

Improving turnaround time at warfarin clinics

Monitoring of anticoagulant effect is an important facet of warfarin treatment. Now, patients who undergo regular international normalised ratio testing can reap the benefit of microcentrifugation, as Afruj Ali Ruf and his colleagues in West Yorkshire explain.

Over recent years, there has been a dramatic increase in the number of patients receiving long-term anticoagulation with warfarin. Multiple indications for long-term anticoagulation are now accepted, including stroke prevention in atrial fibrillation, patients

with prosthetic heart valves and those suffering recurrent venous thrombosis and antiphospholipid syndrome.

The management of individuals on warfarin is problematic due to inter-individual and intra-individual variation in dosage requirements. Many factors

have been reported to influence warfarin dosage, including concomitant medication, diet, increasing age, liver volume, vitamin K status and occult malignancy. More recently, it has become clear that genetic factors that lead to differences in warfarin sensitivity are also important.¹⁻³

These difficulties have led to the need for an entire warfarin-associated industry and infrastructure devoted to the clinical use and therapeutic monitoring of this single drug. Anticoagulant services based in hospitals and the community involve doctors, nurses, pharmacists and laboratory staff. In addition, patient self-testing is increasingly common.

Reliable results

The quality of warfarin therapy management requires reliable results for the prothrombin time/international normalised ratio (PT/INR). The INR, adopted by the World Health Organization (WHO) in 1983, attempts to address the many variables associated with the measure of warfarin effectiveness. The INR is a standardised system of reporting PT, based on a referenced calibration model, calculated by comparing the patient's PT with a control value. Factored in this calculation is the international sensitivity index (ISI), also developed by WHO, which is a determination of each reagent's degree of sensitivity, compared with that of a specific reference thromboplastin (which is assigned an ISI of 1.0).⁴ The ISI allows the associated PT ratio to be normalised to an international reference preparation.⁵

Routine coagulation assays are performed with platelet-poor plasma obtained following centrifugation of whole citrated blood. Usually, clinical laboratories centrifuge blood at 2000–2500 xg for 10–30 minutes. Preparation, in particular centrifugation, of blood specimens can be the cause of bottlenecks in laboratory throughput. Reliable strategies for reducing the time required for specimen centrifugation without affecting quality should be



The StatSpin Express 2 microcentrifuge, available from Rapid Sample Processing.



Microcentrifugation using the StatSpin Express 2 can reduce centrifugation time without compromising the quality of results for routine coagulation tests.

acknowledged, especially by laboratories performing short turnaround time (STAT) analysis and running warfarin clinics.

It has been suggested that microcentrifugation can reduce centrifugation time without compromising the quality of results for routine coagulation tests.⁶⁻⁹ In this study, laboratory staff at Airedale General Hospital compare a 30-second microcentrifugation at 4440 *xg*, using a StatSpin Express 2 microcentrifuge (available from Rapid Sample Processing), against a five-minute centrifugation at 2000 *xg*, using a Jouan B4i centrifuge, to evaluate whether or not turnaround time can be reduced in warfarin clinics without compromising the quality of the INR result.

'Studies show that test results obtained after microcentrifugation are comparable with results using conventional centrifugation'

Airedale experience

Currently, Airedale General Hospital has approximately 1800 patients on long-term warfarin therapy. These patients are monitored in warfarin clinics provided at four remote sites and two weekly hospital-based out-patient clinics. On average, approximately 60


patients are booked in each of the remote clinics, each of which runs for two and a half hours.

A phlebotomist provides a venepuncture service, collecting blood in tubes containing 0.109 mol/L buffered trisodium citrate (Becton Dickinson Vacutainer). Laboratory staff then centrifuge the blood sample and a PT/INR test is performed on the plasma using a Sysmex CA50 portable coagulometer. The INR result is recorded in the patient's warfarin book and returned to the patient, who is then seen by a pharmacist and advised on the dose to be taken.

Previous studies show that coagulation test results obtained after microcentrifugation are comparable with results obtained using conventional centrifugation.⁶⁻⁹ This study compared INR results after 30 seconds' microcentrifugation and after five minutes' conventional centrifugation on 30 randomly selected patients on warfarin, and found no significant difference between INR results using the two centrifugation methods.

Using conventional centrifugation at remote clinics, the mean time from receipt of sample/patient's warfarin book by laboratory staff to recording the INR result and the return of the warfarin book to the patient was 10.5 minutes (range: 7-15 minutes). The mean time using the StatSpin Express at the same remote clinics was 4.3 minutes (range: 4-5 minutes). Samples that required repeat testing as a result of a high INR were excluded from the evaluation.

The Airedale experience shows that

the StatSpin Express reduces the turnaround time by an average of 6.2 minutes, and eliminates the bottleneck that is a common feature of conventional centrifugation. In addition, variation in testing time was eliminated, and patient flow from venepuncture to the point where they see the pharmacist was more streamlined, with a consequent overall improvement in the patient experience. 

References

- 1 Casner PR, Sandoval E. Increased sensitivity to warfarin in elderly Hispanics. *J Clin Pharmacol* 2002; **42**: 145-50.
- 2 Aithal GP, Day CP, Kesteven PJ, Daly AK. Association of polymorphisms in the cytochrome P450 CYP2C9 with warfarin dose requirement and risk of bleeding complications. *Lancet* 1999; **353**(9154): 717-9.
- 3 Hummers-Pradier E, Hess S, Adham IM, Papke T, Pieske B, Kochen MM. Determination of bleeding risk using genetic markers in patients taking phenprocouman. *Eur J Clin Pharmacol* 2003; **59**: 213-9.
- 4 Eckman MH, Levine HJ, Pauker SG. Effect of laboratory variation in the prothrombin time ratio on the results of oral anticoagulant therapy. *N Engl J Med* 1993; **329**: 696-702.
- 5 Brigden ML. When bleeding complicates oral anticoagulant therapy. *Postgrad Med* 1995; **98**: 153-68.
- 6 Lippi G, Salvagno GL, Montagnana M, Manzato F, Guidi GC. Influence of the centrifuge time of primary plasma tubes on routine coagulation testing. *Blood Coagul Fibrinolysis* 2007; **18**(5): 525-8.
- 7 Boudaoud L, Divaret G, Marie P, Bezeaud A. Rapid centrifugation for routine coagulation testing (in French). *Ann Biol Clin (Paris)* 2006; **64**(4): 315-7.
- 8 Foster K, Datta P, Orswell M, Tasaico K, Alpert A, Bluestein B. Evaluation of a centrifuge with rapid turnaround time for the preparation of plasma samples for measurement of common STAT markers on the ACS: 180 system. *Clin Lab* 2000; **46**: 157-60.
- 9 Nelson S, Pritt A, Marlar RA. Rapid preparation of plasma for 'Stat' coagulation testing. *Arch Pathol Lab Med* 1994; **118**(2): 175-6.

Dr Afruj Ali Ruf is consultant healthcare scientist in the haematology department, Airedale General Hospital, Steeton, West Yorkshire BD20 6TD.