Strategies for reducing the exposure to donor blood

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Why is there a need to reduce the use of blood?

The quality and safety of blood in the UK are among the best in the world but, like all other clinical procedures, the transfusion of donor blood is not risk free. The most logical approach to reducing the risk of transfusion is to use blood only when strictly clinically necessary and where there are no alternatives. There have been recent, essentially unfunded, initiatives to promote the appropriate use of blood and the avoidance of transfusion,[1,2] and the Chief Medical Officer made a number of practical recommendations in his 2003 annual report (Table 1).[3] It appears that these efforts are having some effect: the demand for blood in England and North Wales, which steadily increased during the 1990s, has successively reduced by 1%, 1% and 6% over the last three years. However, it is likely that blood usage could be further reduced without compromising patient safety.

High quality evidence about clinical outcomes associated with blood transfusion has only recently been provided. Recent randomised controlled trials have shown that using less blood neither impairs nor improves patient outcome.[4,5] Current practice in surgery and critical care has been strongly influenced by one of these trials which found that a 'restrictive' transfusion strategy using a haemoglobin (Hb) concentration trigger of 7 g/dl showed a trend towards better clinical outcome than a 'liberal' strategy with an Hb trigger of 10 g/dl.[4] Data from over 24,000 patients with acute coronary syndromes demonstrated an association between transfusion and higher 30-day mortality for patients with a nadir haematocrit greater than 25%, suggesting that a haematocrit as low as 25% may be tolerated in otherwise stable patients with ischaemic heart disease.[6]

The safety of blood transfusion

The risk of transfusion-transmitted infection (TTI) by donor blood transfusion has never been lower. During the period 1996–2003, data from the UK haemovigilance scheme (Serious Hazards of Transfusion (SHOT)) show that the incidence of death and major morbidity associated with transfusion was 0.39 and 1 per 100,000 units, respectively.[7] The most frequent causes of death were non-infectious complications (Table 2). Major morbidity due to TTI was mostly due to bacterial contamination associated with stored platelet concentrates. The chance that donor transfusion will transmit one of the viruses for which blood is currently tested is very low. The incidence of viral transmission of HIV, HBV and HCV is 4.58, 0.41 and 22.09 per million blood donations, respectively (K Davison; personal communication).

Two of the 50 recipients of blood from blood donors known to have developed variant Creutzfeldt-Jakob disease (vCJD) have themselves become infected; one recipient died of vCJD,[8] and the other died of unrelated causes but with histological evidence of vCJD.[9]

The cost of providing blood in the UK has greatly increased since 1995, mostly due to measures to reduce the risk of transmission of vCJD and to new microbiological tests. Further measures, such as prion removal filtration, have been estimated to add £100 million to the current £500 million cost to the NHS for blood.[10]

Where does blood go?

A joint study between the National Blood Service and the Medical Research Council found that the average age of patients receiving red cells was 60 years, with the peak decade for transfusion 71–80 years; 58%, 37% and 5% of red cell units were used for medical, surgical and obstetric and gynaecology patients, respectively. The most frequent reasons for red cell use in medicine were cancer and gastrointestinal bleeding, and in surgery cardiac and orthopaedic procedures (Table 3).[11]

Strategies for reducing blood use in surgical patients

There is evidence of wide variation between hospitals in the use of blood for

Table 1. Action recommended by the Chief Medical Officer.[3]

- Clinical governance reviews in every hospital should ensure that best practice guidance, protocols and safe procedures are being complied with for blood and blood product use
- Orders for blood or blood products for individual patients should usually be made only by a trained doctor
- Postgraduate education and training programmes for doctors, nurses and other relevant health professionals should place more emphasis on safe, appropriate use of blood and blood products
- Participation in the SHOT scheme should be demonstrably active, with reports of adverse events and near misses made by all hospitals
- Hospital contingency planning should include plans for potential blood shortages
- Hospitals must improve information technology systems to facilitate better blood stock management, ensure traceability from donor to recipient and routinely monitor blood usage by clinical specialty
- Financial incentives to encourage hospitals to use blood more appropriately should be explored

SHOT = Serious Hazards of Transfusion.

common surgical procedures.[12] A recent audit in primary hip replacement surgery showed a range of 23–58% of patients transfused (Table 4). Most patients who were transfused received only one or two units of blood, and most of these were discharged with an Hb above 10 g/dl. If they had not been transfused, their Hb would still have been above 8 g/dl which would not be expected to impair postoperative recovery.[13]

