AGE ASPECTS IN THE DEVELOPMENT OF VASOPRESSIN-INDUCED CORONARY INSUFFICIENCY

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Electrocardiogram (ECG) changes (enlargement of the T wave, displacement of the S—T segment, disturbances of atrioventricular conduction) arising under the influence of vasopressin in old rats (24-26 months) occur in response to smaller doses of the hormone than in middle-aged (10-12 months) animals. After injection of equal doses the coronary insufficiency was more severe in the older group of animals and was accompanied more often by a disturbance of atrioventricular conduction in the heart of the second to third degree and by distinct disturbances of the hemodynamics.

KEY WORDS: vasopressin; aging; ECG; coronary insufficiency.

Coronary insufficiency is one of the commonest diseases of old age. However, it is usually studied experimentally without consideration of the age of the animals or of age changes in the system of neurohumoral regulation.

The importance of this factor was investigated in coronary insufficiency induced by vasopressin [1, 4, 8].

EXPERIMENTAL METHOD

Experiments were carried out on old (24-26 months) and middle-aged (10-12 months) male Wistar rats anesthetized with urethane (80 mg/100 g body weight). Since differences in sensitivity and reactivity of the cardiovascular system may exist [9], a wide range of doses of synthetic vasopressin (Koch-Light laboratories Ltd.) was used, from 0.005 to 0.2 unit/100 g body weight; the hormone was injected intravenously, slowly (in the course of 20 sec), in 0.5 ml of physiological saline. The ECG was recorded on a 6-channel Élkar-6 electrocardiograph, in standard and chest leads, with a tape winding speed of 100 mm/sec and amplification of 1 mV = 2 cm. The ECG was analyzed by the usual methods [6], allowing for age differences among the rats [10, 15]. The cardiac output was determined by the thermodilution method [5, 11]. The blood pressure (BP) was recorded in the femoral artery.

EXPERIMENTAL RESULTS

Among the ECG changes in vasopressin-induced coronary insufficiency the dynamics of the amplitude of the T wave, the position of the S—T segment, and the rhythm of the cardiac contractions are particularly important [8, 13, 14]. In the first 10-20 sec after the beginning of hormone administration the T wave was increased and was typically pointed in shape, whereas the S—T segment was displaced upward (Fig. 1). In the second period the T wave was reduced and the S—T segment was below its initial level. The times of onset and the duration of the second period depended on the dose of vasopressin and the animal's age and ranged between 20-30 sec and 3-5 min. The third period was characterized by a fresh increase in amplitude of the T wave followed by a gradual decrease to its initial level and by gradual normalization of the S—T segment in the course of 15-30 min.

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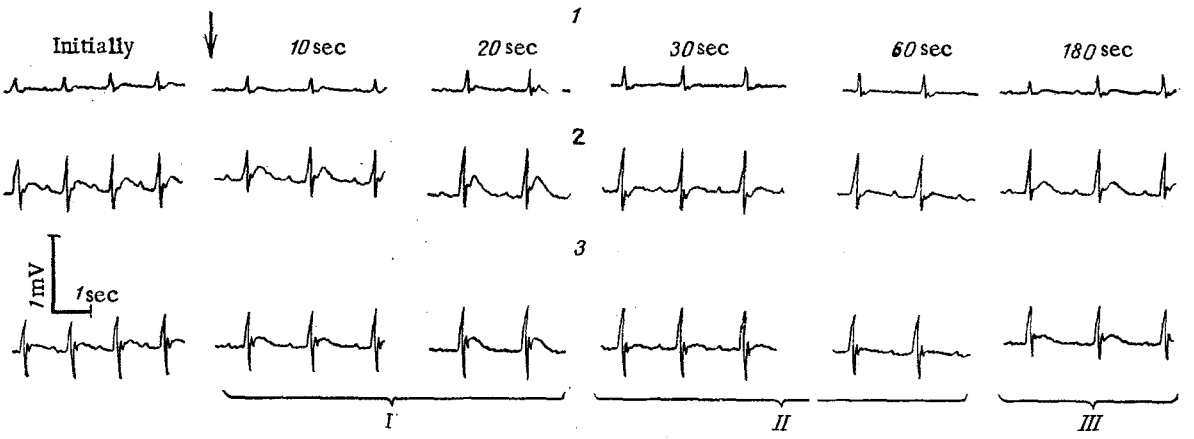

Fig. 1. ECG changes in old rats following injection of vasopressin (0.02 unit/100 g body weight): 1,2,3) standard ECG leads. Arrow marks injection of vasopressin. Numbers above show time after injection of vasopressin. I, II, III) Periods in dynamics of T wave and S–T segment.

