EFFECT OF PARATHYROID EXTRACT ON THE COURSE OF EXPERIMENTAL ACUTE MYOCARDIAL ISCHEMIA IN RATS

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KEY WORDS: myocardial infarction; hypocalcemia.

Disturbances of the hormonal regulation of homeostasis and, in particular, of water and electrolyte homeostasis, linked with the powerful postaggressive response of the body to a pathological focus in the heart muscle, are the most important aspect in the pathogenesis of acute myocardial infarction. One of the most characteristic manifestations of these disturbances is hypocalcemia, due to inhibition of parathyroid function [1, 5]. However, the possibility cannot be ruled out that a fall in the plasma parathormone level may cause the development of other metabolic disorders and they also induce disturbances of the functions of various organs, because the parathyroid glands are closely connected functionally with activity of the kidneys [4, 8] and the cardiovascular [6, 10, 11] and endocrine [7, 9] systems.

A fall in the plasma parathormone concentration in patients with myocardial infarction is an unfavorable prognostic sign, and artificially created experimental parathyroid hypofunction increases the mortality of the experimental animals from acute myocardial ischemia [1]. It is logical to suggest that the use of parathormone may be pathogenetically indicated in acute myocardial infarction.

It was accordingly decided to study the effect of parathyroidin, the Soviet pharmacopoeial preparation consisting of a purified extract of bovine parathyroid glands, on the course of acute experimental myocardial ischemia in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 187 noninbred albino rats of both sexes weighing 180-200 g. Acute myocardial ischemia was produced in 137 animals by coagulation of the descending branch of the left coronary artery [12] under ether anesthesia. In the first 3 days after the operation 57 rats each received 0.5 ml of physiological saline daily by intraperitoneal injection. Eighty rats with acute myocardial ischemia were given parathyroidin at the same times in a dose of 1 U/100 g body weight daily in 0.5 ml of physiological saline; 50 rats undergoing a mock operation served as the control group.

The calcium concentration in samples of blood plasma was determined spectrophotometrically by means of Bio-Lab-Test kits, and lactic acid concentration and activity of creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) were determined by kits from Boehringer.

For the period of the experiment the animals were kept in metabolism cages and the 24-hourly urine was collected for determination of the calcium concentration, by a trilonometric method, and the 24-hourly Ca^{++} excretion was calculated.

Mortality of the animals from acute myocardial ischemia was calculated during the period from 1 h to 5 days after the beginning of the experiment. Early postoperative mortality was disregarded for it was identical in the groups of rats with experimental myocardial ischemia and in rats undergoing the mock operation.

The results were subjected to statistical analysis with determination of $(M \pm m)$.

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TABLE 1. Parameters of Calcium Exchange and Blood Enzyme Activity and Lactic Acid Level in Rats with Acute Myocardial Ischemia Not Receiving (I) and Receiving (II) Parathyroid Extract

Parameter studied	Control	Ischemia					
		1st day		2nd-3rd day		5th day	
		I	II	I	II	I	II
Diuresis, ml/min	5,58±0,31	1,00±0,12*	2,58±0,51*	2,51±0,30*	3,47±0,26*	4,50±0,42*	4,91±0,11
Blood calcium concentration, mM	2,53±0,02	2,17±0,02*	2,25±0,05*	2,22±0,07*	2,31±0,05*	2,25±0,05*	2,47±0,04
Calcium excretion, μmoles / 24 h	6,31±0,34	2,94±0,17	3,09±0,10	3,85±0,65	4,46±0,15	4,61±0,79	5,90±0,13
CPK, units/liter	70,0±6,1	135,0±14,6*	54,4±8,8	142,1±10,8*	63,5±10,5	—	—
LDH, units/liter	120,5±14,6	141,8±13,4	145,5±7,3	—	—	130,0±5,9	109,0±2,5
Lactate, mM	0,50±0,03	0,81±0,15*	0,55±0,11	—	—	0,70±0,09*	0,59±0,06

Legend. Blood CPK activity measured on 2nd day, calcium metabolism parameters on 3rd day after start of experiment. *P < 0.05 compared with control.

