Editorial
Assessing Coagulation

The process of coagulation is extremely complex, with an extraordinary array of checks and balances that generally maintain the blood in a fluid state across a wide variety of circumstances whilst at the same time permitting rapid and effective control of episodes of bleeding. The complex interplay of the numerous components of the coagulation system varies, as it must, with the circumstances in each individual and the stressors to which an individual is exposed. The cell-based concept of coagulation also emphasises the critical role of cellular components in the clotting pathway.[1] Assessment of coagulation must take all of these factors into consideration

Given the complexities of the system, it is not surprising that consistent and meaningful assessment of coagulation is problematic. The standard laboratory tests (SLTs) that are most widely used are the prothrombin time (PTT), its internationally standardised derivative, the international normalised ratio (INR) and the activated partial thromboplastin time (aPTT). In most circumstances, these are the only coagulation tests available to clinicians outside major central hospitals. However, they have severe limitations that are generally not appreciated. The first issue is that these tests were never designed primarily to measure coagulation, rather they were developed to assess the level of activity of the two main early anticoagulant medications, warfarin and heparin. Both tests are performed on cell-depleted plasma, so that only the action of the coagulation proteins in isolation is studied. The prothrombin time is performed using rabbit-brain extracted tissue thromboplastin which maximally stimulates the tissue factor (extrinsic) pathway that triggers the coagulation process. Since warfarin acts predominantly on FVII (also of course on II, IX and X) this is a good test for the adequacy of dosage with this medication. In order to provide more sensitive analysis of the thrombin-dependent amplification (intrinsic) pathway, a thromboplastin extract (partial thromboplastin) was used that does not activate FVII. However, as this proved unreliable, it was further enhanced by the use of an activator such as celite or diatomaceous earth giving the activated PTT. Heparin acts primarily through antithrombin and hence the aPTT is a good measure of heparin activity. These tests are also of some value in evaluating the activity of coagulation factors, but terminate when only 5% of thrombin generation has occurred.[2] They do not assess any of the cellular components of coagulation that are now regarded as an essential part of the process[3] and cannot asses enhanced coagulation.

Seventy years ago, Hartert[4] introduced the concept of whole blood viscoelastic testing using a rotating cup in which a pin on a torsion wire was suspended; he called his device the thromboelastograph (TEG). Acceptance of this device was slow, but the development of liver transplantation resulted in increasing interest in this form of coagulation assessment. This resulted in further development of the TEG and the introduction of a modified version called the ROTEM®. Both devices assess coagulation of whole blood and thus include cellular elements and platelet function as part of the assessment. Standard TEG measurement is made using a celite activator while the ROTEM has assays that are activated by tissue thromboplastin (INTEM) and partial thromboplastin (EXTEM). These assays have the advantage that they assess whole blood coagulation as opposed to merely the plasma component and they are also able to assess hypercoagulable states that the SLTs cannot do. Correlation between these tests and the SLTs is poor, but this should not be surprising given that the techniques are very different.[5,6]

The paper from Veronese et al. in this edition of SAJAA[7] reports a pilot study comparing viscoelastic testing to standard laboratory assays of coagulation in patients with mild to moderate liver disease. As with other studies, it shows poor correlation between TEG r-time and INR. It is of interest that, as with other reports, they found that several patients with liver disease had a hypercoagulable state on TEG analysis. Again, this should not be entirely surprising as liver disease is complex, and the main anti-coagulant serine proteases, protein S and protein C, are also vitamin K-dependent and may be reduced in liver disease similarly to the procoagulant factors. They also reported some patients who had prolonged INR values, but normal TEG results. Without TEG, these patients may well have been administered FFP and other coagulation factors unnecessarily.

Assessment of coagulation in liver disease is complex and, where serious disease is present, assessment of bleeding risk in these patients requires more than the use of SLTs alone. SLTs are relatively cheap and readily available but may be misleading. When faced with serious haemorrhagic risks, viscoelastic monitoring appears to offer substantial additional information that may prove critical in managing perioperative haemorrhage.[8]

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References

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