EFFECT OF DENERVATION OF THE HEART ON ITS FUNCTION IN ASPHYXIA

A. A. Podkolzin, S. O. Trenin, A. P. Legoshin, and A. V. Khokhlov

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During transplantation of the human heart at the present time the organ is completely denervated. Consequently, the study of function of the myocardium deprived of its central nervous regulation becomes of exceptional importance. Previous investigations have been devoted to the study of the function of the denervated heart both at rest and under various functional loads [1, 4, 5, 9]. However, the work of the denervated heart during hypoxia has not been adequately studied.

This paper describes an attempt to study activity of the denervated heart during and after asphyxia.

EXPERIMENTAL METHOD

There were two series of experiments on 23 mongrel dogs weighing 6-8 kg. Under hexobarbital anesthesia (50 mg/kg) and artificial respiration, bilateral intercostal thoracotomy was performed on the animals. In the experimental series both the ventral and the dorsal parts of the thoracic aortic nerve plexus were divided in the chest. The cardiac nerves of the pulmonary and esophageal plexuses also were isolated and divided. In the control series, nerves innervating the heart were separated from the surrounding tissues but not divided. After true or mock denervation of the heart, artificial ventilation of the lungs was stopped for 3 min with both pleural cavities opened. During and after asphyxia the changes in the electrocardiogram (ECG), arterial blood pressure (BP), and venous pressure (VP) were recorded on the MKh-01 monitor, and the systolic volume of the heart (SV), cardiac output (CO), specific peripheral vascular resistance (SPVR), and the work of the left ventricle of the heart (A) were calculated by methods in [3, 6]. The results were subjected to statistical analysis by Student's method.

EXPERIMENTAL RESULTS

Denervation of the heart did not lead to significant changes in the hemodynamics, and before asphyxia the heart rate (HR) was 110 ± 5.6 beats/min, the systolic BP (Ps) was 113 ± 8.9 mm Hg, the diastolic BP (Pd) 86 ± 5.7 mm Hg, the pulse pressure (Ps-Pd) 27 ± 4.6 mm Hg, VP 14.8 ± 1.3 mm Hg, SV 9.6 ± 1.1 ml, CO 1.1 ± 0.2 liter/min, SPVR 52 ± 4.8 conventional units, and A 1227 ± 102 g/cm.

During the first 2 min of asphyxia HR of the denervated heart was unchanged, but after 3 min it was lowered by 19%. By this time Ps had risen by 35%, Ps-Pd by 103%, VP by 34%, SV by 89%, and A by 82%; CO and SPVR showed no statistically significant change (Fig. 1).

At the first minute after asphyxia the various parameters showed a sharp increase. HR was 54% above the background level, Ps 112%, Pd 76%, Ps-Pd 230%, SV 220%, CO 291%, and A 518% above the initial values. Meanwhile VP returned to normal and SPVR fell by 50%.

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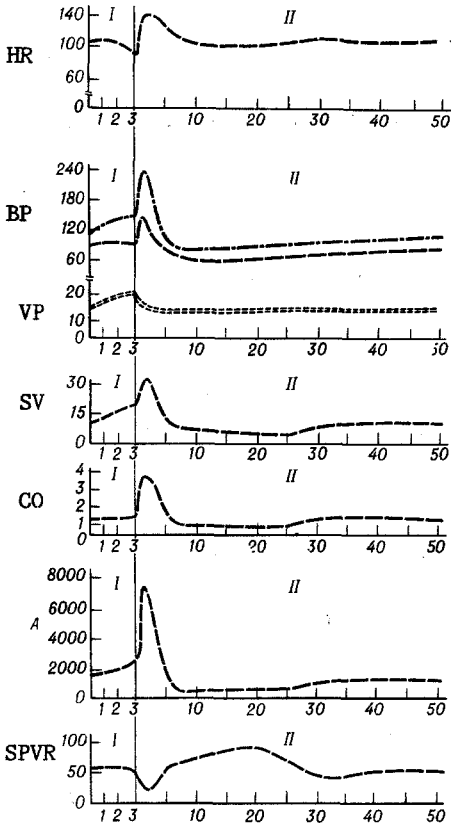

Fig. 1. Changes in hemodynamics during asphyxia, with denervated heart. I) Period of asphyxia, II) Period after asphyxia; ordinate: HR — heart rate (beats/min), BP) arterial blood pressure (in mm Hg), VP) venous pressure (in mm water), SV) systolic volume of the heart (in ml), CO) cardiac output (liters/min), A) work of left ventricle (g/cm), SPVR) specific peripheral vascular resistance (conventional units); abscissa, time (in min).

The parameters then gradually decreased, to reach their background values after 5 min. However, the hemodynamics continued to be inhibited, and by the 10th minute Ps was reduced by 23%, SV by 31%, and A by 50%, whereas SPVR was increased by 31%. Not until the 30th minute was stable normalization of the hemodynamic parameters achieved.

In the control experiments, at the first minute of asphyxia HR was increased by 19%, but later it gradually fell and by the 3rd minute it was 44% below the background level (Fig. 2). By the 3rd minute of asphyxia Ps was increased by 109%, Pd by 69%, Ps-Pd by 288%, VP by 36%, SV by 165%, CO by 53%, and A by 393%, and SPVR by 22%.

Starting with the first minute after asphyxia there was a gradual decrease in the values of the hemodynamic parameters, and by the 3rd-5th minutes they were fully restored to normal.