EXPERIMENTAL RESULTS

In rats with acute myocardial ischemia and not receiving parathyroid extract the blood CPK activity doubled on the 1st and 2nd days after the beginning of the experiment; the LDH level also was a little higher, but the increase was not statistically significant compared with the control (Table 1). The blood lactate level was statistically significantly raised on the first day of acute myocardial ischemia and remained high until the 5th day of the experiment inclusive. The calcium exchange also showed considerable changes. The plasma Ca^{++} concentration fell from the 1st through the 5th days after the beginning of the experiment. Diuresis and the 24-hourly calcium excretion with the urine were depressed. The mortality among the experimental animals during 5 days of observation was 27%.

In the group of animals receiving parathyroid extract the parameters of calcium exchange (the plasma Ca^{++} level and its excretion with the urine) were restored to normal by the 5th day of the experiment. CPK activity on the 1st and 2nd days after the beginning of the experiment was almost halved compared with the corresponding value in the group of rats not receiving parathyroid extract, i.e., it did not differ from the CPK level in animals undergoing the mock operation. The blood lactate level also returned to normal. The blood LDH activity in animals receiving parathyroid extract, just as in the untreated animals, did not differ significantly from the control. Mortality in the group of rats receiving parathyroid extract fell to 15%.

It can be concluded from these results that parathyroid extract had a favorable effect on the course of experimental myocardial infarction. This is confirmed by the fall in the blood CPK activity to the control level under the influence of parathyroidin. An increase in the blood CPK activity in myocardial infarction is known to be the result of death of cardiomyocytes. Conversely, a fall in the CPK level may be evidence of limitation of the zone of necrosis of the heart muscle under the influence of parathyroid extract. This latter explanation may be connected with the fact that parathyroid hormone can play the role of antagonist of β-adrenoreceptor stimulators [11], and it can accordingly protect the myocardium against the harmful action of catecholamines [1], whose role in the development of acute myocardial infarction is not disputed [2].

Elevation of the blood lactate level in shock and shock-inducing states, including myocardial infarction, is connected with a disturbance of tissue metabolism. Since the blood LDH concentration was not increased by parathyroid extract and, consequently, it could not have been a factor lowering the blood lactic acid level, the fall in the serum lactate in the present experiments can be regarded as the result of normalization of tissue metabolism.

The decrease in the 24-hourly diuresis in rats with acute myocardial ischemia was the result of the strong stress reaction and was due, on the one hand, to liberation of large quantities of varopressin, angiotensin, and aldosterone into the blood and, on the other hand, to a disturbance of the microcirculation in the kidney. Inhibition of diuresis is an unfavorable factor not only in myocardial infarction, but also in other postaggressive states.

The increase in diuresis in rats receiving parathyroid extract is evidence of normalization of renal function under the influence of this preparation. In that case, the mechanism of action of parathyroid hormone may be based on blockade of the peripheral effects of vasopressin [4] and also on an increase in velocity of the renal blood flow [8].

A fall of the plasma calcium concentration is an unfavorable prognostic sign in myocardial infarction [3] and is connected with parathyroid insufficiency [1]. Consequently, normalization of the parameters of calcium exchange under the influence of parathyroid extract in the present experiments can also be interpreted as a favorable effect of the treatment given.

It can thus be concluded from the results that administration of parathyroid extract in acute experimental myocardial ischemia has a beneficial action. Solid evidence in support of this conclusion is given by the reduction in mortality of the experimental animals from acute myocardial ischemia by 1.8 times after administration of parathyroidin.

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EFFECT OF STAPHYLOCOCCAL TOXIN ALONE AND TOGETHER WITH ANTISTAPHYLOCOCCAL GAMMA-GLOBULIN ON ELECTRICAL AND CONTRACTILE ACTIVITY OF THE GUINEA PIG MYOCARDIUM

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KEY WORDS: staphylococcal toxin; myocardium; action potential; amplitude of contractions.

One of the key factors in septicemic shock is the direct action of microbial toxins and, in particular, of staphylococcal toxin (ST) on the cardiovascular system. Observations on patients in a state of septicemic shock have shown that the stroke ejection of the heart and cardiac output may be either reduced [1, 2, 14] or increased [7, 10, 12, 15]. Electrophysiological experiments have shown that ST reduces the amplitude of intracellular potentials and the amplitude of contractions of preparations of the guinea pig and rabbit myocardium [9]. Differences in values of the cardiac output obtained in patients with septicemic shock suggest that ST may have not only an inhibitory, but also a stimulating action on the myocardium.

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