Role of the Autonomic Nervous System in the Development of Cardiac Arrhythmias in Cats with Acute Myocardial Ischemia Receiving Thyroliberin

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The role of the autonomic nervous system in the development of ischemic cardiac arrhythmias was studied in acute experiments on cats receiving thyrotropin-releasing hormone. Bilateral vagotomy attenuated, while bilateral transection of cardiac branches of the stellate ganglia completely abolished the antiarrhythmic effect of thyrotropin-releasing hormone.

Key Words: *thyrotropin-releasing hormone; acute myocardial ischemia; cardiac arrhythmias; autonomic nervous system*

Our previous studies showed that thyrotropin-releasing hormone (TRH) produces a pronounced antiarrhythmic effect under conditions of acute myocardial ischemia and stimulation of the sensorimotor cortex [4,5].

The heart is a potent reflexogenic zone and therefore various damaging factors, *e.g.* myocardial ischemia, undoubtedly affect the type of afferent information from this organ. The sympathetic and parasympathetic autonomic nervous systems play a major role in this process [1,3]. However, little is known on the role of the nervous system in the development of ischemic arrhythmias after treatment with TRH. Here we studied whether the parasympathetic and sympathetic autonomic nervous systems are involved in the development of ischemic cardiac arrhythmias during TRH administration.

MATERIALS AND METHODS

Acute experiments were performed on 42 adult cats weighing 2.5-5 kg. The animals were narcotized with nembutal (40 mg/kg intraperitoneally) and the thorax was opened. Artificial ventilation was performed on a Vita-1 device. Acute myocardial ischemia was produced by ligation of the left coronary artery circumflex branch near the place where it arises from the main branch. The development of arrhythmia was monitored during 15-min occlusion and 15-min reperfusion.

TRH (Bokiron) in a dose of 20 μg/kg was injected intravenously 15 min before coronary artery ligation.

Bilateral vagotomy was performed on the neck. Two incisions were made on the left and right sides of the neck. Both vagus nerves were separated from sympathetic nerves and ligated. Vagotomy was performed 5 min before TRH administration.

Access to the stellate ganglion was obtained through the first intercostal space to perform transection of sympathetic nerves. Ligatures were placed above the inferior cardiac nerve and branch of the subclavian loop. Bilateral transection of cardiac branches of stellate ganglia was performed 5 min before TRH administration.

Electrocardiogram was recorded on a Biokomb-8 polyphysiograph (ORION/EMG, lead II). Blood pressure (BP) in the femoral artery was measured with an EMT-35 electromanometer. Idioventricular cardiac

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TABLE 1. BP during Cardiac Denervation and TRH Administration (mm Hg, *M*±*m*)

Treatment	Baseline BP before transection	BP after transection and before TRH administration	BP before coronary artery ligation	BP after 30-sec ischemia
Bilateral vagotomy				
control (*n*=10)	BP_S 145.2±12.1		BP_S 154.5±16.3	BP_S 155.7±16.8
	BP_D 112.6±11.3		BP_D 118.7±15.2	BP_D 124.7±16.1
TRH administration (*n*=13)	BP_S 131.4±13.8	BP_S 134.7±12.9	BP_S 142.4±11.5	BP_S 139.7±12.3
	BP_D 103.4±10.5	BP_D 106.2±9.6	BP_D 113.8±10.4	BP_D 110.5±9.4
Bilateral transection of sympathetic nerves:				
control (*n*=9)	BP_S 148.1±10.3		BP_S 126.7±7.9*	BP_S 102.9±10.6*
	BP_D 114.5±9.6		BP_D 98.4±8.5	BP_D 83.7±7.3
TRH administration (*n*=10)	BP_S 138.4±8.5	BP_S 121.1±6.3*	BP_S 122.3±6.5*	BP_S 111.2±6.6*
	BP_D 109.6±9.3	BP_D 97.5±5.8	BP_D 97.8±5.9	BP_D 88.7±5.4

Note. *p<0.05 compared to baseline BP. Here and in Table 2: *n*, number of experements.

arrhythmias included multiple extrasystoles, ventricular tachycardia, and ventricular fibrillation. The results were analyzed by Student's *t* test and χ^2 test.

