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Central Circulation in Rats with Different Tolerance to Acute Blood Loss

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Study of the dynamics of cardiac output in rats with different tolerance to acute massive blood loss showed that the pumping ability of the heart remains intact during the entire posthemorrhagic period in all high-resistant and in 65% low-resistant rats. In 35% rats that were low-resistant to blood loss, the cardiac output deficiency syndrome developed after cessation of bleeding against the background fall in arterial pressure and a decrease in the hepatic blood flow, which are the signs of rapid variant of the dysfunction produced by acute blood loss.

Key Words: *blood loss; tolerance to blood loss; ultrasound; cardiac output*

In pathophysiology hemorrhagic shock is considered as a result of circulatory insufficiency [10]. The state of cardiovascular system after acute blood loss was studied in detail [6,11-14]. However, little attention was paid to the individual resistance to a single massive blood loss followed by hypoxia [1,6,7], which is reflected in unified approach to the treatment of patients with shock caused by blood loss and partially accounts for unsuccessful treatment of severe posthemorrhagic hypotension in some patients in which the well-known effective preparations could drastically aggravate hemodynamics and sometimes lead to fatal outcome [9,10]. We have shown that rats with different tolerance to acute blood loss evaluated by the lifetime after a single massive blood loss of the standard volume principally differ from each other in the type of reaction of systemic arterial pressure (AP), hepatic and cerebral blood flow, and portal microcirculation [3-5].

We used constant ultrasonic Doppler monitoring to study the systemic hemodynamics: AP, cardiac output, total peripheral vascular resistance (TPVR), heart rate, and portal blood flow after acute blood loss in rats with different tolerance to a single loss of a great volume of blood. Cardiac output was measured in a closed thorax using an ultrasonic intravascular blood flow sensor.

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MATERIALS AND METHODS

Experiments were performed on 56 male Wistar rats (200-250 g) under Urethane anesthesia (1.25 mg/kg intraperitoneally). AP in the femoral artery was measured with a micromanometer. Blood flow rate was measured in the ascending aortic arch with the help of a 0.6 mm ultrasound catheter inserted into the right carotid artery. The transducer was made of a miniature piezo crystal working at 26.8 MHz [7]. To measure TPVR (mm Hg/cm/sec), the blood flow signal from the ascending aortic arch was fed into an analog-to-digital converter. An electronic device measured the dynamics of the stroke volume and cardiac output. The heart rate (beats/min) was recorded with a cardiotachometer triggered by the pulse wave of aortic blood flow. Linear velocity and volume blood flow rate in the hepatic portal vein

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were measured with the use of a bandage-type ultrasonic sensor [5]. An acute blood loss was attained by a single bloodletting from the femoral artery in the amount of 2.5% body weight for 10 min. The observation period was determined by the lifetime of a rat.

The data were analyzed by the Fisher-Student test. The tolerance of the rats to acute blood loss was assessed by the lifetime after cessation of bleeding and by the posthemorrhagic dynamics of AP and portal blood flow.

RESULTS

Irrespective of individual tolerance to blood loss, AP, TPVR, and portal blood flow decreased in all the rats during a single rapid bloodletting. By the end of bleeding, AP in all the rats was 25.71±8.86 mm Hg, while TPVR and blood flow rate did not exceed 30% of the initial level. By contrast, changes in cardiac output in this period were not uniform. In some rats cardiac output changed after removal of first milliliters of blood: there were incidental increases in the aortic blood flow, stroke volume, and cardiac output which were followed by their normalization. By the end of bleeding, cardiac output decreased in most rats, although to a lesser degree than AP and portal blood flow, while in some rats it remained at a subnormal level. In the majority of rats the heart rate decreased by 27.8±15.87 beat/min, and in 30% rats a minor tachycardia was observed.

The rats were subdivided into two groups according to the lifetime after the standard blood loss, the character of posthemorrhagic AP dynamics, and the blood flow. The rats with lifetime greater than 3 h, temporal posthemorrhagic AP rise, and blood flow restored to 70-80% of the initial level, the relative stabilization of these parameters before their irreversible fall during the terminal phase, comprised the group that was high-resistant (HR) to the blood loss (60%). Other rats (40%) had gradually decreased AP and blood flow without the compensatory phase and died 1.5 h after cessation of bleeding. They comprised the group of low-resistant (LR) rats with decompensated posthemorrhagic period.

