Service provision and use of anticoagulants in atrial fibrillation

C M Sudlow, H Rodgers, R A Kenny, R G Thomson

Several large trials have shown that the risk of stroke in patients with non-valvar atrial fibrillation is reduced by treatment with warfarin. Implementing this research evidence requires not only an understanding of the trials' results and of the changes that they imply for clinicians' treatment decisions but also an appreciation of the organisation, quantity, and quality of services required to support these changes. Understanding of these implications is crucial for developing services that allow changes in practice to produce reductions in stroke incidence while minimising the risks of treatment. This article considers the developments in service provision that will probably be required to support the changes in clinical practice suggested by the trials' results. These services will be provided largely by doctors, and their development has implications for doctors in both primary and secondary care.

Recent trials have shown that treatment with warfarin significantly reduces the incidence of stroke among patients with non-valvar atrial fibrillation, and there have been calls for increased use of anticoagulant drugs in such patients.¹⁻⁶ However, while it has considerable potential for preventing stroke, a large increase in warfarin treatment would have knock on effects for diagnostic, investigative, and therapeutic services. The effectiveness of anticoagulant treatment for atrial fibrillation depends on the quality of services provided; without appropriate changes in provision, wide adoption of prophylaxis with anticoagulant drugs could produce more harm than benefit.

Factors that will influence the service needs include the criteria for selection of patients, patient choice, requirements for monitoring and follow up, prevalence of atrial fibrillation, and prevalence of relative and absolute contraindications to anticoagulant treatment. Much information on the quality of services required can be derived from careful examination of the above trials and their applicability to patients receiving routine services. Considerable further work is needed to assess the quantity of services required and their organisation.

Quality of services required

PATIENT SELECTION

Patients in the published trials were recruited from hospital practice and by self referral and referrals from interested doctors. Thus, even at recruitment, they were not representative of patients with atrial fibrillation in the community. Potential subjects were investigated and excluded if their risk of complications was thought to be high or if there was an alternative indication for anticoagulant treatment. Assessments included blood tests, electrocardiography, chest x ray examination, and echocardiography. A substantial proportion of patients were excluded because of findings on assessment, although in the case of echocardiography this was usually because another indication for treatment was detected. Many patients were also excluded because they or their doctor refused participation, and this may have been because of a perceived

but undocumented higher risk from anticoagulants in this group. As a result of these stringent criteria, only 3-40% of the population recruited were eventually randomised to treatment.¹⁻⁵ This is not a criticism of these trials, but it is important to note that the study groups were highly selected and that selection of patients required considerable resources.

A report that aspirin may be as effective as warfarin in treating patients at low risk of stroke has raised the possibility of stratifying patients with atrial fibrillation into groups appropriate for different treatments.⁷ Ongoing trials will hopefully allow further development of this strategy.⁸ Exactly how stratification of risk might be carried out is unclear. Clinical factors alone may be sufficiently accurate,⁹⁻¹⁸ but echocardiography may be necessary in many patients as left atrial size and left ventricular function seem to provide useful extra information on risk.^{11 15 16 18-21} If stratification were to become accepted practice then patients with atrial fibrillation would require more careful clinical and echocardiographic study.

MONITORING AND FOLLOW UP

The trials reported a low incidence of major bleeding events (1.3% a year in patients given warfarin and 1% in controls)⁹ compared with the incidence (3%) and relative risk (6.6) reported in an overview of 25 studies of patients in routine practice who were given anticoagulants.²² Similarly, the trials reported a low rate of intracerebral haemorrhage in patients given warfarin (0.3% a year)⁹ compared with the rate recorded in a large observational cohort (2%).²³ At the higher rate of bleeding the number of strokes is reduced no more by warfarin than by aspirin.²⁴

The difference between the incidence of adverse events in the trials and in routine practice is probably related to the selection of patients but may also be related to the intensity of monitoring and follow up. There is evidence that the incidence of bleeding is closely related to the intensity of the anticoagulant effect.²² Checks of the anticoagulant effect were performed at least every three to four weeks in those trials that reported frequency, and between 0.6% and 15% of the tests showed the effect to be greater than intended.^{1-4 6} In contrast, in a study of use of anticoagulants for atrial fibrillation in a health maintenance organisation in the United States, the mean interval between tests was 36-41 days and 30% of values were above the target range.²⁵ Current practice in Britain may produce even poorer control.²⁶⁻²⁸

Furthermore, patients in the trials were followed up at intervals of three to six months, and attention was paid to the occurrence of complications and to compliance, with treatment being withdrawn if necessary.^{1-4 6} This level of follow up may partially explain the low incidence of complications in the trials, but it is probably not matched in routine British practice.