RESULTS

For evaluation of the role of the parasympathetic system in the antiarrhythmic effect of TRH we used bilateral vagotomy. In control animals (*n*=10) BP slightly increased immediately before coronary artery ligation after nerve transection and on the 30th second of ischemia (p>0.05, Table 1). Cardiac arrhythmias developed in 60% cats. Multiple extrasystoles, ventricular tachycardia, and ventricular fibrillation were observed in 50, 40, and 50% animals, respectively (Table 2).

TRH had no effect on BP in vagotomized cats (*n*=13, p>0.05, Table 1). In these animals the incidence of idioventricular cardiac arrhythmias decreased by 20%. The incidence of multiple extrasystoles, ventricular tachycardia, and ventricular fibrillation decreased by 11.5% and by 2.6 and 3.2 times, respectively, compared to cats not receiving TRH (Table 2).

These data suggest that the antiarrhythmic effect of TRH in cats subjected to bilateral vagotomy was less pronounced than in animals with intact innervation of the heart (Table 2). It cannot be excluded that the parasympathetic autonomic nervous system contributes to a decrease in the incidence of ischemic cardiac arrhythmias after TRH administration.

In the next series we evaluated the effect of TRH on the development of cardiac arrhythmias during blockade of sympathetic impulses to the heart. In control cats (*n*=9) BP decreased by 15% after sympathetic nerve transection and continued to decrease to the 30th

TABLE 2. Incidence of Cardiac Arrhythmias during Cardiac Denervation and Thyroliberin Administration (%)

Treatment	Total incidence of ischemic cardiac arrhythmias	Multiple extrasystoles	Ventricular tachycardia	Ventricular fibrillation
Intact innervation (*n*=13)				
control	69.2	53.8	30.7	53.8
TRH administration	23.3*	23.3	15.4	7.7*
Bilateral transection of sympathetic nerves				
control (*n*=10)	60	50	40	50
TRH administration (*n*=13)	38.5	38.5	15.4	15.4
Bilateral vagotomy				
control (*n*=9)	44.4	11.1	11.1	22.2
TRH administration (*n*=10)	40	30	30	20

Note. *p<0.05 compared to the control.

sec of ischemia ($p<0.05$, Table 1). Cardiac arrhythmias developed in 44.4% animals subjected to bilateral transection of cardiac branches of stellate ganglia. Ventricular fibrillation was observed in 22% cats with cardiac arrhythmias (Table 2). In rats subjected to sympathetic nerve transection and receiving TRH BP decreased by 12% and continued to decrease after coronary artery ligation ($p<0.05$, Table 1).

In contrast to animals with intact innervation of the heart, TRH administration does not prevent the decrease in BP at the early stage of acute myocardial ischemia in cats subjected to bilateral transection of cardiac branches of stellate ganglia [4]. It can be hypothesized that BP rise produced by TRH is mediated by the sympathetic nervous system. Our results are consistent with published data [2,7,13]. Under these conditions idioventricular arrhythmias were observed in 40% animals. The incidence of multiple extrasystoles and ventricular tachycardia was 2.7-fold higher compared to other disturbances. In these animals ventricular fibrillation developed as frequently as in cats not receiving TRH (Table 2). High incidence of ventricular tachycardia was probably associated with the ability of TRH to elevate blood catecholamine level and increase the sensitivity of cardiac β-adrenoceptors to these hormones [8-12,14]. Moreover, the sensitivity of β-adrenoceptors increases during blockade of sympathetic impulses to the heart [6]. The antiarrhythmic effect of TRH was not observed after bilateral sympathetic denervation of the heart.

Our results indicate that the protective effect of TRH on the development of ischemic cardiac arrhythmias is primarily realized via the sympathoadrenal system. The involvement of the parasympathetic system in this process cannot be excluded.

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