Analysis of the posthemorrhagic dynamics of TPVR and cardiac indices in HR rats made it possible to divide them into 2 subgroups. In 70% HR rats, TPVR was markedly decreased during bleeding, but it started to rise after cessation of bleeding, although remaining lower than the baseline by 22.86±6.36%. In these rats heart rate decreased slowly, while aortic blood velocity, stroke volume,

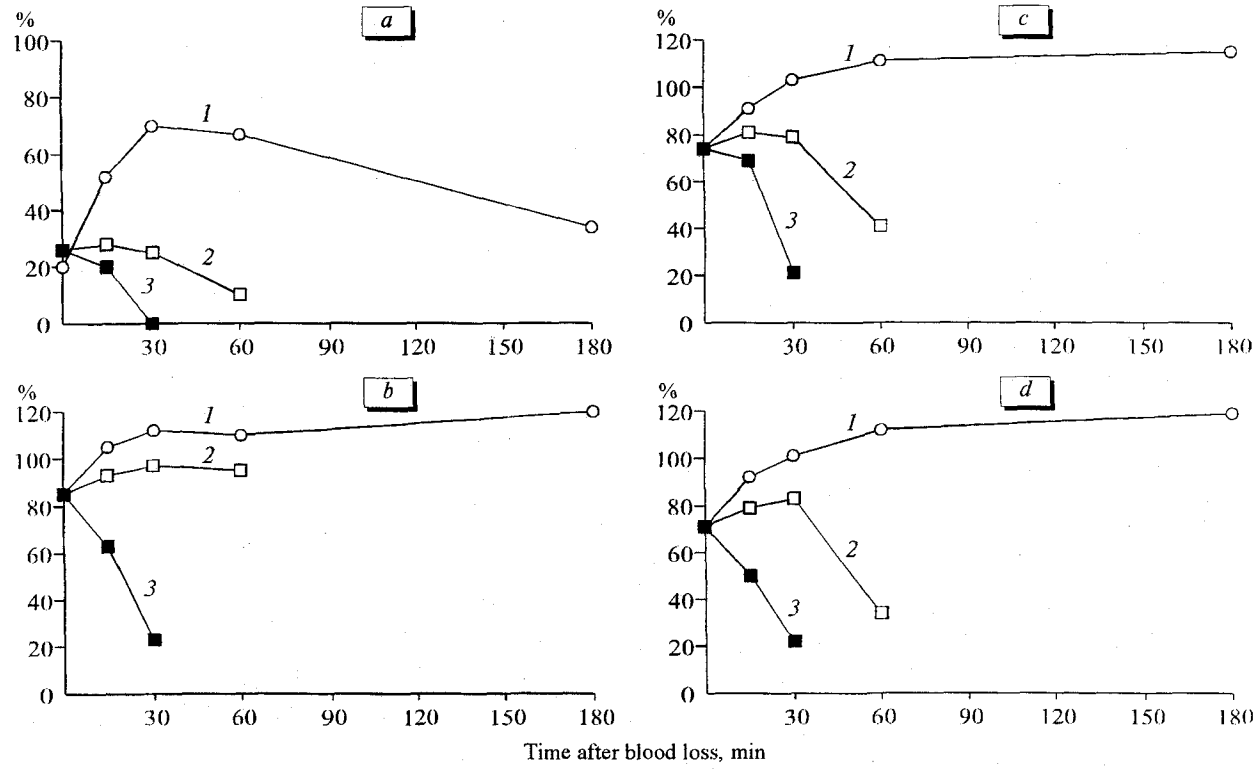

Fig. 1. Posthemorrhagic dynamics of central circulation in the rats with high (*1*) and low tolerance (*2*, *3*) to blood loss. Lifetime of low-resistant rats was lower than 1.5 h (*2*) or lower than 0.5 h (*3*). *a*) Arterial pressure; *b*) aortic blood flow; *c*) stroke volume, and *d*) cardiac output.

