Hemotherapy (pediatrics)

Hemotherapy is the replacement of a certain part of the blood which content is reduced in the circulation or its function is impaired. It is the transfer of biological material from the donor organism to the recipient organism. The goal is the maximum therapeutic effect with minimal risk.

A blood product is any medicinal substance prepared from human blood. Although blood and blood products are considered drugs, their therapeutic use has certain specifics, as hemotherapy is a type of transplant. At present, there is a tendency to produce and use blood products in the purest possible form, with a minimal admixture of other blood components.

Erythrocyte concentrate

General Information

Hematocrit erythrocyte concentration is usually 0.50–0.70, depending on the type of preparation, the volume of the *transfusion unit* (TU) is approximately 250 ml.

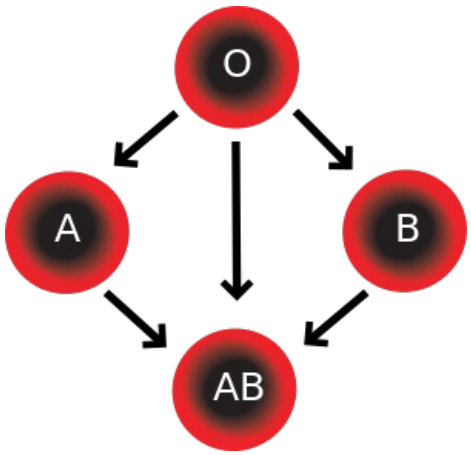
The erythrocyte concentrate must be of the same group in both the AB0 and Rh systems. The universal donor is group 0. In acute, life-threatening conditions, erythrocytes of group 0, Rh-negative can be administered. The universal recipient is group AB.

Applications

- for the application of erythrocytes, a universal donor is a blood group 0 donor, the universal recipient is a patient of blood group AB.
- sick 0 -> can 0,
- sick A -> can A or 0,
- sick B -> can B or 0,
- sick AB -> can AB or B or A or 0.

Side effects of erythrocyte concentrate

Immediate complications



AB0 compatibility

- **Circulatory overload:** symptoms are dry cough, feeling of heaviness in the chest, cyanosis, dyspnea. On examination, we find an increased filling of the jugular veins and symptoms of pulmonary oedema.
- **Haemolytic post-transfusion reaction** (incompatibility, erythrocyte damage): the most common cause is intravascular destruction of erythrocytes by transfusion recipient antibodies. Symptoms include severe chest and/or back pain, dyspnea, restlessness, febrile illness, chills, vomiting. This is followed by hypotension, only with the development of the shock state. If the patient survives the shock, jaundice, renal failure, DIC symptoms appear within 24 hours. Even 50 ml of incompatible blood is sufficient to induce this reaction.
- **Leukocyte and platelet antibody response:** repeated transfusions may induce the production of antibodies to leukocyte and platelet antigens. About 1/3 of patients with these antibodies may develop fever chills, chills, headache, erythema, cough, and chest pain 30 to 180 minutes after blood transfusion.
- **Non-haemolytic reactions:** chills, fever (caused by donor granulocytes), sepsis (in case of bacterial contamination), hyperkalemia (in case of massive transfusion), hypocalcemia, anaphylaxis in the presence of anti- IgA antibodies). The symptomology is urticaria, laryngospasm.
- **Post-transfusion purpura, ARDS, pulmonary oedema** (in the presence of anti-leukocyte antibodies, in complement activation).

Late complications

- alloimmunization against HLA and erythrocyte antigens (caused by contact with donor antigens)
- late hemolysis (caused by anamnestic antibody response to erythrocyte antigens)
- post-transfusion GVHD = graft versus host disease (caused by a proliferation of transfused functional lymphocytes)
- transmission of syphilis
- virus transmission hepatitis, CMV, HIV
- transmission of parasites: malaria
- Overload of iron in polytransfusion