The emphasis on blood management by clinical teams varies greatly. Some teams avoid transfusion completely by close attention to patient care throughout the peri-operative period (Table 5). The combination of algorithms for blood management and restrictive transfusion thresholds offers a better approach to blood conservation than the implementation of single interventions such as autologous transfusion.[14,15] Much of the evidence suggesting a benefit from autologous transfusion is derived from methodologically poor studies with inadequate clinical outcomes.[15]

Pre-operative

Sufficient time should be allocated for the identification and treatment of anaemia, ideally in the setting of a surgical pre-assessment clinic.[14] Drugs that interfere with haemostasis should be discontinued wherever possible. Predeposit autologous transfusion is no longer recommended as a strategy for blood conservation because there is no evidence of better clinical outcome; there are also practical problems in scheduling surgery, which causes inconvenience for patients. Any benefits are offset by a higher incidence of pre-operative anaemia.[15,16]

Table 2. Morbidity and mortality associated with the major complications of blood transfusion (data from Ref 7).

	Total	IBCT	TA-GvHD	TRALI	TTI	Other
Death associated with transfusion:						
total number	90	16	13	33	8	21
number/100,000 units transfused	0.39	0.07	0.06	0.14	0.03	0.09
Major morbidity:						
total number	249	85	0	89	34	41
number/100,000 units transfused	1.1	0.37	0	0.39	0.15	0.18
Minor or no morbidity:						
total number	1,580	1,191	0	9	2	378
number/100,000 units transfused	6.87	5.18	0	0.04	0.01	1.6

IBCT = incorrect blood component transfused; TA-GvHD = transfusion-associated graft-versus-host disease; TRALI = transfusion-associated acute lung injury; TTI = transfusion-transmitted infection.

Table 3. Use of red cell transfusions by clinical specialties (data from Ref 11).

	Red cell units (%)	Reason for use	%
Medicine	58	Treatment of cancer	51
		Diseases of the digestive tract	19
		Non-malignant blood disorders	13
		Other	17
Surgery	37	Orthopaedics	18
		Cardiac	18
		Abdominal surgery	16
		Other	48

Intra-operative

Good anaesthetic and surgical technique is essential. Acute normovolaemic haemodilution is relatively ineffective, but intra-operative cell salvage (ICS) reduces blood use in cardiac, vascular and orthopaedic surgery.[15,17] ICS is currently underutilised in the UK.

Systematic reviews have concluded that aprotinin reduces transfusion requirements, particularly where there is major blood loss such as in cardiac, vascular and liver transplant surgery; tranexamic acid has an inconsistent effect and desmopressin is ineffective.[18,19]

Postoperative

General measures for reducing the use of blood postoperatively include:

- adequate oxygenation
- avoidance of hypertension and over-anticoagulation, and
- careful observation for excessive blood loss, indicating the need for further surgery.

Postoperative cell salvage is frequently used in orthopaedic and cardiac surgery, although there is no evidence for improved clinical outcomes.

Implementation of a local policy for the use of blood based on national guidelines, with education, audit and feedback of data, can be effective in reducing blood use. After the introduction of guidelines in one large hospital in Scotland, data on blood use in relation to Hb before and after transfusion were fed back to clinical teams with suggestions about appropriate blood use. Audits carried out before the initiative and after one year showed that red cell use had decreased by 20%, with no demonstrable effect on morbidity or mortality.[20]

Strategies for reducing blood use in medical patients

Opportunities for reducing blood use have been less well explored in medical than in surgical patients. Good blood management depends on many of the principles described for surgical patients, including:

- identification of the cause of anaemia and its correction with appropriate treatment (eg with haematinics, the timely estimation of blood counts and haemostasis in massive blood loss)
- the implementation of local policies and guidelines for blood use, based on national guidelines, with education, audit and feedback of data to clinical teams.

Recombinant erythropoietin (EPO) improves quality of life by effective treatment of anaemia in patients with chronic renal failure. It is also effective in avoidance of blood transfusion in cancer patients.[21-23] The benefit of treatment with EPO is limited in the presence of functional iron deficiency because the intense erythropoiesis stimulated by EPO causes a demand for iron greater than the ability of stores to release it. Intravenous iron is frequently needed to achieve a maximal response to EPO.[24] The West Midlands Health Technology Assessment Group has been commissioned by the National Institute for Clinical Excellence to undertake a systematic review and health economic study of the use of EPO in cancer.

