The performance of clinics for outpatient control of anticoagulation

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If properly applied, oral anticoagulants provide powerful and safe protection against venous and arterial thrombosis and thromboembolism [1]. Favourable results are more likely where anticoagulation is maintained consistently at a high level of intensity [2], but the therapeutic ratio is narrow, over-anticoagulation carrying the risk of potentially life-threatening haemorrhage. The response to anticoagulants is affected by many factors of which the underlying pathological state [1] and drug interactions [3] are particularly important. Thus, clinics monitoring anticoagulation require accurate documentation of the patient's medical condition and of the drugs prescribed.

We have examined the efficacy of anticoagulation in patients attending two similar but independent hospital-based anticoagulant clinics in an attempt to evaluate factors contributing to anticoagulant control and the risks of complications.

Materials and methods

The outpatient notes of all patients attending two anticoagulant clinics in two teaching hospitals were reviewed. Patients were referred to these clinics from within the hospitals after anticoagulation had been established. The major source was cardiology (49.2 per cent) but patients were also monitored at the request of general physicians (32.4 per cent) and others. At each clinic visit intensity of anticoagulation was estimated by a haematology technician using Thrombotest® [4], a reliable [5] and well standardised [6] modification of the prothrombin time assay. Anticoagulant dosage was regulated on the basis of that information, but the therapeutic range for any patient was at the discretion of the clinic doctor (usually registrar or senior house officer grade). Patients attended at weekly or less frequent intervals until the decision to discontinue anticoagulation was made by the attending or referring physician. On average, 48 patients were seen in 1½ hours, allowing approximately two minutes for each consultation. There was no formal arrangement for clinical assessment. Doctors made free recordings of symp-
toms and physical signs including evidence of thrombotic events and complications of treatment. Some patients were also under surveillance at other out-patient departments but such information was not available in the anticoagulation clinic records.

The study was an analysis of all patients registered with the clinics at a given time, excluding those treated for less than four weeks and those no longer attending the clinics. Case records were studied retrospectively and the following patient information was extracted: age, sex, duration of treatment, indication for anticoagulation, anticoagulation control, haemorrhagic episodes, medical records and treatment records. Anticoagulant control (intensity of treatment) in the three months before review was expressed in terms of International Normalised Ratios (INRs). In patients treated for less than the standard observation period, control was assessed from Thrombotest results during the time of attendance at the clinic. Control was classified as excellent if INR was consistently 2.7-4.5, a range accepted as providing effective prophylaxis with a low incidence of bleeding complications [1,2,7,8]; intermediate if INR was consistently in the range 2.0-4.5 where satisfactory prophylaxis against venous thrombosis has been reported [9], but which may not be of sufficient intensity to protect against arterial thrombosis or thromboembolism [1]; or poor where INR was less than 2.0 or more than 4.5 on at least one occasion. Values greater than 4.5 may be associated with an unacceptable incidence of haemorrhage and values less than 2.0 have little or no therapeutic effect [8]. Haemorrhagic complications were calculated from all recorded events in all patients during attendance at the clinics. Thus, bleeding episodes in those withdrawn from anticoagulation because of serious morbidity or mortality were not included. Medical records were considered adequate when they included details of patient factors which might influence anticoagulation such as compliance, alcohol consumption, liver function and potential bleeding sources. Treatment records were defined as adequate if concomitant drug therapy had been entered.

Statistical analysis was by Chi-squared test for differences in proportions with Yates' correction for small numbers where indicated.
Table 1. Documented indication for anticoagulation in patients attending the clinics.

| Indication                                                                 | Female | Male   | All     |
|---------------------------------------------------------------------------|--------|--------|---------|
| Rheumatic heart disease (including patients with valve replacement, + atrial fibrillation, + arterial thromboembolism) | 269 (75.4%) | 78 (55.3%) | 349 (69.8%)* |
| Others (including patients with peripheral vascular disease, cerebrovascular disease, coronary artery bypass grafts) | 25 (7.0%) | 23 (16.3%) | 48 (9.6%) |
| Unknown                                                                   | 46 (12.9%) | 17 (12.1%) | 63 (12.6%) |
| Totals                                                                    | 357 (100%) | 141 (100%) | 500 (100%) |

*Sex not documented in two patients

Results

A total of 500 patients attended the clinics. The anticoagulant was warfarin in 496 patients and phenindione in four. The populations of the clinics were similar with respect to age (mean ± s.d.) 53.8 years ± 10.3 and 61.6 years ± 9.2, respectively, with 27.2 per cent patients aged 65 years and over; duration of anticoagulation: 53.3 months ± 47.67, and 49.3 months ± 49.8, with 25.1 per cent in the first year of treatment and 9.8 per cent treated for ten years or more; and indication for anticoagulation. The major indication was rheumatic heart disease and these patients were on life-long therapy, but the reason for treatment was not recorded in 63 patients (Table 1).