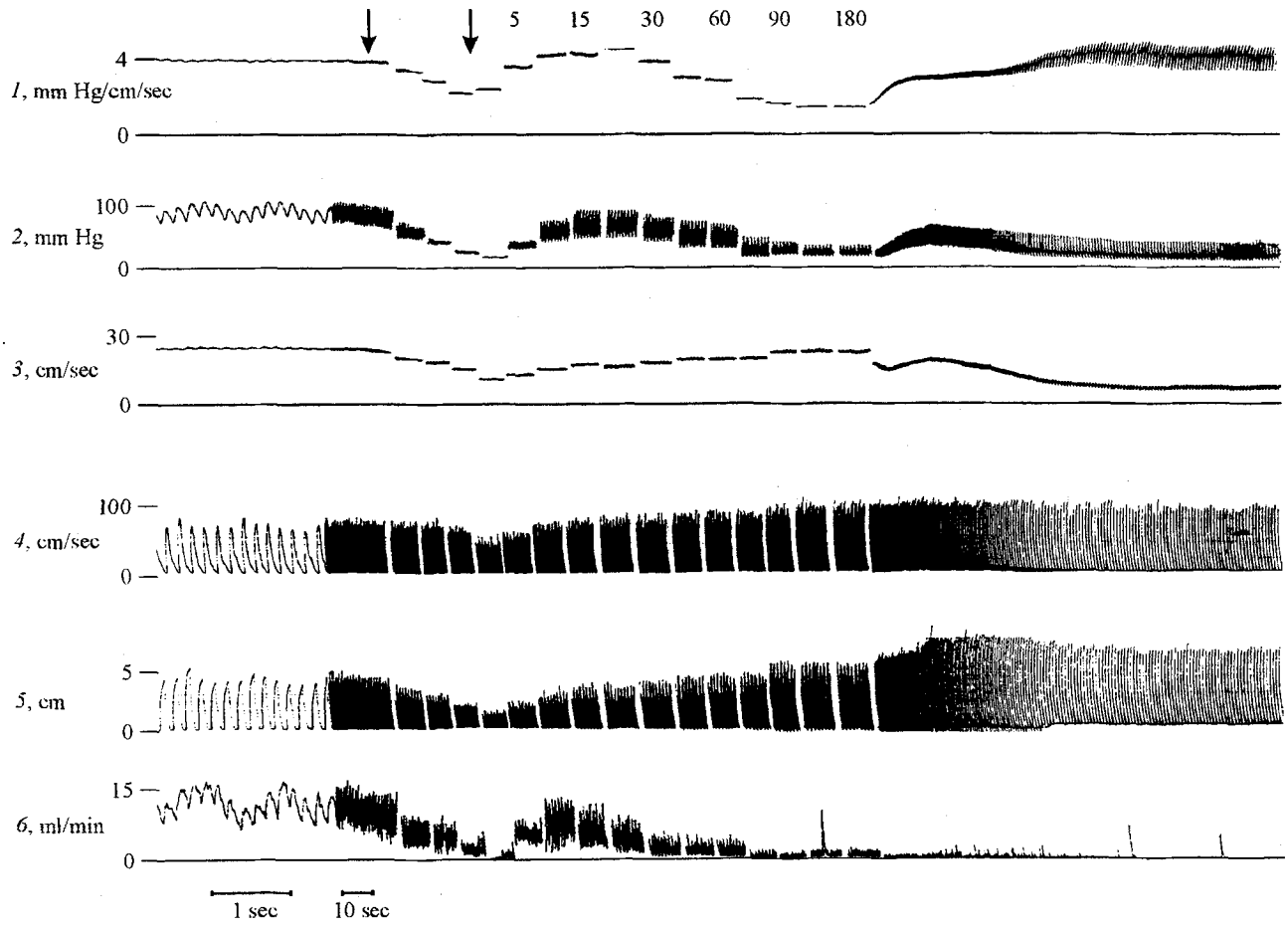

Fig. 2. Systemic hemodynamics and portal blood flow in rat with a high tolerance to blood loss and with posthemorrhagic elevation of the total peripheral vascular resistance (original records). Here and in Fig. 3: the arrowheads indicate the onset and cessation of bleeding while the upper numbers shows time after the end of bleeding (min). *1*) total peripheral vascular resistance; *2*) arterial pressure; *3*) cardiac output; *4*) linear velocity of blood in the ascending arch of aorta; *5*) stroke volume; *6*) blood flow in the portal vein.

