Review Article

Blood transfusion practices in sepsis

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ABSTRACT

Sepsis is a clinical syndrome characterised by systemic inflammation due to infection. There is a spectrum with severity ranging from sepsis to severe sepsis and septic shock. Even with optimal treatment, mortality due to severe sepsis or septic shock is significant and poses a challenge to management. Antibiotics, source control, resuscitation with fluids, vasopressor and inotropic agents are the main-stay of treatment for septic shock. These may be supplemented with transfusion of red blood cells and or blood products, in the case of anaemia to sustain sufficient oxygen delivery[1] or to manage associated haematological issues. Transfusion in sepsis has always been a debatable issue, especially in relation to choice of the fluid and the role of blood or blood product transfusion.

Key words: Hypotension, intravenous fluids, red blood cell transfusion, sepsis

INITIAL APPROACH BEFORE BLOOD TRANSFUSION IN SEPSIS

The early administration of fluids and antibiotics are the cornerstone of management for patients with severe sepsis and septic shock. Therapeutic priorities for patients with severe sepsis or septic shock include:[1]

a. Early initiation of supportive care to correct physiologic abnormalities, such as hypoxemia and hypotension,[2] and to distinguish sepsis from systemic inflammatory response syndrome and if an infection exists, it must be identified and treated as soon as possible. This may require appropriate antibiotics as well as surgical procedures[3,4]
b. Improve oxygenation – supplemental oxygen should be supplied to all patients with sepsis and oxygenation should be monitored continuously with pulse oximetry. Intubation and mechanical ventilation may be instituted depending on the need at the earliest[5,6]
c. Assess perfusion – once the patient's respiratory status has been stabilized, the adequacy of perfusion should be assessed.

CLINICAL SIGNS OF IMPAIRED PERFUSION

Hypotension

Hypotension is the most common indicator that perfusion is inadequate; it is important that the blood pressure be assessed early and often. An arterial catheter may be inserted if blood pressure is labile or restoration of arterial perfusion pressures is expected to be a protracted process.[7] Attempts to insert an arterial line should not delay the prompt management of shock. Patients with chronic hypertension may develop critical hypoperfusion at a higher blood pressure than healthy patients.

Elevated lactate

An elevated serum lactate (e.g. >1 mmol/L) can be a manifestation of organ hypoperfusion in the presence or absence of hypotension and is an important component of the initial evaluation.[3] A serum lactate level ≥4 mmol/L is consistent with, but not diagnostic of, severe sepsis.

Others

Tests that combine output from many organs (e.g. arterial lactate) may obscure the presence of significant ischaemia in an individual organ. Gastric

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tonometry indirectly measures perfusion to the gut by estimating the gastric mucosal pCO_2. It can be used to detect gut hypoxia by calculating the gastric to arterial pCO_2 gap.[8] Additional laboratory studies that help characterise the severity of sepsis include a low platelet count, and elevated international normalized ratio (INR), creatinine, and bilirubin.

Measures to restore perfusion

The rapid restoration of perfusion is predominantly achieved by the administration of intravenous fluids, usually crystalloids. Modalities such as vasopressor therapy, inotropic therapy, and blood transfusion are added, depending on the response to fluid resuscitation, evidence for myocardial dysfunction, and the presence of anaemia.

TRANSFUSION IN SEPSIS/SEPTIC SHOCK

a. Intravenous fluids: In patients with sepsis, intravascular hypovolemia is typical and may be severe, requiring rapid fluid resuscitation. The volume of fluid that is administered within the initial 6 h of presentation is targeted to the set physiologic endpoints (e.g. mean arterial pressure). Thus, rapid, large volume infusions of intravenous fluids are indicated as initial therapy for severe sepsis or septic shock, unless there is coexisting clinical or radiographic evidence of heart failure
b. Fluid therapy should be started in well-defined (e.g. 500 mL), rapidly infused boluses.[3] Volume status, tissue perfusion, blood pressure, and the presence or absence of pulmonary oedema must be assessed before and after each bolus. Intravenous fluid challenges can be repeated until blood pressure and tissue perfusion are acceptable, pulmonary oedema ensues, or fluid fails to augment perfusion. Careful monitoring is essential because patients with sepsis typically develop noncardiogenic pulmonary oedema (i.e. adult respiratory distress syndrome). Thus, while the early, aggressive fluid therapy is appropriate in severe sepsis and septic shock, fluids may be unhelpful or harmful when the circulation is no longer fluid-responsive
c. Choice of fluid: Randomised trials have found no difference between using albumin solutions and crystalloid solutions (e.g. normal saline, Ringer's lactate) in the treatment of severe sepsis or septic shock, but they have identified potential harm from using pentastarch or hydroxyethyl starch rather than a crystalloid solution.[9] In clinical practice, the use of a crystalloid solution is better than albumin solution because of the lack of clear benefit and higher cost of albumin. Giving a sufficient quantity of intravenous fluids rapidly and targeting appropriate goals is more important than the type of fluid chosen[3]
d. Vasopressors: These are second line agents in the treatment of severe sepsis and septic shock. These are useful in patients who remain hypotensive despite adequate fluid resuscitation or who develop cardiogenic pulmonary oedema.[10,11]

