How to evaluate the performance of oral anticoagulation clinics

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Abstract

Increasing numbers of patients are receiving warfarin therapy, with atrial fibrillation being the main indication. If warfarin therapy is to be effective, however, good therapeutic control is important. Recent advances in models of management, including primary care clinics and patient self-management, has meant that patients have an increasing choice as to how and where they have their warfarin monitored. Comparison of performance between these different models of care has been historically difficult due to the use of different reporting techniques. This paper highlights the different methods of reporting therapeutic control, including adverse event reporting, and recommends that at least two measures from a set of recognised parameters should be used. This makes comparison of control between centres possible.

Key words: anticoagulation, warfarin, clinic, audit.

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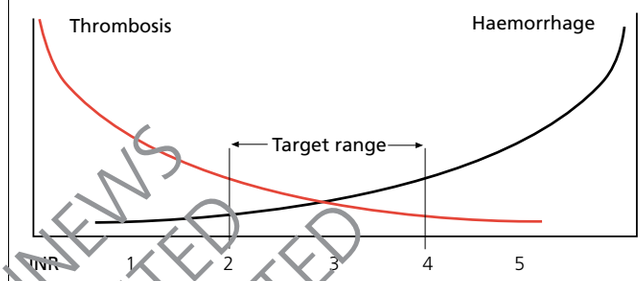
Introduction

The number of patients receiving oral anticoagulants (predominantly warfarin in the UK) continues to rise exponentially due to its reported effectiveness in stroke prevention for patients with non-rheumatic atrial fibrillation (AF).[1,2] There are currently around 500,000 patients receiving warfarin in the UK, with around 15% of these patients being managed outside the traditional hospital out-patient clinic. AF now accounts for around 60% of all patients receiving warfarin.[3] Warfarin unfortunately has a narrow therapeutic window and therefore requires regular titration of dose against anticoagulant effect, as determined by the International Normalised Ratio (INR). Deviation from the target range, in either direction, is associated with a sharp increase in the risk of adverse events, both thrombotic and haemorrhagic (figure 1).

Figure 1. Risk benefits of anticoagulation



Key: INR = International Normalised Ratio

The purpose of this article is to help answer the question: can we be certain that our anticoagulant clinics are doing their job? In other words are we actually doing what we think we are doing and how does what we do compare to predetermined standards?

Audit of laboratory measurements

Is the INR being determined both precisely and accurately? This is usually ascertained by the measurement of control samples, which are handled in exactly the same way as routine, clinical samples. There are two types of quality control (QC) material. The first is a sample of blood with an ascribed (i.e. 'known') INR value (internal QC) which is tested frequently. In a busy laboratory this may be with each batch of samples. The series of results obtained should remain within tight limits around the known INR value. Results falling outside these limits will alert the operator to 'drift' in the equipment or the reagents.

The second type of QC is a sample of unknown INR value, again tested by the same method as routine samples. This material is provided, and the results assessed, by an independent external body. The largest UK body providing external QC for anticoagulation is NEQAS (National External Quality Assurance Scheme).* External QC samples are issued at regular intervals – monthly for laboratories and quarterly for near-patient INR test-

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Table 1. Standards for audit (British Society Haematology guidelines)

- Provision of adequate data for safe transfer of anticoagulant follow-up
- Provision of anticoagulant cards for patients on hospital discharge
- Patient information: awareness of needs for anticoagulation and possible side effects of treatment
- Hospital notes contain information that the patient is currently on warfarin
- The use of heparin/warfarin dosage schedules in hospital setting
- Follow-up arrangements for patients failing to attend appointments
- Achievement of target INR: 50% of INRs within 0.5 INR units and 80% within 0.75 INR units of target

ing. Individual results are compared with all results from across the country, segregated according to equipment type and reagents used. In no sense is there a 'right' answer, but merely the reassurance of how 'your' results compare with every other laboratory.

Dosing

Once the INR has been determined correctly it is important to know that the appropriate dose of anticoagulant is being prescribed. Computer-aided systems are now used frequently and commercially available software has usually been verified. Nevertheless, systems do differ and it is important to verify that a safe and therapeutic INR has been achieved, regardless of whether a computer is used or not. One end point for this is the incidence of adverse events, although there are two drawbacks to using this as an audit parameter. Firstly, serious adverse events are relatively rare and may be extremely difficult to identify. Secondly, the occurrence of these complications may not necessarily be a reflection on the efficacy of the anticoagulant clinic.

The level of therapeutic control may be expressed in terms of the proportion of all INRs which are within the therapeutic range. Methods of expressing this include:

- Point prevalence. The proportion of patients with therapeutic INRs.
- Proportion of tests performed which are within the therapeutic range.
- The proportion of time spent by individuals in the therapeutic range.

