10 Autologous Hemotherapy

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Note: Autologous blood or blood components collected prior to surgery are pharmaceutical products and as such are subject to regulations of the Arzneimittel- und Wirkstoffherstellungsverordnung (AMWHV), the German Medicinal Products Act (Arzneimittelgesetz; AMG), the German Transfusion Act (Transfusionsgesetz; TFG) as well as the German Guide for Obtaining Blood and Blood Components and for Application of Blood Products (Hemotherapy) [11].

10.1 Autologous RBC Products

10.1.1 Preparation

Autologous RBC products can be prepared in three ways: by preoperative autologous blood donation, by presurgical normovolemic hemodilution and by salvaging of wound/drainage blood shed during, and/or after surgery by means of mechanically processed autologous transfusion (MAT).

The advantages of autologous hemotherapy include: the exclusion of rare adverse reactions like plasma-associated incompatibilities or transfusion-associated graft-versus-host disease (GVHD), formation of irregular erythrocyte blood group-specific alloantibodies or delayed hemolytic transfusion reactions and above all the avoidance of transmitting viral pathogens. In view of the considerable progress made in the virus safety of allogeneic blood products, however, this aspect has lost significance [6, 38]. Reduction of postoperative infections after exclusive administration of autologous RBC concentrates in comparison to leukocyte-depleted allogeneic RBC concentrates is subject of discussion [25]. Autologous blood donation and transfusion exposes the patient to principally the same risks as homologous blood donors [11].

The capability of the individual patient to donate autologous blood [11] is to be judged by the attending physician.

10.1.1.1 Preoperative Autologous Blood Donation

Prior to elective surgical interventions with an at least 10% likelihood of blood transfusion (defined by in-house data) according to German Guide for Obtaining Blood and Blood Components and for Application of Blood Products (Hemotherapy), the patient is to be informed in due course and individually of the risks of homologous blood transfusion, of the possible application of autologous blood, and of the potential risks and benefits of autologous hemotherapy [11]. The attending physician is responsible for defining the indication as well as deciding on the amount of blood products required while observing the German Guide in force [11]. Each case of autologous hemotherapy requires exact decisions for or against hemotherapy, taking contraindications into account. Based on the necessary underlying data (blood count and hematocrit, minimum acceptable levels of intra- and postoperative hematocrit/hemoglobin, blood volume, expected loss of blood during the intended procedure according to the hospital’s current requisition lists), planning should be started as early as possible [2].

Current investigations document the benefit of preoperative donation of autologous blood, in particular in cardiovascular surgery [15, 29], hip replacement and spinal surgery [20, 23]. In contrast, a prospective, randomized study on the benefit of preoperative autologous blood donation for hip replacement surgery could demonstrate no advantages [5]. The problem of increased wastage of predonated RBC units that were not used should also be taken into account [4]. No general recommendation can be given regarding the use of preoperative autologous blood donation in primary total knee arthroplasty [18] and in oral and maxillofacial surgery [26, 32, 33].

The essential goal of preoperative autologous blood donation is a substantiated gaining in erythrocyte mass (extracorporeal deposit plus in vivo regeneration). The decisive factor for this increase is the concept of blood collection with a minimum time interval of 3 weeks between the last predonate and elective surgery. Only in this way can an adequate RBC regeneration take place due to the time-dependent physiological basics of erythropoiesis. Because there is an inverse exponential correlation between hematocrit and erythropoietin levels in plasma, erythropoiesis is intensified with declining hematocrit levels. Taking this essential factor into account, conventional concepts for the collection of autologous predeposits (1 unit each with an interval of 1–2 weeks up to shortly before the date of surgery) do not lead to an optimal increase in RBC mass. New, intensified concepts for the collection of autologous predeposits with brief time intervals between the collection of 2 RBC concentrates (within 1 week) results in an increased erythropoietic stimulus and a significant increase in RBC mass compared with the ‘conventional concept’ of collecting RBC [40, 41].

When collecting autologous predeposits, an ‘intensified’ concept for collection is recommended where 2 autologous blood donations are performed within a short time (1 week), provided the clinical status of the patient permits this. In addition to a larger decline in hematocrit levels, there is also a longer time period before surgery, allowing regeneration of erythrocytes.

