

EDITORIAL

EMERGING ALTERNATIVES TO ALLOGENEIC BLOOD TRANSFUSIONS

In 1808 J.W. Goethe wrote, "Blut ist ein ganz besonderer saft" (blood is a very special substance). Although not referring specifically to the biological properties of blood, this statement rings true, particularly as we enter the twenty-first century. It is exactly 100 years since Karl Landsteiner opened the door to the prospect of allogeneic blood transfusions(1). Modern transfusion medicine practice, however, began only during the latter part of the twentieth century.

Modern medicine depends on accurate diagnosis. Modern transfusion practice demands that patients be given the specific blood products they require. Thus, the ability to separate a single unit of whole blood into its components including red blood cells, platelets and plasma products, has enabled complex and effective therapeutic interventions to occur(2). However, as is the case with many effective therapies, recipients of blood products can experience significant morbidity and mortality(3,4). Although the risk of adverse effects from blood product transfusion has lessened considerably over the past decade, concerns about safety, inventory and cost of allogeneic blood still exist and have led investigators to look for several alternatives to reduce or avoid the transfusion of allogeneic blood products.

Efforts to prevent surgical bleeding by improved surgical techniques have been at the forefront of reducing or avoiding allogeneic blood transfusion. Such techniques have included drain clamping using epinephrine, using ultrasonic scalpels and percutaneous microwave coagulation, amongst others(5,6).

Iron and/or recombinant human erythropoietin has been used to raise haemoglobin levels pre - and post - surgery and in anaemia due to other causes(7). Additionally, erythropoietin has been demonstrated to be effective in increasing the volume of autologous blood that can be collected prior to elective orthopaedic surgery(8). More recently, Novel Erythropoiesis Stimulating Protein (NESP) has been confirmed to have similar effects(9).

A number of blood substitutes have been available. These include oxygen-carrying substitutes(10), plasma expanders(11) and platelet substitute(12). Two classes of oxygen-carrying substitutes have been available for sometime: (i) cell-free, cross-linked and modified haemoglobin solutions, known as haemoglobin based oxygen carriers (HBOCs) and; (ii) emulsions of synthetic organic compounds, known as perfluorocarbons. The oncotic property of albumin in the circulation has been shown to be replaceable by a number of synthetic plasma expanders including hydroxyethyl starch, dextran, polyvinyl pyrrolidone and various gelatins. Albumin, fractionated from human plasma, had been used for this purpose for many years, but recently it has been suggested that albumin, apart from the expense, may be associated with increased mortality(13). The newest class of blood

substitute, platelet substitute(12) has become available for potential use in the treatment of patients with thrombocytopenia. To date, however despite showing considerable promise, neither the oxygen-carrying blood substitutes nor the platelet substitute have reached the clinical arena(11,13). More recently, pathogen inactivated allogeneic blood, which is likely to reach the clinical arena within three to five years, has been undergoing research(14).

Despite the above discussed alternatives to allogeneic blood transfusion, autologous blood transfusion has been the most widely studied and used(15) and it is this that makes the study by Magoha *et al*(16) on autologous blood transfusion in elective surgery, published in this issue of the journal relevant. The objective of an autologous blood transfusion programme is to offer, to as many patients as possible, the opportunity of avoiding or at least limiting the risks of allogeneic blood transfusion. In the study by Magoha *et al*(16), only five per cent of all surgical patients benefited from this mode of transfusion. This is in contrast to some studies where autologous blood represented, 55% and 72% of all transfused blood in all patients and in elective surgery patients, respectively(17) but compares well with some studies done fifteen years ago in other countries(18). It is also to be noted that in countries like the USA autologous blood transfusion has fallen steadily from the high prevalence of 50 to 75% reported earlier(17) to four to five per cent now(19).