The British Society of Haematology (BSH) has produced guidelines relating to several readily obtainable measures of the dosing efficiency of the clinic (table 1). With regards to dosing, the recommendations are: 50% of INRs within 0.5 INR units and 80% within 0.75 INR units of target. Other simple measures include mean INR with standard deviation for the whole clinic.

Whichever audit parameter of INR dosing is chosen, allowances must be made for inter-individual variations in response to oral anticoagulants. For a given target INR (for example 2.5) a wide range of doses are required – with warfarin this may range from less than 1 mg to more than 20 mg daily. Reasons for this variation include age, size, liver function, diet, compliance, alcohol use and other medications. Even making allowances for these factors, it is clear that patients vary in 'sensitivity' to changes in warfarin dose, for reasons which are not well understood. Some have argued that, in some cases, this sensitivity may be due to borderline vitamin K deficiency. Others have shown that variations in cytochrome P450 (a liver enzyme which metabolises warfarin) is associated with lower maintenance dose requirements and an increased risk of haemorrhagic complications on starting anticoagulation. It is important to note that audit parameters of dosing will be influenced by the proportion of 'sensitive' patients attending the clinic.

Table 2. Differences in observed values from the same INR data sets

	Tests in range (%)	Point prevalence (%)	Time in range (%)
Intervention	62	71	69
Control	58	64	62

Adapted from: Fitzmaurice D *et al.*[6]

A recent systematic literature review demonstrated a wide variation in the form of audit data presented within published studies.[4] None of the studies included in the review reported point prevalence despite this being a relatively easy measure to calculate and it being one of only two published methods for assessing therapeutic control.[5] The most widely reported measures were: percentage time in range; mean INR; proportion of tests in range; and mean warfarin dose. The first three of these measures relate to therapeutic control whilst warfarin dose is only likely to be discrepant if there is a problem with the INR estimation between centres. It is recommended that, whichever audit parameters are chosen, at least two are reported.

Given the diversity of audit parameters reported, comparison of findings between different centres is very difficult. In a sense this mirrors problems encountered within laboratory comparisons prior to the introduction of the INR system. Our own data have shown that there are differences in the observed efficacy depending upon the parameters chosen, with differences of up to 10% found in terms of INR control (table 2). This is important as INR control gives a proxy measure for clinical outcomes which are relatively infrequent. Thus, improved INR control should correlate to improved clinical outcome.

Administration

This may now be the most important element of an anticoagulant service requiring audit. Patients 'lost' to the system such that they: remain on anticoagulants but fail to have this monitored; remain on anticoagulants after these should have stopped; or have stopped taking anticoagulants when these should continue, are at serious risk of an adverse event. It could be argued that this risk is at least as great as those engendered by failings in testing or dosing elements. Thus, care should be taken to monitor all patients in the system, to chase those failing to attend appoint-

Key messages

- Deviation from the target INR is associated with a sharp increase in adverse events
- Warfarin service components for regular audit and review are:
  - laboratory measurements
  - dosing
  - level of therapeutic INR control
  - patient satisfaction
  - clinic administration
- Clinical outcomes should be determined – as with any therapy – as the final determinant of its therapeutic value
- Patients on warfarin may suffer a significant bleed whilst the INR is in the therapeutic range which has clinical significance but provides little useful information concerning the workings of an anticoagulant clinic itself

ments and, where relevant, to ensure that transfer of patients (and their details) between secondary and primary care is timely and complete. Similarly, it makes sense to ensure that both target INRs and the duration of anticoagulation are consistent with the diagnosis. Most importantly, no patient should be anticoagulated for longer than necessary. The benchmark for this element of the service should be 100% compliance.

Clinical outcomes

It is extremely important to determine clinical outcomes – as with any therapy – as the final determinant of its therapeutic value. However, this may represent a research topic as opposed to audit. Both haemorrhagic and thrombotic complications of oral anticoagulants are closely related to the INR. For instance, the relative risk of serious bleeding doubles with each unit increase in INR.[7] The problem can be looked at the other way around. One series examined all cases of intracranial haemorrhage presenting to a tertiary referral centre over a five-year period, of whom 116 were taking anticoagulants. Two thirds of this group experienced haemorrhage when the INR was either in or below the therapeutic range whilst one third should not (by accepted guidelines) have been on anticoagulants in the first place.[8] Thus, a patient on warfarin may suffer a significant bleed whilst the INR is in the therapeutic range. The reason for this apparent paradox is that although the relative risk of haemorrhage increases dramatically with the INR, the great majority of anticoagulated patients are in, or close to, the therapeutic range. Thus, it is to be expected that many, if not most, patients suffering a haemorrhagic complication will come from this non-overanticoagulated group.

This obviously has clinical significance and may engender debate on patient selection and indications for anticoagulation, but provides little useful information concerning the workings of an anticoagulant clinic itself.

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