EFFECT OF TAURINE ON DENSITY OF ADRENERGIC NERVE ENDINGS AND RECOVERY OF CARDIAC FUNCTION AFTER ISCHEMIA

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How to increase the resistance of the myocardium to ischemia is an urgent problem in modern cardiology. Myocardial ischemia is accompanied by the release of potassium ions from the myocardial cells and their accumulation in the extracellular space [4], and also by release of catecholamines from nerve endings. These factors play an important role in the genesis of reperfusion arrhythmias and, consequently, they also affect the restoration of myocardial contractility during reperfusion.

Taurine (2-aminoethanesulfonic acid) has been shown to have both inotropic and antiarrhythmic effects [2, 6, 7]. The ability of taurine to reduce the release of catecholamines from sympathetic granules of the adrenals and brain, induced by an increased potassium ion concentration, also has been demonstrated [5].

The aim of this investigation was to study the effect of taurine on restoration of the contractile function of the heart and its automatism and also on the density of adrenergic nerve endings after ischemia.

EXPERIMENTAL METHOD

Experiments were carried out on the hearts of guinea pigs weighing 200-300 g, anesthetized with urethane, 1.6 g/kg, intraperitoneally. The isolated hearts were perfused through a cannula inserted into the aorta, by means of a Multiperpex 2215 peristaltic pump, at the rate of 11 ml/min. Perfusion was carried out with Krebs–Henseleit solution (pH 7.38 ± 0.02), saturated with carbogen, at 37°C. A small balloon filled with liquid was introduced into the chamber of the left ventricle through an incision in the wall of the left atrium. The pressure in the isovolumic balloon, reflecting the tension of the ventricular fibers, was measured by means of a Gould Statham P23 DB electromanometer and recorded on a Gould 2200 instrument. The rate of spontaneous cardiac contractions was 3.5-4 Hz. The heart was perfused for 30-40 min until the parameters of cardiac function had stabilized. Next, by stopping the operation of the peristaltic pump total cardiac ischemia was produced for 40 min, during which time the air temperature in the chamber was kept constant (36°C). Reperfusion was carried out by restarting the coronary blood flow at its previous speed. The state of the adrenergic nerve plexuses in the right and left ventricles was studied 30 min later (Fig. 1). Catecholamines in the nerve plexuses were demonstrated with a 2% solution of glyoxylic acid [3], and they were assayed quantitatively by the dot planimetric method [1]. The nerve endings become visible only if catecholamines are present in them. Taurine in a concentration of 2 mM was added in the different series of experiments either before and after ischemia or only after ischemia. Hearts to whose perfusion fluid no taurine was added served as the control. The results of recording the developed, systolic, and diastolic pressures, the frequencies and rhythm of contractions, and the results of investigation of the state of adrenergic nerve plexuses in the right and left ventricles were all subjected to statistical analysis by Student's test.