The management of massive blood loss

The usual presentation of major blood loss is as an emergency in accident and emergency, obstetrics or surgery. The restoration of an adequate circulating volume is the most important immediate aim, followed by treatment of any surgical source of bleeding and correction of haemostatic abnormalities with blood components.[25] Good communication is essential between clinicians and blood bank staff about the timely and effective use of blood components.

Recombinant activated factor VII (rVIIa) is effective in the treatment of severe haemorrhage unresponsive to standard management. However, there are few data on its safety and effectiveness.[26] Currently, the decision on whether to use rVIIa in a patient with uncontrolled bleeding must be made by individual clinicians guided by hospitals' medicines and transfusion committees.

Table 4. Audit of blood use in primary hip replacement surgery in seven hospitals (data from the Oxford Regional Transfusion Committee).

	Blood use	
	Mean	**Range**
Patients transfused (%)	41	23–58
Discharge Hb (g/dl):		
● untransfused patients	10.8	8.6–13.5
● patients transfused with 1–2 units of blood	10.9	8.9–13.1
Patients transfused with 1–2 units of blood with discharge Hb >10 g/dl (%)	72	50–75

Hb = haemoglobin.

Table 5. Strategies for reducing blood use in surgical patients.

Pre-operative	● Identification and correction of anaemia ● Avoidance of drugs interfering with haemostasis (eg anticoagulants, drugs with antiplatelet activity)
● Intra-operative	● Good anaesthetic and surgical techniques ● Avoidance of hypothermia ● Reduction of regional vascular pressure ● Cell salvage ● Point-of-care testing (for blood count and haemostasis) to guide the use of blood components ● Use of drugs such as aprotinin
● Postoperative	● Implementation of local guidelines for the use of blood based on national guidelines, with education, audit and feedback of data to clinical teams ● Minimising the volume of blood collected for laboratory samples ● Washed or unwashed cell salvage

Key Points

Blood usage is reducing, but there remains wide variation between clinical teams

There is potential for further reduction in blood use by avoidance of inappropriate transfusion and greater use of alternatives to donor blood

Recent data from a small number of randomised controlled trials indicate that reduced use of blood does not impair clinical outcomes, but more high quality evidence is needed about blood transfusion practice

The combination of algorithms for blood management and the adoption of restrictive transfusion thresholds is the best approach to blood conservation

Blood usage is greater in medical than in surgical patients, but most efforts for blood conservation so far have been in surgery

Specific methods for reducing blood usage in surgery include the identification and treatment of pre-operative anaemia, and the use of intra-operative cell salvage and drugs such as aprotinin in selected groups of surgical patients

KEY WORDS: algorithms for blood management, blood conservation, clinical trials, comparative audit, intra-operative cell salvage, patient safety, recombinant erythropoietin, recombinant factor VIIa, restrictive transfusion thresholds, treatment of pre-operative anaemia

Future prospects

There has been better recent recognition of the risks of transfusion and the safety of restrictive transfusion policies. Blood usage is reducing, but there is evidence both of considerable variation in the usage and of some inappropriate use. Better education about good transfusion practice, wider adoption of algorithms for blood management and conservative transfusion thresholds, supported by local and national comparative audit initiatives, should result in further reductions. Computer requesting of transfusions and referral of unapproved requests to a haematologist have been shown to reduce blood usage;[27] wider adoption of this approach should be considered as part of the development of electronic prescribing.

Better quality evidence is needed about good transfusion practice. A recent editorial made a strong case for balancing the large and recurring expenditure on blood safety against the costs of clinical trials to develop the evidence base for the effective use of donor blood transfusion and strategies for the avoidance of transfusion.[10]

References

1 Department of Health. *Better Blood Transfusion*: *Appropriate Use of Blood*. Health Service Circular, HSC 2002/009. www.doh.gov.uk/bbt2

2 Report from the Working Parties on Autologous Transfusion and Alternatives to Transfusion of the NBS subgroup on Appropriate Use of Blood. *A national blood conservation strategy for the National Blood Transfusion Committee and the National Blood Service*. www.dh.gov.uk/assetRoot/04/08/95/13/04089513.pdf

3 Donaldson L. *On the state of the public health*. Annual Report of the Chief Medical Officer 2003. London: DH, 2003. www.dh.gov.uk/PublicationsandStatistics/Publications/AnnualReports

4 Hebert PC, Wells G, Blajchman MA, Marshall J *et al*. A multicenter, randomized, controlled trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 2004;**340**:409–17.