Additional therapies

Use of additional therapies such as inotropic therapy or red blood cell (RBC) transfusion are targeted at increasing the cardiac output to improve tissue perfusion and thereby raise the central venous (superior vena cava) oxyhaemoglobin saturation toward normal ($ScvO_2$ ≥70%). Their use be limited to those with refractory shock in whom the $ScvO_2$ remains <70% after optimisation of intravenous fluid and vasopressor therapy. A trial of inotropic therapy may be warranted in patients who have refractory shock/who also have diminished cardiac output.[12] Inotropic therapy should not be used to increase the cardiac index to supranormal levels.[13] Epinephrine is the usual inotropic agent.[3] Dobutamine at low doses, may cause the blood pressure to decrease because it can dilate the systemic arteries. However, as the dose is increased, blood pressure usually rises because cardiac output increases out of proportion to the fall in vascular resistance.

TRANSFUSION OF BLOOD PRODUCTS FOR SEPSIS AND SEPTIC SHOCK

Patients with severe sepsis and septic shock frequently experience what could be termed "haematologic failure" – abnormalities of blood cell lines and clotting/antithrombotic proteins that can occur in complex, protean patterns. Anaemia, thrombocytopenia, leucopoenia, disseminated intravascular coagulation, and functional deficiencies of coagulation factors are all common in people with severe sepsis or septic shock.

RED BLOOD CELL TRANSFUSIONS

Packed RBC transfusion in the early goal directed therapy (EGDT) for severe sepsis and septic shock has not made it into the latest Surviving Sepsis Guidelines as a graded recommendation. Rather, blood transfusion as part of EGDT for severe sepsis/septic shock is considered an "option" co-equal with dobutamine infusion to improve perfusion. During the first 6 h of resuscitation, if $ScvO_2$ < 70% or SvO_2 equivalent of <65% persists with what is judged to be adequate intravascular volume repletion in the presence of persisting tissue hypoperfusion, then dobutamine infusion (to a maximum of 20 μg/kg/min) or transfusion of packed RBCs to achieve a haematocrit of ≥30% in attempts to achieve the $ScvO_2$ or SvO_2 goal are options.[3]

Several problems were documented with RBC transfusions, such as infection, pulmonary complications such as TRALI and transfusion-associated circulatory overload, transfusion-related immunomodulation and multiorgan failure, and increased mortality. Until better evidence is available, a "restrictive" strategy of RBC transfusion (transfuse when haemoglobin [Hb] <7 g/dL) is recommended except in acute haemorrhage, or in patients with acute myocardial ischemia when an Hb trigger of 8 g/dl is reasonable.

The Surviving Sepsis Guidelines advocate restricting RBC transfusion in adults with severe sepsis/septic shock until Hb falls below 7.0 g/dL, and not transfusing above 9.0 g/dL, if ischemic heart disease, severe hypoxemia, or active bleeding is not present.[3,14]

Erythropoietin

Although certain patients with severe sepsis and septic shock may have other reasons to receive erythropoietin, the Surviving Sepsis Guidelines advice against giving the erythropoietin as treatment for anaemia associated with severe sepsis/septic shock.[3,14]

Fresh frozen plasma

No clinical studies have been done to determine whether correcting coagulation abnormalities (elevated prothrombin time [PT]/INR) with transfusion of fresh frozen plasma (FFP) affects outcomes in severe sepsis and septic shock. However, there are no studies that show that correction of coagulation abnormalities helps patients who are not bleeding, even if their INR is severely elevated. Given this absence of any demonstrated benefit, the Surviving Sepsis Guidelines suggest reserving transfusion of FFP for those patients with severe sepsis/septic shock who have increased PT, partial thromboplastin time, and/or INR, and who either have active bleeding, or are planned to undergo surgery or invasive procedures.[3,14]

Platelets

Thrombocytopenia in sepsis is due both to impaired platelet production and also increased platelet destruction. There is no solid evidence to guide platelet transfusion in severe sepsis and septic shock, but a restrictive approach is suggested, unless bleeding or the risk thereof is present. For patients with severe sepsis and septic shock, the Surviving Sepsis Guidelines suggest transfusing platelets prophylactically only when platelets fall to 10,000/mm^3, assuming no bleeding is present. In patients considered at significant risk for bleeding, a threshold of 20,000/mm^3 is suggested, and for those with active bleeding or who are undergoing surgery or invasive procedures, transfusing platelets to 50,000/mm^3 is suggested.[3,14]

Antithrombin

The Surviving Sepsis Guidelines advise against the use of antithrombin III for severe sepsis or septic shock.

SUMMARY

For patients with severe sepsis and septic shock, it is recommended to use intravenous fluids, rather than vasopressors, inotropes, or RBC transfusions as first-line therapy for the restoration of tissue perfusion (Grade 1B). Therapy should be initiated as early as possible, within 6 h of presentation. Fluid boluses are the preferred method of management and should be repeated until blood pressure and tissue perfusion are acceptable, pulmonary oedema ensues, or there is no further response. Blood and blood products are indicated when specific situations warrant. Managing septic shock remains debatable especially in the area of transfusion related issues, and additional research is needed in this area of critical care.

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