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An update on INR monitoring

By Dr Shane Jackson, Dr Luke Bereznicki, Professor Gregory Peterson, Ella Jeffrey

Learning objectives

After reading this article the pharmacist should be able to:

- Understand key educational points for patients taking warfarin
- Understand the importance of maintaining the INR in the therapeutic range
- Understand the potential role of patient self-testing of the INR
- Be aware of possible future roles of pharmacists in the management of warfarin therapy.

An 88-year-old male was admitted to hospital with heart failure, and a past medical history including paroxysmal atrial fibrillation. He was initiated on warfarin due to the presence of a thrombus in the left atrium, visualised on transoesophageal echocardiography, and was subsequently discharged on a dosage of 2.5mg daily. After eight days, it was determined by a pharmacist that the man had been attempting to take 2.3mg of warfarin daily. The patient had confused his most recent INR result with his intended warfarin dose. He was unaware that his dose and the INR were actually two different things. Fortunately, this did not result in any adverse consequences because the dose he was meant to be taking and the actual dose being taken were very similar.

A 65-year-old lady was admitted to hospital with a diagnosis of ischaemic heart disease. She had a past medical history of hypertension, peripheral vascular disease, reflux oesophagitis, previous coronary artery bypass graft (CABG), and hypothyroidism. Another CABG was completed, and was complicated by post-operative atrial fibrillation. The patient was initiated on warfarin, to be of six weeks' duration if she remained in sinus rhythm and to then start aspirin after she ceased warfarin. She was discharged on warfarin 3mg daily, with a satisfactory INR at 2.0. The day following discharge, her general practitioner ordered an INR test and it was found to be 2.0. The doctor suggested to the patient that she increase her dose of warfarin from 3mg daily to 'alternate 3mg and 4mg'. The patient, however, assumed this message to mean 3mg in the morning and 4mg at night. In effect, she had actually doubled the intended dose from 3.5mg per day to 7mg per day. Her INR was found to be greater than 8.0 at five days after discharge. This error was perpetuated as the patient forgot to telephone the doctor for her INR result, and the doctor did not contact her until the next day.

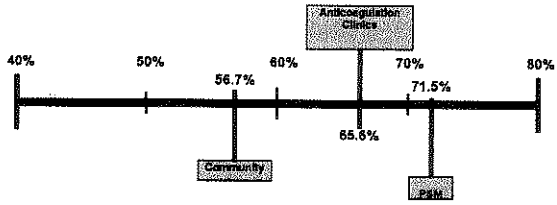
Warfarin has been in widespread use since the 1950s and is currently the most commonly prescribed vitamin K antagonist worldwide. The use of warfarin is now increasing at a steady rate (approximately 10% per year),[1] largely due to its use for stroke prevention in chronic atrial fibrillation. Adverse events (over-use, under-use and misuse) from warfarin in Australia were estimated to cost over $100 million per annum in direct hospital costs alone (in 1992).[2] While the benefits of warfarin are greatest in the elderly, so are the difficulties of anticoagulant management and the risk of adverse outcomes. Health care systems need to improve to counter this therapeutic dilemma, as warfarin is likely to remain the only widely available oral anticoagulant for the foreseeable future.

Aspects of warfarin management that require close attention are:

- The careful selection of patients in whom treatment with warfarin is appropriate;
- Initiating therapy in a low dose (e.g. 2.5-5 mg/day);
- Close monitoring, especially with any change in the patient's regular drug therapy or comorbidities;
- Thorough education of patients and carers;
- Clear and comprehensive communication between patients, health care professionals and interfacing health care systems (e.g. hospitals and community-based care);
- Involving patients more in the management of their warfarin therapy (self-monitoring/management in suitable patients); and
- Ongoing review of the appropriateness of therapy as circumstances change.

