GUIDELINES FOR THE CLINICAL USE OF RED CELL TRANSFUSIONS

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This document provides general recommendations for the clinical use of red cell transfusions. Background information is provided after the section on recommendations, and the appendix provides control (audit) measures for the use of red cell transfusions.

Recommendations

These have been adapted from a number of existing guidelines (American College of Physicians, 1992; American Society of Anesthiologists Task Force on Blood Component Therapy, 1996; Consensus Conference on Red Cell Transfusion, Royal College of Physicians Edinburgh, 1994), and a recent systematic review of published recommendations and guidelines for the transfusion of red cells (Calder et al, 1997). They are primarily intended to guide practice for adults.

General principles

- clinicians prescribing red cell transfusions should be aware of the appropriate indications, and the risks and benefits of transfusion.
- patients should be given information about the risks and benefits of red cell transfusion, whenever possible, and possible alternatives including autologous transfusion. Patients have the right to refuse transfusion, but signed consent is not required.
- the cause for anaemia should be established, and treatment with red cell transfusions should not be given where effective alternatives exist e.g. treatment of iron deficiency, megaloblastic and autoimmune haemolytic anaemia.
- there is no universal 'trigger' for red cell transfusions i.e. a given level of haemoglobin at which transfusion of red cells is appropriate for all patients. Clinical judgement plays a vital role in the decision to transfuse red cells or not.
- in acute blood loss, crystalloids or synthetic colloids, not blood, should be used for rapid acute volume replacement. The effects of anaemia need to be considered separately from those of hypovolaemia. It is accepted that in massive blood loss empirical decisions have to be taken, but it is still important to define patients' needs for blood components and fluid replacement as specifically as possible to ensure that blood is prescribed rationally.
- local arrangements should be in place to provide compatible blood urgently for patients with major bleeding.
- the reason for administration of red cell transfusions should be documented in patients' medical records.

Indications for the use of red cell transfusions

To treat acute blood loss:-

Patients with acute massive blood loss (>40% loss of blood volume) should ideally be managed by experienced clinicians in a suitable setting such as high dependency units.

A blood sample should be sent to the hospital blood bank for compatibility testing and for urgent provision of blood according to hospital policy.

It may be difficult to assess the amount of blood loss, but consideration of lost circulating volume may be useful in guiding transfusion management. See Table 1 for a classification of hypovolaemic shock according to % blood loss, and the associated clinical signs (Baskett, 1990).

First estimate lost circulating volume:

⇒ <15% loss of blood volume (750mL in an adult): do not transfuse unless blood loss is superimposed on pre-existing anaemia or when the patient is unable to compensate for this level of loss because of severe cardiac or respiratory disease.

⇒ <30% loss of blood volume (800-1500mL in an adult): will need to transfuse crystalloids or synthetic colloids, the need for red cell transfusion is unlikely unless the patient has pre-existing anaemia, reduced cardiorespiratory reserve or if blood loss continues.

⇒ <40% loss of blood volume (1500-2000mL in an adult): rapid volume replacement is required with crystalloids or synthetic colloids, and red cell transfusion will probably be required.

⇒ >40% loss of blood volume (>2000mL in an adult): need rapid volume replacement including red cell transfusion.

Next consider the haemoglobin: Have in mind a target value at which to maintain the patient's haemoglobin. The haemoglobin should be considered along with other factors such as the rate at which blood is being lost in formulating red cell use. Broadly speaking:

⇒ red cell transfusion is not indicated when estimates of actual and anticipated haemoglobin level are > 10g/dL.

⇒ red cell transfusion is always indicated when the haemoglobin level is < 7/g/dL. Transfuse according to ongoing red cell loss. If otherwise stable transfuse 2 units in adults (or equivalent in children according to size) and reassess.

⇒ patients with haemoglobin levels between 7-10g/dL are in a grey area. Clinicians often transfuse red cells, although available evidence suggests that this is not strictly justified.

⇒ in patients who may tolerate anaemia poorly e.g. patients over the age of 65 years, and patients with cardiovascular or respiratory disease, consider raising the level at which transfusions are indicated to < 8g/dL.

