CASE REPORT

Walking the Razor's Edge—Anticoagulation-induced Intracerebral Hemorrhage and the Perplexity in Choosing between International Normalized Ratio and Point-of-care Tests as a Reliable, Definitive, Coagulation Testing Parameter in Neurosurgical Management

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Abstract

Urgent reversal of anticoagulation in patients on warfarin therapy for neurosurgical procedures can be quite tricky as well as risky. Anticoagulation reversal using blood products has its own challenges and their administration must be guided with effective, investigative tools such as international normalized ratio (INR) and point-of-care coagulation tests. However, the superiority of either in neurosurgical procedures has not been established. Hence, a careful risk calculation must be done considering the overall clinical picture of the patient as well. We present a case report in which we faced such a dilemma.

Keywords: International normalized ratio, Neurosurgery, Thromboelastography (TEG), Warfarin.

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Introduction

The greater longevity of the aging population is affiliated with the escalating use of anticoagulants which is deemed mandatory for prevalent conditions such as atrial fibrillation and in those with mechanical heart valves. It is comparable to having the sword of Damocles over their head-discontinuation of which can lead to thrombotic events while its use is associated with a 7- to 10-fold increase in intracerebral hemorrhage.[1] The mortality rate is driven in part due to hemorrhage expansion and tissue damage which hence warrants urgent reversal of the anticoagulant scenario and immediate surgical intervention. The onus of accelerating this process lies with the anesthesiologist while keeping in mind the overall bleeding risk to ensure patient safety and sagaciously choosing the appropriate point-of-care coagulation testing (POCCT) alongside the conventional coagulation tests.

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Case Description

A 60-year-old woman complained of sudden onset headache, dizziness, and multiple episodes of vomiting. On evaluation in a multispecialty hospital, her Glasgow Coma Scale (GCS) was 11/15, her left pupil was <2 mm, and both pupils were sluggishly reacting to light. Head CT scan showed a hyperdense hematoma with minimal edema (4 × 3.5 × 4 cm) noted in the right cerebellar hemisphere with compression over the fourth ventricle and medulla with a descent of the right cerebellar tonsil through the foramen magnum. The international normalized ratio (INR) was 3.3. The rest of her labs were normal. Vitamin K 10 mg was administered intravenously and she was shifted to our hospital for further treatment. On arrival, her GCS was 7/15. She was immediately intubated. Medical history revealed surgery for rheumatic heart disease with a mitral valve replacement (metal prosthetic valve) in 2015. She was on anticoagulation therapy with tablet warfarin 2.5 mg on an alternate day for the same. The last dose was taken a day earlier. She was a known hypertensive since 2014 and during the same year, she suffered a stroke from which she fully recovered. Labetalol infusion was started due to high blood pressure recordings. The neurosurgeon decided to proceed with an emergency surgical decompression and evacuation. Since a lot of precious time was lost in transit during shifting the patient to our care, we were pressurized for a swift reversal of anticoagulation and to expedite the shifting to the operating theater. Echocardiography showed a left ventricular ejection fraction of 50% with the septal wall mildly hypokinetic. The cardiologist advised optimizing the INR. A hematologist's opinion was sought who advised infusion of about 900 mL of fresh frozen plasma (FFP) and administration of prothrombin complex concentrates (PCCs) at a rate of 30 IU/kg till the INR

was corrected to 1.4. A thromboelastography (TEG) was sent immediately which also acknowledged the need for transfusion of FFP (Fig. 1). The PCCs were not available at that time and hence not administered. Post-infusion of FFPs, INR was sent and the patient was shifted to the operating theater after 3 hours of receiving them in the intensive care unit (ICU). Blood and blood products were arranged and kept on standby for intraoperative transfusion. An additional dose of 80 µg fentanyl and vecuronium 8 mg were administered and anesthesia was maintained with oxygen + air + sevoflurane. Standard monitoring was continued in addition to securing central venous access and an arterial line. A TEG sample was sent. The INR value came to be 1.27 while the TEG revealed a more thrombotic picture (Fig. 2). Clinically, there was not much bleeding. Hence, we decided not to transfuse the PCCs which by then had arrived. Intraoperative hemodynamics were maintained uneventfully with a blood loss of about 500 mL. No further blood products were transfused. The patient was shifted back to the ICU for elective postoperative ventilation in view of poor preoperative GCS. She received one unit of packed red blood cells (PRBC) postoperatively. Patient condition and GCS improved, and she was extubated on the second postoperative day with no residual neurological deficit. Low molecular weight heparin (LMWH) was started on postoperative day 1 and it was decided to start anticoagulation 1 week later.