The eligibility of a patient for autologous blood donation is examined following the specifications for healthy blood donors [11]. Patients with leukocyte counts of more than 10.5 × 10⁹/l should donate autologous blood only if an infection is unlikely or can be ruled out as the cause. Depending on the clinical state of the patient, an adequate volume substitution should be performed after each autologous blood donation.

Prior to autologous blood donation the hemoglobin level should be at least 11.5 ± 0.5 g/dl (7.13 ± 0.31 mmol/l).
In individual cases the administration of erythropoietin (in combination with iron supplementation) can become necessary in order to retain endogenous erythrocyte reserves [37, 42, 48]. Iron substitution therapy should be applied if at least 3 autologous blood donations are planned or if the ferritin level is <50 μg/l [51].

Autologous RBC concentrates are prepared from whole blood or by using cell separators. Blood collection follows regulations laid down for the production of homologous RBC units (see chapter 1). Autologous whole blood may also be used unprocessed after inline filtration. By setting a correspondingly low extracorporeal volume (e.g. 250 ml), the cell separator can be adapted for use in children and older patients [34, 35].

It is prohibited to pass on unused units of autologous blood to other patients or to use them for the preparation of other blood products.

Cryopreservation of autologous blood is established only in some centers [31]. Its indication is limited to patients with a complex spectrum of antibodies as well as patients with rare blood groups and the potential risk of forming antibodies against high-frequency antigens.

**10.1.1.1 Quality Criteria**

On principle, all the requirements of homologous RBC concentrates must be met (see chapter 1). In individual cases it is possible, due to a physician’s decision, to deviate from the requirements of homologous blood donors, especially regarding threshold values for erythrocyte counts and hemoglobin/hematocrit [11].

**10.1.1.2 Preoperative Normovolemic Hemodilution**

Preoperative normovolemic hemodilution can be considered for patients with preoperative hematocrit/hemoglobin concentrations at the upper limit of normal and for whom an intraoperative blood loss is anticipated of >50% of the blood volume, and who are able to tolerate hemodilution-derived anemia due to their general clinical state [27, 43]. Within the framework of any risk-benefit analysis, the physician should also bear in mind that the maximum possible saving (which is only achievable when preoperative hemoglobin concentrations are at the upper limit of normal) does not exceed 1–1.5 homologous RBC concentrates [7, 39].

The patient is to be informed about the risks and benefits of hemodilution.

The blood bag is to be labeled with patient data (last name, first name, date of birth) as well as the time and date of collection and is to be tested for intactness, possible hemolysis and clot formation. Collected autologous blood cannot be stored and is to be tested for intactness, possible hemolysis and clot formation. The physician collecting the blood is responsible for proper preparation.

**10.1.1.2.1 Quality Criteria**

Preoperative normovolemic hemodilution can only be recommended as a method with a limited effect for patients with hemoglobin concentrations at the upper limit of normal. No reduction in the demand for allogeneic RBC concentrates could be documented in controlled trials.

**10.1.1.3 Mechanically Processed Autologous Transfusion**

The patient is to be informed about the potential risks and benefits of MAT. MAT is especially indicated in operations in which major blood loss is anticipated (e.g. orthopedic or vascular surgery) or occurs unexpectedly (emergency operations) [3, 12]. Although more than 50% of the blood shed from wounds can be retransfused in this way, the rate of recovery varies considerably; thus it cannot be anticipated and budgeted in preoperative transfusion planning [50].

The blood shed from the wound is mechanically salvaged under sterile conditions and retransfused as a washed RBC suspension. MAT may not be used when bacterial contamination of the aspirated blood is strongly suspected (e.g. gastrointestinal surgery) as the washing and filtration steps in the preparation process do not eliminate bacteria. As a rule the collected RBC must be retransfused immediately. In exceptional cases RBC collected by MAT can be stored up to 6 h at 2–6 °C. This period of time covers the complete process.

The transfusion of salvaged blood shed from wounds or drainage intra- or postoperatively without previous treatment (washing) is not recommended due to the risk of clotting activation or retransfusion of cytokines and possibly endotoxins as well as of other biological active substances.