Next consider the risk of further bleeding from disordered haemostasis and perform appropriate screening tests: Abnormal haemostasis associated with acute blood loss is usually due to thrombocytopenia or platelet dysfunction; treat with platelets according to guidelines. Coagulopathies which require replacement of clotting factors are less common, and treat according to guidelines. Seek the advice of a haematologist about the appropriate investigation and management of abnormal haemostasis, including the use of platelet and coagulation factor replacement before invasive procedures.

Postoperative transfusion:-

The same target values for haemoglobin levels should be applied as for acute blood loss. There is no case for transfusion back to a "normal" haemoglobin, and to avoid transfusion when the haemoglobin is >10g/dL is in line with current practice. Patients may need iron supplements (iron stores should be built up preoperatively in patients with suspected or definite evidence of iron deficiency).

Anaemia in Critical Care:-

The same target values should be applied as for acute blood loss. There is strong evidence that over-transfusion increases mortality in this group (Hebert, 1999).

Chronic anaemia:-

It is worth repeating that the cause for anaemia should be established, and treatment with red cell transfusions should not be given where effective alternatives exist. Treat patients' symptoms not the haemoglobin level. Transfuse to maintain the haemoglobin just above the lowest level which does not cause symptoms of anaemia. Note that many patients will be asymptomatic with a haemoglobin level <8g/dL.

Background

There is agreement that red cell transfusions are required to increase the oxygen-carrying capacity of the blood by raising the haemoglobin level of patients with acute and chronic anaemia. However, it has not been possible to reach a consensus on the precise indications for their use despite numerous attempts in the form of guidelines and at Consensus Conferences.

There is evidence of very significant variation in the use of red cell transfusions, for example as provided by the Sanguis study, indicating that currently available guidelines have little impact on clinical practice (The Sanguis Study Group, 1994). This variation does not correlate with patient characteristics, appearing to be more dependent on the individual clinician ordering the transfusion, strongly suggesting that inappropriate use is widespread. Several recent events in relation to blood transfusion in the UK support the view that renewed efforts should be made to encourage better use of red cell transfusions, including:-

- the continuing rise in the use of red cell transfusions by approximately 2% per year.
- waiting list initiatives for elective surgery, which are likely to increase further the demand for red cell concentrates; about 45% of red cell transfusions are given to surgical patients (Murphy et al, 1998).
- concern about the National Blood Service's ability to meet this increasing demand and the possibility of more frequent and prolonged periods of blood shortages.
- renewed concerns about the safety of transfusion, in relation to both infectious and non-infectious complications of transfusion as highlighted in the Serious Hazards of Transfusion (SHOT) initiative, and including the risk of transmission of new variant Creutzfeldt-Jacob disease (nvCJD).
- new safety requirements such as leucocyte-depletion and nucleic acid testing which are increasing the cost and complexity (which leads to some losses) of the production of blood components.

All the randomised controlled trials on which evidence-based guidelines for the transfusion of red cells should ideally be based have not been carried out. **The purpose of this document is to set 'pragmatic' guidelines for the use of red cell transfusions. While recognising they are not wholly evidence-based, it is hoped that they can be used to encourage more consistent transfusion practice and provide a benchmark for clinical audit.**

There is evidence that the use of transfusion algorithms (Despotis, 1994), and prospective audit allied to educational programmes can be effective in modifying clinicians' behaviour in ordering transfusions (Toy, 1994). Clinical governance can be used to support this process, and hold clinicians accountable if they are unwilling to change their practice without providing a valid explanation for refusing to do so (Eisenstaedt, 1997). Meanwhile, it is hoped that randomised controlled trials will be carried out to provide the clinical outcome data for evidence-based transfusion practice in the future.

What parameters can be used to indicate the need for red cell transfusion?