Although widely interpreted as being studies of warfarin treatment, these trials were in fact studies of packages of care that included drugs, monitoring, and follow up. If the benefits are to be realised in routine practice equivalent care may be needed. This implies that much thought will need to be given to the services required to support anticoagulant treatment.

Departments of Medicine and Epidemiology and Public Health, Medical School, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH

C M Sudlow, *MRC training fellow in health services research*

H Rodgers, *senior lecturer in stroke medicine and services*

R A Kenny, *senior lecturer in geriatric medicine*

R G Thomson, *senior lecturer in epidemiology and public health*

Correspondence to: Dr Sudlow.

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SHEILA TERRY/SPL

MARK CLARKESPL

FIG 1—Selection of patients can have a considerable influence on the outcome of clinical trials

Quantity of services required

The quantity of services required depends on the number of patients with atrial fibrillation and the number likely to benefit from treatment. We are currently setting up a community study in Northumberland to address these issues.

PREVALENCE OF ATRIAL FIBRILLATION

Estimates of prevalence in the community vary widely around the world.²⁹⁻³² A study from Australia reported a prevalence of atrial fibrillation of 3% in people aged 65-69, 7% in those aged 70-74, and 11.6% in those aged over 75.²⁹ A recent study in the United States, however, reported prevalences of 0.3% in people aged 65-69, 1.5% in those aged 70-79, and 3% in those aged over 80.³⁰ The higher mortality from cerebrovascular and cardiovascular disease in the United Kingdom would suggest that atrial fibrillation may be more prevalent here, but British studies of prevalence have involved small numbers of elderly patients from unrepresentative populations.³³⁻³⁸ Best estimates are therefore based on the Australian and North American studies. Projecting these estimates on to figures from the 1991 census would predict that between 160 000 and 644 000 patients aged over 65 in Great Britain have atrial fibrillation.³⁹ Such a fourfold difference in estimates of prevalence renders predictions of service requirements highly doubtful.

PROPORTION OF PATIENTS NEEDING TREATMENT

Reports on the proportion of patients that might benefit from anticoagulant treatment have not been based on community samples but on the assumption that patients without recorded contraindications should be treated with warfarin.^{25 40 41} However, factors other than firm contraindications to warfarin—such as compliance, cognitive function, disability, and quality of life—are also likely to affect general practitioners' and patients' decisions about treatment. Documented variations in general practitioners' willingness to give anticoagulant treatment in different cases⁴² may have been affected by such factors. Predictions of practitioners' likely views have not been tested in the field.⁴³ Moreover, patients' perceptions of inconvenience, risk, and benefit are likely to have a major influence on the uptake of treatment. Evidence suggests that patients felt that their quality of life was improved by taking anticoagulant treatment in a trial setting,⁴⁴ but, despite predictions, it is uncertain whether unselected patients with atrial fibrillation would share this perception or what their reactions to the offer of treatment would be.^{45 46}

Organisation of services

Patients who are taking warfarin for atrial fibrillation require a range of services including those for phlebotomy, laboratory tests, and anticoagulation clinics. Patients will also require investigations to ensure that appropriate treatment is chosen and services to deal with the complications of treatment.

Phlebotomy services and expertise in interpreting the results of tests and adjusting warfarin doses may be based in hospital clinics or in primary care (there is considerable local variation in distribution of the workload at present). In either case the additional number of patients will have implications for facilities and staff time. While there is some evidence that monitoring in primary care is at least as effective as hospital based services,²⁶ many general practitioners feel unable to take on this additional work without further resources.^{47 48} Furthermore, if primary care is to take responsibility for a substantial part of the monitoring and phlebotomy then there is likely to be need for considerable expansion of the ability of

haematology laboratories to handle requests for clotting studies and to provide results rapidly, a problem that is avoided by the use of portable capillary blood monitors in many dedicated anticoagulant clinics.

