SUCCESSIVE REPLACEMENT OF LETHAL BLOOD LOSS IN DOGS WITH POLYGLUCIN AND PERFLUOROCARBON EMULSION

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The study of perfluorocarbon (PFC) emulsion as the gas-carrying basis for a blood substitute and oxygen carrier is of great interest. A PFC emulsion alone cannot maintain the hemodynamics for a long time because proxanol, the only component of the emulsion to possess an oncotic pressure, leaves the blood stream rapidly [6]. PFC emulsion is therefore usually injected together with colloidal solutions with hemodynamic action. For instance, in the case of the preparation Fluosol DA (from Green Cross Corporation, Japan), hydroxyethyl-starch is added immediately before infusion [6]. As plasma expander for the Soviet PFU emulsion (perfluorodecalin—perfluorotripropylamine in the ratio of 7:3), we have used polyglucin* (PG), an antishock plasma substitute widely used in clinical practice. Preliminary experiments *in vitro* showed that PG, added to PFC emulsion, does not disturb its stability if the resulting mixture is constantly stirred in the presence of a small quantity of albumin. Clearly these conditions are entirely satisfied in the blood stream.

Guided by these considerations, and also by the absence of advantages to be obtained by mixing the two preparations before intravenous infusion over infusing them separately, we decided on successive injection of PG and of PFC emulsion to replace lethal blood loss in dogs. The aim of this investigation was to study the state of the hemodynamics and gas exchange under these conditions.

EXPERIMENTAL METHOD

Experiments were carried out on six mongrel dogs of both sexes weighing 12-14 kg, bled to the extent of 50 ml/kg body weight (50-60% of the circulating blood volume) by the method in [1]. The animals were under neuroleptanalgesia (total dose of fentanyl per experiment 0.028 mg/kg, of droperidol 1.4 mg/kg). During manipulations of the femoral vessels, additional local anesthesia with procaine was used. After the blood pressure had fallen to 0-5 mm Hg, PG was injected (35 ml/kg body weight and the oxygen supply was connected (85%); 10 min after the end of infusion of PG, PGF emulsion (25 ml/kg) began to be infused at a rate of 10-15 ml/min. The oxygen capacity of 24 vol. % of emulsion at 760 mm Hg and 37°C was 11 vol.%. The arterial pressure (Pa), heart rate (f), cardiac output (Q), and circulating blood volume (V), measured by the dye dilution method (Cardio-Green), were recorded. The oncotic pressure of the plasma (P_{onc}) was determined on a "Knauer" osmometer with "fine" membrane. Plasma was obtained by centrifugation (4000g) for 15 min. The PFC concentration (Ft) in the blood was determined on an F-21 chromatograph from Perkin-Elmer (Sweden). Blood gases were determined by "Lex-O-Con" (USA) and AVL-940 (Switzerland) gas analyzers. The degree of hemodilution was monitored as hemoglobin concentration, measured by the hemoglobin cyanide method. Samples of arterial blood were taken from the femoral artery and of venous blood from the right ventricle. The oxygen demand (rO_2) was calculated as the product of Q and the arteriovenous oxygen difference $(A - V)_{O_2}$, and the systemic oxygen transport was calculated as the product of Q and the oxygen concentration in the artery (caO_2). The individual contribution of the emulsion to the total oxygen capacity was determined as the product of the coefficient of solubility of oxygen in the PFC used and of Ft and the given pO_2 [7]. The results were subjected to statistical analysis.

*A Soviet dextran equivalent.

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TABLE 1. Principal Parameters of Hemodynamics before and after Successive Replacement of Blood Loss by PG and PFC Emulsion (M ± m, n = 6)

Parameter studied	Initial value	After replacement of blood loss				
		10 min		10 min	2 h	24 h
		PG	PFC			
Pa, mm Hg	122±3	116±6	126±6	126±7	120±5	—
f, beats/min	126±18	144±17	158±14	155±16	167±16	—
Q, ml/kg·min	176±11	263±20*	369±30*	224±20	177±5	—
V, ml/kg	91±5	81±4	101±7	85±6	72±4*	—
P_{onc}, mm Hg	19,0±1,1	23,3±1,2	26,4±2,0*	21,0±0,9	20,1±0,8	15,8±1,8

Legend. *P < 0.05 here and in Table 2.

