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Use of blood and blood products in trauma

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According to the global study of the burden of disease, violence and accidental injury account for 12% of deaths worldwide; 30–40% of trauma mortality is attributable to haemorrhage. The highly complex haemostatic system is severely impaired as a result of haemorrhagic shock, acidosis, hypothermia, haemodilution, hyperfibrinolysis, and consumption of clotting factors. Thus it is important to prioritize the prevention of the development of coagulopathy. Timely transfusion of red blood cells and plasma products becomes essential to restore tissue oxygenation, support perfusion, and maintain the pool of active haemostatic factors. The limits to this strategy to compensate for the loss of blood and coagulation factors are discussed. In the absence of international guidelines, there is an ongoing debate about a generally accepted treatment algorithm, mass transfusion protocols, and adverse events that have been observed as a result of transfusion. Thus many recommendations are based upon expert opinion rather than on evidence. In this chapter we address key issues of transfusions of red blood cells and plasma products in the acute control of bleeding in traumatized patients.

Key words: trauma; haemorrhage; haemostasis; coagulopathy; blood products.

Exsanguination after trauma has been identified to be the leading cause of early in-hospital mortality.[1,2] Uncontrolled bleeding after trauma is usually caused by a combination of surgical and coagulopathic bleeding, requiring an interdisciplinary approach. On admission to hospital, 25–36% of trauma patients already show signs of coagulopathy.[3,4]

Coagulopathic bleeding is multifactorial and includes dilution and consumption of coagulation factors, hypothermia, hypocalcaemia, acidosis and activation of fibrinolysis.

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Surgical control of bleeding is unlikely to be successful if a combination of hypothermia, acidosis and coagulopathy – also called the 'the lethal triad' – is present.[5]

Hypothermia is an independent risk factor for bleeding and death[6], causing an impairment of clotting, a reduction in the synthesis of coagulation factors, altered platelet function, and increased fibrinolysis.[7] Since most laboratory tests – activated partial thromboplastin time (aPTT), prothrombin time (PT) – are performed at 37 °C, the effect of hypothermia on coagulation in the patient is often underestimated.[8]

Acidosis may develop as a result of reduction in tissue perfusion and consequent release of anaerobic metabolites, compromising the function of platelets and coagulation enzymes. Compared to pH 7.4, prothrombin activation at pH 7.0 is reduced by 70%.[9] Thus the maintenance of tissue oxygenation and oxygen delivery remains one of the most important goals in the treatment of trauma victims.

Coagulopathy may further be aggravated by the infusion of large volumes during initial fluid resuscitation. The magnitude of dilution coagulopathy depends on the volume and the type of volume infused.[10]

The early recognition of haemorrhagic shock in the initial management phase is essential for the prevention of coagulopathy. Early signs of shock are[11]:

- altered level of consciousness as a result of reduced cerebral perfusion;
- delayed capillary refilling, mottled skin as a consequence of reduced peripheral perfusion; and
- oliguria.

Analysis of lactate and base excess will further help to differentiate the severity of shock.[12,13] A blood loss of <15% of total blood volume is usually well tolerated, while a loss of 30–40% will lead to haemorrhagic shock. A massive haemorrhage is defined as[14,15]:

- loss of an entire blood volume equivalent within 24 h; or
- loss of 50% of blood volume within 3 h; or
- continuing blood loss at a rate of 150 mL/min; or
- continuing blood loss at a rate of 1.5 mL/kg/min over 20 min; or
- rapid blood loss leading to decompensation and circulatory failure, despite the support of blood products, volume replacement, and all accepted surgical and interventional treatments to stop bleeding.

For a targeted therapy it would be ideal to establish a relation between the volume of blood loss and reduction in coagulation factors and platelets. However, because of the high dynamic of blood loss, inter-individual variations in clotting factors, and the functionality of involved organ systems, this has not yet been accomplished.[16] In order to preserve tissue oxygenation and maintain the pool of procoagulant factors, red blood cells (RBCs), plasma, and coagulation factors are transfused, but monitoring both the effects and the timing of the substitution is highly complicated. Therefore this review highlights selected issues in the transfusion of RBCs and plasma products.