Control of anticoagulation is summarised in Tables 2 and 3. Standards at the two clinics were similar. In the poor control group, 176 patients (90.3 per cent) had at least one INR less than 2.0, and 55 (28.2 per cent) had values greater than 4.5. In only 19 patients was control considered poor exclusively because of INRs greater than 4.5 while 140 patients had values less than 2.0. Control was significantly better in those treated for more than one year (excellent, 32.9% vs 9.1%; χ² = 26.3, p < 0.001; poor, 33.4% vs 57.0%, χ² = 21.4, p < 0.001). There was no significant relationship between anticoagulant control and age or sex.

Haemorrhagic events are summarised in Tables 4 and 5. At both clinics, there was a striking risk of bleeding in the first treatment year with one haemorrhagic event in every three treatment-years as compared to one per 14.2 treatment-years in those on longer term treatment. Bleeding events were not related to age or sex.

Medical records were adequate in 115 patients (23 per cent), treatment records in 95 (19 per cent) and both in 69 (13.8 per cent). In patients treated for more than one year, an unknown indication for anticoagulation was more common in those with poor control compared to the remainder (19% vs 8.8%, χ² = 8.3, p < 0.01), and was less frequently associated with bleeding events (11.1% vs 25.6%, χ² = 3.8, p = 0.05); medical records were less often adequate in poorly controlled patients (12.7% vs 17.1%, χ² = 1.24, NS), but treatment records were adequate significantly more often (18.9% vs 8.4%, χ² = 4.9, p < 0.05).

Table 2. Anticoagulant control in clinic patients treated for one year or less and in patients treated for more than one year.*

| INR          | One year or less | More than one year | All   |
|--------------|------------------|--------------------|-------|
| 2.7–4.5      | 11 (9.1%)        | 124 (32.9%)        | 135 (27.1%) |
| 2.0–4.5      | 41 (33.9%)       | 127 (33.7%)        | 168 (33.7%) |
| <2.0 or >4.5 | 69 (57.0%)       | 126 (33.4%)        | 195 (39.2%) |

*Data missing in two subjects

Table 3. Anticoagulant control in relation to indication for treatment.

| Indication                                                                 | 2.7–4.5 | 2.0–4.5 | <2 or >4.5 |
|---------------------------------------------------------------------------|---------|---------|------------|
| Rheumatic heart disease                                                  | 106 (30.4%) | 119 (34.1%) | 124 (35.5%) |
| Deep venous thrombosis/pulmonary thromboembolism                         | 6 (12.5%)  | 11 (22.9%)  | 31 (66.6%)  |
| Others                                                                   | 16 (40.0%) | 2 (5.0%)   | 22 (55.0%)  |
| Unknown                                                                  | 7 (11.1%)  | 40 (63.5%) | 16 (25.4%)  |

Table 4. Documented haemorrhagic events in patients attending the clinics.

| Patients                      | Haemorrhagic events | Patients with haemorrhagic events | Treatment years/haemorrhagic event |
|-------------------------------|---------------------|----------------------------------|-----------------------------------|
| All                           | 168                 | 109 (21.8%)                      | 12.8                              |
| Treated for more than one year| 148                 | 90 (23.9%)                       | 14.2                              |
| Treated for one year or less  | 20                  | 19 (15.7%)                       | 3.0                               |
Table 5. Recorded haemorrhagic events in patients attending the clinics.

| Events                        | Number |
|-------------------------------|--------|
| Serious haemorrhages          |        |
| Epistaxis                     | 50     |
| Haematuria                    | 24     |
| Bleeding per vagina           | 21     |
| Haemoptysis                   | 14     |
| Haematemesis                  | 7      |
| Retinal haemorrhage           | 1      |
| Skin haematoma                | 1      |
| Other haemorrhages            |        |
| Bruising                      | 31     |
| Local rectal bleeding         | 13     |
| Subconjunctival haemorrhage   | 4      |
| Bleeding ear                  | 1      |
| Other                         | 1      |
| **TOTAL**                     | **168**|

\[ \chi^2 = 17.3, p < 0.001 \]. In all patients, adequate treatment records were again more frequent in the poor control group (28.2%) than in the remainder (13.2%), \[ x^2 = 17.3, p < 0.001 \]; there were no differences with respect to knowledge of indication or medical records in terms of anticoagulation control or bleeding events.

Discussion

Overall, 75 per cent of patients spent variable periods outside optimal control (INR 2.7-4.5), and in these the value of anticoagulation must be questionable. At each clinic, there was a tendency to under-anticoagulation which may be just as dangerous as over-anticoagulation since it predisposes to a considerable risk of sometimes fatal thrombotic events [1]. Historically, most patients have received inadequate treatment [7], and it would appear that more recent recommendations for increased intensity of treatment have yet to be accepted by those directly involved in monitoring treatment.