Case Description

Warfarin acts by inhibiting the reactivation of vitamin K epoxide to hydroquinone, thus inhibiting gamma-carboxylation of glutamate at the amino terminus of coagulation factors synthesized in the liver (factor II, VII, IX, X). This results in the prolongation of prothrombin time (PT) (INR). Hence, INR is ideal to gauge the safety against bleeding due to warfarin.[2] Warfarin is employed to prevent thromboembolism in patients with mechanical heart valves. The INR targeted for this category of patients according to the set guidelines is 3 (range of 2.5–3.5). The reported risk of subdural hematoma (SDH) with anticoagulation is 4- to 15-fold.[3,4] The reported mortality of anticoagulant-related SDH is between13 and 20%.[5] For a better outcome and a decreased mortality, this INR must be appropriately reversed preoperatively. Current guidelines recommend reversal of anticoagulation and normalization of INR to 1.4 which is suitable for most of the neurosurgical procedures.[6] Anticoagulation can be reversed using vitamin K, FFP, or factor concentrates. However, vitamin K and FFP are not ideal when urgent reversal to maintain an INR <1.5 is required as their action takes a long time. Required volumes of FFP often exceed 1,000 mL, requiring significant infusion time and additional problems in patients with volume constraints because of impaired renal or cardiac function.[7] Prothrombin complex concentrates are the gold standard therapy and recombinant activated factor VIIa can cause a complete reversal in 10 minutes but they both may cause thrombotic complications (PCC has a high level of factor II) and their availability is a concern in many centers. Warfarin anticoagulation management presents a myriad of clinical challenges. Few of these hurdles could be overcome by recruiting POCCT. Point-of-care coagulation testing may be defined as the rapid specific testing of bodily fluids at the bedside. The PT and activated partial thromboplastin time (aPTT) provide information on the first phase of coagulation up to fibrin formation. Conversely, viscoelastic POCCT devices produce information in all phases of coagulation, providing insight into interactions between the cellular and plasma components of whole blood and the activity of the fibrinolytic system; all of which are vital for successful hemostasis.[8] The main advantages of TEG include guiding transfusion therapy and decreasing the use of blood products, detecting dynamic changes in blood coagulation during resuscitation, and predicting the clinical efficacy of therapeutic agents affecting blood coagulability. In our case, we were directed to chase an INR of 1.4 and instructed to infuse PCC. Due to their non-availability, there was a delay in the administration. Fortunately, a TEG done around the same time revealed no further administration of blood products, thus saving us from an unwarranted transfusion and its related complications. Hence, it is questionable whether PT/INR can be considered a good reference standard to diagnose coagulopathy. TEG has convincingly demonstrated its usefulness to help improve outcomes in cardiac surgery. A meta-analysis of 17 randomized controlled trials (RCTs) demonstrated that TEG decreases blood product transfusions and surgical re-exploration due to postoperative bleeding in cardiac surgery patients.[9]

There is conflicting evidence for TEG's usefulness in trauma patients. A recent Cochrane database systematic review found insufficient data to compare the accuracy of TEG and RoTEM vs PT/INR in the diagnosis of trauma-induced coagulopathy.[10]

In major trauma, r-TEG is better in predicting the need for transfusion of FFP, RBCs, and platelets compared to conventional coagulation tests of PT, aPTT, INR, platelet count, and fibrinogen.[11] Based on another large systematic review, TEG/RoTEM can diagnose coagulopathy and may predict blood components transfusion and mortality in trauma patients.[12]

There is limited evidence for the use of TEG in intracranial bleeding due to anticoagulants.

In about half of patients on warfarin therapy, R-time may be normal in both TEG and rapid TEG tests, with a poor correlation between TEG and INR.[13] This is a good example of how TEG may miss a clinically significant coagulopathic state. Hence, INR is still the gold standard for monitoring warfarin therapy.

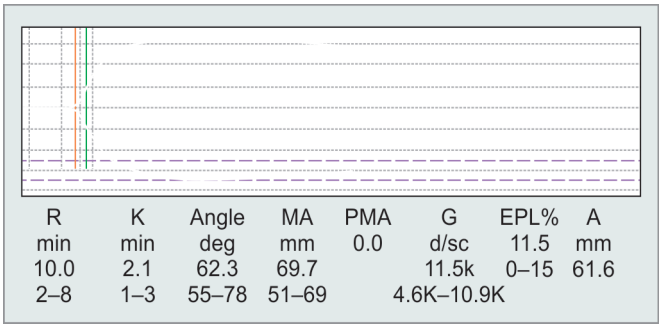

Fig. 1: Preoperative TEG prior to transfusion of fresh frozen plasma

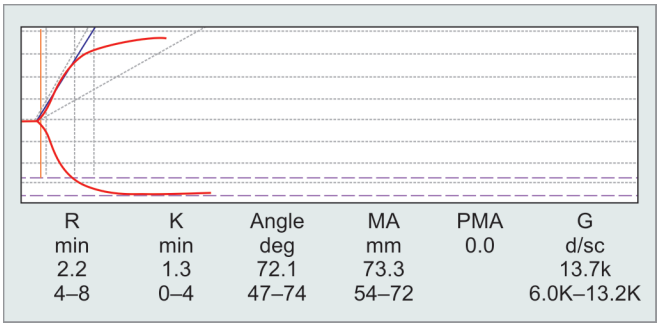

Fig. 2: Intraoperative TEG after the transfusion of fresh frozen plasma

Conclusion

"The essence of fighting is the art of moving at the right time" quoted Bruce Lee. While the risk of death from bleeding far exceeds the risk of death from thromboembolism reversing the anticoagulation must be done carefully and swiftly choosing the appropriate monitoring tools. Though INR has been frequently incorporated for the same, it should be borne in mind that it may be overrated and TEG might help in balancing and regulating the need for unnecessary blood transfusions.

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