Preoperative Autologous Blood Donation – a ‘Confessor’s’ Point Of View

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Summary
This contribution was part of a public pro and con discussion during the 4th CAT symposium in Nottwil (Switzerland) and will focus predominantly on the pro arguments for preoperative autologous blood donation (PABD). A major advantage of PABD is the avoidance of the immunological problems associated with allogeneic transfusions. These can result in the delay of later transfusions and unavailability of compatible blood after immunization, leading to severe hemolytic transfusion reactions when red cell antibodies cannot be taken into account. Arguments will be presented that clearly show that transfusion of the wrong patient is expected less frequently with autologous blood products as long as general transfusion standards are observed. Unavoidable delayed hemolytic transfusion reactions, which occur after boosting of an undetectable antibody produced after an immunization in the past, cannot happen when autologous blood is administered. Furthermore, despite comprehensive testing for infectious diseases, allogeneic blood still bears the risk of transmission of infections due to blood donation in the window period, low-carrier status of the blood donor, or the emergence of new infectious agents. However, PABD should be adapted to the individual transfusion need of a patient for a given surgical intervention, should be carried out under optimized conditions, and should be included in a comprehensive concept of autologous hemotherapy. As part of such a concept, PABD constitutes a key element because it is, in contrast to other techniques, a preventive measure.
Introduction

During the last couple of years the demand for preoperative autologous blood donation (PABD) is declining. In Germany, the major reasons for this development are the high safety of allogeneic blood components, a diminishing fear of contracting AIDS, decreasing transfusion needs particularly in orthopedic surgery as well as considerable logistic and legal hurdles that render PABD both cumbersome and costly. Clinicians who have to decide upon the indication for PABD and patients are faced with so many arguments, both right and wrong, against the use of autologous blood that they increasingly refrain from utilizing this procedure, particularly since this clearly facilitates planning of surgery. It is for this reason that this paper concentrates, as a counterbalance, entirely on arguments in favor of PABD. The author of this article is aware of the bias of his statements and has consequently given it the title ‘a confessor’s point of view’. For a neutral discussion of the pros and cons of PABD refer to [1].

Theses

PABD Contributes to Blood Procurement

In Germany, blood shortages of red cell concentrates repeatedly occur [2], which may lead to the postponement of elective surgery. This holds especially true for Rh-negative red cells, but does sometime also concern blood group O and A Rh-positive blood. Indeed, because of the decreasing willingness of the population to donate blood on the one hand and the still increasing demand for blood products owing to a shift of surgical procedures to an increasingly older patient population on the other hand, a rise in the frequency of blood shortages is to be anticipated. This is why PABD, with a shared approximately 4% of all red cell concentrates manufactured in Germany between 1999 and 2001, is considered a significant contribution to the blood supply, which however, according to the figures in earlier years, could be substantially higher. By the end of the 1980s, it was concluded that 15–20% of the transfusion need for elective surgical procedures could be covered by PABD [3, 4]. A meta-analysis performed by Henry et al. [5] showed that the application of PABD is able to reduce the consumption of allogeneic blood by 63%. With an optimal scheduling, PABD results in a real gain in red cells, patients can be operated with hemoglobin concentrations similar to concentrations found after allogeneic blood by 63%. With an optimal scheduling, PABD is able to reduce the consumption of allogeneic blood by 63%. With an optimal scheduling, PABD results in a real gain in red cells, patients can be operated with hemoglobin concentrations similar to concentrations found prior to PABD and can be discharged postoperatively with hemoglobin values higher than after allogeneic transfusion.

Autologous Blood Is Not an Inferior Blood Component

As long as donation, processing and storage of autologous blood takes place under optimal conditions, autologous blood components are not of inferior quality compared to allogeneic blood. This though requires for example the exclusion of patients with possible infections spreading via the blood stream – especially those of the gastrointestinal tract –, repeated disinfection of the venipuncture site, reliable administration of iron medication for support of erythropoiesis, double red cell apheresis, and the manufacturing of blood components in the facility where they are to be administered. By avoiding the frequent temperature changes which allogeneic red cells are often exposed to as a result of transportation and repeated cross-matching procedures, the quality of autologous blood is similar to that of allogeneic blood. After leukocyte depletion, even when stored as whole blood, these autologous components can be stored as long as red cell concentrates suspended in an additive solution [6]. Whole blood has the additional advantage that less volume replacement solutions are needed.