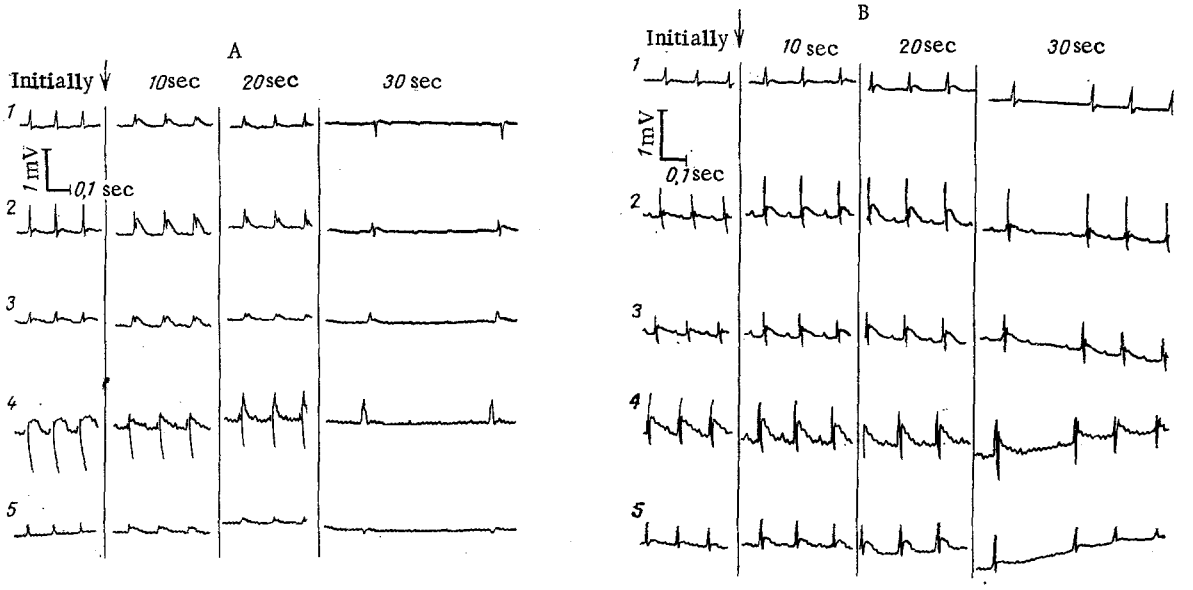

Fig. 2. Disturbance of atrioventricular conduction in old (A) and middle-aged (B) rats following injection of vasopressin (0.2 unit/100 g body weight): 1,2,3) standard ECG leads; 4,5) chest leads V_1 and V_5. Arrows indicate injections of vasopressin. Numbers above curves show time after injection of vasopressin.

TABLE 1. Changes in Indices of T Wave and S–T Segment (in μV) Compared with Initial Values after Intravenous Injection of Various Doses of Vasopressin into Middle-Aged and Old Rats (M ± m)

Character of changes	Middle-aged rats		Old rats	
	0.01–0.02 unit/100 g body weight (n = 34)	0.1–0.2 unit/100 g body weight (n = 23)	0.01–0.02 unit/100 g body weight (n = 38)	0.1–0.2 unit/100 g body weight (n = 34)
Initial enlargement of T wave	97,5± 6,5	136,5± 10,5	172,5± 21,5	161,5± 6,0
Initial elevation of S–T segment	80,0± 10,0	100,0± 4,5	160,0± 15,6	155,0± 9,0
Subsequent temporary fall of S–T segment	—	40,0± 5,0	62,5± 12,0	76,0± 6,1
Subsequent temporary reduction of T wave	—	46,5± 5,5	59,0± 14,0	76,0± 3,5

TABLE 2. Maximal Slowing of Sinus Rhythm (in % of initial) following Intravenous Injection of Various Doses of Vasopressin into Middle-Aged and Old Rats (M ± m)

Animals	Dose of vasopressin (in units/100 g body weight)	
	0,01—0,02	0,1—0,2
Middle-aged	29,2±1,8	41,9±3,4
Old	22,9±1,3	28,3±1,1

After injection of vasopressin in a dose of 0.005 unit/100 g body weight, which caused no changes in the EEG of the middle-aged animals, enlargement of the T wave was found in 65% and upward displacement of the S—T segment in 40% of the old animals. The second period of changes was not found after this dose. With an increase in the dose of vasopressin to 0.01-0.02 unit/100 g body weight, a marked increase in the T wave was observed in the old animals in 100% of cases, but in only 70% of the middle-aged rats. With this dose of the hormone, moreover, the second period of the ECG dynamics was found only in the old animals (in 60% of cases). A further increase in the dose of vasopressin to 0.1-0.2 unit/100 g body weight led to an increase in the T wave in 100% of cases in both middle-aged and old animals. However, the frequency of appearance of the second period of the ECG dynamics in the old animals was much higher (90%) in the old animals than in the middle-aged group (55%).