These investigations showed that in both series of experiments an increase in hemodynamic parameters was observed during asphyxia. In the experimental series, however, the increase was much smaller. We know that the response of the denervated heart to functional loads develops more slowly than in the normally innervated heart [8]. In the present experiments, in the experimental series, BP, A, and SV, in the course of 3 min, were unable to reach the levels of these parameters in the control series at the 3rd minute of asphyxia. It was also noted that HR of the denervated heart did not increase, whereas in the control tachycardia developed during the first minute of asphyxia. This is in agreement with data in the literature indicating that a functional load on the denervated heart does not lead to any significant change in its rate of beating [10].

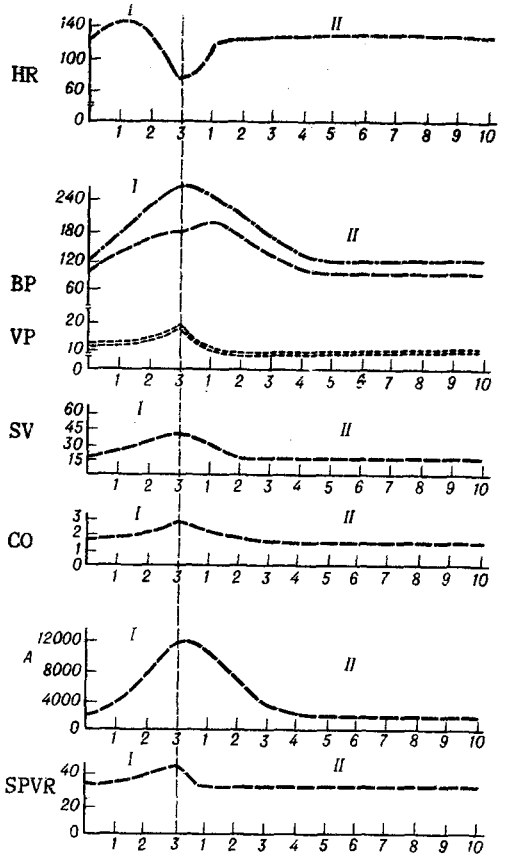

Fig. 2. Changes in hemodynamics during asphyxia, with innervated heart.
Legend as to Fig. 1.

In our experiments cardiac failure developed by the 3rd minute of asphyxia, leading to an increase in VP, which was the same in both series. Bradyacardia appeared, and was much less marked in the experimental series than in the control. In the presence of myocardial hypoxia, to preserve its energy resources, the heart reduced its rate. However, self-regulation was disturbed in the denervated heart and it continued to work at a relatively high HR.

Previous investigations showed that the heart responds after denervation to excitation by an inappropriate strengthening of its work [2, 5]. In our experiments this did not happen during asphyxia to begin with, probably because of delay of the response to stimulation, and later because of the development of heart failure. However, at the first minute after asphyxia, the work of the heart increased variously in intensity. BP, A, SV, and CO all rose much more than in the control experiments during asphyxia. They then decreased. However, the inappropriate work of the heart during asphyxia and after its end probably led to overfatigue of the myocardium, which was accompanied by inhibition of the hemodynamic parameters, which was observed in the period after asphyxia.

Thus the denervated heart does not raise HR during asphyxia and only very slowly achieves an increase in BP, SV, and A. Moreover, self-regulation of its work is depressed and the action of mechanisms aimed at protecting the myocardium against hypoxic damage is retarded. In the first minutes after asphyxia there is a sharp increase in activity of the denervated heart, which is not determined by the needs of the body. The uneconomic work of the denervated heart during asphyxia and the inappropriate activity in the period after asphyxia lead to inhibition of its function, and normalization of the hemodynamics after 3 min of asphyxia takes place 6-10 times more slowly than in the innervated heart.

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EFFECT OF DALARGIN ON PROLIFERATION OF THE GASTRIC EPITHLIUM DURING REPEATED EXPOSURE TO STRESS

S. S. Timoshin, S. I. Shvets, M. I. Radivoz, A. G. Aleksandrovich, and E. I. Mel'nik

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Dalargin, a synthetic analog of Leu-enkephalin, has a broad spectrum of biological activity [8]: it accelerates physiological and reparative regeneration [9, 10], has an immunomodulating action [13], and possesses antistress activity [8]. Dalargin depresses poststress ulcer formation [6]. According to the results of our previous investigations, this property of dalargin is realized through preservation of noradrenalin reserves in the gastric tissue, reduced accumulation of lipid peroxidation products in the tissues, weakening of poststress depression and activation of compensatory proliferative cell division in the epithelium of the pyloric part of the stomach, in response to a single exposure to fixation stress [12]. In our previous investigations we found that dalargin can increase the histamine content in the gastric tissues, and this is accompanied by lowering of the blood histamine concentration [1]. According to one view [15], this trend of histamine metabolism promotes activation of reparative regeneration in the gastric mucosa.

The aim of this investigation was to determine the effect of dalargin on DNA synthesis in the epithelial cells of the mucosa of the pyloric part of the stomach during repeated exposure to various kinds of stress, and also to evaluate the role of histamine in the regulation of cell division of the gastric epithelium under these conditions.

EXPERIMENTAL CONDITIONS

Experiments were carried out on female albino rats weighing 160-190 g. Fixation stress was produced by immobilizing the animals in the supine position by the method described previously [11]. Hypoxic stress was created by elevation

*Deceased.

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