Point-of-Care Coagulation Testing: Stepping Gently Forward

As a specialist in diagnostic coagulation, I am frequently faced with a patient who does not want to drive into Boston to be monitored for warfarin (coumadin) therapy at our anticoagulation clinic. This fact has not been lost on instrument manufacturers, who have produced multiple point-of-care devices for home monitoring of the prothrombin time/international normalized ratio (PT/INR). The number of individuals taking coumadin for atrial fibrillation, recurrent venous or arterial thrombosis, and other conditions is tremendous. The total number of prescriptions for warfarin in 1999 exceeded 20 million. The report by Ambrose et al. (1) in this issue of Clinical Chemistry investigates the performance of a point-of-care testing (POCT) analyzer for activated clotting time (ACT) measurement in a population of children undergoing extracorporeal membrane oxygenation. The performance of the POCT analyzer was equivalent to that of other commercially available POCT instruments for ACT measurement, but the results showed no relationship to the gold standard test of plasma heparin concentration. This study highlights several issues relevant to point-of-care coagulation assays. One of the most important is whether the tests are performed at a clinical site or at home.

A recent survey of coagulation analyzers identified 17 devices (2). Of these, 15 had been cleared for use by the Food and Drug Administration as of October 1, 2000. Of these, 12 can be used to perform a PT/INR, 11 can perform an ACT or related test to manage heparin therapy, and 8 are available for partial thromboplastin time (PTT) measurements. Four of the instruments have had a patient self-testing program for home monitoring of PT/INR to optimize coumadin therapy. POCT for coagulation at a clinical site by certified health professionals has some unique aspects, as noted below, but the major practice change for point-of-care coagulation studies is home testing for coumadin dose adjustment. As expected for any product, the financial return from a new product is the major driver in the move toward point-of-care coagulation testing, especially home testing because it increases the market by several orders of magnitude over POCT for coagulation only at clinical sites.

A clinical driver for home monitoring of coumadin therapy is the limited knowledge of many general physicians on how to manage coumadin therapy and the inadequate number of well-run anticoagulation clinics to assist physicians (3). I have seen much coumadin monitoring by the “yo-yo method”. In this unfortunate situation, the patient has a high INR value, so the physician discontinues the coumadin therapy completely for several days. The physician then reinitiates coumadin therapy at too high a dose after the INR has fallen well below the therapeutic range, which produces a value well above the therapeutic range, and the cycle is repeated over and over again. The yo-yo method is less of an issue with heparin because dosage adjustment can be made quickly, as heparin has a short half-life of ~60 min.

Another clinical driver for home testing is the apparent benefit from more frequent INR monitoring than is currently performed. Several studies found that self-tested patients were more often within the therapeutic range than patients managed by standard methods, largely because of more frequent testing in the self-test group (4–7). A recent report involving 325 patients ≥65 years of age showed that more frequent monitoring at home reduced the frequency of major bleeding and increased the proportion of time that the INR was within the therapeutic range (8). Because patients are generally asked to travel to an anticoagulation clinic or a hospital laboratory for sample collection, monitoring not performed at home occurs at most weekly, and when patients are stable, as infrequently as once each month. Experience with glucose monitoring for diabetics indicates that more frequent monitoring and more careful management of insulin therapy lead to fewer complications. Evidence now indicates that the same is likely to be true for coumadin monitoring and possibly heparin monitoring by the PTT at a clinical site.

A laboratory-based driver for home testing is that the assay result is produced by a single meter and the same operator, a situation preferable to the use of a myriad of different reagent/instrument combinations for INR testing. This advantage is not usually in place for PTT monitoring for heparin at a clinical site because there typically are many different users of the POCT device.

With all of the drivers toward point-of-care coagulation testing at home, one must consider whether POCT by the patient is the ideal option or whether point-of-care coagulation testing at a more convenient site than a hospital or anticoagulation clinic, such as a pharmacy or a blood drawing station, by a person trained to do the test is a better answer.

Consider the consequences of an abnormal glucose value and its potential impact on clinical outcome. If hyperglycemia is unrecognized because a high blood glucose is misread as normal, the consequences are not likely to be acutely life-threatening. The mistake of misreading a truly low blood glucose as normal could have acute consequences, but the patient often is symptomatic as he or she becomes hypoglycemic. The appearance of symptoms typically prompts the patient to ingest a source of glucose to increase blood sugar.

Consider on the other hand, the PT/INR in a coumadin-treated patient and the PTT in a heparinized patient. One potential consequence of having an INR or a PTT above the therapeutic range and misreading it as therapeutic is that the patient suffers a lethal or irreversibly damaging hemorrhage in the central nervous system, from which there is no chance for recovery. Similarly, if the patient has an INR or a PTT value below the therapeutic range and the result is misread as therapeutic, the
patient may suffer a lethal thrombosis, the entity that anticoagulant therapy was initiated to combat in the first place. Thus, the consequences of missing a high or low PT/INR or PTT by mistake could be catastrophic and irreversible, and in both cases, the patient may not have warning symptoms to prevent the bad outcome. Non-therapeutic concentrations misread as therapeutic, because they are the “expected values”, are the most dangerous because these results do not generate a “red flag” for subsequent action.

Most proponents of home monitoring for anticoagulation argue that with good training by an expert trainer, a patient can effectively perform coumadin testing. One danger of this approach is that the patient is certified at one age and then months to years later, when he or she may no longer be as physically able to perform the test, there is still permission to use the device. Certification twice per year (at least) for use of the instruments at home would be highly recommended. It must be appreciated that once patients have been using a device for monitoring the INR, they (like many physicians) assume that the number on the display is always correct, and will therefore be reluctant to begin a program of point-of-care coagulation testing outside the home because they can generate a number (right or wrong). It goes without saying that patients are much less likely to identify errors in technique or understand interferences in the test than are healthcare professionals. The compromise of having the testing performed at a local pharmacy or clinic obviates the need to drive long distances and reduces the risk of operator error because the test would be performed by a certified allied health professional.

I would like to conclude by providing a real-life circumstance for consideration. Imagine that your grandmother is taking coumadin and makes a mistake in the performance of the test. She generates an INR of 2.5, the middle of the therapeutic range, when the actual value was 6.8. This is extremely dangerous because it predisposes to major hemorrhage, but it is not reflected by the test result. Grandma, who lives alone, has a major hemorrhagic event in the brain and expires. No autopsy is performed. What is the likelihood that an operator or instrument error-related death will be detected? The answer is that it will be almost impossible to implicate anything wrong with the test reagents or the performance of the test until there are a significant number of deaths associated with the use of a coagulation POCT instrument at home. Because of this impossibility, I would argue that it is better to develop the solution of allied health professionals performing the point-of-care test more frequently than once a week as the appropriate answer, despite the modest disadvantages of this option.

For point-of-care coagulation testing within a clinical site, this requirement is easily met. The use of point-of-care coagulation testing at a clinical site by a certified individual—if it provides accurate enough information on which to base clinical decisions—provides certain advantages over central laboratory testing, especially in institutions without a pneumatic tube and reliable STAT turnaround times.

In the report by Ambrose et al. (1) in this issue of Clinical Chemistry, the lack of agreement with heparin concentrations by anti-Xa methods used in the clinical laboratory does not negate its clinical benefit if useful information is provided on heparin management. However, I am concerned that the pendulum has swung too far toward home testing of INR for coumadin therapy.

References

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