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# Autologous blood transfusion – a review

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## Summary

The discovery of HIV and other transfusion-transmissible infections has increased the demand for alternatives to allogeneic blood transfusion. One such alternative is autologous transfusion. This review presents an analysis of autologous transfusion. We conclude that autologous transfusion should form part of a strategy to minimise the risk associated with allogeneic transfusion in Nigeria and other developing countries.

Allogeneic transfusion is a ubiquitous practice. Once an unquestioned adjunct to patient care, it is currently being re-evaluated and alternatives are being considered in response to concerns about its safety.[1]

Some of the complications are immunological, and are thought to be responsible for the increase in tumour recurrence after surgical resection,[2,3] increased postoperative infection rates,[2,4] increased progression of HIV infection,[5] decreased cell mass and occasional transient hypotension,[1] and multiorgan failure.[6] These sequelae can be reduced by the use of syngeneic or autologous blood, or leucodepleted allogeneic blood components.[7]

Autologous blood transfusion is extremely safe. Cross-matching is not required; iso-immunisation to foreign protein is excluded; allogeneic blood is conserved for those who need it, particularly for emergencies; and the fear of transfusion-transmissible disease can be ignored.[8]

The greatest risk of autologous blood transfusion is clerical error and bacterial contamination of the autologous unit. Meticulous attention to standards can eliminate these problems.

Autologous transfusion is indicated for most elective operations that do not involve 'type and screen'. It is indicated for patients with very rare blood groups or complex red cell antibodies for whom it is difficult to find compatible blood, and also for some religious sects (such as Jehovah's Witnesses, in whom only intra-operative cell salvage is permissible).[9]

However, this practice is still under-appreciated in Nigeria and most developing countries. This review aims to provide information on the nature, clinical outcomes and cost benefits of autologous blood transfusion.

## Forms of autologous blood transfusion

Three main techniques for autologous transfusion are predeposit autologous donation (PAD), acute normovolaemic haemodilution (ANH), and perioperative cell salvage (PCS).

### Predeposit autologous donation (PAD)

PAD entails repeated preoperative phlebotomy, 4 - 5 weeks before surgery, during which time 4 or 5 units of in-date blood can be collected with ease.[1] This technique reduces exposure to allogeneic blood. It avoids many of the risks of transfusion, especially immunisation to red cell/platelets/HLA antigens and the transmission of infection. Any patient who is medically fit for elective surgery is fit to donate blood preoperatively. The reductions in haematocrit and blood viscosity that accompany preoperative donation improve microcirculation and tissue perfusion, and reduce the risk of thromboembolism.[8]

However, PAD is associated with increased risk of donation (severe vasovagal reaction and angina, or trauma due to the venepuncture) and wastage of unused units.[9] To reduce these, the medical exclusion criteria adopted by the British Committee for Standards in Haematology (BCSH) are advocated. The patient should be free from cardiovascular, cerebrovascular and respiratory diseases, and active infections; the patient should also have a confirmed and reliable surgical date, have good venous access and also be free from anaemia.

Pregnancy with impaired placental blood flow, intrauterine growth retardation, pregnancy-related hypertension, pre-eclampsia, renal disease, and insulin-dependent diabetes mellitus are other relative contraindications.[10,11]

## Acute normovolaemic haemodilution (ANH)

Acute normovolaemic haemodilution ('haemodilution') is a form of autologous donation performed preoperatively in the operating theatre or anaesthetic area. It is usually restricted to patients in whom substantial blood loss (> 1 litre or 20% of blood volume) is predicted. Whole blood (1.0 - 1.5 l) is removed, and simultaneously intravascular volume is replaced with crystalloid or colloid, or both, to maintain blood volume. The anticoagulated blood is then reinfused during or shortly after surgical blood loss has stopped in reverse order of collection.[1] The blood-sparing benefit of haemodilution is the result of the reduced red cell mass lost during surgical bleeding.

Patients of any age may be considered for ANH. ANH should only be considered when the potential blood loss is likely to be greater than 20% of blood volume. It should not be considered unless the preoperative haemoglobin (Hb) is > 11g/dl.[11] The amount of blood withdrawn depends on the target haematocrit and can be calculated using a standard formula, viz. $V = EBV \times (H_o - H_f)/H_{av}$ (where V = volume to be removed, EBV = estimated blood volume (usually taken as 70 ml/kg body weight), $H_o$ = initial $H_b$, $H_f$ = desired $H_b$ and $H_{av}$ = average $H_b$ (mean of $H_o$ and $H_f$)).