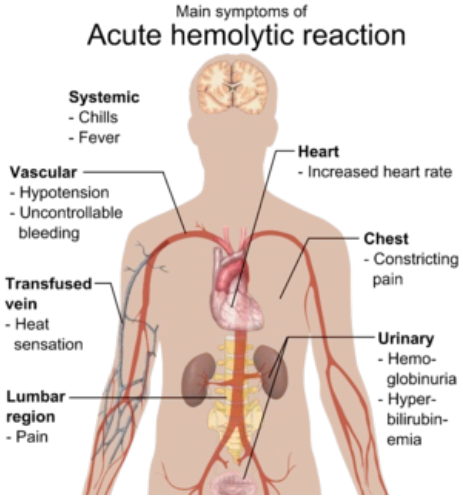
Preventing adverse effects

- examination of urine, temperature, blood pressure, SF before and after transfusion
- patient monitoring during transfusion
- accurate documentation
- when the reaction is recorded, we immediately interrupt the transfusion, but we also leave access
- the rest of the product is left for 24 hours at T 4 ° C
- the post-transfusion reaction is reported

Application procedure

If blood from the vital indication is not required, erythrocyte concentrate is ordered from the transfusion station according to the patient's blood group according to the AB0 and Rh system. Prior to each scheduled transfusion, the laboratory requires a so-called **"crossmatching"** (this is the reaction of the recipient's serum/plasma and the blood cells of the product segment). After receiving the blood, we perform this "crossmatching", i.e. an orientation examination of the blood group in the AB0 system at the patient's bedside just before the transfusion. During the start of the transfusion, we perform a so-called **"bioassay"**. We perform it at the beginning of each transfusion to detect an incompatibility or any other reactions early. In the case of unconsciousness, general anaesthesia, in a newborn, a biological test is not clearly indicated.

Fatal post-transfusion reactions are almost always an administrative mistake!



Main symptoms of Acute hemolytic reaction

Indications

The decision to transfuse should not be based on hemoglobin alone. The indications are as follows:

- Hb < 40 g/l (HCT < 0.12) in any patient condition
- Hb 40 to 60 g/l (HCT 0,12–0,18) with concomitant hypoxia, acidosis, dyspnea, impaired consciousness
- Hb < 70 g/l (HCT < 0.21) in clinical anemia intolerance
- Hb < 80 g/l (HCT < 0.24) in simple operations
- Hb < 90 g/l (HCT < 0.27) in cardiopulmonary or cerebrovascular disease
- Hb < 100 g/l (HCT < 0.30) in planned cardiac surgery

The above values are fixed, they do not take into account, for example, the possibility of further progression of anaemia (eg in hemolytic anaemias, bleeding conditions). Here, the requirement for transfusion would come even at higher Hb values. In intensive care patients, the criteria for packed red blood cells transfusion are completely different. The optimal possibility of oxygen transfer is taken into account here. It is recommended that a hematocrit of 0.25 to 0.35 be maintained in these patients. Values below 0.25 already represent a low transport capacity for oxygen, while values above 0.40 already worsen the rheological properties of the blood. In patients in intensive care, but a stable state, a "restrained" policy is preferred today, transfusion is recommended only with a decrease in Hb <70 g / l.

Transfusion of red cell products in children

- Total volume 10-15 ml / kg
- Recommended speed 4-8 ml / kg / hour
- 4 ml of the product / kg body weight assumes an increase in Hb of 10 g / l

Types of blood products containing erythrocytes

Bedside test

Whole Blood

Whole blood comes from one donor, we usually take 450 ml of blood into the anticoagulant solution. It serves primarily as a raw material for the preparation of other transfusion products. Whole blood is practically no longer used for transfusion. The hematocrit is usually > 0.30. After collection, it is cooled and centrifuged. Resuspension solution is added to the separated red blood cells. As a result, we obtain 3 types of transfusion products:

- plasma
- thrombocytes from the buffy coat (= buffy coat platelets + leukocytes)
- resuspended erythrocytes without a buffy coat

Packed red blood cells (erythrocyte concentrate = plasma-depleted blood=**erymass**) represents about 150 to 200 ml of erythrocytes, from which most of the plasma has been removed.

The following products are used in practice far more often than whole blood.

Erythrocytes without buffy coat resuspended

Erythrocytes without buffy coat resuspended (EBR) represent the most common form of erymass for transfusion in adult patients without specific burden (polytransfused patients, hematooncological problems, requirement for CMV negativity). They have a low leukocyte content (leu <1.2 x 10/9) and a minimal, residual amount of plasma. The resuspension is performed in a solution of NaCl, glucose, mannitol, adenine, guanosine etc. The resuspended eryconcentrate contains an insignificant amount of plasma. HCT is in the range of 0.55-0.65.

