EFFECT OF INJECTION OF HOMOCARDIAC ANTIGEN ON ACTION OF STROPHANTHIN IN ANIMALS WITH EXPERIMENTAL MYOCARDIAL INFARCTION

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UDC 615.22:[547.918.582.937].03:
616.127-005.8-092.9

Sensitivity to strophanthin and its hemodynamic effect were investigated in rabbits during immunization with homocardiac antigen on the 1st, 3rd, and 5th day after formation of experimental myocardial infraction. The titer of anticardiac autoantibodies was found to be lowered on the 10th day after ligation of the coronary artery, and sensitivity to strophanthin was sharply reduced, as reflected in the values of the minimal lethal dose and the toxic dose (producing cardiac arrhythmia). Changes in tolerance to strophanthin after injection of myocardial antigen in the presence of infarction are connected with the intensity of the immunopathological changes in the heart.

KEY WORDS: experimental myocardial infarction; cardiac glycosides; autoantibodies.

In connection with the possible participation of anticardiac autoantibodies in the pathogenesis of myocardial infarction [5-7], the study of the reactivity of the cardiovascular system to cardiac glycosides, allowing for the intensity of autoimmune processes.

The object of this investigation was to study hemodynamic indices and the character of action of strophanthin in animals with experimental myocardial infarction when immunized with homocardiac antigen.

EXPERIMENTAL METHOD

Experiments were carried out on 47 chinchilla rabbits weighing 2-3.5 kg. A myocardial infarct was produced by ligature of the descending branch of the left coronary artery. The animals (24 rabbits) of the experimental group received an intravenous injection of homocardiac antigen in a dose of 3 mg protein/kg body weight on the 1st, 3rd, and 5th days after ligature. An extract of minced myocardium from the focus of necrosis was used as the antigen. Control rabbits (23) received an injection of isotonic sodium chloride solution at the same time.

Circulating anticardiac antibodies were determined by the passive hemagglutination test (PHT), complement fixation test (CFT), and Hoigne's test in the modification of Klemparskaya and Raeva [2]. The systemic arterial pressure (BP) was recorded in the femoral artery and the heart rate was calculated from the ECG. The minute blood volume was determined by the thermodilution method [1]. The thermodilution curve was recorded on an apparatus consisting of an electronic potentiometer (ÉPP-09) and thermistor probe for measuring the intravascular temperature. After semilogarithmic correction of the thermodilution curve, the minute and systolic blood volumes, cardiac index, and other parameters of the hemodynamics were determined. The character of the action of strophanthin was studied on the 10th, 15th, and 21st days after production of the infarct. Injection of strophanthin started with a dose of 0.05 cat unit (c.u.)/kg (6.7 μg/kg), after which 0.1 c.u./kg (13.4 μg/kg) was injected every 10 min, and the dose causing arrhythmia (toxic dose)

Department of Pharmacology, Kursk 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. 79, No. 5, pp. 89-92, May, 1975. Original article submitted December 22, 1973.

TABLE 1. Effect of Strophanthin on Hemodynamics of Rabbits with Experimental Myocardial Infarction (Control) and Receiving Homocardiac Antigen (Experiment)

Hemodynamic index	10th day after ligature				21st day after ligature			
	experiment		control		experiment		control	
	initial data (n = 8)	strophanthin 0.05 c.u./kg (n = 8)	initial data (n = 7)	strophanthin 0.05 c.u./kg	initial data (n = 8)	strophanthin 0.05 c.u./kg (n = 8)	initial data (n = 7)	strophanthin 0.05 c.u./kg
BP (in mm Hg)	94±10,4	93±4,9	79±7,6	72±7,9	88±7,4	93±6,6	89±2,2	86±4,92
HR (beats/min)	262±13,6	263±12,3	303±13,3	300±17,3	292±9,4	283±9,6	300±10,0	287±6,54
MVB (in ml)	505,6±54,7	618,0±81,2[1]	467,9±61,5	546,4±87,5	494,9±41,9	494,2±40,5	484,5±20,6	543,5±29,7[1]
SBV (in ml)	1,83±0,250	2,43±0,350[1]	1,53±0,211	1,81±0,290	1,71±0,164	1,77±0,153	1,63±0,091	1,90±0,129[1]
CI (in ml/m²/min)	2205,5±123,8	2772,1±294,3	1856,7±202,5	2130,2±749,1	2089,1±173,5	2103,6±118,4	3395,7±169,27	2641,2±260,7[1]
SI (in ml/m²)	8,96±1,06	10,90±1,49	6,14±0,62	7,14±0,96	7,26±0,77	7,49±0,51	7,21±0,92	9,35±0,78[1]
TPR (in dynes/sec/cm^{-5})	16 040±2 956	14 070±2 373	14 793±2 410	12 577±2 739	14 860±1 746	16 312±1 934	14 720±621	12 667±1 026[1]
WILV (in kg/m²/min)	2,85±0,256	3,43±0,314[1]	1,93±0,283	2,05±0,411	2,43±0,258	2,63±0,235	2,88±0,082	3,04±0,241
WSILV (in g/m²)	11,17±1,24	13,38±1,60	6,30±1,0	6,68±1,05	8,27±0,679	9,20±0,12	9,54±0,68	10,62±0,86

