GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Effect of TRH on the Development of Ischemic Cardiac Arrhythmias in Cats

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Acute experiments on cats showed that intravenous injection of thyrotropin-releasing hormone prevented blood pressure drop and produced a pronounced antiarrhythmic effect.

Key Words: *thyrotropin-releasing hormone; myocardial ischemia; cardiac arrhythmias*

Coronary heart disease is accompanied by changes in external respiration, which plays an important compensatory role in the development of ischemic cardiac arrhythmias [2,6,7,9]. Thyrotropin-releasing hormone (TRH) involved in the regulation of respiratory activity is of particular interest in this respect [3,8,12]. Little is known about the effect of TRH on functional activity of the cardiovascular system [10-12].

We found no data on the influence of TRH on the development of ischemic cardiac arrhythmias. Here we studied the effect of TRH on the development of cardiac arrhythmias during experimental myocardial ischemia.

MATERIALS AND METHODS

Acute experiments were performed on 31 male and female cats weighing 2.5-4.0 kg and narcotized with nembutal (40 mg/kg intraperitoneally). Myocardial ischemia was produced by 15-min ligation of the circumflex branch of the left coronary artery near the place where it arises from the main branch with doderone thread, which was followed by reperfusion. The development of arrhythmia was monitored during 15-min occlusion and 15-min reperfusion.

In series I (18 animals) we studied the incidence of cardiac arrhythmias during coronary occlusion. In series II (13 animals) we studied the incidence of cardiac arrhythmias after treatment with TRH. TRH (Bokiron) in a dose of 20 mg/kg was injected intravenously 15 min before ligation of the coronary artery [1]. The animals were subjected to tracheostomy. A Vita-1 volume-frequency respirator was used for artificial ventilation. Electrocardiogram was recorded using a Biokomb-8 polyphysiograph (ORION/EMG, lead II). Blood pressure (BP) in the femoral artery was measured with an EMT-35 electromanometer. The results were analyzed by methods of variational statistics.

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RESULTS

In series I coronary occlusion was followed by a significant decrease in BP in 91.7% cats ($p<0.01$). Baseline BP was 152.5±7.1/108.8±7.5 mm Hg. It sharply decreased to 121.8±12.2/84.3±10.2 mm Hg 30 sec after occlusion ($p<0.01$). The systolic pressure remained practically unchanged during ischemia (122.35± 12.20 mm Hg). After reperfusion BP was 159.4±13.2/ 110.3±9.5 mm Hg. Individual extrasystoles, multiple extrasystoles, ventricular tachycardia, and ventricular fibrillation developed in 66.5, 50, 27.7, and 55.5% animals, respectively (Fig. 1). Therefore, coronary occlusion led to a rapid and sharp decrease in BP and rhythm disturbances, including ventricular fibrillation.

In 75% cats TRH administered before coronary occlusion increased BP by 10.8% from the baseline level. The baseline BP was 132.86±6.37/93.50±3.66

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mm Hg. After 5 min BP increased to 156.43±5.32/115.00±4.35 mm Hg ($p<0.05$). Immediately before coronary occlusion BP was 140.83±5.53/110.00±5.87 mm Hg ($p<0.05$). In 62.5% animals BP before coronary occlusion surpassed the baseline by 28.2%. BP remained unchanged during 15-min occlusion. Thus, TRH prevented the drop of BP produced by coronary occlusion. The decrease in BP to 133.57±7.94/97.14±6.31 mm Hg was observed only 15 min after ligation of the coronary artery. After removal of the ligature BP remained practically unchanged and returned the baseline level by the 15th minute (131.67±4.52/95.00±5.53 mm Hg). These data show that TRH prevents BP drop induced by myocardial ischemia at various stages of the experiment.

TRH increased BP, but did not change heart rate (HR). The initial HR was 158.2±1.94 bpm. Before ligation of the coronary artery HR insignificantly decreased to 153.34±2.08 bpm. During occlusion HR increased and by the 15th minute reached 169.2±3.84 bpm. Fifteen minutes after removal of the ligature HR was 147.28±3.12 bpm.

In this series ligation of the coronary artery was less frequently accompanied by the development of cardiac arrhythmias. Single and multiple extrasystoles, ventricular tachycardia, and ventricular fibrillation were observed in 61.5, 23, 15.4, and 7.7% animals, respectively (Fig. 1). Thus, TRH decreased the incidence of multiple extrasystoles, ventricular tachycardia (by 2 times), and ventricular fibrillation (by 6 times).

Our results show that TRH prevents BP drop during myocardial ischemia and reduces the incidence of severe cardiac arrhythmias, including ventricular fibrillation. Our previous studies revealed a correlation between the decrease in BP at the early stage of myocardial ischemia and development of ventricular fibrillation [5]. Experiments with massive blood loss demonstrated that TRH increases BP [3,4]. X. Zhou *et al*. [12] showed that TRH markedly increases the mean BP and survival rate in rats with hemorrhagic shock. V. V. Zakusov *et al*. [3] reported that the effect of TRH on BP is realized via α-adrenoceptors in the vascular wall. These data show that TRH stabilizes BP and decreases the incidence of severe arrhythmias during myocardial ischemia.

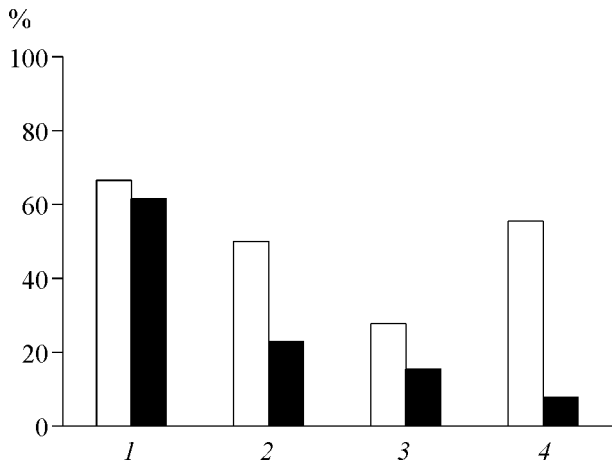

Fig. 1. Effect of TRH on the development of cardiac arrhythmias during experimental myocardial ischemia: individual extrasystoles (*1*), multiple extrasystoles (*2*), ventricular tachycardia (*3*), and ventricular fibrillation (*4*). Incidence of cardiac arrhythmias during myocardial ischemia (dark bars) in cats receiving TRH (light bars).

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