Erythrocytes without buffy coat resuspended and deleucotized

Eryconcentrate corresponds to the previous type, in addition, **leukodepletion** is performed. Leukocyte removal takes place at various stages (during production, before release from the transfusion department or at the bedside via a single-purpose filter). The number of leukocytes is significantly reduced (<1 x 10/6), HCT is usually in the range of 0.55 to 0.65. This preparation is an alternative to the CMV negative erythrocyte preparation. It is suitable for the positivity of antibodies against leukocytes, in polytransfused patients (hematooncology, young children).

Washed Erythrocytes

Washed erythrocytes are obtained from whole blood by centrifugation and washed with isotonic solution, resulting in the removal of plasma, platelets and leukocytes. HCT ranges up to 0.65-0.75. The indication is patients with proven antibodies against plasma proteins, eg. in IgA deficiency, in hemolytic anaemia with complement activation (eg. paroxysmal nocturnal haemoglobinuria), in severe transfusion reactions.

Eryconcentrate must be administered as soon as possible, i.e. no later than 24 hours after preparation.

The disadvantage of this preparation is the risk of contamination and the impossibility of storage when opening a closed system, as well as damage to the cells by washing.

Cryopreserved erythrocytes

These are erythrocytes frozen at −80 ° C. They do not contain protein, granulocytes and platelets. The indications are rare blood types and as an alternative to CMV negative erythrocyte preparation.

Irradiated erythrocytes

Irradiation of erymass eliminates T-lymphocytes. **Irradiated erythrocytes** have special indications:

- patients before and after TKD
- hereditary immunodeficiency syndromes
- intrauterine transfusion
- hematooncological diseases
- oncology patients on chemotherapy and radiotherapy
- polytransfused patient

From today's point of view, irradiated, deleukotized and resuspended eryconcentrate without a buffy coat is the safest variant of erythrocyte transfusion for young children. This type of eryconcentrate should certainly be used in premature babies and newborns, preferably also in children under 6 years of age.

Disadvantages of irradiation include a negative effect on the stability of the erythrocyte membrane (increased value of potassium and Hb during storage), preparations with erythrocytes can be irradiated within 14 days after collection. Irradiation is recommended just before application, storage is only possible within 24 hours.

Platelet concentrate

When administering platelets, we follow the blood groups in the AB0 system, no agreement in Rh is required. In acute conditions, group 0 platelets can be administered, as in erythrocyte concentrate.

Types of platelet replacement products

- **platelets from buffy coat.** They are obtained from whole blood by centrifugation (platelets are obtained together with leukocytes). They should be used in children exceptionally, as they represent a large antigenic load. 4 to 6 TU buffy coats must be used to replace 1 platelet unit = 1 TU of separated platelets from apheresis. The buffy coat dosage corresponds to the plasma dosage, ie 15 ml / kg and dose. The platelet count is usually> 0.6 x 10/11.
- **apheresis platelets.** They represent the most commonly indicated form of platelet substitution. 1 TU contains platelet concentrate collected using a cell separator from a single donor. The volume of TU is usually 150 to 300 ml. The dose is 10 - 15 ml / kg. Platelet counts are usually> 2 - 8 x 10/11.
- **platelets from leukocyte-poor apheresis** (leukocyte value is <2 x 10/9)

- **platelets from deleukotized apheresis** (leukocyte value is <1 x 10/6). Deleukotized preparations are indicated in patients at risk of alloimmunization with leukocyte antigens, at risk of CMV transmission (immune defects, CMV negative newborns), in polytransfused, transplanted, in aplastic anaemia, after bone marrow transplantation, in case of leukocyte antibody detection, in febrile reaction after thrombocurrent application.

Irradiated platelets represent prevention against GVHR (graft versus host reaction). Irradiation blocks the proliferation of immunocompetent lymphocytes, preventing clonal expansion of donor T cells. Irradiated platelets are recommended in children <6 years of age, in haemato-oncology patients and after transplantation organs.

All transfusion products administered in pediatric patients in severe conditions should, as far as possible, be deleukotized and irradiated.

Platelet aggregation

Indications and contraindications

indication

- thrombocytopenia <5,000 in patients with ITP with manifest bleeding,
- thrombocytopenia <5,000 - 10,000 even in asymptomatic patients,
- thrombocytopenia <25,000 in patients with DIC without manifest bleeding, with manifest bleeding an indication <50,000,
- thrombocytopenia <50,000 when planning surgical procedures (including the introduction of CVK) or current thrombocytopathy,
- thrombocytopenia <50,000 - 100,000 in major surgical procedures (cardiac surgery, neurosurgery),
- neonatal alloimmune thrombocytopenia: platelets <20,000 - 30,000 x10 / 9 (compatible donor required),

contraindication

- TTP = thrombotic thrombocytopenic purpura (cryoprotein-depleted plasma, so-called “K plasma”, is prepared for the treatment of patients with TTP.

