The 16-acetylgitoxin was injected intramuscularly into the rats in a dose of 0.1 mg/kg daily for 2 weeks. An increase in the adrenalin concentration and in the total catecholamine concentration was observed under the influence of 16-acetylgitoxin in the animals with coarctation of the aorta; this may play an essential role in the cardiotonic action of cardiac glycosides.

The concentration of catecholamines in the myocardium has been shown to play an essential role in the mechanism of the positive inotropic action of the cardiac glycosides [1, 6, 7, 9, 10]. In this connection it is interesting to examine whether the catecholamine concentration is changed after administration of cardiac glycosides during a functional load on the heart.

In the investigation described below the effect of 16-acetylgitoxin (16-AG), synthesized in East Germany, was studied on the concentrations of adrenalin (A) and noradrenalin (NA) in the myocardium of the left ventricle and in the adrenals of rats with experimental coarctation of the aorta.

EXPERIMENTAL METHOD

Forty albino rats weighing 200-250 g were used. A metal spring clip was applied to the abdominal aorta to constrict its lumen by about 2.5 times. The relative weight of the left ventricle and of the adrenals was calculated. Determination of A and NA was carried out by a fluorimetric method with the Farrand Mark I spectrofluorimeter in the modification of Matlina and Rakhmanova [4]. 16-AG was injected intramuscularly in a dose of 0.1 mg/kg daily for 2 weeks.

The animals were divided into four groups. The rats of group 1 (intact) acted as the control. The rats of group 2 received 16-AG for 2 weeks. Coarctation of the aorta was produced 2 weeks before sacrifice in the animals of group 3. Coarctation of the aorta was also produced in the animals of group 4 which received 16-AG for 2 weeks. At the end of the experiment the animals were decapitated.

EXPERIMENTAL RESULTS

The relative weight of the left ventricle in the animals with coarctation of the aorta was increased by 25% and the relative weight of the adrenals by 70% compared with the control. Injections of 16-AG caused no change in these values either in the intact animals or in the animals with coarctation of the aorta.

The results of determination of the catecholamine concentration in the myocardium of the left ventricle and in the adrenals are given in Table 1. In animals in which coarctation of the aorta was produced the

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TABLE 1. Catecholamine Concentration in Myocardium of Left Ventricle and Adrenals of Rats ($M \pm m$)

Groups of animals	Adrenalin content (in μg)			Noradrenalin content (in μg)		
	myocardium		adrenal	myocardium		adrenal
	as a whole	per gram fresh tissue	as a whole	per gram fresh tissue	as a whole	per gram fresh tissue
1. Intact rats (control)	0,146 \pm 0,038	0,30 \pm 0,05	19,47 \pm 2,9	0,673 \pm 0,08	1,33 \pm 0,24	5,03 \pm 0,882
2. Intact rats receiving 16-AG	0,219 \pm 0,036	0,42 \pm 0,07	24,57 \pm 2,7	0,422 \pm 0,09	0,905 \pm 0,223	4,09 \pm 0,563
3. Rats with coarctation of aorta	0,076 \pm 0,004	0,13 \pm 0,0093	26,10 \pm 4,0	0,442 \pm 0,03	0,73 \pm 0,08	3,29 \pm 0,694
4. Rats with coarctation of aorta and receiving 16-AG	<0,05	<0,01	>0,1	<0,05	<0,05	>0,1
	0,156 \pm 0,03	0,30 \pm 0,065	37,14 \pm 2,9	0,433 \pm 0,15	0,90 \pm 0,35	5,88 \pm 0,570
	<0,05	<0,001	<0,05	>0,5	>0,5	<0,02
						143 \pm 14
						<0,05

content of the catecholamines in the myocardium calculated per gram fresh weight was reduced. In the adrenals (calculated in the same way) the changes were not significant. Under the influence of the glycoside a slight tendency was observed in the intact rats for the A concentration in the myocardium and adrenals to increase, but the decrease in their NA concentration was not significant. In the animals with coarctation of the aorta and receiving 16-AG, the A concentration rose sharply in the myocardial tissue but remained unchanged in the adrenals by comparison with the animals undergoing coarctation of the aorta only. The NA concentration in the adrenals of these animals was considerably increased, but in the myocardium there was nothing more than a tendency for it to increase.

The changes in the catecholamine concentrations calculated per gram of fresh weight of the organ were attributable not only to an increase in the relative weight of the left ventricle and adrenals, but also to the injection of 16-AG. This is shown by the results of the calculation of the catecholamine concentrations in the whole organs (Table 1) and by the fact that 16-AG, which does not affect the relative weight of the left ventricle and adrenals, at the same time changes the relative content (per gram tissue) of catecholamines.

The catecholamine content in the whole organ and calculated per gram tissue showed similar changes under the influence of 16-AG. The only difference was in the degree of the changes, resulting from the increase in weight of the left ventricle and adrenals. The increase in weight of the adrenals was evidently due to the stressor effect of the operation.

In animals receiving 16-AG the A/NA ratio changed as a result of an increase in the A concentration. Since the specific action of the glycosides on the heart is connected with their steroid structure, it is interesting to note that administration of ACTH to patients with rheumatoid arthritis and into healthy subjects is accompanied by a decrease in the excretion of NA and an increase in the excretion of A [3, 8]. Other investigations [11] have shown that the degree of methylation of amines in the adrenals depends on the size of the adrenal cortex; the larger the cortex relative to the medulla, the higher the percentage of methylation of NA.

These results suggest that under the influence of 16-AG the conversion of NA into A may be increased. Since the A concentration in the myocardium increased more under the influence of 16-AG than in the adrenals, other mechanisms must evidently be involved, such as increased ability of the heart to adsorb A.

The effect of 16-AG on the total catecholamine concentration in the intact animals differed from its effect on rats with coarctation of the aorta. It fell slightly in the former and increased in the latter. These results accord with the view that cardiac glycosides exert their effect only on the pathologically changed heart.

The increase in the total catecholamine concentration occurring under the influence of 16-AG is evidently one of the changes which can play an essential role in the cardiotonic action of the glycoside. The cardiotonic effect of the cardiac glycosides is in

fact reduced as the catecholamine reserves in the myocardium are exhausted [6, 9], and it is potentiated by an increase in their concentration [1, 7, 10].

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