and cardiac output were higher than the control by 20-25%. In the terminal phase of the posthemorrhagic period, the HR rats of this subgroup demonstrated an extra monotone increase in the cardiac output until the fatal outcome, and this increase was observed simultaneously with the second irreversible decrease in AP, blood flow, TPVR, and progressive bradycardia (Fig. 1). The lifetime in this subgroup was 233.18±42.68 min.

In 30% HR rats TPVR was not only restored in the posthemorrhagic period, but it exceeded the control value by 26.42±7.48% and remained at this level during the entire period of relative stabilization of AP and blood flow. As a rule, in such HR rats the aortic blood velocity, stroke volume, and cardiac output increased, but they never exceeded the initial level, while the heart rate dropped to 35.0±8.16 beats/min. In the terminal phase of the posthemorrhagic period characterized by the second irreversible fall of AP and blood flow, this subgroup of HR rats demonstrated a decrease in TPVR and progressive bradycardia. By contrast, the indices of cardiac performance slightly increased, this increase proceeding until the complete arrest of breathing (Fig. 2). The lifetime in the HR rats in this subgroup was 208.75±27.81 min.

The group of LR rats was also heterogeneous in the respect of the indices of central circulation, and it was also divided into 2 subgroups. In LR rats of the first subgroup (65%), cessation of bleeding was followed by some increase in stroke AP, the mean AP increase was no more than 10-15% of the initial level. The aortic blood velocity restored to the subnormal level and slightly decreased at the end of the terminal phase. In these rats the stroke volume and cardiac output increased, but to a lesser degree than in HR rats, being less than the control level by 20-30% in most of them (Fig. 1 and 3). They had increased TPVR, which, however, did not reach the initial values; the heart rate was unstable. All LR rats of the first subgroup demonstrated progressive bradycardia and a decrease in cardiac output

and stroke volume at the end of the posthemorrhagic period. Lifetime in this subgroup was 72.85± 12.86 min. In LR rats of the second subgroup (35%), the aortic blood velocity and stroke volume decreased irreversibly after cessation of bleeding (Fig. 1). These rats demonstrated the periods of rise of the stroke volume and cardiac output by 15-20% against the background decrease in these cardiac indices, and they had unstable heart rate. TPVR in some rats of the second subgroup remained decreased, while it markedly exceeded the initial level in other rats of this subgroup. These rats died during the first 30 min after cessation of bleeding.

This study showed that the majority of LR rats did not differ from HR rats in the respect of changes in cardiac indices, in contrast to posthemorrhagic AP dynamics, portal blood flow, and microcirculation [3,5]. According to modern data, the pumping action of the heart is preserved in all HR rats and in 65% LR rats until the fatal outcome, which agrees with the data on functional isolation of the heart from the nervous control during hypoxia. One of the reasons for the revealed lower cardiac output in LR rats with decompensated blood loss may be the development of irreversible generalized posthemorrhagic constriction of microvessels [5], which prevents the regulation of fluid balance at the microcirculatory level by hydrostatic and colloid-osmotic gradients. In such animals it leads to disturbances in autohemodilution as well as in posthemorrhagic restoration of AP and volume of circulating blood. About one-third of LR rats developed the cardiac output deficiency syndrome after cessation of bleeding, which developed against the background of irreversible decrease in AP, blood flow, and sustained constriction of portal microvessels [5], resulting in a rapid development of disturbances produced by acute blood loss. Thus, the therapeutic strategy for LR species of this subgroup should differ from treatment of posthemorrhagic states of the