The clinical benefits of warfarin are highly dependent on maintaining the international normalised ratio (INR) within the therapeutic range (generally 2.0-3.0 in patients with chronic atrial fibrillation). Poor adherence, variable dietary intake, drug interactions, inadequate knowledge, and miscommunication between the patient and health care professionals and institutions, have all been cited in the literature as potential causes for fluctuations in the INR. Unfortunately, patients taking warfarin in the community spend only about 50-60% of their time within this INR range (Figure 1).[3] Patient self-monitoring (PSM) is considered the gold standard for warfarin management, which can result in over 70% of time spent in the therapeutic range. Extrapolating from international observational studies, optimal control of INR would be expected to prevent 1,750 major bleeds and 700 ischaemic strokes each year in Australia.[4]

Figure 1: Effect of monitoring process on anticoagulation control.[3]



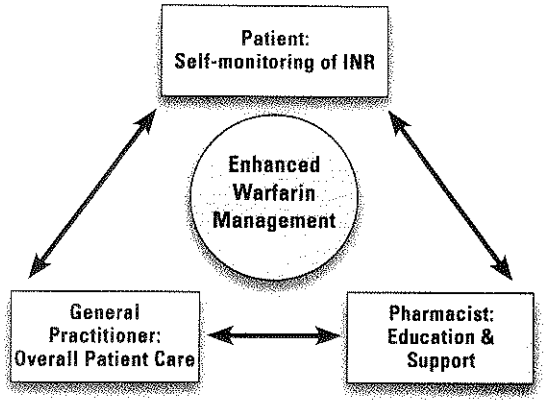
Traditionally, anticoagulant therapy in Australia is managed by GPs and pathology providers. The patient visits their GP or pathology specimen collection centre to have a venous blood sample taken (or the aged care facility transfers a blood sample to a pathology service), and the result is subsequently reported to the GP, who determines the need for dosage adjustments. The GP or pathology provider must then communicate the dosage requirements back to the patient (or carer) or aged care facilities in a timely manner to ensure dosage adjustments, if needed, are implemented. The inability to make timely contact with the patient or nursing home, and the potential for misinterpretation of information conveyed by the GP has been shown by ourselves and others to result in dosage errors.[5,6]

Small point of care (POC) INR monitors with high accuracy and ease-of-use have been available for a number of years (e.g. the *CoaguChek XS*, Roche Diagnostics). Self-monitoring involves patients measuring their INR with a portable device and referring to a health care practitioner for guidance on dosage changes, while with self-management patients measure most or all of their INRs, interpret the results themselves, and translate this into dosage adjustments.

Pharmacists are in an ideal position to screen patients taking warfarin for their suitability to monitor or manage their own therapy.

After performing a systematic review and meta-analysis of 14 randomised controlled trials that assessed the effects of self-monitoring (either self-monitoring alone or self-monitoring and self-adjustment of the warfarin dose) of anticoagulation compared with standard monitoring, Heneghan, *et al.* concluded that self-monitoring improves the quality of oral anticoagulation.[7] The clinical outcomes of patients who self-monitored alone and those who also self-adjusted their warfarin dose were similar. However, self-monitoring is not feasible for all patients, and requires identification and education of suitable candidates. It is estimated that with appropriate training, self-monitoring is safe and reliable for a sizeable proportion (approximately 25%) of patients receiving oral anticoagulation treatment.[8]

Figure 2: Conceptual model for patient self-monitoring of warfarin



Patient self-monitoring of oral anticoagulation is now practised in a number of European countries, including Germany, Italy, the Netherlands and England, and also in the USA. Australia is lagging behind in introducing similar strategies to improve the quality of anticoagulation. The authors have recently received funding from the Department of Health and Ageing, through the 4th Community Pharmacy Agreement, for two projects which have the potential to establish the clear role of pharmacy in the management of warfarin in the Australian community setting:

- Pharmacy-Based Model Enabling Patient Self-Monitoring of Warfarin: Development and Evaluation (Figure 2).
- The Role of Community Pharmacy in Post Hospital Management of Patients Initiated on Warfarin (Figure 3).

Pharmacists are in an ideal position to screen patients taking warfarin for their suitability to monitor or manage their own therapy. Under existing funding structures, pharmacists can refer these patients to their general practitioner to further discuss the concept, with a view to referral to the community pharmacy to organise a visit by an accredited pharmacist for specialised training, delivered as a home medicines review (HMR). While POC devices are presently costly, private health insurers are now offering significant rebates on the cost of these devices on a case-by-case basis (with an 80% rebate, the cost of a *CoaguChek XS* is approximately $150). Roche Diagnostics (Australia) have made their *CoaguChek XS* monitor available through pharmacy wholesalers, so that community pharmacies can order in or stock the device for interested and suitable patients. With a critical mass of trained pharmacists soon to be available to train suitable patients, the Australian pharmacy profession will be able to offer people taking warfarin a streamlined model of care that has the potential to greatly improve health outcomes.

