Module 1: Critical bleeding. Massive transfusion protocol

Critical bleeding:
• Major haemorrhage that is life threatening and is likely to result in the need for massive transfusion
• Haemorrhage of a smaller volume in a critical area or organ (e.g. intracranial, intraspinal or intraocular), resulting in patient morbidity or mortality.

Massive transfusion:
In adults, 'massive transfusion' may be defined as a transfusion of half of one blood volume in 4 hours, or more than one blood volume in 24 hours (adult blood volume is approximately 70 mL/kg).
In children, 'massive transfusion' may be defined as a transfusion of more than 40 mL blood/kg. (The normal blood volume of a child is approximately 80 mL/kg.)
Management of critical bleeding should focus on early recognition of blood loss, rapid control of the source of bleeding and restoration of circulating blood volume.

Patient blood management aims:
To improve clinical outcomes by avoiding unnecessary exposure to blood components. It includes the three pillars of:
• optimisation of blood volume and red cell mass
• minimisation of blood loss
• optimisation of the patients tolerance of anaemia.

Permissive hypotension and minimal volume resuscitation
Aggressive volume resuscitation can cause serious problems, including:
• oedema, compartment syndrome and acute lung injury
• exacerbation of anaemia, thrombocytopenia and coagulopathy due to haemodilution
• exacerbation of bleeding due to possible clot disruption.

Permissive hypotension and minimal volume resuscitation are strategies in which systolic blood pressures of 80–100 mm Hg are tolerated while bleeding is controlled. Several studies have shown survival benefit.
Permissive hypotension and minimal volume resuscitation are generally preferable to aggressive volume resuscitation while active bleeding is being controlled.
Permissive hypotension is contraindicated in patients with traumatic brain injury.
The safe low threshold for systolic blood pressure is unknown, and elderly patients require specific consideration.
The maximum safe duration for permissive hypotension is unknown

Early surgical management
Damage control surgery may be indicated for patients with severe haemorrhagic shock. The decision to switch over to damage control mode should be made early.

Blood: Shelf life up to 42days, leukodepletion may extend this.
Storage lesion with RBC include:
• reduced levels of 2,3 diphosphoglycerate
• increased oxygen affinity
• shape change
• reduced deformability
• decreased viability
With increased storage time – generation of inflammatory mediators, cytokines and lipids implicated in immunomodulation, TRALI,, febrile transfusion reactions and cellular injury. But no evidence to restrict RBC stored for only a short time in critically ill patients.
Additive solutions:
CPDA-1 (citrate, phosphate, dextrose and adenine)
SAG-M (sodium chloride, adenine, glucose and mannitol)

1. In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

Parameters to measure early and frequently	Critical physiologic derangement
Temperature	<35
Acid – Base staus	pH<7.2 BE>-.6 Lactate>4
Ionised Ca	<1.1
Haemoglobin	
Platelet count	<50
INR	>1.5
APTT	>1.5xnormal
Fibrinogen	<1.0

Mortality was found to be highest where acidosis and hypothermia occurred with coagulopathy

2. In patients with critical bleeding requiring massive transfusion, does the dose, timing and ratio (algorithm) of RBCs to blood component therapy (FFP, platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate?

In trauma patients, a ratio of RBC:FFP:platelets of ≤ 2:1:1 was associated with improved survival.
In non-trauma patients, there were insufficient data to support or refute the use of a defined ratio of blood component replacement

Blood component replacement should be guided by clinical assessment and results of coagulation tests. Keep fibrinogen level above 1.0 g/L.

- In critically bleeding patients requiring, or anticipated to require, massive transfusion, an MTPa should be used.
- In patients with critical bleeding requiring massive transfusion, insufficient evidence was identified to support or refute the use of specific ratios of RBCs to blood components.

3. In patients with critical bleeding requiring massive transfusion, is anaemia an independent risk factor for adverse outcomes?
Anaemia (WHO) Hb < 130 g/L in males and females.
Unlikely that the effects of anaemia will be able to be independently assessed in this group of patients.

-In patients with critical bleeding requiring massive transfusion, haemoglobin concentration should be interpreted in the context of haemodynamic status, organ perfusion and tissue oxygenation.

4. In patients with critical bleeding requiring massive transfusion, what is the effect of RBC transfusion on patient outcomes?
- In patients with critical bleeding requiring massive transfusion, the use of blood products may be lifesaving but also independently associated with increased mortality and ARDS.
- In patients with critical bleeding requiring massive transfusion, the use of an MTP to facilitate timely and appropriate use of RBC and other blood components may reduce the risk of mortality and ARDS.

5. In patients with critical bleeding requiring massive transfusion, what is the effect of non-transfusion interventions to increase haemoglobin concentration on morbidity, mortality and need for RBC transfusion? Unknown!

6. In patients with critical bleeding requiring massive transfusion, what is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?
- The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality
- An MTP should include advice on the administration of rFVIIa when conventional measures – including surgical haemostasis and component therapy – have failed to control critical bleeding. initial dose of 90 µg/kg.

7. In patients with critical bleeding requiring massive transfusion, what is the effect of FFP, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?
In trauma patients with critical bleeding **r**equiring massive transfusion, an RBC:FFP ratio of ≤ 2:1 is associated with reduced mortality

8. In patients with critical bleeding requiring massive transfusion, at what INR (or PT/APTT) for FFP, fibrinogen level for cryoprecipitate and platelet count for platelets concentrates should patients be transfused to avoid risks of significant adverse events?
• FFP: INR 1.5 ⟹ 15 mL/kg
• platelets: <50 ⟹ 1 adult therapeutic dose
• cryoprecipitate: fib <1-1.5 ⟹ $1\text{unit}/30\text{kg}$.

9. Effect of Tranexamic Acid (CRASH 2)
In trauma patients with, or at risk of, significant haemorrhage, tranexamic acid should be considered. (1g bolus, 1g infused)

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