BLOOD AND BLOOD COMPONENTS IN MASSIVE HAEMORRHAGE

Red blood cells (RBCs)

Transfusion of RBCs is a mainstay in trauma management. The concept of specific component therapy was developed during the 1960s. Whole blood units are separated

into RBCs, platelets and plasma, and these may be separated further (e.g. by cryopre-cipitation). The advantage of this strategy is to allocate resources according to the needs of the individual patient, resulting in both economic and logistic benefits. One disadvantage is that, the substitution with plasma-free and thrombocyte-depleted RBCs can lead to coagulopathies at an earlier stage compared to the substitution of whole blood. An analysis from the Vietnam war revealed that the platelet count did not fall below 10^3/L, despite massive transfusion of 6 L of whole blood.[17] In contrast, 85% of patients receiving at least 10 units of RBCs developed thrombocytopenia.[18] The use of whole blood continues in military settings because frozen components and platelets cannot be stored[19], and large amounts of blood can be delivered in a timely manner even in the case of mass casualties.[20]

Although it is known that the haematocrit influences coagulation, the specific effects are generally unknown. One mechanism is attributed to the margination of platelets. This means that platelets have to be pushed by red cells to the margin of the vessel to make contact with injured endothelial cells.[21] Clinically, an acute reduc-tion in the haematocrit leads to a prolongation of the bleeding time.[22] In contrast, a moderate isolated reduction of haematocrit in vitro did not reveal an effect on thrombelastography except for the clot formation time.[23] Erythrocytes support thrombin generation[24] and maintain oxygen delivery, securing aerobic metabolism. However, there are well-described short-term and long-term negative effects of RBC transfusion encompassing haemolytic reaction and transmission of infectious diseases. With regard to trauma, RBC transfusion might also cause multiple organ failure (MOF) and increase the incidence of post-traumatic infections.[25–28]

There is no randomized controlled trial (RCT) available comparing a liberal versus a restrictive transfusion regimen in trauma patients. Reanalysed data from the Trans-fusion Requirements in Critical Care trial showed that a restrictive regimen (transfu-sion trigger <7 g/dL) compared to a liberal regimen (transfusion trigger <10 g/dL) resulted in reduced numbers of RBCs transfused.[29,30] Although the analysis did not show a beneficial effect of a restrictive transfusion regimen, reflected by similar inci-dences of MOF and post-traumatic infections, this could still be the case, since the study was not primarily designed or powered to answer this question. In contrast, an observational study with 15,534 patients by Malone et al revealed different results; in this trial 1703 trauma victims received on average 6.8 ± 6.7 units RBCs.[31] After con-trolling for potential confounders – injury severity score (ISS), Glasgow coma score (GCS), shock variables, age, race – RBC transfusion was associated with increased mortality, admission to ICU and ICU length of stay. Until further RCTs adequately address these issues, it is generally agreed that the haemoglobin level in a bleeding patient should be maintained at 7–8 g/dL at least.[32] Primary efforts in treating trauma victims should also include measures to reduce the need for RBC transfusion.

Platelets

Platelets are separated from whole blood by centrifugation or by apheresis. After preparation they can be stored for up to 5 days at room temperature (20–24 °C) with constant movement to prevent clotting. In massive bleeding, a relevant thrombo-cytopenia develops much later than plasma deficits, and will occur after the replace-ment of approximately 220% of circulating blood volume.[33] The decline of platelet count is individually different due to different capabilities for recruiting platelets from spleen and lung and the release of premature platelets from the bone marrow.

Since some patients even have high platelet counts despite ongoing bleeding, it is important to measure the platelet count repeatedly after admission. However, the number of platelets does not correlate with their ability to coagulate, and there are no practical methods for testing their activity.

A platelet count $<50 \times 10^9$/L in a bleeding patient or a patient with a pre-existing coagulopathy is generally regarded as an indication to transfuse platelets. In most patients one aphaeresis concentrate will increase the platelet count by 20×10^9/L (one platelet aphaeresis concentrate is approximately equivalent to a pool of 4–8 platelet concentrates).[34,35] The adequacy of transfusion should be confirmed after 10–15 min post-transfusion[36], since ongoing bleeding, platelet consumption, or human leukocyte antibodies (HLA) may cause a lower increase in platelets than expected.[37] In the case of diagnosed HLA antibodies, only matched HLA platelets will be effective. The recovery rate of 5-day-old platelets is about 50%. Non-viable platelets are sequestered in the spleen.[38] No data are available about the time taken for these non-viable platelets to be removed from circulation in massive trauma. This might lead to falsely high platelet counts. Platelets become fully functional after 4 hours of administration.[39,40]

A platelet count $>100 \times 10^9$/L is usually sufficient and requires transfusion only if severe platelet dysfunction is present. In the absence of bleeding or coagulopathy, a low platelet count is not an indication to transfuse platelets.