In tumor patients it is recommended to irradiate MAT blood at 50 Gy before retransfusion [24]. The relevant terms and regulations of the AMG regarding the operation of a qualified radiation institution must be observed.

Taking the contraindications into account, application of MAT can be recommended when major blood loss is anticipated as well as when acute bleeding occurs during surgery.

In tumor surgery the application of MAT can be recommended, when the blood shed from the wound is irradiated prior to retransfusion.

**10.1.2 Storage and Shelf Life**

Autologous red blood cell preparations are principally to be stored at 2–6 °C clearly separated from homologous blood products.
Blood derived from hemodilution or MAT must be re-transfused as soon as possible if indicated. The maximum time span between collection and transfusion is 6 h.

10.1.3 Range of Application, Dosage and Mode of Administration

Autologous whole blood concentrates and RBC concentrates are prescription-only medical products and therefore an integral part of medical treatment [11]. Indications for transfusion differ in no way from those for homologous preparations. This also applies to RBC concentrates obtained in the context of acute normovolemic hemodilution.

10.1.4 Adverse Reactions

See chapter 11.

10.1.5 Documentation, Informed Consent

Documentation of administration is done according to article 14 TFG (patient data, batch number, identification of the preparation, volume administered, time and date of collection, adverse reactions). The German Guide for Hemotherapy should be considered [11].

Before autologous blood donation the patient is to be informed in writing about the individual risk-benefit ratio involved in donating and receiving autologous blood components and about the possibility that homologous blood components may still have to be transfused.

10.2 Autologous Platelet Preparations, Autologous Fresh Frozen Plasma, Autologous Fibrin Glue, Autologous Platelet-Rich Plasma

The use of these blood products is based on reports from isolated centers and is limited to only a few indications. Controlled prospective studies have not been performed. Therefore, no recommendations concerning indications, dosage, quality requirements or mode of administration can be made.

10.2.1 Autologous Platelet Concentrates

This application is restricted to specific indications. Autologous platelet concentrates have been used by ophthalmologists to treat macular holes [21, 22, 28]. Single reports have been published about the use of autologous platelet concentrates in cardiac surgery [52] and as supportive treatment in high-dose chemotherapy [45].

10.2.2 Autologous Fresh Frozen Plasma

In the production of autologous RBC concentrates autologous fresh frozen plasma (AFFP) is routinely produced as part of the separation process and is available during or after surgery [11]. Indications for fresh frozen plasma are described in chapter 4. In elective surgery in which high blood losses can be anticipated (e.g. revision of total hip arthroplasty, surgery), the presurgical collection of several units of AFFP via plasmapheresis in combination with intraoperative MAT is a well-established means of providing ‘physiological’ fluid replacement perioperatively, even in the event of massive blood loss.

10.2.3 Autologous Fibrin Glue

Various working groups have reported on the preparation and use of autologous fibrin glue in surgery [13, 44, 49]. Standard methods have not yet been established [46].

10.2.4 Autologous Platelet-Rich Plasma

Autologous platelet-rich plasma (APRP) is obtained from small amounts (around 10–80 ml) of autologous blood by centrifugation. Usually it is mixed with a few drops of blood from the wound and human bone material or synthetic bone substitute material and is used for filling bone defects in dentistry. The only prospective trial published so far [30] as well as a few case studies or data from animal experiments who reported benefits [1, 16, 47] or no significant effect [17, 19, 36] in the application of APRP or platelet-rich plasma in bone graft surgery do not allow to make recommendations for application beyond clinical trials. Randomized trials on the efficacy of APRP are still lacking.

A general application of APRP beyond clinical trials is not recommended.

10.3 Autologous Stem Cell Preparations

The German Guide for Obtaining Blood and Blood Components and for Application of Blood Products (Hemotherapy) [11], the guides for transplantation of peripheral blood stem cells [9], for bone marrow transplantation [8] and for cord blood stem cells [10] as well as the recommendations of the German Society for Transfusion Medicine and Immunohematology on blood stem cell apheresis [14] should be observed.

10.4 Documentation

See section 10.1.5.
References


