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Perftoran is reliable alternative of blood transfusion

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The first Russian gas-carrier blood substitution named Perftoran consist of perfluorocarbonic substances and stabilizers. Perftoran carries out oxygen delivery by capillaries and supplies body compartments with oxygen by the smallest capillaries, enlarging effective square of vessels and minute circulatory volume. Perftoran is only drug demonstrates a high immediate effect in the treatment of fat embolism at once in contrast with other drugs which act within 12-18 hours. The infusion of Perftoran emulsion raises steadiness of animals to the bleeding in experiments, supplies the high level of cardiac output and systemic oxygen circulation. Since 1986 Perftoran is used for treatment of acute and chronic hypovolemia; disorders of microcirculation, impairment of gases interchange, metabolic disorders of different etiology (infections, sepsis, respiratory distress syndrome of adults, cerebral circulation impairment, disseminated intravascular coagulative syndrome). Different approaches for Perftoran usage are: protection of graft (in order to transplantation prepare); in apparatus of artificial blood circulation; regional perfusion of heart and limbs; lavage of wounds and lungs. Perftoran has small contraindications (hemophilia) and a few of adverse effects (allergic reactions, tachycardia, hypotension).

Key words: blood substitutes, gas transport, perfluorocarbons, Perftoran, artificial oxygen carriers.

Blood Bank Transfus Med 2003; 1(2): 93-95

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The transfusion of allogenic blood components is associated with certain risks including potential complications in the form of incompatibility reactions, influence on the recipient’s immune system and transfer of infectious agents.

Most of the wide-spread blood substitutions do not provide the basic function of the human blood which is the oxygen delivery to the body compartments. Throughout the last decades, two ways in the problem of gas-transport blood substitutions searching have been discussed. Firstly, it is offered to use the modify forms of hemoglobin as a reliable gas carrier. The second way was to have perfluorocarbonic substances (PFCs) in role of substrate for delivery of gases.

In contrast to hemoglobin, PFCs do not make chemical combination with oxygen, but dissolves it as the same as the other gases. PFCs create the linear connection. The level of oxygen solubility has direct proportion to the partial pressure of oxygen (in contrast to dissociation curve of oxyhemoglobin).

PFCs are the part of intravenously administrated emulsion which considered to be biologically inertness, i.e. PFCs don’t cause any metabolic changes in the body. PFCs’ particles are rapidly removed from circulation within 4-12 hours. They accumulate in lungs, spleen and liver and excreted with respiration in further.

PFCs for i. v. administration consist of proper PFCs; salt composition; chemicals provided emulsion stability.

The choice of PFCs are determined by its oxygen capacity, the time of semi-excretion and body retention. The oxygen capacity depends on chemical structure of fluorocarbonic substance, concentration of emulsion and the size of PFC particles.

PFCs as the blood substitutions should comply following demands:
• sufficient oxygen capacity;
• absence of tissues’ accumulation;
• high purification;
• absence of side effects.

The first Russian gas-carrier blood substitution named Perftoran has been created in the Institute of Theoretical and Experimental Biophysics Russian Academy of sciences (Pushchino Moscow region 142290 Russia)

At this time Perftoran is allowed to the clinical use

**Perftoran consist of:**
Perfluorodecaline - 13.0 g
Perfluoromethylcyclohexilpiperidine - 6.5 g
Proxanol 268 - 4.0 g
Sodium Chloride (NaCl) - 0.6 g
Potassium Chloride (KCl) - 0.039 g
Magnesium Chloride (MgCl2 *6 H2O) - 0.019 g
Sodium Hydrocarbonate (NaHCO3) - 0.065 g
Sodium Hydrophosphate (NaH2PO4*2 H2O) - 0.02 g
Glucose (C6H12O6 *6 H2O) - 0.2 g
Water for injection - to 100 ml

**Perftoran Characteristics**
Oxygen solubility - 6-7 vol.%
Relative viscosity - 2.5 sP
Osmolarity - 280-310 mOsm /l
pH - 7.2-7.8