Platelet inhibitors – acetylsalicylic acid, glycoprotein (GP) IIb/IIIa inhibitors, etc – severely reduce the capability of platelets to aggregate. In cardiac surgery it has been shown that the inhibitory platelet effect caused by clopidogrel doubles the need for RBCs and causes an eight-fold increase in the need for platelet substitution.[41] In conclusion, the platelet count has to be interpreted in the specific clinical context.[42]

Adverse reactions of platelet transfusion include transmission of infectious diseases, allergic reactions, transfusion-related lung injury (TRALI), graft-versus-host disease (GVHD), and bacterial infections, which might cause a septic platelet transfusion associated with a high mortality.[43]

Fresh-frozen plasma (FFP)

Fresh-frozen plasma is human donor plasma separated from whole blood or obtained by plasmapheresis. It is frozen within 6–8 h after collection, stored at a temperature below −30 °C, and must be thawed at 37 °C before use. The volume of a typical unit contains 150–250 mL. FFP contains near-normal physiological levels of all plasma proteins – including procoagulant and inhibitor components of the coagulation cascade such as antithrombin – except FVIII, which rapidly decays.

Coagulation factors are diluted by approximately 15% during the preparation process with anticoagulant solution. During the freezing and thawing process further losses might occur. Also, the activity of coagulation factors depends on the donor's concentration of coagulation factors. Thus concentrations might vary between 60 and 140%. In contrast, solvent-detergent plasma (SD-FFP) contains pooled plasma from multiple donors, balancing the variations in factor concentrations.

According to guidelines from the American Society of Anesthesiologists (ASA), the indication for the use of FFP in trauma is a prolongation of prothrombin time and activated thromboplastin time of more than 1.5 times.[34] Furthermore, FFP is advised in patients with clinical signs of a bleeding coagulopathy, such as diffuse bleeding, massive transfusion, or disseminated intravascular coagulation (DIC). Other recommendations suggest transfusing FFP prophylactically after a certain number of units of RBCs have

been transfused.[18] Nonetheless, there is no evidence for the dose that should be transfused, nor for the ratio of FFP to RBC that should be applied (1:1, 1:2 or 1:3). Also, it has not been proven whether prophylactic substitution of FFP prevents the development of coagulopathy or improves bleeding control[44,45], and there is no apparent correlation between the degree of bleeding and the total volume of plasma transfused.[46]

Current recommendations on dosage are based on personal experience and expert opinion rather than on evidence. A dose of 10–15 mL/kg is widely accepted. However, if no volume deficit is present, patients with impaired cardiac or renal function might decompensate under volume overload.

Despite the lack of evidence, the number of FFP individually transfused has increased steadily over the last two decades in many countries.[47] Stanworth et al therefore did a systematic review of RCTs on the clinical effectiveness of the use of FFP.[48] From the 57 RCTs identified, only six could demonstrate a potential benefit with the use of FFP.

For life-threatening bleeding caused by warfarin overdosage, guidelines recommend the use of FFP only if prothrombin complex concentrate (PCC) is unavailable or contraindicated.[10] It has been well documented that the effectiveness in correcting coagulopathy as reflected by the international normalized ratio (INR) and the levels of vitamin-K-dependent clotting factors is lower using FFP than using PCC.[49,50] This is attributed to the level of factor IX in FFP, which is often too low to reach haemostatic concentrations. In order to achieve sufficient haemostatic concentrations of coagulation factors, the associated volume overload might become problematic. Besides, it has been shown that the administration of FFP is more prolonged than PCC. If PCC is not available, a dose of 15 mL/kg FFP is generally sufficient to correct warfarin-induced coagulopathy.[51–53] Disadvantages of FFP usage include the time delay (turn-around time) of a minimum of 30 min for thawing and transport of FFP from the blood bank to the patient. In addition, FFP contain varying amounts of citrate or citric acid for anticoagulation purposes. Since citrate binds calcium, it is necessary to monitor the calcium concentration closely.[54] Special attention should be give to patients with reduced capacity to metabolize citrate, such as patients with hypothermia or liver failure. Moreover, the transfusion of FFP is associated with risk of TRALI and transmission of infectious diseases.