TABLE 2. Parameters of Gas Exchange before and after Consecutive Replacement of Blood Loss by PG and PFC Emulsion (M ± m, n = 6)

Parameter studied	Initial value	After replacement of blood loss			
		10 min		10 min	2 h
		PG	PFC		
Hb, g%	14,9±0,7	9,0±1,1*	6,4±1,0*	7,0±1,1*	9,7±1,0*
caO_2, vol. %	19,1±1,8	11,7±0,9*	9,2±0,5*	11,9±0,9*	13,7±0,6*
$(A-V)O_2$, vol. %	5,4±0,8	3,5±0,6	3,3±0,6	6,3±0,7	6,7±0,7
PaO_2, mm Hg	106±3	445±11*	495±23*	491±9*	500±6*
PvO_2, mm Hg	46±2	55±1	119±20*	54±5	47±4

EXPERIMENTAL RESULTS

Infusion of PG and the emulsion after blood loss led to restoration and stabilization of Pa and f. The level of V at this time was very slightly higher than initially, but after 2 h it was about 80% of initially. P_{onc} after infusion of the emulsion was 38% higher than initially, but 1 h later it was back to normal, at which level it remained until the end of the experiment. After 24 h it was approximately 83% of the initial value (Table 1). The time course of the changes in P_{onc} described above and also a small decrease in the level of V toward the end of the period of observation evidently depends on the properties of proxanol and the low-molecular-weight fractions of PG, which, since they possess a considerable oncotic pressure, leave the blood stream rapidly [1, 6]. After infusion of PG the value of Q rose by 1.5 times, but injection of the emulsion caused an increase in this parameter by 2.5 times compared with initially, which is partly attributable to temporary hypervolemia (the volume of blood substitute was 20% greater than the volume of blood lost). After 2 h Q had returned to its initial value.

Switching the animals to breathing oxygen after infusion of PG was accompanied by a rise of pO_2 in the artery to 445 mm Hg, and after the infusion of PFC emulsion there was an additional rise to 500 mm Hg (Table 2). Calculations showed that infusion of traditional plasma expanded under similar conditions gave an addition of not more than 1.2 vol.% to the total oxygen capacity). One of the principal parameters of homeostasis, namely rO_2, was restored after replacement of the lost blood, and subsequently increased (Fig. 1). This may have been due to improvement of the microcirculation [2, 8].

What contribution to the total oxygen balance is made by the emulsion? Calculations showed that about 75% of the total rO_2 and 34% of pO_2 were provided by the infusion of PFC emulsion. This high contribution of the emulsion to satisfaction of the oxygen demand of the body can evidently be explained by the high values of pO_2 in the vein (119 mm Hg), which were observed previously [3-5]. At that pO_2 level the Hb dissociation curve is shifted to the right, and this interferes with the giving up of oxygen by the erythrocytes, so that only oxygen of the PFC emulsion and plasma is utilized. After 2 h, when Q had fallen to its initial level and oxygen utilization was increased, the emulsion accounted for 37% of rO_2 and 24% of qO_2 (Fig. 1).

All the experimental animals survived.

After successive injection of PG and of 24 vol. % of PFC emulsion, and during inhalation of medical oxygen, the principal parameters of the hemodynamics disturbed as a result of blood loss, were restored in lethally exanguinated dogs and maintained at stable levels, the

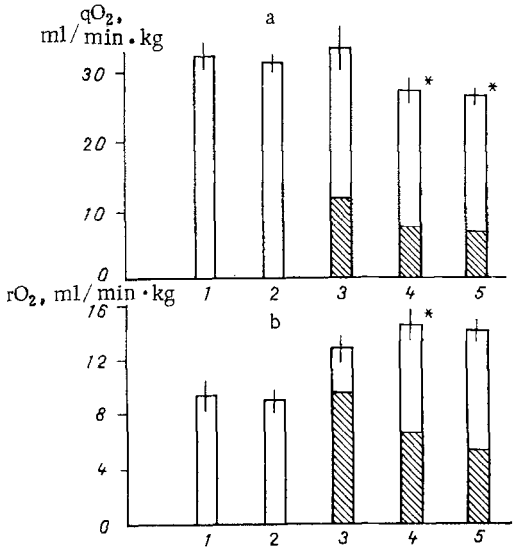

Fig. 1. Systemic transport and consumption of oxygen before and after successive replacement of lethal blood loss by PG and PFC emulsion (M ± m, n = 6). 1) Initial data; 2) 10 min after infusion of PG; 3) 10 min; 4) 1 h; 5) 2 h after infusion of PFC emulsion. *P < 0.05. Shaded area of column denotes individual contribution of PFC emulsion.

oxygen capacity of the blood was increased by 3 vol. %, pO_2 in the arteries was raised to 500 mm Hg, and the total oxygen consumption also was increased.

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