Point of view

Should the replacement of acute blood loss with non-red blood cell solutions in the elderly be called resuscitation or embalming?

The patient was an 84 year old man who had a past history of hypertension, ischaemic heart disease and chronic obstructive airways disease. He had just been admitted to the intensive care unit (ICU) following an elective repair of an abdominal aortic aneurysm, pale, hypotensive and in fulminant pulmonary oedema with the anaesthetic registrar beginning the 'hand over' as he struggled to help position the bed into the ICU bay.

It appeared that the operation was technically complicated. However, no blood had been given throughout the procedure even though an assessed blood loss of 4 L was recorded. Instead, 3 litres of 4% albumin in 0.9% saline, 3 litres of Gelofusine® and 6 litres of Hartmann's solution were administered "for intravascular loading" and to replace the "volume loss". During our conversation it also emerged that at the latter part of the 3 hour operation the patient's ST segments "sagged" so he was given atenolol "15 mg all up" but then developed hypotension which required metaraminol which had been intermittently administered during the final stage of the operation. As the pulse oximeter recorded an ever decreasing saturation, the F_IO_2 gradually increased from 40% to 100%, with 10 cm H_2O of PEEP being finally applied to stop the blood stained froth from entering the expiratory limb of the anaesthetic circuit. A blood gas, which was performed just before leaving the operating theatre, suddenly appeared and revealed a PaO_2 65 mmHg, $PaCO_2$ 57 mmHg, pH 7.01, lactate 9 mmol/L and haemoglobin 61 g/L.

"You didn't use blood because…?" I left a pause for the anaesthetic registrar to reply.

"We are not using blood routinely" he said "ever since the Canadian study showed that it increases mortality"

"Increases mortality!" I uttered.

"Yea, it increases mortality if used routinely" he blurted.

I could not help myself. "But he is now in cardiogenic shock and severe pulmonary oedema. In fact, I can't think of anything else you could have done that would have made his condition worse. He was generously preloaded, his haemoglobin was more than halved, with resultant myocardial ischaemia; he was then beta blocked, reducing inotropism, and the metaraminol selectively increased his afterload, increasing cardiac work and left atrial pressure. Voilà! - cardiogenic shock and fulminant pulmonary oedema"

His chin protruded. "OK, what would you have done?"

"I would have given blood – the other problems would not have occurred"

He put his metaraminol syringe into his top pocket, looked at me for a second and smirked. "Enjoy" he said, then turned and left, leaving me to regret my outburst.

'Blood and blood products are a limited resource and should be used within strict guidelines' is a statement that has no rebuttal and every major hospital will have their protocol for transfusion. However, many confuse the indications for a red blood cell (RBC) transfusion in the elderly patient who is acutely anaemic (e.g. during fluid resuscitation for active haemorrhage) for those indications that are based on studies performed in young isovolaemic patients with chronic anaemia.

Fundamentally, the equation is relatively simple. Life cannot exist in humans without RBCs and the closer we get to this point, the greater we jeopardise life. Nonetheless, a RBC transfusion is not risk free and is indicated when its benefit (i.e. to sustain life) is greater than its risk (i.e. to threaten life).

In a young and healthy human, an acute isovolaemic reduction of haemoglobin to 50 g/L does not produce evidence of inadequate systemic oxygen delivery (as assessed by rise in arterial blood lactate and ST segment changes on ECG),[1] and the minimal haemoglobin level required in the absence of disease and at rest (i.e. where a maximum extraction of oxygen and maximum increase in cardiac output is required to achieve normal oxygen requirements) is 30 g/L.[1] Indeed, a patient who survived with maximum cardiovascular and respiratory support with a haemoglobin level of 14 g/L has been recorded.[2] Nonetheless, in the elderly patient with co-morbid conditions that include ischaemic cardiac disease, an acute isovolaemic reduction in RBC mass can produce profound effects as their ability to increase cardiac output and to selectively vasodilate threatened organs to improve oxygen supply is often severely limited.