The degree of enlargement of the T wave and elevation of the S—T segment in the old animals after injection of vasopressin in a dose of 0.01-0.02 unit/100 g body weight was greater than in the middle-aged rats (Table 1). With an increase in the dose of vasopressin to 0.1-0.2 unit/100 g body weight, no further enlargement of the T wave or elevation of the S—T segment was observed in the old animals, whereas their subsequent decrease was more marked. In the middle-aged rats, following an increase in the dose of vasopressin the increase in amplitude of the T wave and the height of the S—T segment grew proportionally; when a temporary fall in these indices followed, it was less marked than in the old rats.

The P—Q intervals (normal duration 0.04-0.05 sec for middle-aged and 0.05-0.06 sec for old rats [10, 12, 15]) were almost doubled after administration of vasopressin both in the old (to 0.10-0.13 sec) and the middle-aged (to 0.07-0.09 sec) rats. Atrioventricular conduction was disturbed to the second to third degree or sometimes to complete transverse heart block much more often (in 58.4% of cases) in the old animals than in the middle-aged group (2.9%; Fig. 2).

Injection of vasopressin was followed by sinus bradycardia, reaching a maximum 2-3 min after the injection, in 100% of cases in rats of both groups. However, in the old animals, with all the doses used, the sinus bradycardia was less marked than in the middle-aged rats (Table 2).

Injection of vasopressin disturbed the hemodynamics in all the animals, but in the old rats the changes were more severe than in the middle-aged group with all doses used. For instance, the cardiac output of the old animals fell by 41.9 ± 3.1%, whereas in the middle-aged group it fell by only 28.8 ± 4.1%. In the old animals, after the BP had increased for 20 sec, it decreased temporarily (depressor phase) in 82% of cases; not until 1.5 min after the injection did it start to rise again, to reach a maximum after 3 min. In the middle-aged animals during the first few minutes after injection an initial rapid rise was followed by a slow but steady rise in BP, ultimately to a greater degree than in the old animals. The most marked ECG changes, characteristic of coronary insufficiency and including disturbances of atrioventricular conduction, sometimes amounting to complete heart block, were recorded during this depressor phase. The depressor wave of BP after injection of vasopressin into the old animals in a dose of 0.1-0.2 unit/100 g body weight was thus a reflection of cardiogenic collapse, due on the one hand to weakening of the cardiac contractions and, on the other hand, to the development of bradycardic arrhythmia.

The results indicate that signs of coronary insufficiency appear in old animals after injection of smaller doses of vasopressin; if the same dose of vasopressin is given the coronary

insufficiency in old animals is more severe and is more often accompanied by the development of arrhythmia and disturbance of the hemodynamics. This difference can be considered to be due both to increased sensitivity of the coronary vessels in old animals to the action of vasopressin [3] and to increased sensitivity of their myocardium to restriction of its blood supply [2, 7].

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ARTIFICIAL VENTILATION OF THE LUNGS AFTER PARALYSIS OF THE DIAPHRAGM

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To maintain a normal arterial pCO_2 in phrenicotomized rabbits artificial ventilation of the lungs must be increased to almost double the normal level. The reason is that phrenicotomy causes a decrease not only in pulmonary, but also in alveolar ventilation.

KEY WORDS: diaphragm, phrenicotomy, artificial ventilation of the lungs.

Division of the phrenic nerves leads to increased inspiratory activity of the respiratory center. The resulting paralysis of the diaphragm causes a decrease in the respiratory volume of the lungs, as a result of which the inhibitory reflex from the lungs on the respiratory center is reduced. However, the role of a reduction in the respiratory volume of the lungs in the increased activity of the respiratory center, demonstrated in experiments on rabbits with an open chest [1] or a closed chest (i.e., the conditions under which resuscitation is carried out on patients with paralysis of the respiratory muscles) may prove to be con-

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