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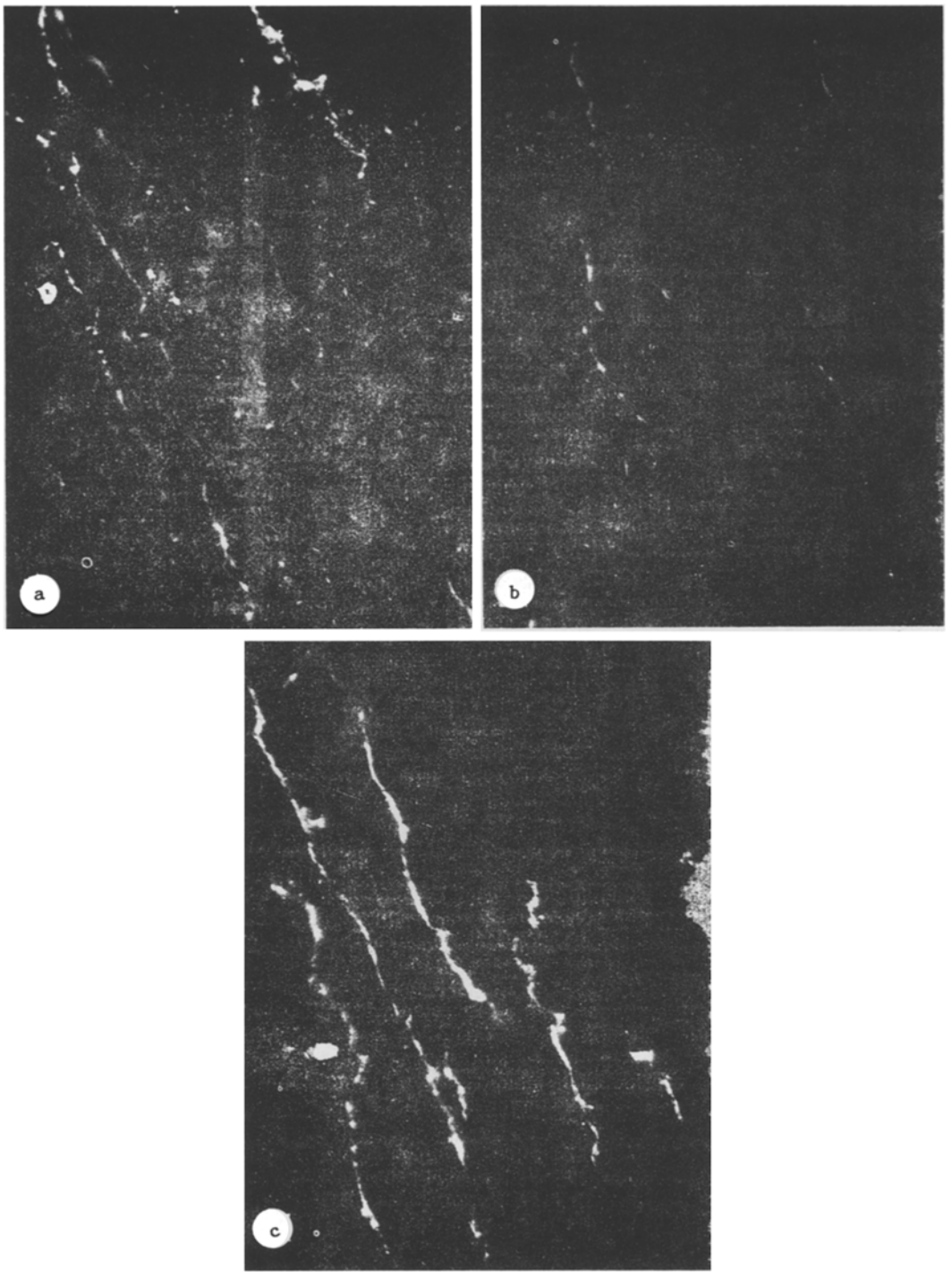

Fig. 1. Microscopic preparation of left ventricle. State of adrenergic nerve endings in left ventricle of guinea pig heart. a) Control animal, b) after ischemia for 40 min, c) after administration of taurine before and after ischemia. Incubation in 2% glyoxylic acid solution; ×120.

EXPERIMENTAL RESULTS

The original data characterizing function of the isovolumic hearts at the beginning of the experiments (developed pressure, diastolic pressure, heart rate) were virtually identical in all series of experiments (89 ± 7 mm Hg; 10 mm Hg; 203 ± 6 beats/min respectively). Data characterizing recovery of function of the isolated guinea pigs' hearts after ischemia for 40 min are

TABLE 1. Restoration of Function of Guinea Pig Hearts after Ischemia for 40 min

Parameters of cardiac function	Control (after ischemia, without taurine, eight experiments)	Taurine, before and after ischemia (six experiments)	Taurine after ischemia (five experiments)
Degree of recovery of developed pressure, in % of initial value	47±8	51±7	69±13
Degree of recovery of heart rate, in % of initial value	101±5	104±1	96±2
Presence of fibrillation during recovery (No. of experiments)	5	6	–
Time of initial and final restoration of regular rhythm, in min	4.0±0.4	3.5±1.2	1.4±0.3*
Rise of diastolic pressure toward end of reperfusion period, in mm Hg	22±3	21±5	12±3**
	25±4	15±6	8±7

Legend. *$p < 0.001$, **$p < 0.05$ compared with control.