1) The haemoglobin level

The benefit of red cell transfusion is usually thought of in terms of increasing the oxygen carrying capacity of the blood, but a more relevant consideration is the avoidance of tissue hypoxia. Adequacy of tissue oxygenation is a balance between oxygen consumption and delivery. Many factors influence oxygen consumption including exercise, body temperature, sympathetic and metabolic activity, heart rate and the effect of drugs. Oxygen delivery is the product of the oxygen content of the blood and the amount of blood delivered (or blood flow). When the haemoglobin level falls, there is a compensatory increase in the cardiac output and blood flow, and other factors such as reduced blood viscosity, and peripheral vasodilatation act to maintain oxygen delivery to the tissues.

Clinicians may underestimate the effectiveness of such adaptive mechanisms, perhaps explaining the tendency towards over-reliance on measurement of the haemoglobin level and excessive use of red cell transfusions. Chronic anaemia is even better tolerated than acute anaemia because of better oxygen delivery associated with an increase in 2,3 DPG and a shift in the oxygen dissociation curve. The reserve of oxygen carrying capacity is such that cardiac output does not usually increase until the haemoglobin level falls below 7g/dL.

For many years, it was traditional to use a trigger of a haemoglobin level of 10g/dl for red cell transfusion prior to surgery, during surgery and for transfusions to medical patients. However, evidence accumulated of renal transplant patients and Jehovah's witnesses with lower haemoglobin levels undergoing surgery successfully (Stehling & Simon, 1994; Carson et al, 1988). In the study of Jehovah's witnesses, no patient with a pre-operative haemoglobin level of greater than 8g/dl and with blood loss less than 500mL died (Carson et al, 1988). Furthermore, acute isovolaemic anaemia to a haemoglobin level of around 5g/dL in volunteers and patients produced no evidence of inadequate oxygenation (Weiskopf et al, 1998), and a recent review of the literature on red cell transfusion found insufficient evidence to justify the use of a single haemoglobin level as a threshold for the transfusion of patients with acute or chronic anaemia (Hebert et al, 1997).

Numerous guidelines for the use of red cell transfusions have been produced; up to 15 quoted in one paper (Weiskopf, 1998) with various suggestions for the trigger for transfusion, and with a tendency for the level of haemoglobin as the trigger for transfusion to be lowered. Some now suggest that this has gone too far and that many patients are undertransfused (Valeri et al, 1998). Although it is difficult to know to what extent this view is correct, there should be support for audit of transfusion practice for both under- and over-transfusion (Lenfant et al, 1992), and concern about under-transfusion should be considered when drawing guidelines for the use of red cell transfusions.

2) Parameters other than the haemoglobin level

Are physical findings and routine clinical investigations better at indicating the need for red cell transfusion than the haemoglobin level alone? Symptoms such as fatigue and shortness of breath are subjective, but are still useful in determining the need for red cell transfusion in patients with chronic anaemia. Changes in respiratory rate and pulse may be difficult to interpret and may merely be an adaptive response to the anaemia rather than indicating impending adverse clinical effects. Mental function deteriorates with cerebral hypoxia, but the effect is probably too subtle to be clinically useful. Myocardial ischaemia is not always associated with changes on the electrocardiogram (ECG) or echocardiography, and does not necessarily lead to serious outcomes such as myocardial infarction or death.

There are few trials in this area, but a recent study used physical activity as a measure of the adequacy of post-operative haemoglobin level, and found no difference between

patients who received transfusions to maintain the haemoglobin level above 10g/dL and patients receiving transfusions when they were symptomatic or when their haemoglobin level fell below 8g/dL (Carson et al, 1998).

Acute anaemia. This is usually due to acute blood loss, where the effects of anaemia should be separated from those of hypovolaemia. Experience has shown that losses up to 30-40% can be treated with crystalloids alone in young healthy patients, and as described above, acute isovolaemic anaemia to a haemoglobin level of around 5g/dL in a study of volunteers and patients produced no evidence of inadequate oxygenation (Weiskopf et al, 1998). A recent study showed that a transfusion threshold of 7g/dL was as safe and possibly superior to a threshold of 10g/dL (Hebert et al, 1999).