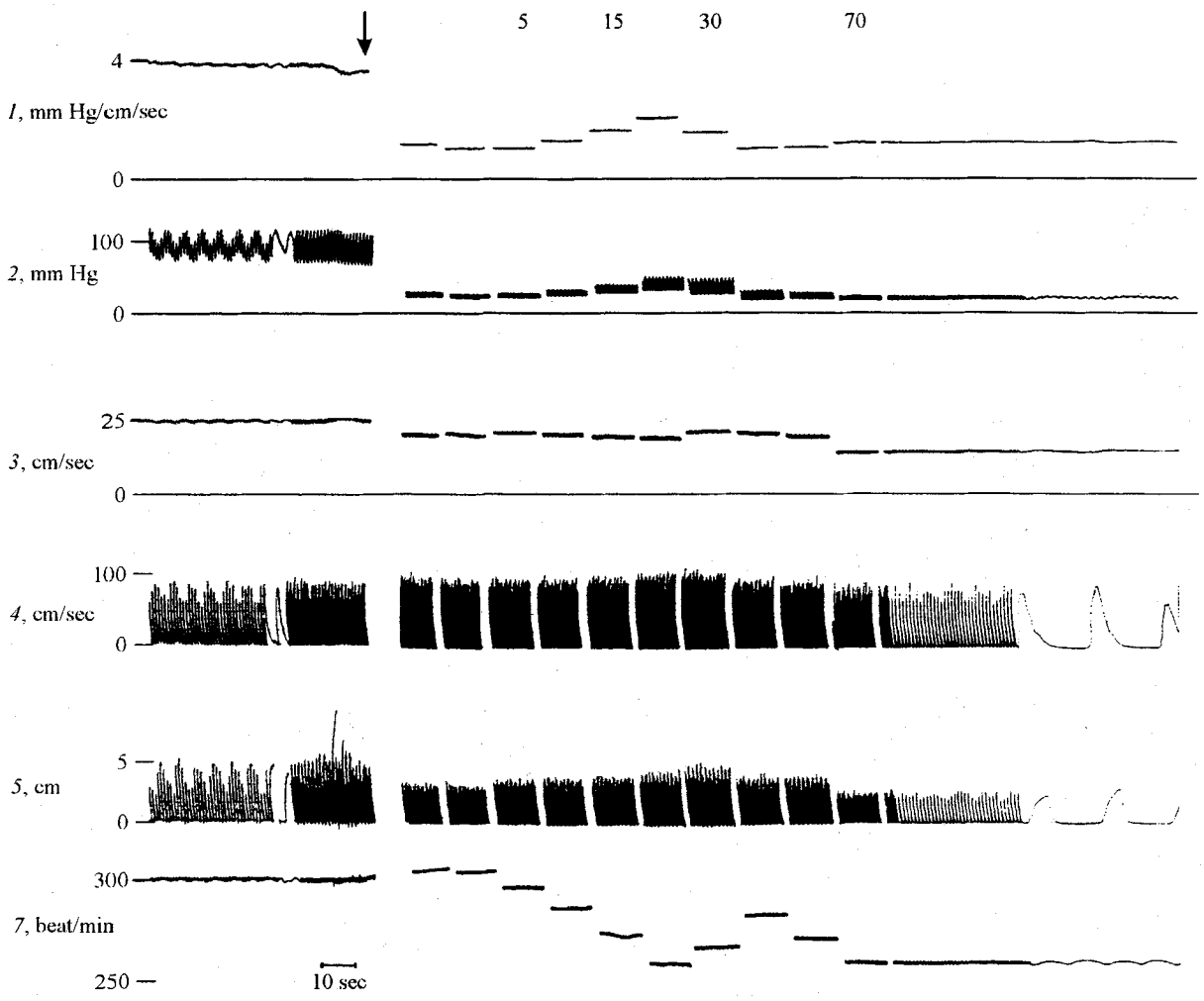

Fig. 3. Posthemorrhagic changes in arterial pressure, cardiac output, stroke volume and the heart rate (7) in low resistant rats with lifetime 75 min (original recordings).

species with other types of dysfunction development produced by an acute blood loss, and it needs intensive therapy for inotropic support to the heart and for elimination of pathologic constriction of the microvessels.

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