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What's new in hemorrhagic shock?

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Hemorrhagic shock is a life-threatening condition requiring a series of immediate interventions. Although several details are still debated, there have been some important achievements with great potential to influence the care and outcomes of these patients.

The recognition of hemorrhagic shock should be based on a combination of clinical, hemodynamic and biochemical signs. The presence of low blood pressure should not be a prerequisite of shock diagnosis, and assessment of inadequate tissue perfusion by thorough examination of cutaneous perfusion, urine output and altered mental status together with laboratory signs of anaerobic metabolism such as serum lactate and metabolic acidosis should all be taken into account [1].

The main goals of the treatment of hemorrhagic shock include the correction of the imbalance between oxygen delivery (DO_2) and consumption (VO_2), maintaining adequate perfusion pressure, and preventing or treating coagulopathy (Fig. 1) [2].

The cornerstone of the initial management of the bleeding patient is fluid resuscitation. Discussion of the crystalloid-colloid debate goes well beyond the scope of this article [3, 4]. However, based on a recent retrospective cohort study it has been proposed that low-volume resuscitation with hypertonic saline may be preferable to large-volume fluid loading before active bleeding has been controlled in hemorrhagic shock [5, 6]. Therefore, prospective studies are strongly warranted on this topic.

Tissue perfusion may also be improved by early vasopressor administration. With careful blood pressure-targeted titration of norepinephrine, life-threatening hypotension and unnecessary fluid overload can be avoided. It is important to note, as stated in international guidelines, that a low systolic blood pressure should be tolerated until the cause of bleeding has been controlled (in the absence of severe traumatic brain injuries) [1].

Tailoring fluid and vasopressor treatment requires resuscitation end points. Pulse-contour-driven dynamic variables such as stroke volume and pulse pressure variation may serve as useful measures to avoid both under- and over-resuscitation. The parameters of tissue perfusion and oxygen debt, such as lactate and base deficits, central venous oxygen saturation ($ScvO_2$) and a venous-to-arterial CO_2 gap, should also be put into context during treatment [1, 7].

Apart from fluid resuscitation, the early administration of blood products, such as red blood cells (RBCs), fresh frozen plasma (FFP) and platelets, is often inevitable in order to maintain DO_2 and correct coagulation.

Regarding hemostasis management, the administration of RBCs should be supplemented as soon as possible with FFP to compensate for the deficit in coagulation factors. There are two strategies for correcting hemostasis. So-called 'formula-driven' resuscitation with a predetermined RBC:FFP ratio serves as a fast and easy-to-use approach to early correction of hemostasis. Recent retrospective studies suggested an RBC:FFP ratio of approximately 1:1 [8]. Although this concept is gradually expanding from trauma to non-trauma bleeding