Haemodilution combines the advantages of PAD and some additional benefits, with controversies. Elaborate mathematical modelling studies have been published that take into account the dynamic nature of the patient's red blood cell (RBC) mass as it affects blood loss, fluid replacement, and blood transfusions.[12] Haemodilution is probably less expensive to accomplish than PAD, and it may be the only option available when surgery is performed in other than elective settings.[13] In orthopaedic and cardiovascular surgery, reductions in allogeneic blood use have been reported after extreme haemodilution.[14] More modest haemodilution may also be beneficial,[15] but this is not accepted by all.[12] The severity of the anaemia could affect oxygen transport, although the concomitant drop in blood viscosity, and compensatory cardiac output increase, could restore oxygen delivery. However, one group has suggested that haemodilution may jeopardise patients at risk for myocardial infarction.[9]

## Perioperative cell salvage (PCS)

Intraoperative RBC salvage entails the collection and reinfusion of blood lost during or after surgery. Shed blood is aspirated from the operative field into a specially designed centrifuge. Citrate or heparin anticoagulant is added, and the contents are filtered to remove clots and debris. Centrifuging concentrates the salvaged red cells, and saline washing may be used. This concentrate is then reinfused. Devices used can vary from simple, inexpensive, sterile bottles filled with anticoagulant to expensive, sophisticated, high-speed cell washing devices. Postoperative salvage refers to the process of recovering blood from wound drains and reinfusing the collected fluid with or without washing.[1]

Many surgical patients who undergo procedures in which transfusions are likely can benefit from intraoperative blood salvage, especially where PAD is impossible or inadequate.[8]

Relative contraindications to the use of PCS include infection (contamination of the operative field by bacteria) and presence of malignant cells. However recent published work suggests that the risk of dissemination of malignant disease is minimal.[9] Patients undergoing cell salvage need not be screened for viral markers. Universal precautions to protect staff from the risks of virus transmission must always be observed.[11]

The haematocrit of salvaged unprocessed blood is typically low because of a combination of dilution from irrigation fluids and some degree of mechanical haemolysis.[16] After blood has been exposed to serosal surfaces in operative fields, it becomes depleted of coagulation factors and platelets;

**TABLE I. DIRECT COST OF ALLOGENEIC BLOOD TRANSFUSION AND VARIOUS FORMS OF AUTOLOGOUS BLOOD TRANSFUSION**

| | Cost per unit (US$) | | | |
|---|---|---|---|---|
| Item | Allogeneic | PAD | ANH | PCS |
| **Collection** | | | | |
| **Labour** | **1.41** | **2.1** | **0.7** | **4.2** |
| **Equipment** | **2.82** | **3.5** | **2.82** | **6.3** |
| **Infectious disease testing*** | | | | |
| **Initial** | **11.9** | **-** | **-** | **-** |
| **Confirming** | **6.3** | **-** | **-** | **-** |
| **Blood processing and inventory management** | | | | |
| **Labour** | **2.82** | **2.82** | **2.1** | **2.82** |
| **Equipment** | **1.42** | **1.41** | **3.5** | **1.41** |
| **Compatibility testing** | | | | |
| **Labour** | **3.5** | **-** | **-** | **-** |
| **Equipment** | **2.82** | **-** | **-** | **-** |
| **Total** | **32.99** | **9.83** | **9.12** | **14.73** |

*Blood is tested for syphilis, hepatitis B surface antigen, antibodies to hepatitis B core antigen, antibodies to hepatitis C virus, antibodies to HIV 1 and 2.
PAD = predeposit autologous donation; ANH = acute normovolaemic haemodilution; PCS = perioperative cell salvage.

a clinical consequence termed 'salvaged blood syndrome' has been described, which involves multiorgan failure and consumption coagulopathy.[1] Nevertheless, renal sequelae are uncommon.[17] Qualitative coagulation abnormalities often observed in recipients of large volumes of salvaged blood include hypofibrinogenaemia, elevated fibrin degradation products, thrombocytopenia, and prolonged prothrombin and partial thromboplastin times.[18] During open-heart operation, mediastinal blood may contain very high levels of cardiac muscle enzymes, especially creatine phosphokinase, as well as lactate dehydrogenase from haemolysed RBCs.[19] The reinfusion of shed mediastinal blood can result in increased levels of these enzymes and can confound the diagnosis of myocardial infarction in the postoperative period.[20]

Salvage is a safe and efficacious alternative to allogeneic red cell transfusion if standards are maintained, but fewer data are available on clinical outcomes than for PAD and ANH. These techniques offer advantages similar to those of haemodilution but do not require infusions of crystalloid or colloid to preserve blood volume. Many litres of blood can be salvaged intraoperatively during extensive bleeding, far more than with other autologous techniques. Intraoperative salvage is used extensively in cardiac surgery, trauma surgery, and liver transplantation. Salvage can be one of the most expensive autologous techniques because costly capital equipment and disposables are used, and it is usually restricted to procedures resulting in substantial blood loss (> 1 - 2 l).[1]

## Data on clinical outcomes

Blumberg *et al.*[1] evaluated 16 observational studies and concluded that autologous blood transfusion is associated with significant reductions in postoperative infection.