Other products

Fresh frozen plasma (FFP)

Fresh frozen plasma (FFP) must be of the same group, the universal plasma donor is group AB (in practice, universal AB plasma is usually administered without testing, as there is often a need for urgent administration). A can containing plasma separated from one donated full blood contains normal levels of persistent plasma clotting factors, albumin and immunoglobulin. The level of factor VIII is> 70% of the level in fresh plasma. The greatest use is in patients with severe bleeding diathesis who have not previously been diagnosed with bleeding disorders. The advantage is just a wide "scope" in the content of coagulation factors.

FFP must be of the same group, the universal plasma donor is group AB.

Freshly Frozen Plasma

Indications and contraindikations

indication:

- bleeding in patients with coagulation factor V and IX deficiency or if deficiency factor concentrates are not available (ff. II, VII – X),
- DIC in the consumption phase,
- TTP.

Obsolete indications today include volume expansion and immunotherapy. Volume expansion is not indicated (except for hemorrhagic causes), as it is safer to administer crystalloids and synthetic colloids. In septic shock, flat-rate plasma administration is also not appropriate. Purified immunoglobulins are now available in the indication of immunotherapy.

contraindications:

- pulmonary oedema,
- cardiac decompensation,
- IgA deficiency,
- DIC without treatment of the underlying cause.

Application and dosage

- for plasma application, a universal donor is a blood group AB donor, the universal recipient is a blood group patient 0,
- patient 0 -> can 0 or A or B or AB,
- patient A -> can A or AB,
- patient B -> can B or AB,
- patient AB -> canned AB.

dosage

- the usual dose for hypocoagulation conditions is 10-15 ml / kg,
- for volume expansion (today used only in the indication of hypovolemia due to hemorrhagic cause) 20 ml / kg.

Albumin

Albumin is one of the proteins in the blood plasma, accounting for 60% of all plasma proteins. In addition to blood, it also occurs in other body fluids (interstitial fluid, cerebrospinal fluid). It is important for the transport of various substances in the blood (fatty acids, minerals, bilirubin, drugs) and helps maintain a stable environment (its colloidal-osmotic (colloidal) pressure retains fluid intravascularly). Albumin is synthesized in the liver, unlike other plasma proteins, it is not glycoprotein. It used to be the most commonly used colloid in hypovolemia. From today's point of view, we distinguish the following indications:

- plasma replacement in plasmapheresis,
- swelling resistant to diuretic therapy in conditions with hypoproteinemia. As a rule, substitution is recommended at values <20 g / l, for nephrotic syndrome <15 g / l,
- use as a colloid in the treatment of hypovolemia. Although albumin is still used in this indication, there are no studies to demonstrate its benefit over hydroxyethyl starch-type crystalloids or colloids. Empirically, it is usually administered as 5% albumin at a dose of 20 ml/kg.

The recommended dose is 0.5 - 1.0 g / kg for dose, administered within 30 - 120 minutes. Albumin is administered in a concentration of 5, 10 or 20%.

Cryoprecipitate, fibrinogen substitution

Cryoprecipitate is prepared from FFP during controlled melting and resuspension. It contains mainly fibrinogen, f. VIII and XIII. Compatibility testing is not strictly required but is an advantage. Its main indication is fibrinogen substitution for DIC consumption. It is only a backup option for the treatment of haemophilia and von Willebrand's disease, as the availability of recombinant factor VIII is certainly more therapeutically advantageous. It is practically no longer used today. At a low level of fibrinogen, ie <1 g/l, we prefer the administration of fibrinogen. Dosage in adults ranges from 1 to 8 g, in children, it is lower (according to the weight and severity of the condition).

Prothrombin complex concentrate

The prothrombin complex concentrate contains factors II, VII, IX and X. The indication for administration is the bleeding of patients with acquired prothrombin complex factor deficiency caused by p.o. anticoagulants, severe liver disease or vitamin K deficiency. In patients with DIC, the administration is indicated only to manage life-threatening bleeding and only after appropriate antithrombotic therapy has been initiated.

