Laboratory Screening for Abnormalities of Primary Hemostasis: What’s Next?

To the Editor:

The diagnostic approach to abnormalities of primary hemostasis is still a major challenge for clinical laboratories. In clinical practice, the investigation of unexplained bleeding ideally uses easy, reliable, and inexpensive screening tests, eventually followed by second-line analyses (1). Because of a lack of reliable alternatives, the bleeding time (BT) test has been widely used for decades. However, the BT test is relatively insensitive and nonspecific with respect to identifying abnormalities of primary hemostasis. The diagnostic efficiency of the BT test for prediction of abnormal perioperative bleeding has been critically questioned (2–5), suggesting the need for alternatives.

The interaction of citrated whole blood with biochemically active membranes coated with physiologic agonists (collagen and adenosine diphosphate or collagen and epinephrine) can be used to trigger platelet activation under high shear rates and generate a stable platelet plug. Abnormal prolongation of clot development can be automatically recorded by the PFA-100® Analyzer (Dade), which reflects potential qualitative and quantitative abnormalities of platelet function. The clinical usefulness of this test has been studied in some clinical settings, including evaluation of uremia, the laboratory approach to the diagnosis of von Willebrand disorder and platelet dysfunction, and the monitoring of therapy with antiplatelet drugs (6–8). The within- and day-to-day (total) imprecision (CV) of the test are reportedly <10% (8). The test may be especially useful in children (9) because the analysis does not require the active cooperation of the patient and uses <2 mL of blood. We agree with Lehman et al. (5) on the limited clinical impact of discontinuing the BT test, and we believe that automated, in vitro analyzers can be useful for the identification of some defects of primary hemostasis. The PFA-100 analysis has replaced the BT test in the evaluation of disorders of primary hemostasis in our laboratory (9).

References


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To the Editor:

Currently there is no simple test to detect pancreatic cancer (PC). Fasting plasma islet amyloid polypeptide (IAPP) was reported to be increased in patients with PC (1), and a soluble factor from PC cells was reported to stimulate IAPP secretion (2), suggesting the possibility of an increase of IAPP in the plasma of patients with PC. In a recent clinical study, however, IAPP was not a satisfactory marker for detecting PC (3).

Human IAPP is easily degraded by proteases present in serum or plasma and also degraded during the clotting process. A possible cause for the loss of utility of IAPP for PC detection could be degradation of the polypeptide before analysis. Therefore, we designed a study to reevaluate this marker using plasma samples carefully collected in tubes containing protease inhibitors, with the plasma separated immediately and stored at −80 °C before analysis. Unfortunately, this improved sample handling did not improve the utility of IAPP for detection of PC.

Blood samples were collected in tubes containing protease inhibitors (2 mg/L antipain dihydrochloride, 25 mg/L elastatinal, 0.5 mg/L leupeptin, and 0.5 g/L EDTA). Our IAPP assay procedure was a modification of the method described by Perment et al. (1). Tracer was made by iodiumination of synthetic human IAPP with the iodogen method and purified by HPLC. BeforeRIA, plasma samples were extracted with 600 mL/L acetonitrile on Sep-Pak C18. For RIA, anti-human IAPP antibody (RAS 7321) was used. The detection limit was 1.5 pmol/L, and the intra- and interassay CVs were <10%.

IAPP was stable for 2 h at 4 °C when synthetic IAPP was incubated...