5 Finfer S, Bellomo R, Boyce N, French J *et al*; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004;**350**:2247–56.

6 Rao SV, Jollis JG, Harrington RA, Granger CB *et al*. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. *JAMA* 2004;**292**:1555–62.

7 *Serious hazards of transfusion*. Annual report 2003. Serious Hazards of Transfusion scheme, Manchester, UK, 2004. www.shotuk.org

8 Llewelyn CA, Hewitt PE, Knight RS, Amar K *et al*. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. *Lancet* 2004;**363**:417–21.

9 Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. *Lancet* 2004;**364**:527–9.

10 McClelland B, Contreras M. Appropriateness and safety of blood transfusion. *BMJ* 2005;**330**:104–5.

11 *Epidemiology and Survival of Transfused Recipients Study. Interim report*. National Blood Service/Medical Council Clinical Studies Unit, May 2004.

12 The Sanguis Study Group. Use of blood products for elective surgery in 43 European hospitals. *Transfus Med* 1994;**4**:251–68.

13 Carson JL, Terrin ML, Magaziner J, Jay M. Anemia and postoperative rehabilitation. Review. *Can J Anaesth* 2003;**50**(6 Suppl):S60–4.

14 Slappendel R, Dirksen R, Weber EW, van der Schaaf DB. An algorithm to reduce allogenic red blood cell transfusions for major orthopedic surgery. *Acta Orthop Scand* 2003;**74**:569–75.

15 Carless P, Moxey A, O'Connell D, Henry D. Autologous transfusion techniques: a systematic review of their efficacy. Review. *Transfus Med* 2004;**14**:123–44.

16 Henry DA, Carless PA, Moxey AJ, O'Connell D *et al*. Pre-operative autologous donation for minimising perioperative allogeneic blood transfusion. Review. *Cochrane Database Syst Rev* 2001, Issue 2.

17 Carless PA, Henry DA, Moxey AJ, O'Connell DL, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. Review. *Cochrane Database Syst Rev* 2003, Issue 4.

18 Henry DA, Moxey AJ, Carless PA, O'Connell DL *et al*. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. Review. *Cochrane Database Syst Rev* 2001, Issue 1.

19 Carless PA, Henry DA, Moxey AJ, O'Connell D *et al*. Desmopressin for minimising perioperative allogeneic blood transfusion. Review. *Cochrane Database Syst Rev* 2004, Issue 1.

20 Garrioch MA, Sandbach J, Pirie E, Morrison A *et al*. Reducing red cell transfusion by audit, education and a new guideline in a large teaching hospital. *Transfus Med* 2004;**14**:25–31.

21 Bohlius J, Langensiepen S, Schwarzer G, Seidenfeld J *et al*. Erythropoietin for patients with malignant disease. Review. *Cochrane Database Syst Rev* 2004, Issue 3.

22 Rizzo JD, Lichtin AE, Woolf SH, Seidenfeld J, Bennett CL. Use of epoetin in patients with cancer: evidence-based clinical practice guidelines of the American Society of Clinical Oncology and the American Society of Hematology. *J Clin Oncol* 2002;**20**:4083–107.

23 Samol J, Littlewood TJ. The efficacy of rHuEPO in cancer-related anaemia. Review. *Br J Haematol* 2003;**121**:3–11.

24 Ford PA, Mastoris J. Strategies to optimize the use of erythropoietin and iron therapy in oncology patients. Review. *Transfusion* 2004;**44**(12 Suppl):15S–25S.

25 Stainsby D, MacLennan S, Hamilton PJ. Management of massive blood loss: a template guideline. Review. *Br J Anaesth* 2000;**83**:487–91.

26 Roberts HR, Monroe DM, White GC. The use of recombinant factor VIIa in the treatment of bleeding disorders. Review. *Blood* 2004;**104**:3858–64.

27 Lapierre V, Oubouzar N, Tramalloni D, Hartmann O. Implementation of a specific approval process for blood-components prescription. *Lancet* 2000;**355**:465.