Need for a Point-of-Care Assay for Monitoring Antiplatelet and Antithrombotic Therapies

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The Framingham studies instituted by the National Institutes of Health in the 1950s identified the major risk factors for the development of cardiovascular disease. Specific lipid-lowering drugs and a variety of blood pressure-lowering drugs were developed to better manage these cardiovascular disease risk factors. Along with the use of these therapeutic modalities, the means to monitor risk factors after medical intervention was also developed. However, despite the fact that antiplatelet therapies are in use for a long time than statin therapy, no simple, specific, cost-effective assays are available for monitoring antiplatelet therapy.

The need for such an assay for monitoring antithrombotic therapies is greater in patients with stroke. According to the American Heart Association update, on average, every 45 seconds, someone in the United States has a stroke. Of all strokes, 88% are ischemic and 9% are intracerebral hemorrhagic. Therefore, the majority of patients with stroke are on antiplatelet therapy. Drugs of choice for antiplatelet therapy are aspirin, Plavix, or a combination of both. Because there is some concern that patients with cardiovascular disease may have variable responses to the action of aspirin, there is a tendency to recommend Plavix, a combination of aspirin and Plavix, or Aggrenox (combination of aspirin and extended-release dipyridamole). In view of this, there is a great need to monitor the antiplatelet therapy in these patients so that the therapy could be optimized to suit the individual requirement.

Several methods are available for monitoring platelet function. Hurlen et al have used the method of Wu and Hoak to determine the platelet aggregate ratio as a marker of assessing platelet function.2,3 Gum et al have used aggregometry to evaluate aspirin sensitivity by monitoring platelet response to adenosine 5’-diphosphate and arachidonic acid.4 They also used the Platelet Function Analyzer (PFA-100; Dade International Inc), a method that measures platelet function, to study their patient population. Malinin et al used Ultegra RPFA-ASA (VerifyNow; Accumetrics, Inc, San Diego, Calif) to monitor the effect of single-dose aspirin (325 mg) in subjects with multiple risk factors.5 Despite the fact that researchers are monitoring platelet function over 5 decades, there are no simple, specific, cost-effective assays available for monitoring antiplatelet therapies. However, we strongly feel that platelet aggregation studies will still provide valuable information to clinicians on the status of platelet reactivity.

Studies in our laboratory over several decades using both optical and impedance aggregometry have failed to show any aspirin resistance or clopidogrel resistance in normal healthy subjects. Performing whole blood aggregometry is simple and results are reproducible. Whole blood is drawn into sterile plastic syringes using a butterfly needle (20g) and mixed with 3.2% sodium citrate (anticoagulant; 9:1 ratio). Platelet aggregation studies are performed with whole blood diluted 1:1 with 0.9% saline. Like in optical aggregometry with platelet-rich plasma, during whole blood aggregometry, adenosine 5’-triphosphate secretion from the dense granules of platelets could be monitored by using firefly luciferin and luciferase reaction. Using arachidonic acid or adenosine 5’-diphosphate as agonists, one can monitor aspirin or clopidogrel resistance in patient populations using whole blood aggregometry. Studies from our laboratory as well as that of others have demonstrated that whole blood aggregometry by the impedance method is superior to the optical method.6,7

According to the American Heart Association, every 3 minutes, someone in the United States dies of a stroke. It is noteworthy that 8% to 12% of ischemic strokes and 37% to 38% of hemorrhagic strokes result in death of patients with stroke within 30 days. It is therefore essential to monitor activation profiles of both platelet and coagulation pathways so that better therapeutic protection could be provided to those with high risk for acute vascular events. In the absence of a point-of-care assay capable of monitoring both the mechanisms that promote thrombosis, whole blood aggregometry is a good choice for monitoring antiplatelet therapies.
Disclosures
None.

References

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