Lower Risk of Infectious Complications of Autologous Blood

Transfusion of allogeneic blood bears the minimal risk of transmitting the infectious agents HIV, HCV and HBV if donation takes place during the so called window phase, if the donor is known negative state or if rare genetic variants of a virus are encountered. Furthermore, infections might be transmitted such as HTLV/II, parovirus B19, West Nile virus or SARS virus which the donor is not or cannot be tested for. One has always to reckon with the emergence of ‘new’ transfusion-transmissible infectious agents. After 3 known cases of variant Creutzfeldt-Jakob disease (vCJD) in patients having been transfused with blood of vCJD-infected donors, this disease must also be considered an infectious risk of blood transfusion. However, currently, the risk of bacterial contamination of blood products is considered to be a more relevant problem, and this risk also exists for autologous blood transfusions. The assumption that this risk is even higher for autologous blood is not justified when PABD is carried out under state-of-the-art conditions that apply to the manufacturing of blood components in general (see above). Contamination rates assessed from multicenter studies which were compiled by the Paul-Ehrlich-Institut (PEI) are not considered relevant in this context because of the uneven distribution of the regional origin of allogeneic and autologous blood products. However, when compared directly, in a sufficiently representative sample, bacterial contamination rates in autologous blood components actually appeared not to be different to those in allogeneic blood products [7].

Autologous Blood Is Not More Costly than Allogeneic Blood

In general, autologous blood is more expensive than allogeneic red cell concentrates. This is predominantly due to the fact that the German guidelines require measures that unnecessar-
稍稍increase the cost of autologous blood [8]. There is however no real need for separating autologous blood into components because the patients do not usually develop hemostatic disturbances during surgery. If, however, autologous plasma is available, it should be regarded as an optimal volume replacement solution. The risk of transfusing the wrong patient is not a convincing argument for the requirement of autologous blood to be submitted to virological testing. The main reason why these incidents must be avoided is the risk of hemolysis due to ABO incompatibility. The leukocyte content of autologous blood is irrelevant for how well these products are tolerated and has no influence on the postoperative outcome of the patients [9–11]. Thus universal leukocyte depletion of autologous blood is considered unnecessary. Leukocyte depletion might only be reasonable in order to prolong the postdonation period if this is necessary for the restoration of the hemoglobin level of the patient. The costs of PABD can be further reduced by optimizing organization and logistics. In addition, wastage rates can be decreased by adapting the number of donated units to the individual need of a patient. The predeposit of autologous blood should not only rely on the average blood loss or number of transfused red cell units for a given surgical intervention. In contrast, individual patient characteristics such as baseline and tolerable hemoglobin level, total blood volume as well as expected blood loss of the patient should be taken into account [12]. Finally, we question that restrictive transfusion based on critical hemoglobin values is warranted in autologous transfusion. This approach is undoubtedly justified in the allogeneic setting where the numerous risks of allogeneic blood components have to be considered. However, if, given optimized manufacturing, autologous units do not have most of these risks, which is the firm belief of the author, then autologous transfusion should be guided by the goal of maintaining the optimal hemoglobin level in order to accelerate rehabilitation, improve the outcome of the patients and reduce the total cost of the recovery process [13].

As shown in table 1, the cost for leukocyte-depleted autologous whole blood are not much higher than those of allogeneic red cell concentrates, even if a wastage rate of 50% and virological testing in an external laboratory are taken into account – at least under conditions that ensure optimal organizational and logistic circumstances in the conduction of a PABD program.

When the cost of allogeneic blood production are calculated, some of the expenses are usually not taken into account. This also holds true for the above calculation. These include reservation of cross-matched red cell concentrates that are eventually not transfused (on average the number of cross-matched red cell concentrates exceeds the number of red cell concentrates that are finally transfused by 2–4 times), additional antibody screening tests and blood group typing of all patient samples sent in for cross-matching, loss of units because of transfusion reactions, costs for diagnosis and treatment of transfusion reactions and expenditures for look-back procedures.

There Is No Increased Risk of the Donation Procedure

There are conflicting reports concerning the side effects of autologous donations for patients [14, 15]. Whereas Popovski et al. [14] found a 12 times higher risk of severe donation complications in autologous compared to allogeneic blood donors [14], McVay et al. [15] could not confirm these results and found no differences in reaction rates. Other authors demonstrated that autologous donation was as safe as donation by healthy individuals, even with an increased donation risk due to relevant co-morbidity [16–18]. Empirical evidence shows that autologous blood donations are not associated with a higher frequency of side effects as long as the blood drawing team provides an atmosphere of experience and confidence. On the contrary, young (allogeneic) donors exhibit vasovagal reactions more often because they have a much more labile autonomic nervous system. This is especially seen on their first donation.

Thus, PABD should be carried out by experienced staffs who are able to correctly estimate the health status of the patients, identify patients eligible for PABD, are able to adapt the donation procedure and the monitoring to the health status of the patients, and inform the patients about necessary rules of conduct for the time period after blood drawing. Moreover, the individual patient is usually more inclined to accept the risk of donation which he or she believes is able to control and influence, as opposed to a more theoretical risk the occurrence of which is stochastic. PABD provides the patients with a feeling of self-determination and to actively contribute to the safety of the medical intervention they have to undergo. In particular, when PABD takes place in the facility where the surgical procedure is to be performed, they develop a higher sense of safety and self-assurance. In Germany, current jurisdiction puts considerable emphasis on the right of patients to...
Self-determination such that the patients’ desires have to be respected as long as they are appropriate.

