The Complex Process of Haemostasis and Interactions due to Hyperosmotic Fluids

Kompleks Hemostaz Süreci ve Hiperozmotik Sıvılarдан Kaynaklanan Etkileşimler

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Natural haemostasis includes a variety of physiological events by which bleeding stops in case of vascular injury. Haemostasis is a complex process that involves several steps to achieve the final objective of haemorrhage cessation. Classically, the first step is the constriction of injured blood vessels to decrease local blood flow, leading to platelet adhesion and aggregation, which are referred to as 'primary haemostasis'. Afterwards, the process of fibrin formation and stabilisation begins, referred to as 'secondary haemostasis', which involves many intermediate enzymatic reactions with coagulation factors. These steps have a feedback restricting haemostasis to prevent thrombotic events through the activation of the fibrinolytic system that allows the beginning of the repair of the vascular and tissue defect (1).

This course of haemostatic events has been explained by developing theories to elucidate all interactions between platelets, coagulation factors via the waterfall model, cofactors without enzymatic activity, antithrombotic mechanisms, and so on. In previous years, the cell-based model of haemostasis, in which the endothelium has a central role, has been accepted because of its best explanation of haemostasis. In this model, which was first proposed in 2001 (2), three overlapping phases can be differentiated. In the initiation phase, which is the first phase, coagulation starts when the vasculature is injured and subendothelial cells expose tissue factor (TF), which is the key initiator of haemostasis, that binds to coagulation factor VII, leading to its activation to FVIIa. The TF/FVIIa complex begins the activation of other coagulation factors, with the final objective of the formation of small amounts of thrombin (3). In the amplification phase, which is the second phase, thrombin activates platelets that have adhered to the site of injury and several coagulation factors. They bind to thrombogenic platelet surfaces and intensify and amplify prothrombinase activity (4). In the third phase (propagation phase) activated factors on catalytic platelet surfaces activate prothrombin (factor II) resulting in a massive generation of thrombin (factor IIa). The generated ‘thrombin burst’ converts fibrinogen into fibrin to form a sufficiently large clot. In the final step, thrombin-activated factor XIII (FXIIIa) catalyses the formation of crosslinks between fibrin fibres to form an elastic and stable fibrin clot (5).

This ‘perfect system’ is disrupted in current clinical practice by the administration of several drugs. The most commonly known are antiplatelet and anticoagulant agents, but some others can also disturb coagulation. For example, if the infusion of large amounts of fluids is needed to restore intravascular volume and maintain tissue perfusion when an important blood loss occurs, a nonspecific coagulopathy due to the dilution of coagulation factors and platelets could impair the coagulation. It is related to the amount of infused fluid rather than to its type.

Nevertheless, in addition to this dilutional coagulopathy, specific anticoagulant side-effects could appear to be related to the kind of fluid infused. In case of colloids (mainly dextrans, starches and gelatines), a transient decrease in factor VIII amounts, acquired von Willebrand syndrome, impaired thrombin–fibrinogen interactions, impaired factor XIII–fibrin polymer interactions and decreased platelet adhesion and aggregation, with impairment of primary and secondary haemostasis, have been described (6, 7). These haemostasis alterations have been studied and defined using viscoelastic tests such as thromboelastometry (TEG®) and thromboelastography (TEG®), showing that clot strength is reduced and that platelet dysfunction is present after dilution with artificial colloids (8).

In this issue of this journal, Ali et al. (9) published a very interesting study focusing on coagulation impairment through ROTEM® measurement after in vitro blood dilution with hypertonic–hyperoncotic solutions with or without the addition


The results of the study showed that the administration of mannitol or hypertonic saline with or without the addition of starch could be related to haemostasis impairment, although hypertonic saline seems to be safer due to less alteration in coagulation. In both cases, induced disorders are mainly dependent on fibrinogen–fibrin interactions as demonstrated by ROTEM®. The results are consistent with those of previously published studies (12-14), although the new contribution is the combination of both osmotic solutions with starch currently used in current practice.

So, what is the importance of the paper from Ali et al (9)? As the avoidance of perioperative bleeding and postoperative haematomas is of prime importance in neurosurgery to prevent poor outcomes, it seems essential to adopt a multimodal approach including the best fluid therapy (type and amount of fluid) to prevent the impairment of haemostasis. If it is necessary to infuse an osmotic agent to prevent or control the intracranial pressure, the administration of hypertonic saline could be a better option than the administration of mannitol, mainly in patients with intracranial haematomas or those who are at a high risk of bleeding. Moreover, as we know that most colloids can impair the haemostasis, its indication in neurosurgery or in cases of traumatic brain injury should be full justified and individualised.

The results of the study by Ali et al. (9) should be demonstrated in vivo, with different degrees of haemodilution and fluid combinations, but this first contribution will outline the importance of fluid administration in neurosurgery and haemostasis monitoring with a viscoelastic point-of-care.

References

12. Luostarinen T, Niiya T, Schramko A, Rosenberg P, Niemi T. Comparison of hypertonic saline and mannitol on whole blood coagulation in vitro assessed by thromboelastometry. Neurolcrit Care 2011; 14: 238-43. [CrossRef]