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CHANGES IN HEMODYNAMICS AND OXYGEN SUPPLY DURING MASSIVE INJECTION OF HOMOLOGOUS BLOOD THROUGH AN ARTERIOVENOUS SHUNT

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KEY WORDS: blood transfusion; complications of blood transfusion.

Injection of an excess of homologous blood during major operations on the heart, lungs, and great vessels causes an increase in the number of posttransfusion complications. These complications, affecting the recipient, exhibit considerable polymorphism and have been called the "massive transfusion syndrome" or "homologous blood syndrome" [1-8].

One of the main manifestations of this syndrome is a disturbance of the general hemodynamics and of the oxygen supply to the recipient at different levels. It was therefore decided to study these disturbances experimentally in order to elucidate certain aspects of its pathogenesis. An arteriovenous shunt [8] was used as experimental model of the extracorporeal circulation in this investigation.

EXPERIMENTAL METHOD

Experiments were carried out on 42 dogs weighing 9-20 kg (nine recipients and 33 blood donors). The animals were first heparinized (3 mg/kg) and anesthetized with pentobarbital (30 mg/kg). Blood was obtained from the donors on the day of the experiment by bleeding from the femoral artery into a vessel containing heparin (50 mg/liter). Before the blood was taken the blood of the donors and of the donor and recipient was cross-matched. The total volume of donors' blood to be exchanged was introduced into a vessel connected to the femoral artery and vein. Normovolemic injection of freshly prepared homologous blood (taken from at least three donors) was then carried out into the experimental dogs by means of an arteriovenous shunt. Exchange of blood took place on account of the arteriovenous pressure gradient at a rate of 90-110 ml/min. The volume of donors' blood injected in all the experiments was 110-120 ml/kg body weight of the recipient. The duration of perfusion was 30 min.

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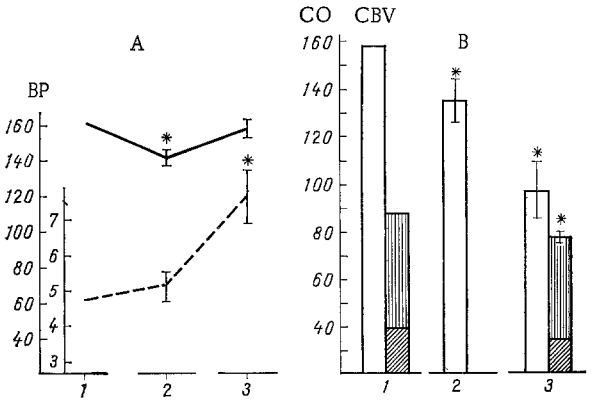

Fig. 1. Changes in BP, TPVR, CO, and CBV during massive injection of homologous blood by means of an arteriovenous shunt. Abscissa, stages of experiment: 1) initial data, 2) immediately after massive injection of homologous blood, 3) 2 h after injection of homologous blood; ordinate: A: continuous line BP (in mm Hg), broken line TPVR (in dynes·sec·cm^{-5}); B: unshaded columns — CO (in ml/min/kg), shaded columns — CBV (in ml/kg); vertical shading — plasma volume, oblique shading — erythrocyte volume. Asterisks denote statistically significant deviations ($P < 0.05$).

The arterial blood pressure (BP) and central venous pressure in the experiments were determined on the Mingograph-81 apparatus (from Elema), the circulating blood volume (CBV) by the dye (T-1824) dilution method, the total O_2 consumption on the Lex-O_2-KON apparatus (from Lexington), and the concentration and partial pressure of O_2 in arterial and mixed venous blood on the Gas-Check-937 apparatus (from AVL). The cardiac output (CO) by Fick's method, the arteriovenous O_2 difference, the degree of saturation of arterial and venous blood with O_2, and the total peripheral vascular resistance (TPVR) were calculated. The parameters studied were determined in the initial state, immediately after perfusion, and 2 h later. The numerical results were subjected to statistical analysis by the difference method.

EXPERIMENTAL RESULTS

Values of the main indices of the hemodynamics are illustrated in Fig. 1. Immediately after the end of perfusion the mean value of BP fell ($P < 0.01$). However, after 2 h BP was almost completely restored. The level of BP depends on two variables: CO and the resistance of the vessels to the blood flow. Analysis of CO and TPVR showed that 2 h after perfusion CO was reduced by 39% compared with its initial value, and this activated the principal compensatory mechanism aimed at maintenance of BP, namely spasm of the vessels and an increase in TPVR (by 168%). Parallel to the fall in CO, the stroke volume of the heart fell from 0.72 to 0.5 ml/kg. The heart rate of the experimental animals was not significantly changed, although a tendency for it to become slower was observed. By this period TPVR was 11% lower than initially ($P < 0.05$). The decrease in TPVR took place both on account of sequestration of the liquid part of the blood (plasma) and on account of the number of circulating homologous erythrocytes. It is possible that the mild degree of hypovolemia which was found could have been one of the many causes of worsening of the hemodynamic indices. It should be pointed out that in three cases (about 30%) acute circulatory disturbances of the shock type were found. They occurred in the initial stage of perfusion and were transient in character. These disturbances were probably connected with redistribution of the blood and have been described previously during experiments with excessive injection of homologous blood [7, 8].