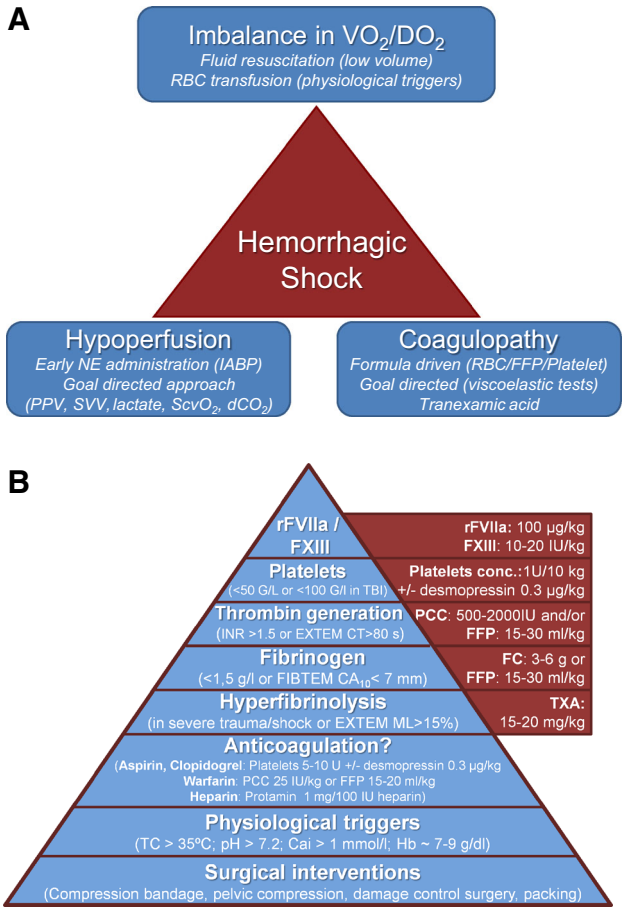

Fig. 1 Cornerstones of pathophysiology-based interventions (**a**) and coagulation management (**b**) in hemorrhagic shock. **a** VO_2 Oxygen consumption; DO_2 oxygen delivery; *RBC* red blood cell; *NE* norepinephrine; *IABP* invasive arterial blood pressure; *PPV* pulse pressure variation; *SVV* stroke volume variation; $ScvO_2$ central venous oxygen saturation; dCO_2 venous-to-arterial CO_2 gap; *FFP* fresh frozen plasma. **b** *Cai* ionized calcium; *Hb* hemoglobin; *PCC* prothrombin complex concentrate; *FFP* fresh frozen plasma; *INR* international normalized ratio; *TBI* traumatic brain injury; *TXA* tranexamic acid; *FC* fibrinogen concentrate; *rFVIIa* recombinant activated factor VII; *FXIII* factor XIII

management, the results of these studies are conflicting and should be interpreted with caution because of the potential for survival bias and substantial differences between civilian and military trauma. In an international prospective cohort, only combined high-dose FFP, cryoprecipitate and platelet therapy with a high total fibrinogen load appeared to produce a consistent improvement in coagulation [9]. Undoubtedly the onset, course and severity of coagulopathy differ depending on the etiology. Therefore, it is likely that a given RBC:FFP ratio does not fit all patients. Furthermore, the timing of FFP administration may play a pivotal role in the outcome; hence, it may be just as important, or even more so, than the RBC:FFP ratio itself [10].

Unnecessary overuse of blood products can lead to several complications [11]. However, individualized 'goal-directed' hemostatic resuscitation may help to rationalize blood product utilization. Dynamic monitoring of whole-blood coagulation provides several advantages as compared to conventional plasma-based tests, such as the prothrombin time, activated partial thromboplastin time, international normalized ratio, fibrinogen and platelet count. The latter tests are slow and mainly reflect the initiation phase of thrombin generation. They cannot be used to evaluate the primary hemostasis, clot strength and fibrinolysis, which are also important pillars of hemostasis and can often be impaired in severe bleeding. Viscoelastic tests (such as the TEG or ROTEM), however, provide rapid and dynamic evaluation of clot formation, strength and stability [12]. There is emerging evidence that point-of-care tests based on 'goal-directed' coagulation management can modify the transfusion strategy by providing better understanding of the underlying pathology and by the targeted use of not only FFP, but also fibrinogen and prothrombin complex concentrates (PCC), hence reducing the need for blood products, which enables the clinician to tailor hemostasis management according to the patient's needs [13]. Current guidelines emphasize the importance of higher target fibrinogen levels (1.5–2.0 g/l) and platelets of >50 g/l in general, or >100 g/l in brain injury [14].

Regarding the adjunctive treatment of hemostasis, there is strong evidence that tranexamic acid reduces mortality; therefore, its early routine administration during hemostatic resuscitation is recommended by international guidelines [14–16]. Recombinant factor VII can be considered only if major bleeding persists after all efforts to support the fundamental pillars of hemostasis have failed. Although we have satisfactory evidence that the effects of vitamin K-dependent anticoagulants should be reversed by PCC, in bleeding patients taking new direct oral anticoagulants, its benefit remains controversial [17]. Nevertheless, in the clinical routine there is no other alternative to PCC at present, and hemodialysis can be considered in patients taking dabigatran.

Considering the later phase of hemorrhagic shock management, in addition to restrictive transfusion protocols with a post-transfusion target of hemoglobin levels of 70–100 g/l, 'physiological triggers' such as the $ScvO_2$ values have also been suggested to aid an individualized approach by tailoring transfusion according to the patient's actual needs instead of a 'numbers-driven' protocolized care.

Finally, coordinated teamwork (including several different specialties) is essential in the management of patients requiring massive transfusions. Implementation of hospital-specific 'massive transfusion protocols' may promote cooperation and accelerate the process, hence improving outcomes in patients with severe bleeding [18].

In summary, this paradigm shift in the management of hemorrhagic shock over the last decade provides several alternatives for improving outcomes in hemorrhagic shock patients; therefore, our current practice should be reviewed and changes implemented if needed.

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