**It was established, Perftoran**

• carries out oxygen delivery by capillaries;
• supplies body compartments with oxygen by the smallest capillaries, enlarging effective square of vessels and minute circulatory volume;
• provides the most effective conditions for oxygen releasing from erythrocytes in the tissues by increasing the constant of oxygen and carbon diffusion in the emulsion by means of change of oxyhemoglobin curve of dissociation;
• reduces viscosity of erythrocytes-plasma-emulsion’s system and thus it lets to grow cardiac output;
• protects by stabilization of transmembrane gradients of potassium, calcium, hydrogen and water;
• increases cell membranes firmness to the osmotic, chemical, mechanical damages;
• reduces haemolysis, aggregability and viscosity of erythrocytes;
• is an effective fluid absorbent with an active absorption surface equals 600 m2 for 100 ml of solution. Perftoran is only drug demonstrates a high immediate effect in the treatment of fat embolism at once in contrast with other drugs which act within 12-18 hours.
• has an antioxidant effect;
• activate hepatic detoxification system;
• does not make toxic effects and mutagenic, cancerogenic, embriotoxic effects either;

The infusion of Perftoran emulsion raises steadiness of animals to the bleeding in experiments, supplies the high level of cardiac output and systemic oxygen circulation.

**Indications and usage**

• acute and chronic hypovolemia;
• disorders of microcirculation, impairment of gases interchange, metabolic disorders of different etiology (infections, sepsis, respiratory distress syndrome of adults, cerebral circulation impairment, disseminated intravascular coagulative syndrome);
• protection of graft (in order to transplantation prepare);
• usage in apparatus of artificial blood circulation;
• regional perfusion of heart and limb;
• avage of wounds and lungs.

The half-life time of Perftoran circulation is 24 hours. Superfiically active substances leave the body throughout the kidney within 24 hours. PFCs are not metabolized in the human body and excrete completely within 18-24 months.

Perftoran is contraindicated in hemophilia and may be used in pregnancy only in life-threatening situations.

Adverse effects are possible in Perftoran infusion, that are allergic reactions (urticaria, itching, redness of skin), tachycardia, hypotension, fever, headache, dyspnea, retrosternal and back pain. In case of development of any complication the infusion should be immediately interrupted not to take the needle out of vein should start the critical care measures which consists of administration of antihistamine, steroid, vasopressive and other drugs used in anaphylaxy’s treatment. Perftoranis compatible with albumin, blood components, isotonic
sodium solution, glucose solution and antibiotics. Infusions of crystalloid solutions do not influence on properties of Perftoran. Colloid solutions abling to support osmotic pressure lead to swelling of middle-sized particles in Perftoran emulsion and therefore it changes to properties of Perftoran.

Before infusion it is mandatory to make compatibility test, which consists of slow administration of the first 15 drips, then infusion interrupts for 3 minutes, then following 30 drips are administrated and the infusion interrupted again for 3 minutes. In absence of sign of complications, infusion continues in usual way. Perftoran infuses intravenously dose is given 5-30 ml/kg (for adults) by steamly or drippy. Single and summary dose depends on severity of patient’s condition and age of patients. Effectiveness of Perftoran’s infusion can be increased if patient has oxygen inhalation simultaneously.

Storage time and keeping

Perftoran should be kept at -4 °C to -18 °C. It is recommended to thaw at room temperature and stored after thawing at 4°C within 2 weeks. After thawing Perftoran should be carefully homogenized and warm to 21-23°C before infusion. It is suitable for five times freezing/thawing procedure.

Storage time for Perftoran is 3 years at -4°C to -18°C and 2 weeks at 4°C.

Perftoran should be kept at the place can not be reached for children. It should not be used after expire date. It is forbidden to thaw at temperature above 30°C and to keep at temperature below -18°C.

Perftoran is put on the market in 50, 100, 200, 500 glass bottles.