Recent studies have questioned the value of preoperative autologous donation (PAD) because the practice is wasteful and not cost-effective(2). One problem with PAD is that approximately 50% of autologous blood that is collected is discarded(21). Thus, it is surprising, but encouraging, that in the study by Magoha *et al*(16) reported in this issue of the journal, all blood collected were used and more was needed. Again, autologous blood donation and the transfusion of autologous blood are also associated with other risks(17). In one study, one in the 16, 783 autologous donations was associated with an adverse reaction severe enough to require hospitalisation, which is twelve times the risk associated with community donations by healthy individuals(22). Myocardial ischaemic events have also been reported to occur in association with autologous blood donation(23). Finally, the transfusion of autologous blood has many of the same complications as transfusion of allogeneic units, including bacterial contamination, haemolysis (ABO blood group-related due to errors in the administration of units) and volume overload(19).

Clinical studies have suggested that the predonation of autologous blood may actually be harmful to patients by lowering their haematocrits(24). The benefit of PAD in the patients who predonated autologous blood in the study by Bierbaum *et al*(25) was that it reduced the likelihood of allogeneic blood exposure by approximately two thirds

in non-anaemic patients and by approximately one third in patients with baseline anaemia (Hct<39%), when compared to patients who did not predonate autologous blood. However, the main benefit of autologous blood predonation practice is reported to be a substantial reduction in risks from viral transmission by allogeneic blood(26). Despite the recent re-evaluation of PAD, this practice remains common in orthopaedic surgery(25) and this is reflected in the study by Magoha *et al* (16) where 79% of the patients were orthopaedic cases.

Recommendations for selecting patients suitable for preoperative autologous blood donation have been published(27). The number of autologous units requested usually conforms to a variation of the maximum surgical blood order schedule, which determines how many blood units should be cross-matched before surgery. Attempts to stratify patients into groups at high and low risk for transfusion based on the baseline haemoglobin and on the type of procedure show some promise. In a Canadian study using a point score system, 80% of the patients undergoing orthopaedic procedures were identified to be at low risk (less than 10%) for transfusion, so that autologous blood procurement for these patients would not be recommended(28). However, one problem with algorithms based on an estimated blood loss and preoperative haematocrit is that blood losses are difficult to predict and many surgical procedures, even by the same surgeon, can be accompanied by a wide range of blood loss.

Studies have demonstrated that preoperative anaemia is the most important determinant for transfusion risk(20,25,26). One important approach to this problem is iron supplementation(29) before surgery. Another approach is erythropoietin therapy, an approved alternative to autologous blood predonation(20). In a recent, multicenter clinical trial, erythropoietin therapy was demonstrated to be equally efficacious to autologous blood predonation in reducing allogeneic blood exposure in patients undergoing orthopaedic surgery(30).

Acute normovolaemic haemodilution (ANH) entails the removal of whole blood from a patient immediately prior to surgery and simultaneous replacement with an acellular fluid, such as crystalloid or colloid, to maintain normovolaemia. The value of haemodilution comes from the fact that losses in red cell volume are reduced during perioperative blood loss because of the attendant lowering of haematocrit levels preoperatively(20). Moderate haemodilution to post-haemodilution haematocrit level of 28% results in the preservation of 100 to 200ml of red cells (the equivalent of one half to one unit of blood)(20). The efficacy of haemodilution can be improved by increasing pre-operative haematocrit levels with erythropoietin therapy and accepting lower post-haemodilution haematocrit levels(20). The aim of haemodilution is to protect patients who might have unpredictable or substantial blood losses, yet maintain perioperative haematocrit values that minimise the risk of myocardial ischaemia(31).

ANH has several advantages over autologous blood donation. First, the units procured by haemodilution require

no testing, so that the costs are substantially lower than those of autologous blood donation(20). Second, since the units of blood are not removed from the operating room, the possibility of an administrative error that could lead to an ABO - incompatible blood transfusion is theoretically eliminated as is the risk of bacterial contamination. Third, blood obtained by haemodilution does not require an additional investment of time by the patient since it can be safely performed at the time of surgery, nor does it prolong the duration of anaesthesia(20).

In conclusion, modern blood transfusion therapy is slowly evolving from its empiric origins towards a more scientifically rational practice. The decision to transfuse is multifactorial. Elements include an assessment of the need to increase tissue oxygen delivery weighed against the risks inherent in the transfusion or the decision not to transfuse. Given the current range of blood transfusion options a blood substitute could be used effectively in the surgical setting to obviate the use of allogeneic blood or augment autologous transfusion practices.

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