COAGULATION FACTORS

Recombinant activated factor VII (rFVIIa)

rFVIIa was originally developed as haemostatic agent for use in haemophilia patients who developed inhibitors to factor VIII or IX. Since its first approval 10 years ago by the US Food and Drug Administration (FDA), it has also been approved in Europe for factor VII deficiency and Glanzmann's thrombasthenia (GT) with past or present refractoriness to platelet transfusion. Haemostasis is induced by exogenous administration of pharmacological doses if rFVIIa plasma concentrations of ≥ 25 nmol/L reached.[55] In these supraphysiological doses rVIIa binds to the phospholipid structures of activated platelets at the site of injury and thereby directly activates factors IX and X. This augmentation of the coagulation process leads to the enhancement of thrombin (thrombin burst). The activation of platelets at the site of injury is the reason for a localized reaction of rFVIIa. Furthermore, it has been demonstrated that rFVIIa influences the fibrin structure in a dose-dependent manner by forming a tight fibrin structure which is resistant to premature lyses.[56]

The efficacy of rFVIIa depends on the pH. An in-vitro study demonstrated that thrombin generation in response to rFVIIa administration was statistically significantly reduced during acidosis.[9] On the other hand, no negative influence on the effectiveness of rFVIIa has been reported during hypothermia.[57]

The first successful treatment of a nearly exsanguinated trauma patient with rFVIIa was reported in 1999.[58] Since then the numbers of case series and reports describing the still off-label use of rFVIIa in controlling massive haemorrhage is increasing.[59]

Dutton et al published a large case series ($n = 81$) of patients with coagulopathic bleeding as a result of different causes, including traumatic haemorrhage and traumatic brain injury.[60] The use of rFVIIa in a dose range of 40–150 µg/kg successfully stopped the coagulopathic bleeding in 75%. The Israeli Multidisciplinary rFVIIa Task Force reports another series with 36 trauma patients in whom the use of rFVIIa (dose range 100–140 µg/kg) prevented exsanguination in 72% of the cases.[61] On the basis of their findings, they developed recommendations for the use of rFVIIa in uncontrolled haemorrhage, suggesting an initial dose of 120 µg/kg followed by further doses (second dose of 100 µg/kg) if required after 15–20 min. Recently Boffard et al published the results from a multicentre, randomized, double-blind, placebo-controlled trial, stratifying for severe blunt and penetrating trauma.[62] Patients were included in the study after receiving 6 units of RBCs and were randomized to obtain either three doses of rFVIIa (200, 100 and 100 µg/kg) or placebo. In addition, damage-control surgery to manage haemorrhage was performed. A significant reduction in the primary end-points, RBC units transfused, and need for massive transfusion (defined as >20 units of RBCs) was observed in patients with blunt trauma who survived for more than 48 h. The need for massive transfusion was reduced from 33% to 14% ($P = 0.03$). The incidence of acute respiratory failure was also significantly lower. Although a trend towards a reduced need for RBC transfusion and fewer mass transfusions was also observed in the group of penetrating injuries, this did not reach statistical significance. The incidence of adverse events was comparable between the placebo and rFVIIa groups, and no thromboembolic events were observed.

As a result of these findings, a European expert panel recommended the use of rFVIIa in blunt trauma with a starting dose of 200 µg/kg (grade B).[63] In contrast, the use of rFVIIa was not recommended in penetrating trauma (grade B). However, in conclusion, the lack of data from randomized trials and the possibility of a publication bias in favour of successful case series were criticized. Furthermore, there is still a considerable lack of evidence about the timing of rFVIIa administration, the dosage, and the identification of the most suitable patients. At present, an international phase-III study is targeting to enrol 1500 patients with the aim to investigate, the effect of rFVIIa on mortality in trauma patients (CONTROL).

An algorithm for the use of rFVIIa based on the current evidence was developed to offer guidance for the practising physician (Figure 1). Most importantly, main factors additionally compromising coagulation (haematocrit, fibrinogen, platelets, pH) have to be corrected before rFVIIa is administered. After the application, close monitoring is advised for possible adverse thromboembolic events.