Legend: HR) heart rate, MBV) minute blood volume, SBV) stroke blood volume, CI) cardiac index, SI) systolic index, TPR) total peripheral resistance, WILV) work index of left ventricle, WSILV) work stroke index of left ventricle, n) number of animals.

[1]Changes in hemodynamic indices after injection of strophanthin statistically significant ($P < 0.05$) when data analyzed by difference method.

TABLE 2. Sensitivity of Rabbits with Experimental Myocardial Infarction to Strophanthin after Injection of Homocardiac Antigen

Group of animals	Dose of strophanthin	No. of expts.	Dose (in μg/kg)	p_1
Intact	Toxic	9	70,0±4,4	
	Minimal lethal	9	95,1±7,2	
With myocardial infarct 10th day after ligature				
Experiment	Toxic	8	110,5±22,5	<0,05
	Minimal lethal	8	135,3±18,7	<0,05
Control	Toxic	8	21,9±6,4	
	Minimal lethal	8	45,2±12,1	
15th day after ligature				
Experiment	Toxic	8	71,8±12,5	>0,1<0,2
	Minimal lethal	8	107,2±1,3	<0,05
Control	Toxic	8	91,1±9,8	
	Minimal lethal	8	163,5±14,6	
21st day after ligature				
Experiment	Toxic	8	40,5±10,0	<0,05
	Minimal lethal	8	67,0±9,5	<0,05
Control	Toxic	7	115,2±30,8	
	Minimal lethal	7	142,0±28,1	

[1]Index of significance of differences between experimental and control group.

and the dose causing cardiac arrest (minimal lethal dose) were recorded. The results were subjected to statistical analysis [3].

EXPERIMENTAL RESULTS

The effect of strophanthin on the hemodynamics of rabbits with experimental myocardial infarction and immunized with homocardiac antigen is illustrated in Table 1.

The results show that strophanthin caused some increase in the hemodynamic indices in the control group on the 10th day after production of the infarct, but it was not statistically significant. On the 15th day after ligature strophanthin caused practically no change in the hemodynamics. On the 21st day the cardiotonic effect of a "therapeutic" dose of strophanthin (0.05 c.u./kg) was more clearly defined (Table 1 – increase in MBV, SBV, SI). In the experimental animals (immunized with homocardiac antigen) the most marked cardiotonic effect was observed on the 10th day after production of myocardial infarction (Table 1 – increase in MBV, SBV, CI, WILV).

Determination of the toxic and lethal doses of strophanthin also revealed differences in the sensitivity of the control and experimental animals to the glycoside at different periods after production of the infarct. Whereas in the control animals the highest sensitivity to strophanthin was observed on the 10th day after reproduction of the infarct (Table 2), in the experimental animals at this period sensitivity to the glycoside was minimal. The tolerance of the experimental animals to strophanthin was sharply reduced on the 21st day. The change in sensitivity to strophanthin correlated with the dynamics of anticardiac antibodies in the experimental animals. In the control group, for instance, on the 10th day Boyden's test was positive in 19 of 29 animals, the CFT in 14 of 21 rabbits, and Hoigne's test in 15 of 20 rabbits. The results are similar to observations described in the literature [3, 4]. Injection of homocardiac antigen lowered the antibody titer and the frequency of positive results of the PHT, CFT, and Hoigne's test at all times of observation.

Differences in the sensitivity of the immunized and control animals can possibly be explained by binding of the anticardiac autoantibodies formed with the homocardiac antigen (10th day after ligature), followed by an increase in the content of autoantibodies fixed by the myocardium by the 21st day of observation. This hypothesis is confirmed by the dynamics of pathohistological changes observed in the heart.

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