The need for decisions on whom to refer, treat, and monitor will also increase the amount of time that general practitioners have to spend with each patient with atrial fibrillation. Present referral practices for atrial fibrillation are unknown. Moreover, if echocardiography is found to be useful in supporting decision making then we can anticipate an increase in the number of referrals to secondary care, even if patients are mainly managed in primary care.

Finally, it is inevitable that there will be an increase in the incidence of anticoagulant related bleeding. This, and the need to investigate the possibility that symptoms are related to treatment, will increase demands on services in primary care, general medicine, geriatrics, gastroenterology, neurology, and radiology.

Funding of services

A cost-benefit analysis of anticoagulant treatment for patients with atrial fibrillation in Sweden concluded that treatment would probably save money overall.²⁴ However, the analysis was unable to take account of many of the variables discussed above: fairly low estimates of prevalence were taken; it was assumed that half of patients would receive anticoagulants; and no account was made of the costs of detecting and investigating patients with atrial fibrillation or of the costs of complications, except for intracranial haemorrhage. Costs of drugs and monitoring may be different in Britain and will certainly vary according to whether primary or secondary care takes on the bulk of this work. More accurate estimates of overall costs will be required, and ways must be found to target appropriate funding to the parts of the health service incurring these costs. Redistribution of resources will certainly be necessary, and, in the context of a fixed health care budget and uncertainty about whether there will be overall savings, difficult decisions may have to be made about what services currently provided ought to be cut to release the necessary resources.

Conclusion

There is need for caution in interpreting the results of trials of the carefully controlled use of a potentially hazardous treatment in selected populations and in extrapolating these results to the British population. To extend the undoubted benefits of this treatment to patients we may need to provide equivalent levels of care in selection and monitoring. The provision of this care could require changes in practice in many areas in the health system. The division of labour between primary care and hospitals will vary according to local interests and expertise. If an adequate service is to be provided then some coordination and planning of its components will be essential. Purchasers and providers should pay close attention to this area and develop:

- Systems that provide an effective, equitable, and convenient service for patients requiring investigation and treatment
- Evidence based guidelines for selecting patients and treatment that can be audited to maintain standards.

Effective planning at an early stage will hopefully prevent the inappropriate treatment of patients and poor monitoring and follow up that will occur if services are overwhelmed or incorrectly used. To enhance the accuracy of this planning, further information is needed on the prevalence of atrial

fibrillation in Britain, on the prevalence of indications and contraindications for anticoagulation, on factors that influence doctors' decisions to offer treatment and patients' decisions to accept it, and on the costs and benefits of anticoagulant treatment in primary and secondary care.

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Commentary: Caution needed in introducing warfarin treatment

K G Sweeney, D J Pereira Gray, R J F Steele, P H Evans

St Leonard's Medical Practice, Exeter EX1 1SF
 K G Sweeney, general practitioner
 D J Pereira Gray, general practitioner
 R J F Steele, general practitioner
 P H Evans, general practitioner

Correspondence to:
 Dr Sweeney.

We welcome the cautious interpretation of the recent trials of warfarin in atrial fibrillation provided by the authors of this article and concur with their concerns about the generalisability of the results of this group of trials. We congratulate them on introducing the concept of packages of care in this context—packages that include not just the prescribing of drugs but rigorous selection of patients and meticulous monitoring and follow up.

The authors' analysis of the trials highlights the huge exclusion rates of patients initially considered eligible

and, correctly in our view, links these stringent exclusion criteria and the intensity of follow up of patients to the uniformly low bleeding rates that were found in all the trials. We would go further and point out that for quite large periods of time in all but one of the trials patients were in fact underanticoagulated according to the individual trial's acceptable range of anticoagulation (table). We also argue that the minor bleeding rates in these trials were not given enough consideration in the reviews that summarised their results.⁷ There was no agreed definition of minor