Fibrinogen and cryoprecipitate

The conversion from fibrinogen to fibrin is the final step in the coagulation cascade to clot formation. In a study enrolling 60 patients, Hiippala et al showed that fibrinogen is
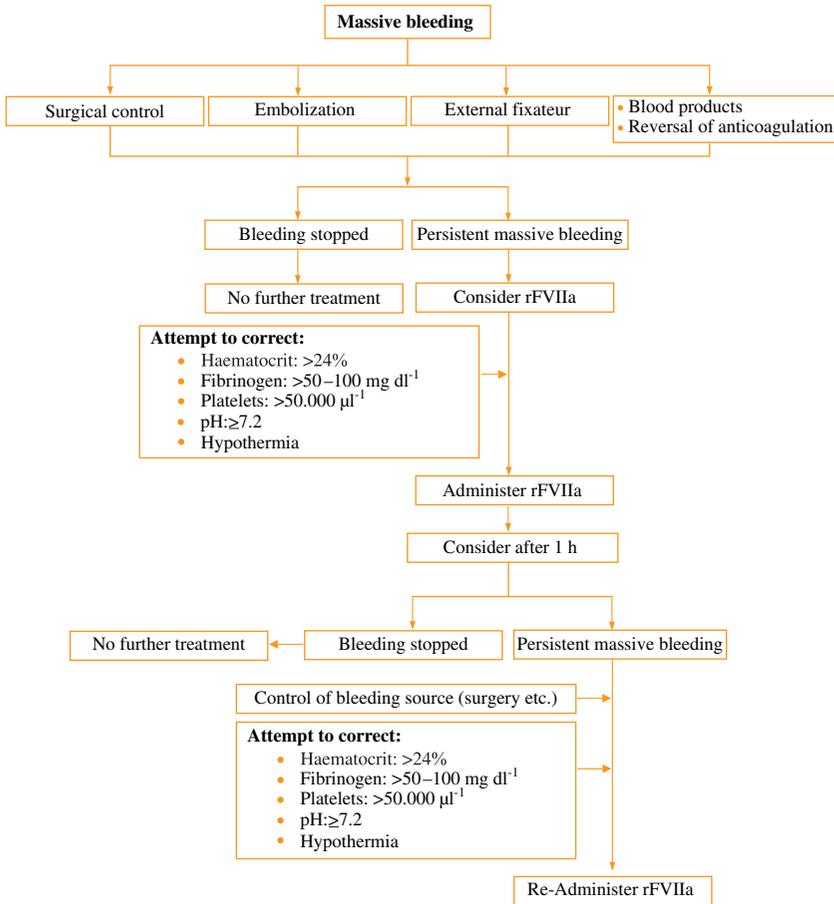
Figure 1. An algorithm for the use of recombinant activated factor VII (rFVIIa), developed by a European panel of experts modified from Ref. [64]

the first coagulation factor to reach critical concentrations when blood loss has reached 142% of the calculated blood volume.[64] Massive blood loss, large wound areas, and consumption and dilution of coagulation factors contribute to the decrease in fibrinogen level. The polymerization of fibrinogen is influenced by the interaction with colloids[65], and the clot firmness can additionally be reduced by concomitant hyperfibrinolysis. The impact of reduced fibrinogen concentration by dilution has been shown in vitro and in vivo.[66,67] Using thrombelastography, Fries et al demonstrated that the impaired fibrin polymerization was reconstituted after the administration of fibrinogen.[67] Using electron microscopy, the exogenous administration of fibrinogen had a recovery effect on the thinner reticular network.

Despite the lack of evidence for the optimal dose of fibrinogen, different algorithms recommend the substitution of fibrinogen in bleeding patients if the level falls below 0.5–1.0 g/L.[61,63] If the application of FFP in a bleeding patient is not sufficient to raise the fibrinogen plasma level to this concentration, the use of fibrinogen concentrate or cryoprecipitate might be indicated.

Fibrinogen concentrates are virally inactivated and are the treatment of choice for patients with inherited deficiencies of fibrinogen. On average, the adult dose is 2–3 g intravenously for acceptable levels to be achieved.