TABLE 2. Effect of Taurine on Density of Adrenergic Nerve Fibers after Myocardial Ischemia

Experimental conditions	Number of experiments	Area of adrenergic nerve fibers, in percent of area of field of vision	
		right ventricle	left ventricle
Control (intact animals)	5	3,7±0,50	3,6±0,23
Ischemia for 40 min, without taurine	6	0,87±0,05	0,65±0,05
Ischemia for 40 min, taurine before and after ischemia	6	3,5±0,21*	2,8±0,2*
Ischemia for 10 min, taurine after ischemia	5	2,1±0,10*	1,9±0,10*

Legend: *$p < 0.001$ compared with control.

given in Table 1. They show that in the reperfusion period, in five of eight experiments of the control series and also in all experiments in which taurine was added before and after ischemia, fibrillation was observed whereas in all experiments in which taurine was added only during the reperfusion period, fibrillation was not found. The time of initial and final (complete disappearance of extrasystoles) restoration of a regular rhythm in the latter was significantly (about 50%) less than in experiments of the two previous series (Table 1). The degree of recovery of the developed pressure and heart rate and the rise of diastolic pressure toward the end of the reperfusion period were about equal in all series.

Thus although the degree of recovery of contractility was the same in all series, restoration of normal automatism took place much faster in experiments in which taurine was added at the beginning of reperfusion.

The results of the study of the state of adrenergic nerve plexuses in the right and left ventricles of the hearts are given in Table 2. They show that the density of adrenergic nerve plexuses in hearts subjected to ischemia was lower than in hearts taken directly from the animals, by a factor of 4 in the right ventricle and of 6 in the left ventricle. If taurine was given only after ischemia the density of the adrenergic nerve endings in both ventricles was about 2.7 times higher than if taurine was not added. An even higher density of nerve endings, close to the control level, was observed in experiments in which taurine was added before ischemia (Table 2).

The results show that the use of taurine in the reperfusion period leads to significantly higher residual catecholamine levels in adrenergic nerve fibers at the end of the reperfusion period after ischemia. Meanwhile, restoration of a regular cardiac rhythm in these experiments took place much more rapidly, and fibrillation was not observed. These results are evidence of the antiarrhythmic effect of taurine, combined with better restoration of the myocardial catecholamine reserves. At the same time, direct correlation was not observed between these parameters, as shown by the results of another series of experiments in which taurine was present in the solution before ischemia. Virtually complete recovery of the catecholamine concentrations in the right ventricle and recovery up to 78% of the initial level in the left was observed. However, fibrillation was present in the reperfusion period in virtually all the experiments.

Thus an increase in the taurine concentration in the perfusion fluid before ischemia leads to much higher residual catecholamine levels in the myocardium, and this may prove useful in ensuring more rapid restoration of cardiac function after operations under cardioplegia. The fact that taurine has an antiarrhythmic effect in the reperfusion period after ischemia provides yet another model of pathology in which this particular effect is noted. A similar effect was demonstrated previously in cases of overdosage of catecholamines and cardiac glycosides or potassium deficiency [2, 7]. This effect can be associated only partially with improved preservation of catecholamine reserves in the myocardium. Further research is required to determine the mechanism of action of taurine.

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EFFECT OF PARATHORMONE ON REACTIVITY OF THE RENAL BLOOD FLOW TO VASOPRESSIN IN NORMOTENSIVE AND SPONTANEOUSLY HYPERTENSIVE RATS

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Hypertrophy of smooth muscles in the arteries of the kidneys [13] and other organs [9] is observed in spontaneously hypertensive rats (SHR) in the prehypertensive stage, and when combined with an increase in calcium concentration in them [14], this leads to enhanced contractile activity of these muscles in response to stimulation by vasopressin [7]. Accumulation of calcium and its binding in the cardiomyocytes and smooth-muscle cells of the vessels in primary hypertension is the result of a genetically determined defect of the cell membranes [4]. Lowering of the ionized calcium level [11] and elevation of the parathormone (PTH) concentration in the blood have been observed under these circumstances [10]. It was shown previously in the writers' laboratory that PTH has a hypotensive action in SHR [1]. The same effect of PTH has been described under other conditions by different workers also [12].

The aim of this investigation was to study changes in reactivity of the renal blood flow to various doses of vasopressin (VP) under the influence of PTH in normotensive rats (NTR) and SHR.

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