Reliable measures of oxygen delivery to critical organs are not available. Even with invasive haemodynamic monitoring in critically ill patients, there is difficulty in knowing which measurements, such as cardiac output and oxygen consumption, should be used for monitoring haemodynamic therapy. In terms of management, the importance of adequate volume replacement, maintenance of blood pressure and the use of inotropic drugs to maintain a normal cardiac output continues to be emphasised (Hinds & Watson, 1995). A recent systematic review of randomised controlled trials suggested that crystalloids should be used in preference to colloids for fluid resuscitation of patients with acute hypovolaemia (Schierhout & Roberts, 1998), but the crystalloids v. colloids debate continues and reviews of the effectiveness of specific colloids are being prepared by the Cochrane Injuries Group (Fluid resuscitation with colloid or crystalloid solutions, 1998).

In acute blood loss, estimation of actual and likely further blood loss is an important factor in the decision about red cell transfusion.

Chronic anaemia. The symptoms of chronic anaemia depend on the patient's age, level of activity, and co-existing medical problems such as cardiovascular and respiratory disease. The association of symptoms with a given level of haemoglobin can be anticipated in individual patients after observation over a period of time.

Conclusions

There are no reliable parameters to guide the need for red cell transfusion. The decision to transfuse red cells is a complex one and depends on factors such as the cause of the anaemia, its severity and chronicity, the patient's ability to compensate for anaemia, the likelihood of further blood loss and the need to provide some reserve before the onset of tissue hypoxia. The risks of transfusion also need to be balanced against the perceived benefits. While guidelines for red cell transfusion often specify a given level of haemoglobin in oreder to be pragmatic, consideration of the patient's clinical condition is an essential part of the decision to transfuse red cells or not and is a matter for clinical judgement.

Red cell components

There are few clinical data on the advantages and disadvantages of different types of red cell components in the management of acute and chronic anaemia. This guideline assumes the use of red cells suspended in optimal additive solution, the standard red cell preparation available from the NBS. That there is a place for whole blood particularly in the treament of acute blood loss is a question which is often raised. Whole blood is not routinely available from blood services in the UK. A position statement is available on this issue on request from the NBS.

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Appendix.

Control (audit) measures for the clinical use of red cell transfusions

- each Blood Bank should have a maximum blood order schedule (MSBOS), and compatible blood should not generally be made available for surgery where the usage is less than 50% of the units provided
- the MSBOS should be reviewed at least annually according to the current blood usage for elective surgery
- local guidelines should be drawn up for peri-operative transfusion, and audited; similarly for other situations where acute haemorrhage is common, e.g. GIT bleeding, obstetrics and trauma services
- comparison of the use of blood for common surgical procedures e.g. primary total hip replacement and coronary artery bypass surgery between surgeons and hospitals should be routine
- documentation of transfusion in the medical notes including the indication for transfusion, the date of transfusion, the number and type of units transfused, and any adverse effects and how they were managed must be routine. Ideally, the notes should also include an assessment of the effectiveness of the transfusion, for example in relieving symptoms of anaemia and in raising the haemoglobin level. These records should be audited

TABLE 1

Classification of hypovolaemic shock according to blood loss (Baskett, 1990)

	Class I	Class II	Class III	Class IV
Blood loss: Percentage Volume (mL)	<15 750	15-30 800-1500	30-40 1500-2000	>40 >2000
Blood pressure: Systolic Diastolic	Unchanged Unchanged	Normal Raised	Reduced Reduced	Very low Very low unrecordable
Pulse (beats/min)	Slight tachycardia	100-120	120 (Thready)	>120 (Very thready)
Capillary refill Respiratory rate	Normal Normal	Slow (>2s) Normal	Slow (>2s) Tachypnoea (>20/min)	Undetectable Tachypnoea (>20/min)
Urinary flow rate (mL/h)	>30	20-30	10-20	0-10
Extremities	Colour normal	Pale	Pale	Pale and cold
Complexion	Normal	Pale	Pale	Ashen
Mental state	Alert	Anxious or aggressive	Anxious, aggressive, or drowsy	Drowsy, confused, or unconscious