Cryoprecipitate contains factor VIII, von Willebrand factor (vWF), factor XIII, fibrinogen and fibronectin. It is the cryoglobulin fraction of FFP when thawed and centrifuged. On average, a dose of 2 mL/kg is used. One unit (10–20 mL) of cryoprecipitate should increase the fibrinogen level by 0.1 g/L. Since fibrinogen concentrates and cryoprecipitate are small in volume, both can be administered rapidly. If available, fibrinogen is the treatment of choice rather than cryoprecipitate.[34,35,51] The effectiveness of substitution should be monitored by fibrinogen levels and clinical signs of bleeding. In addition, thrombelastography is useful to estimate the clot firmness. To our knowledge no specific adverse reactions except allergic reactions and anaphylaxis have been reported.

Prothrombin complex concentrate (PCC)

PCC contains the vitamin-K-dependent factors FII, FVII, FX and FIX. Because of the heterogeneity of available PCCs, the therapeutic amounts of factors vary ("four versus three factor concentrates").[68] Most PCCs also contain heparin and proteins C and S, as well as protein Z of varying concentrations and antithrombin. All plasma products are virally inactivated and have a good safety record. The indications for the use of PCC are a fast reversal of oral anticoagulation with warfarin or a known deficiency of the vitamin-K-dependent factors in potentially life-threatening bleeding. The substitution should be supplemented by intravenous vitamin K to induce the endogenous synthesis of vitamin-K-dependent factors. Dosing recommendations are controversial, suggesting either an adjustment according to INR[69] or standard doses regardless of INR.[70] It seems reasonable to monitor the effect of PCC therapy based on the results of INR and the clinical effect.[71]

Well-known adverse effects include thromboembolism (coronary and cerebral arteries) and disseminated intravascular coagulation, which appear in a dose-dependent manner.[72,73] Moreover PCC is very expensive. Therefore, PCC should be applied only after careful assessment of the individual benefits and risks. The clinical diagnosis or a history of heparin-induced thrombocytopenia (HIT) are contraindications to using PCC.

Single-factor therapy

The substitution of mono-component factor therapy is required for correcting coagulopathy in patients with congenital factor deficiencies such as haemophilia A or B or von Willebrand's disease (vWD). Patients with massive haemorrhage and no history of isolated coagulation factor deficits do not require single-factor replacement.

PHARMACOLOGICAL AGENTS TO SUPPORT COAGULATION

Antifibrinolytic drugs

In trauma patients both hypofibrinolytic and hyperfibrinolytic states have been described[74–76], depending on the time of assessment and the severity of the trauma. Ideally antifibrinolytic drugs should only be used in the evidence of hyperfibrinolysis.

However, RCTs have also shown a blood-sparing effect of aprotinin and tranexamic acid in cardiac surgery in prophylactical use.[77,78]

Antifibrinolytic agents currently in use are the serin protease inhibitor aprotinin and the synthetic analogues ϵ-aminocaproic acid (6-aminohexanoic acid, EACA) and tranexamic acid (TXA).[79] Aprotinin is a naturally occurring polypeptide which unspecifically inhibits serine proteases such as plasmin, trypsin, kallikrein and others; it is isolated from bovine lung. The antifibrinolytic mechanism is mediated by the reversible formation of inhibitor complexes. Since aprotinin inhibits plasmin it interferes neither with fibrin-bound plasmin nor with plasminogen. The activity of aprotinin is expressed in kallikrein inactivator units (KIU). 1 KIU is defined as the amount of aprotinin that decreases the activity of two biological kallikrein units by 50%.[80] To inhibit plasmin, plasma concentrations of 125 KIU/mL aprotinin are usually needed.[81] Although different dose regimens have been proposed, the most common is to administer a loading dose of 1–2 million KIU followed by a continuous infusion of 100,000–200,000 KIU/h.[82] A rapid redistribution in the extracellular space leads to an initial decrease in plasma concentration. Finally, aprotinin is metabolized in a biphasic pattern with metabolism in the proximal renal tubes.[83]

After the administration of aprotinin, anaphylactic reactions have been observed, induced by the circulating foreign polypeptide. The re-exposure to aprotinin within 6 months increases the risk of developing a severe anaphylactic reaction in up to 4.5% of cases.[84] A recently published international observational prospective study by Mangano et al showed that the use of aprotinin in cardiac surgery was associated with an increased risk of renal failure and myocardial infarction.[85] A propensity score case–control comparison of aprotinin and tranexamic acid from Karkouti et al also concluded that the use of aprotinin might be associated with an increased risk of renal dysfunction.[86] Based on those studies, the US FDA advises limiting the use of aprotinin to situations where the clinical benefit of reduced blood loss outweighs the potential risks.[87] Furthermore, the FDA recommends to carefully monitor for adverse events.