**A Major Benefit of PABD Is the Prevention of Immunological Side Effects of Transfusion**

**Immunization**
In approximately 1–2.5% of all hospitalized patients clinically relevant red cell antibodies can be detected. About 40% of these antibodies are actually hemolytic in vivo if they are not taken into account for transfusion. After transfusion of allogeneic red cell concentrates approximately 9% of the patients develop red cell antibodies. After 5 years about 50% of these antibodies are no longer detectable in routine antibody screening and, consequently, cannot be taken into account for the provision of compatible red cell concentrates. Thus, immunological effects of a transfusion will generate several problems in the future. Since universal leukocyte depletion has been introduced in Germany in 2002, only the problems caused by immunization against red blood cells following allogeneic transfusion will be discussed in further detail below.

Diagnostic problems in the identification of red cell antibodies induce delays and increase cost. Out of 34,000 blood samples that were sent to our laboratory for antibody screening and/or cross-matching, 0.74% (156 patients) contained unidentifiable antibodies, prohibiting safe transfusion in these cases. In some of these patients red cell concentrates had to be transfused although cross-match results were positive. Whether those transfusions will always be well tolerated as was fortunately the case here cannot be predicted.

Serious problems with respect to the provision of compatible blood can occur upon later transfusions if multiple antibodies or antibodies against high-frequency antigens develop. If red cell antibodies cannot be taken into account, e.g. in the case of emergency transfusions or when they are not detectable, transfusion reactions may occur.

Under special circumstances, when antibodies of the immunoglobulin IgG class are directed against fetal red cells, hemolytic disease of the newborn may result.

**Allergic Reactions**
Approximately 0.1% of transfusions of leukocyte-depleted allogeneic red cell concentrates are usually associated with mild transfusion reactions. However, in the initial stage the symptoms of these reactions cannot be differentiated from those leading to severe transfusion reactions. Thus, transfusions have to be stopped, and patients require intensive monitoring and often even need symptomatic treatment. Consequently, such reactions result in loss of blood components and increased cost, which are not taken into account in any economic calculation. The reported incidence of serious allergic transfusion reactions is indeed 1:20,000 to 1:50,000 [8].

**Acute Hemolytic Transfusion Reactions (AHTR)**
AHTR occur when hemolytically active, detectable antibodies are not taken into account in the course of transfusion. Their frequency was estimated at 1:10,000 to 1:100,000 red cell concentrates [8]. Given a fatality rate of 5%, this is equivalent to one death in 500,000 to 5,000,000 transfused units. The main reasons for AHTR are organizational failures leading to transfusion of the wrong patients. In our experience, in most of these instances blood samples for blood group typing had been taken from the wrong patients (approximately 80%). Such errors do not occur in autologous transfusion. Only 5–10% of incorrect transfusions are caused by misidentification of the patient immediately before transfusion. The latter are also supposed to occur more rarely in autologous than in allogeneic transfusion when autologous units are not labeled with the blood group of the patient, because this can prevent transfusions only based on the comparison of blood groups. Such insufficient patient identification procedures are still often observed on wards (e.g. intensive care unit), which simultaneously receive red cell concentrates for different patients. Accompanying documents, firmly attached to red cell units, which are aimed at correctly identifying the patient the blood is assigned for, are often removed or are not used for correct patient identification. Unambiguous patient identification of autologous blood can be achieved by comparing the complete particulars of the patient and, if possible, the signature of the patient with the corresponding data on the blood bag label. This undoubtedly decreases the risk of transfusing the wrong patient considerably in comparison to allogeneic transfusion.

**Delayed Hemolytic Transfusion Reactions (VHTR)**
VHTR are unavoidable events if a previous immunization is not detectable and therefore cannot be taken into account at the time of transfusion. Three to 14 days after transfusion red cell concentrates bearing antigens the recipient has been immunized against lead to hemolysis as a result of boosting. Often the hemolysis is mild and not recognized by the clinicians. However, in rare cases a VHTR can be fatal. In a 10-year survey carried out by the Food and Drug Administration covering the period between 1976 and 1985, out of all fatal hemolytic transfusion reactions that occurred, 14% were caused by VHTR [19]. In the SHOT report comprising the years 1996/1997 until 2003, 8 out of 90 fully analyzed severe transfusion complications were caused by VHTR [20]. The incidence of VHTR is reported to be 1:1,000 to 1:4,000 transfusions and that of fatal VHTR 1:1,000,000 transfusions [8]. Our own data are indeed compatible with these results (1:3,500 in 2005). Antibodies most often involved are directed against antigens of the Kidd blood group system (10 cases in 4.5 years) which often, even though highly sensitive detection methods are em-

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ployed, remain undetectable in the patients’ sera and can only be identified and confirmed in eluates [21].