In a study by the 'TRICC' investigators of 4470 critically ill patients, anaemia (e.g. haemoglobin < 100 g/L) was associated with an increased risk of death in patients with cardiac disease, and that blood transfusions decreased this risk.[3] Yet, in a multicentre randomised trial of 838 critically ill anaemic patients

(reported by the same group), a restrictive transfusion approach (i.e. one that kept the haemoglobin between 70 - 90 g/L) was just as effective (and was associated with a lower mortality rate) than when blood transfusions were administered to keep the haemoglobin between 100 - 120 g/L.[4] In a retrospective study of 8787 patients who underwent operative repair of a hip fracture, perioperative transfusion in patients with haemoglobin levels of 80 g/L or higher did not alter the 30 or 90 day mortality[5] although, as a non randomised trial, clinicians may have been astute enough to know when to transfuse the at 'risk patient' to achieve similar mortality in both groups.[6]

However, a relationship between mortality and anaemia has been established in elderly patients with cardiovascular disease.[7,8] In one retrospective study of 78,974 patients who were $\geq$ 65 years old and who were admitted to hospital with acute myocardial infarction, blood transfusion was associated with a lower 30 day mortality in patients who had a haematocrit on admission less than 33% (e.g. 110 g/L).[9] Also, in a randomised trial of patients with congestive heart failure (NYHA class III and class VI), an increase in the haemoglobin from 103 g/L to 129 g/L was associated with an improved left ventricular ejection fraction and a reduction in diuretic dose compared with the control group. During the study, the treatment group had no mortality compared with the control group which had a mortality of 25%.[10] Moreover, the TRICC investigators retrospectively reviewed a subgroup of 357 patients who were anaemic with a diagnosis of coronary artery disease from their study of 836 critically ill patients[4] and reported a trend to a lower survival rate in the group with a restrictive transfusion approach (i.e. one that kept the haemoglobin between 70 - 90 g/L) compared with the liberal transfusion group (i.e. when blood transfusions were administered to keep the haemoglobin between 100 - 120 g/L).[11] Nonetheless, in a recent observational study of three large randomised trials involving 24111 patients who had an acute myocardial infarct, Rao *et al*, using sophisticated analytic methods and in a younger group of patients, concluded that transfusion (which occurred in only 10% of patients) may have increased mortality.[12]

In patients with chronic kidney disease and chronic anaemia a relationship between anaemia and morbidity[13,14] and mortality[15,16] has been reported, leading to guidelines that recommend a haemoglobin be maintained between 110 g/L and 120 g/L in these patients.[17]

Apart from the mechanical effects (e.g. air embolism, micro embolism, hypervolaemia) and febrile reactions (which are rarely life threatening)[18] the risks associated with RBC transfusions include: haemolytic reactions (which may be life threatening when incompatible RBCs are administered),[19] anaphylactoid reactions (which may be life threatening when blood with antibodies to IgA is infused in patients with a selective IgA deficiency),[20] disease transmission (while blood is normally screened, infections may be still be transmitted with an incidence of 1:5,000,000 for HIV, 1:3,000,000 for HCV and 1:1,000,000 for HBV) and bacterial infections. However, of the proposed transfusion-related immunomodulation (TRIM) effects, which include improved renal allograft survival,[21,22] enhancement of metastatic spread of carcinoma,[23-25] increase in postoperative infectious complications[24,26] and graft vs. host disease; improved renal allograft survival is the only TRIM effect that has been demonstrated unequivocally at the clinical level.[21,22,24,27,28]

Traditionally, a RBC mass reduction of 30% (e.g. haemoglobin level of 100 g/L) in a normovolaemic patient is taken as the value below which a transfusion is required, although a single threshold for transfusion applied to all patients is a coarse reference,[29] as current data suggest that the threshold should probably be at a haemoglobin level < 80 g/L in the young patient and < 100 g/L in the elderly patient with cardiovascular disease.[20,30-36]

The use of non-RBC fluid (allowing cardiac output to increase and oxygen delivery to be maintained) rather than RBCs in the actively bleeding patient is tolerated in the healthy young patient, as they may endure an isovolaemic drop in haemoglobin by up to 70%. However, in the elderly patient (e.g. $\geq$ 65 years old) with cardiovascular co-morbid conditions, any acute drop in haemoglobin can be hazardous and deliberate isovolaemic resuscitation using non-RBC fluid rather than RBC in this group may reflect more a process of embalming rather than resuscitation.

L. I.G. WORTHLEY
Department of Critical Care Medicine, Flinders University of South Australia, Adelaide, SOUTH AUSTRALIA

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