One of the times of highest risk associated with warfarin therapy is when patients leave hospital, especially after being commenced on the drug. The authors have previously established that a suitably trained pharmacist visiting patients

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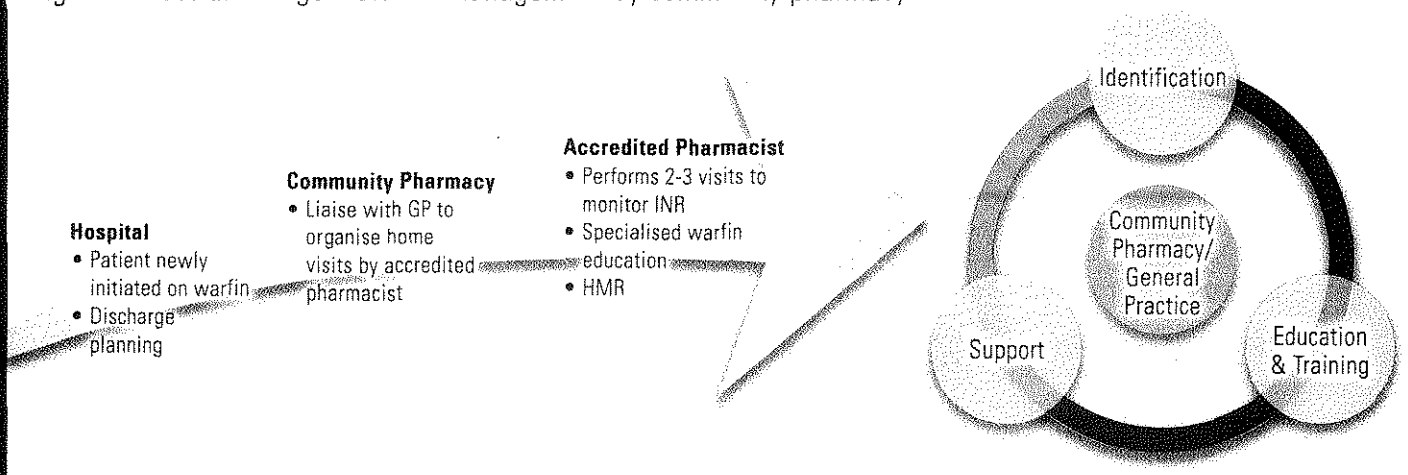
Figure 3: Post-discharge warfarin management by community pharmacy



at home following hospital discharge, and providing education and monitoring the response to warfarin, in consultation with the patient's doctor, significantly reduces the occurrence of major side effects.[9] It is envisaged that home (or within community pharmacy) follow-up and INR monitoring, performed in accordance with appropriate quality assurance procedures, will become a routine and cost-effective service for hospital patients discharged on warfarin.

Studies have generally shown an inverse relationship between patient knowledge and adverse outcomes of warfarin therapy. The best outcomes have been recorded where patients have had increased participation in their care and were encouraged to communicate more effectively with doctors and other health professionals about drug interactions and changes in lifestyle or diet. The outcomes of education and self-monitoring were studied in a group of older patients (aged 65 years or over) with unstable control of anticoagulation.[10] The 125 patients in this study were randomised to continue with usual clinic care or to receive education about warfarin, with and without self-monitoring of the INR. Compared with the previous six months, there was a significant increase in the percentage of time spent within the therapeutic range for the six months following education and following education combined with self-monitoring, compared with those patients following usual clinic care. The authors suggested that patient education regarding anticoagulation therapy is a cost-effective initiative to improve control. Pharmacists should use the following checklist when delivering warfarin education. The authors will also have an educational website (www.anticoagulation.com.au) available in the second part of this year.

Checklist for patient counselling on warfarin

- Mechanism of action
- Compliance (maintaining a diary of INRs, doses)
- Reason for treatment
- Explanation of INR, target range and regular testing
- Possible effects of poor control of anticoagulation
  - o Bleeding or severe bruising
  - o Recurrence of thromboembolism
- Appropriate action if excessive bleeding or bruising occurs
- Appropriate action if diarrhoea or vomiting occurs
- Starting a new treatment or changing a dose of current treatment
- Common prescription and OTC medication interactions, such as aspirin, NSAIDs, paracetamol, complementary therapies and laxatives.
- Role of vitamin K, and the importance of consistency in regards to vitamin K rich foods in the diet, rather than avoidance.
- Alcohol intake
- Minimise high risk activities associated with the risk of physical trauma
- Medical bracelet/necklace and warfarin ID card.

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