**Immunosuppression**

Whether or not autologous blood leads to transfusion-related immunosuppression to a lesser extent than allogeneic blood after the introduction of universal leukocyte depletion, is currently unclear. In a recently published observational study in orthopedic patients there were still significantly fewer secondary infections in the group having donated and received autologous blood (1.2%) compared to the group that received leukocyte-depleted allogeneic red cell concentrates (12%, p < 0.05) [22].

**Discussion**

The arguments presented here show that, despite the high safety standards achieved for allogeneic blood products, these can never reach the level of safety of autologous blood, in particular with respect to immunological problems, as long as the latter is obtained under optimized conditions and according to state-of-the-art standards. In addition, the procurement of autologous blood in the preoperative rather than perioperative period, has the advantage that, at the time of surgery, the transfusion need for a given intervention has already been provided for. Furthermore, latent iron deficiency anemia can be detected early in the preoperative phase and can be treated. As a result of the preoperatively stimulated erythropoiesis, patients can compensate better for any perioperative blood loss, and at the time of discharge often have higher hemoglobin levels than patients who had received allogeneic blood, even if the indication for transfusion was similarly strict. It is thus difficult to comprehend why arguments against PABD were raised at the end of the 1980s especially from those involved in transfusion medicine, at a time when this method really began to flourish. A common criticism involves the comparison of allogeneic blood components manufactured under highly standardized conditions with suboptimally produced autologous blood products, used to highlight the advantages of allogeneic blood. Since for the most part those going against the use of PABD are members of blood donation facilities not affiliated with hospitals, one might suspect that these institutions try to avoid contact with ill people and are afraid of the patients’ allegedly increased risk of side effects during donation. This notion is strengthened by the fact that those institutions usually leave the care of the patients to the hospitals and restrict their services to the processing of the donated autologous blood. Reluctance to PABD may also exist because it cannot be integrated into large-scale blood donation facilities without considerable organizational and logistic effort since clinically trained personnel and special equipment, e.g. monitoring devices, are needed. The higher expenditures for PABD because of the need for different manufacturing procedures may also play a role. Furthermore, the concept of individualized PABD goes against the efforts to increase standardization and automation in transfusion medicine. This is the reason behind the enforcement of unnecessary requirements for PABD such as component processing, leukocyte depletion, virological testing and, meanwhile, even blood group labeling of autologous units. These measures serve the main purpose to integrate PABD in the standardized manufacturing processes of big blood donation facilities in order to cause as little cost as possible. On the other hand, critics of PABD try everything to render this ‘unpopular’ method impossible to be carried out independently by clinicians. This raises the suspicion that reservations against PABD might also be caused by the fact that competence in transfusion medicine might develop independent from the influence of the blood donation facilities, for instance in separate autologous blood banks, which might generate a trend counteracting growing efforts for centralization and monopolization.

The author has difficulties to understand why the use of autologous blood is being dismissed because it is considered not cost-effective whilst the cost of allogeneic blood products is continually rising as a result of the growing efforts to increase the safety of these blood products (e.g. anti-HBc testing, HIV-PCR, bacterial testing, pathogen inactivation and, when possible, prion testing). These additional cost are however not needed when autologous blood is used! Do the opponents of PABD fear that the development towards ever safer allogeneic blood is hampered by PABD? The concern that PABD might threaten allogeneic blood donation is not justified since PABD can of course constitute only a very limited part of the overall blood supply. Furthermore, in the discussion about PABD it is often noticeable that this method is regarded as an egoistic action, whereas allogeneic blood donation arises from an altruistic motivation. One wonders whether PABD simply does not match with the perceptions and values of some blood donation services.

The author’s point of view can be summarized as follows: PABD ought to be carried out only under optimized circumstances. The indication for this procedure has to take into account the individual transfusion needs of the patient and the expected blood loss of the surgical procedures. This includes that autologous hemotherapy methods should be applied sensibly and are also used in combination if feasible. However, PABD is the only method to be regarded as a preventive measure. PABD has to be performed by specially trained and clinically experienced staff. PABD should take place either at the place of residence of the patient or preferably at the hospital where the surgical procedure is to be performed. Organization should be simplified by avoidance of unnecessary involvement of several separate facilities. Last, but not least, guidelines should continuously be critically appraised, and established requirements should be revised according to scientific evidence in order to avoid unnecessary obstacles and rising cost for PABD.
References