EACA and TXA are competitive inhibitors of plasminogen activation. TXA is about 10 times more potent than EACA in vitro, with sustained antifibrinolytic activity.[88]

A systematic review of RCTs from Henry et al investigated wether the use of antifibrinolytics in elective surgery reduces the need for allogenic transfusion.[89] Aprotinin reduced the rate of blood transfusion by 30% (RR = 0.70: 95%CI: 0.64–0.76), whereas TXA reduced the rate by 34% (RR = 0.66: 95%CI: 0.54–0.81). In contrast, EACA showed no significant reduction in the need for RBC transfusion (RR = 0.48: 95%CI: 0.19–1.19). This review also revealed that most data were obtained from RCTs using aprotinin leading to a potentially publication bias. Whether or not antifibrinolytic drugs could contribute to reducing the need for RBC transfusion in trauma patients has not yet been sufficiently investigated.[90]

The CRASH-II trial (clinical randomization of antifibrinolytics in significant haemorrhage) is currently investigating the effects of TXA in a large cohort of 20,000 trauma patients.[91]

Desmopressin (DDAVP)

Desmopressin (1-deamino-8-D-arginine vasopressin) is a synthetic analogue of vasopressin. It increases plasma levels of both FVIII and vWF from endothelial storage sites in healthy individuals as well as in deficient patients.[92] Desmopressin is an effective

treatment in bleeding patients with congenital bleeding disorders, such as haemophilia and certain vWF disease type.[93] Plasma concentrations of factor VIII and vWF are up to quadrupled after administration.[94] Results from different studies using desmopressin after the use of aspirin to reduce haemorrhage after coronary artery surgery bypass grafting are not conclusive.[95–97]

In a meta-analysis, Carless et al showed the effect of desmopressin in elective surgery.[98] Neither the blood loss (WMD $= -114.3$ mL: 95%CI: -258 to 30.2 mL) nor the need for RBC transfusion (WMD $= -0.35$ units: 95%CI: -0.7 to 0.01units) was reduced. The authors concluded that there is no evidence for the administration of desmopressin to reduce the need for blood transfusion in the absence of congenital disorders. Furthermore, there are no data available for its use in trauma patients.

SUMMARY

Coagulopathy after trauma is multifactorial and remains a challenge requiring an interdisciplinary approach. Most effort should be made to prevent the development of coagulopathy. Once the distortion of the complex haemostatic coagulation has developed, a clear strategy is essential for overcoming coagulopathy. Clinical assessment should supplement close laboratory monitoring to identify the cause of persistent bleeding. To preserve tissue oxygenation and maintain the pool of coagluation factors in massive haemorrhage, RBCs, FFP and platelets remain the mainstay of therapy. Supplementing fibrinogen or PCC should be undertaken only on the individual patient's need. The use of rFVIIa in trauma has been shown to be beneficial in blunt injuries, but further data on dosage, timing, and indication are urgently needed. Pharmacological treatments to support coagulation are effective in reducing the need for RBCs transfusion in different clinical settings, but insufficient data are available on the use of these substances in trauma.

Practice points

- hypothermia and acidosis severely impair coagulation and should be avoided or corrected, respectively
- use of RBCs and plasma products should be adapted to clinical monitoring and laboratory tests of haemostasis, including thrombelastography
- FFP is generally required when the PT or aPTT are more than 1.5 times the normal value
- fibrinogen and cryoprecipitate may be used if the fibrinogen level is lower than 0.5–1.0 g/L
- PCC is recommended in a bleeding patient with warfarin anticoagulation
- before the administration of rFVIIa, surgical and interventional methods to control haemorrhage should to be performed; in case of persistent bleeding, an initial dose of 200 µg/kg rFVIIa is recommended and should be followed by 1–2 repeated doses of 100 µg/kg if necessary
- adjuvant therapy with antifibrinolytics might be useful in certain cases of haemorrhage bleeding and hyperfibrinolysis

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