To interpret the oxygen supply to the recipient a simplified diagram of the respiratory function of blood was used (Fig. 2). This not only gives a complete picture of the quanti-

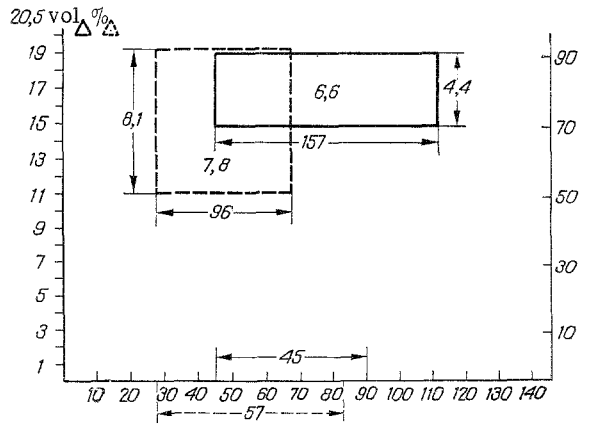

Fig. 2. Oxygen supply to recipient before injection of massive doses of homologous blood through an arteriovenous shunt (continuous line) and 2 h after injection (broken line). Abscissa, pO_2 (in mm Hg); ordinate: left — O_2 concentration (in vol.%), right — degree of saturation of blood with O_2 (in %). Numbers within rectangles show O_2 consumption (in ml/kg/min). Top line of rectangles shows O_2 concentration and saturation in arterial blood, bottom line of rectangles — the same in venous blood. Numbers below rectangles show CO (in ml/min/kg).

tative and qualitative aspects of the tissue O_2 supply, but also takes into account the basic indices of the total gas exchange and hemodynamics and, what is particularly important, it reflects their interdependence.

As Fig. 2 shows, in the initial state the animals' initial O_2 consumption was 6.6 ml/min/kg body weight. This quantity of O_2 was supplied by a CO of 157 ml/min/kg, with an arteriovenous O_2 difference of 4.4 vol.%. The arterial blood contained 18.7 vol.% of O_2. Its oxygen saturation was normal (92%) allowing for the general anesthesia; the partial pressure of O_2 in it also was normal, namely 90 mm Hg. The mixed venous blood contained 14.7 vol.% of O_2 and its oxygen saturation was up to 72%. The partial pressure of O_2 in it was 45 mm Hg, which is quite sufficient for normal diffusion of oxygen from the capillaries into the tissues. Moreover, even greater reserves of unused O_2 remained in the blood (see Fig. 2 — the whole of the free space below the rectangle).

The diagram reflecting the respiratory function of blood 2 h after exchange normovolemic perfusion already differed in its external appearance from that in the original state. The rectangle now had the shape of a square, indicating changes in O_2 transport from the lungs to the tissues. In fact, by this time CO had fallen from 157 to 96 ml/min/kg. The quantity of O_2 assimilated by the recipient was increased, but not statistically significantly (7.8 ml/kg/min). The question naturally arises: What compensatory powers were used by the recipient to maintain the total O_2 consumption at its initial level? The oxygen capacity, the O_2 concentration in arterial blood, and its O_2 saturation remained at the previous level, whereas the mixed venous blood contained only 10.7 vol.% of O_2 and its partial pressure of oxygen fell to 28 mm Hg, much below that required for normal diffusion of O_2 from the capillaries into the tissues. The arteriovenous O_2 difference was almost twice that in the initial state. The essential needs of the recipient for O_2 were thus satisfied by an increase in its utilization from the incoming blood. On the diagram this led to a shift of the venous point downward and to the left, and, consequently, to a fall in pO_2 in the venous blood, thus worsening the conditions for diffusion of O_2 from the capillaries into the tissues. This method of maintaining O_2 transport has comparatively limited possibilities and is observed in cases when the weakened heart cannot increase its work.

During normovolemic exchange perfusion with homologous blood, carried out very rapidly, cardiac failure was observed to develop. Compensation of hypoxia took place entirely through

increased utilization of O_2 from the blood, and this in turn led to exhaustion of the O_2 reserves and to a critical fall of pO_2 in the venous blood. This picture is evidence of a congestive type of circulation and the development of circulatory hypoxia.

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ACTION OF VARIOUS DOSES OF PHYTOMITOGENS ON BLOOD LYMPHOCYTE PROLIFERATION IN SCHIZOPHRENIA

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It was shown previously [1-4] that lymphocytes in the blood of schizophrenic patients are less able to proliferate in response to stimulation by phytohemagglutinin (PHA) and concanavalin A (con A). This phenomenon may be based on a number of factors, including a shift of the optimal dose of stimulator in this disease into the region of lower or higher concentrations of mitogen, as is observed in ataxia-telangiectasia, Bruton's disease, and systemic lupus erythematosus [5-7].

The aim of the present investigation was to compare the proliferative activity of lymphocytes, stimulated by different doses of PHA and Con A, of healthy subjects and patients with schizophrenia.

EXPERIMENTAL METHOD

Lymphocytes from 24 healthy subjects aged from 18 to 49 years and from 19 patients with schizophrenia (10 with a continuous-progressive and 9 with an episodic-progressive type of course), aged from 18 to 59 years, were tested. Blood was taken from the patients and healthy subjects into test tubes with heparin (10 i.u./ml). After sedimentation of the erythrocytes the plasma was drawn up into a Pasteur pipet and $1 \cdot 10^6$ lymphocytes were cultured in 1 ml of medium containing 20% autologous serum and 80% Eagle's medium with glutamine, for 72 h at 37°C. To stimulate the lymphocytes the following concentrations of PHA and Con A were used: 5, 10, 25, 50, 100, and 200 μg/ml. Two hours before the end of culture 1 μCi thymidine-^{3}H (specific radioactivity 19.6 Ci/mmole) was added to each flask. The cells were transferred to membrane filters (Hawg, 0.45 μ) and treated successively with physiological saline, 5% TCA, and 96° alcohol. The radioactivity of the samples was measured on a Mark II liquid scintillation counter. Proliferative activity was calculated on the basis of radioactivity in three parallel cultures.

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