Standards were even worse in those treated for 12 months or less. Control tends to be poor and erratic in patients receiving short-term anticoagulation [10-12]. Our findings suggest that inadequate control may persist for many months, even in those commencing life-long treatment. If, as has been recommended [1], prothrombin time should reach the optimal range within days and be kept in that range for more than 80 per cent of the time, there must be some doubt concerning the value of anticoagulation during the first year of treatment.

Control was particularly poor in those with deep venous thrombosis/pulmonary thromboembolism, probably because of their relatively short period of anticoagulation (81.3 per cent treated for 12 months or less). A modest intensity of anticoagulation provides adequate prophylaxis for venous thromboembolism [9] but only 35 per cent of patients treated for this reason remained within a safe and possibly therapeutic range during the three month period. Furthermore, it is likely that many patients in Scotland are treated with anticoagulants when in fact thrombosis or pulmonary thromboembolism is absent [13]. Our findings suggest that these patients are subjected to an unacceptable risk.

The trend towards under-anticoagulation did not prevent a very high incidence of haemorrhage with one haemorrhagic event occurring in every 12.8 treatment-years. This probably underestimates the true risk since patients with a serious haemorrhagic tendency may have been withdrawn, and enumeration of bleeding manifestations depends strongly on conscientious clinical assessment and recording. Incidents were particularly frequent (one per three treatment-years) in those treated for 12 months or less. Hitherto, the danger of early bleeding in patients at the outset of long-term oral anticoagulation has probably been underestimated, since patients in the first year of treatment have not been evaluated [14,15]. Our failure to identify a relationship between bleeding complications and the observed intensity of anticoagulation was not unexpected since haemorrhagic events were usually recorded some time before the monitoring period.

Standards at the clinics were also poor with respect to record keeping which was much worse than at a general medical clinic [16]. Thus, physicians may be faced with patients where the indications for anticoagulation are unclear and the risks are unknown. One consequence may be that the time when treatment should stop passes unnoticed, so that anticoagulation continues by default [17]. At these clinics, 19 per cent of patients with deep venous thrombosis/pulmonary thromboembolism were treated for more than one year, several times the recommended duration [18]. Moreover, it seems likely that deficient documentation was to some extent responsible for the unsatisfactory clinic performance. In the majority of clinic attenders (ie those treated for over one year), inadequate medical records and unknown indication for anticoagulation were more frequent in the poor control group. Since the desired intensity of anticoagulation depends on the indication [1,8,9], it is probable that aggressive treatment was not pursued where the indication was unclear, which may explain why patients, in whom the reason for treatment was uncertain, suffered less often from bleeding events. The trend towards improved record keeping for concomitant drugs where control was poor may reflect concern on the part of the monitoring physician that drug interactions were contributing to unacceptable control in these patients. Despite the indifferent standards of outpatient anticoagulation at these clinics and elsewhere in the UK [19], requirements for long-term treatment are likely to increase dramatically in the next few years as more patients undergo cardiac surgery. Thus there is an urgent need to improve the efficiency of anticoagulation control. Better management with less danger to the patient might be achieved by improved documentation.

Since this survey was conducted, management practices at our clinics have undergone major changes. Patient numbers have increased but personnel and space have not kept pace. Therefore, new developments have been directed towards facilitating the task of the attending
physician and standardising the recording of important clinical details. On referral, a form incorporating all relevant patient data is completed (Table 6). This is retained in the clinic case records together with a summary of the most recent hospital admission. The patient must also continue to be followed up at another clinic throughout the period of monitoring at the anticoagulant clinics. A comprehensive continuation document formalises systematic recording of vital clinical information at the clinics (Table 6). Both have been designed for ease of completion and interpretation. The continuation document is intended to allow eventual computer storage of data. Preliminary evidence suggests that these changes have been well received by the medical staff involved. It is hoped that these new approaches to management will improve transfer of information, increase the doctor’s awareness of the patient’s state, aid decision making by juniors and lead to an overall enhancement of patient care.

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Table 6. Information included on the referral form and continuation document.

| Both | Patient name/address | Date of birth/hospital number |
|------|----------------------|-----------------------------|

| Referral form | Continuation document |
|---------------|----------------------|
| Anticoagulation indication | Date of visit |
| proposed duration | Thrombotest results |
| potential hazards | Alcohol consumption |
| Cardiac status | Other drugs/doses |
| Thrombotest result/date | Compliance |
| Anticoagulant/dose | Haemorrhagic events |
| Alcohol consumption | Thrombotic events |
| Other drugs/doses | Side-effects |
| Referring doctor | Anticoagulant dose/pre-vis |
| ward/hospital discharge date | ordered |
| General practitioner | Medical/surgical follow up |

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45