Protein C

Protein C (PC) is an anticoagulant protein that plays an important role in the regulation of hemostasis. PC is synthesized in the liver as a vitamin K-dependent plasma protein. It is present in plasma at a concentration of 4 µg/ml. PC circulates in the blood in the form of zymogen (proenzyme). The PC is selectively converted "on-site" and "on-demand" to activated protein C (APC) during coagulation activation. APC has many "braking effects" on the coagulation cascade: it inactivates ff. Va (thereby reducing thrombin production) and VIIIa, prevents pro-inflammatory consequences of thrombin production (including platelet activation, adhesion, and aggregation, the release of vasoactive and pro-inflammatory substances, increased endothelial permeability), promotes fibrinolysis by binding tissue activator of plasminogen I (tPA-I inhibitor). APC also has strong anti-inflammatory effects. All patients with a diagnosis of septic shock have lower plasma PC levels and most have elevated APC levels.

Indications for PC administration are:

- primary PC deficiency,
- gram-negative bacterial sepsis (especially meningococcal),
- DIC,
- liver disease.

Before administration of PC, its plasma level must be examined, as well as AT III, D-dimers, PAI-I activity + antigen. Ceprotin® = non-activated PC is already on the market, whose CIs are only allergic reactions to the product component. Activated PC (Xigris®) is used only in adults, it is contraindicated in children

required amount of AT III (I.U.) = (required concentration - initial concentration) x 0.6 x kg t.h.

The final concentration should always be 125% or higher, the calculated dose of AT III is administered every 8 hours i.v. Routine administration of AT III is not recommended. AT III studies are relatively small, but some include childhood. Some recommend co-administration of heparin, which enhances the effect of AT III.

Recombinant activated f. VII (rfVIIa)

Recombinant activated f. VII (rfVIIa) is commercially available as **NovoSeven®**. It is a substance eptacog α, which acts in the same way as f. VIIa. Its effect is to activate f. X (Xa), which initiates the coagulation process. Through rfVIIa, the formation of thrombin on the surface of activated platelets is increased, at the same time leading to an increase in platelet adhesion and aggregation. Because rfVIIa does not require ff to work. VIII and IX ("by-passing effect"), serves as a universal hemostatic. Official indications for NovoSeven® include haemophilia A, B with the presence of inhibitors, congenital deficiency f. VII, Glanzmann's thrombasthenia. In the indications "of label", it is used as a universal hemostatic in severe bleeding in patients without primary coagulation disorders. For this reason, the UNISEVEN register was established, which is a database of the use of rfVIIa in various indications (the Czech Republic has been included since 2004).

General principles of hemotherapy

pre-transfusion examination

- AB0, Rh,
- screening for irregular antibodies,
- identification of irregular antibodies,
- comparison with the previous examination,
- selection of a suitable product,
- compatibility test = "crossmatching".

vital indications

- dispensing within 20-30 minutes,
- laboratory examination AB0, Rh - lasts 3-5 minutes.

If the recipient cannot be examined, then we administer erythrocytes group 0, Rh-negative, plasma AB, platelets 0.

In general: if a recipient blood sample is not available, if the sample is insufficient, if there is no time to perform a STATIM AB0 and Rh (D) examination or if the result is not evaluable, 0 Rh (D) blood is collected

The safest is the transfusion that is not given.

Possibilities of substitution therapy of hemocoagulation factor deficiency

Possibilities of substitution therapy of hemocoagulation factor deficiency

defficient factor	substitute therapy
Factor I (fibrinogen)	▪ Haemocomplettan P® ▪ cryoprecipitate ▪ FFP
Factor II (prothrombin)	▪ FFP ▪ prothrombin complex concentrate
Factor V	▪ FFP
Factor VII	▪ FFP ▪ prothrombin complex concentrate ▪ recombinant f. VIIa (NovoSeven®)
Factor VIII	▪ f. VIII concentrate ▪ DDAVP
Factor IX	▪ f. IX concentrate ▪ prothrombin complex concentrate
Factor X	▪ FFP ▪ prothrombin complex concentrate
Factor XI	▪ FFP
Factor XIII	▪ cryoprecipitate ▪ FFP
von Willebrand disease	▪ DDAVP ▪ f. VIII concentrate

Links

Sources

- HAVRÁNEK, Jiří: *Hemoterapie*. (modified)

Related articles

- Blood
- Hemostasis
- Koagulace
- Blood transfusion
- Anemia