The number of randomised studies is low; a PUBMED search revealed only 5. Patients randomised to receive autologous rather than allogeneic blood had better clinical outcomes (reduction in postoperative infection and recurrence of cancer) in 4 of 5 studies.[3,21-23] In the only study that supported allogeneic transfusion over autologous, one-third of the patients randomised to receive autologous blood transfusion also received allogeneic blood because allowable blood loss was exceeded.[24]

Few data exist comparing the relative advantage of the various forms of autologous transfusion. Ness *et al.*[15] randomised 50 patients to donate PAD of 3 units of red cells or to undergo ANH before radical retropubic prostatetectomy. They found that ANH could safely replace or augment PAD as a means of decreasing the use of allogeneic blood, and they consider their results applicable to any surgical procedure in which a 1 000 ml blood loss is anticipated. In a randomised trial of patients undergoing total knee arthroplasty who predonated either 1 unit of blood for unilateral, or 2 units for bilateral knee procedures, or who underwent ANH to a haematocrit of 28%, Goodnough *et al.*[25] found no differences in the amount of allogeneic blood transfusions among the PAD and ANH cohorts for all 32 patients. A meta-analysis of all 24 eligible prospective randomised trials (1 218 patients) comparing ANH with control groups showed that ANH effectively reduced the likelihood of exposure to at least 1 unit of allogeneic blood in cardiac and miscellaneous procedures but not in orthopaedic surgery. The overall results of this analysis were inconclusive since sample sizes were small, variable amounts of blood were drawn,[26] and trials involving different surgical procedures had to be pooled.[27]

Data from randomised studies confirm the results of observational studies and the comparative advantage of autologous blood transfusion over allogeneic blood transfusion.

## Cost of autologous blood transfusion

Comparative cost data on the various forms of autologous blood transfusion are rather subjective and inconsistent; the body of literature to date on cost effectiveness compared allogeneic with autologous blood transfusion. Most of such studies concluded that allogeneic is more cost effective than autologous blood transfusion.[9,28] The increased cost comes from unused autologous collection; this problem is magnified by over-collection and unnecessary utilisation, and by the extra work involved in deviation from routine large-scale allogeneic collection practices.[9]

In our setting, we evaluated a hypothetical cost estimate by considering the direct cost accruable for each unit of allogeneic blood transfused and the various forms of autologous blood transfusion procedures. Table I gives a summary of the direct cost for the various procedures less the cost of units discarded and the cost of treating complications of transfusion. Generally, direct cost was estimated by computing the resources required for donor recruitment, infectious disease testing, phlebotomy, cross-matching, administrative and inventory management, and overhead cost. It is obvious from our estimate that an autologous blood transfusion procedure enjoys comparative advantage over allogeneic blood transfusion per unit of transfusion.

In one hypothetical cost-utility analysis of patients undergoing primary elective hip replacement, cost-effectiveness of transfusion per quality-adjusted life-year (QALY) was estimated at an extremely high $3 400 000. However, if allogeneic transfusion was assumed to increase the risk of postoperative bacterial infection, a possibility suggested by some workers,[2,4] the cost of using autologous blood fell to less than $50 000 per QALY, and the procedure became dominant (cheaper to use than allogeneic blood) as the infection risk rose.[29] However, it should be recognised that transfusion medicine in sub-Saharan Africa is practised in a setting that is inherently risk-averse, owing, of course, to heightened public awareness of HIV and other transfusion-transmissible viruses, given their high prevalence and the absence in most of our settings of molecular technologies for earlier and proper detection. In the context of our limitations, it might be erroneous to accept cost effectiveness strictly on the basis of programmes that are less expensive and more effective, but also to accept even programmes that are more expensive and more effective because it is the subjective health outcome that is paramount. Otherwise, how do we compensate for all the negative consequences of immunomodulation and fears?

## Conclusion

An autologous blood transfusion programme must be reliable, effective and safe for patients and practitioners. A hospital wanting to establish an autologous blood transfusion service requires the total commitment of those involved. The essence

of success is motivation and communication and the planning involves all key players. It is quite likely that many of our patients will appreciate the value of autologous transfusion. Although there are considerable organisational problems to overcome, and the need for a strong sense of commitment, the setting up of an autologous blood transfusion service to meet this demand can only be beneficial. Our colleagues will have to be educated to promote the concept that the use of a person's own blood is safest. It will conserve donor blood for those who need it, and result in more effective use of blood supplies. An autologous blood transfusion programme should only be complementary to the established blood transfusion programme. We can make this work even in our centres. First, appreciate the concept; make further investigation with regard to cost benefit; motivate for the establishment of a transfusion committee, then policy; and sell the idea with facts. Let us speak to be heard!

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