

Anticoagulation in patients with atrial fibrillation

Not safe and not cheap

EDITOR,—I am concerned about the potential widespread use of warfarin in asymptomatic atrial fibrillation encouraged by recent articles. Philip M W Bath and colleagues assert that overwhelming evidence from trials suggests that this treatment profoundly reduces strokes, carries small risks of bleeding, and is cost effective. I am sceptical; these trials have to be scrutinised closely and compared with real life.

Patients enrolled in these trials were carefully screened for the slightest characteristics that might place them at any risk of bleeding and were more likely to be more compliant than average. The Veterans Affairs stroke prevention in non-rheumatic atrial fibrillation study excluded 7444 out of 7982 eligible patients; 6.7% were entered.² The stroke prevention in atrial fibrillation study initially excluded 17 046 eligible patients.³ Of the 1330 entered, 703 were considered to be ineligible; only 3.4% were entered. Although atrial fibrillation is more common with advancing age,⁴ four of the five trials were in younger patients at lower risk. Only one trial was in older patients⁵; in this study the numbers of events (thromboses and bleeding) were identical in all groups. Despite careful patient selection there were more side effects and non-compliance with warfarin. Though warfarin has led to fatal bleeding, it may not reduce the incidence of major strokes as shown below.

I have analysed the data in three trials that have detailed the severity of strokes.^{2,3,5} The results are striking (table). No doubt warfarin reduced the incidence of transient ischaemic attacks and minor non-disabling strokes, but none of the trials showed that the incidence of fatal and disabling strokes was reduced beyond statistical doubt. This reduction in mild strokes has been achieved neither safely nor cheaply. A Canadian study showed an annual rate of fatal or major bleeding of 2% despite excluding 94% of eligible patients.⁶ A complication rate exceeding 1.3% is estimated to increase costs.⁷ The incidence and severity of bleeding in ordinary clinical practice is probably even higher. The ratio of risk to benefit will probably also increase with time beyond the

Severity of cerebrovascular accidents in patients given placebo, aspirin, or warfarin in three trials^{2,3,5}

| | Placebo | Aspirin | Warfarin | p Value (warfarin v placebo) |
|--|----------|----------|----------|------------------------------|
| <i>Veterans Affairs stroke prevention in non-rheumatic atrial fibrillation</i> | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 19 (265) | | 4 (260) | 0.001 |
| Severity: | | | | |
| No impairment | 9 | | | |
| Minor | 7 | | 3 | }0.32 |
| Major | 2 | | 0 | |
| Fatal | 1 | | 1 | |
| <i>Atrial fibrillation aspirin anticoagulation study</i> | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 19 (336) | 17 (336) | 5 (335) | |
| Severity: | | | | |
| Transient ischaemic attacks | 3 | 2 | | |
| Minor | 2 | 1 | | |
| Non-disabling | 3 | 7 | | |
| Disabling | 7 | 4 | 4 | }0.13 |
| Fatal | 4 | 3 | 1 | |
| <i>Stroke prevention in atrial fibrillation</i> | | | | |
| No of cerebrovascular accidents (No of patients in arm) | 17 (211) | | 6 (210) | 0.01 |
| Severity: | | | | |
| Minimal | 10 | | 4 | |
| Moderate | 7 | | 2 | }0.093 |
| Fatal | 0 | | 0 | |

Advice to authors

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trials' short 1.3-2.2 years of follow up. Strokes tend to cluster in the first months after the diagnosis of atrial fibrillation⁸ and survivors with atrial fibrillation tend to have a similar risk of recurrence to those in sinus rhythm.⁹

Clinicians may argue that several strokes in groups given warfarin occurred either when warfarin was stopped or with subtherapeutic anticoagulation. Warfarin withdrawal may induce transient rebound hypercoagulability that could enhance thrombosis. Patients in trials were seen every three to four weeks, each time by a doctor, and had their tablets counted to check for compliance. If anticoagulation was unsuccessful despite this stringent follow up clinicians are unlikely to be successful in their overstretched clinics.

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- Bath PMW, Prasad A, Brown MM, MacGregor GA. Survey of use of anticoagulation in patients with atrial fibrillation. *BMJ* 1993;307:1045. (23 October.)
- Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Coling CL, Gornick CC, et al. Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. *N Engl J Med* 1992;327:1406-12.
- Stroke Prevention in Atrial Fibrillation Investigators. Stroke prevention in atrial fibrillation study. *Circulation* 1991;84:527-39.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 1991;22:983-8.
- Petersen P, Boysen G, Godteredsen J, Andersen ED, Andersen B. Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet* 1989;ii:175-8.
- Connolly SJ, Laupacis A, Gent M, Roberts R, Cairns JA, Joyner C. Canadian atrial fibrillation anticoagulation (CAFA) study. *J Am Coll Cardiol* 1991;18:349-55.
- Gustafsson C, Asplund K, Britton M, Norrving B, Olsson B, Marke L-A. Cost effectiveness of primary stroke prevention in

atrial fibrillation: Swedish national perspective. *BMJ* 1992;305:1457-60.

- Sandercock P, Bamford J, Dennis M, Burn J, Slattery J, Jones L, et al. Atrial fibrillation and stroke: prevalence in different types of stroke and influence on early and long term prognosis (Oxfordshire community stroke project). *BMJ* 1992;305:1460-5.
- Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. The effect of low dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. *N Engl J Med* 1990;323:1505-11.

Underuse of warfarin is multifactorial

EDITOR,—Philip M W Bath and colleagues recently surveyed the use of warfarin in hospital inpatients with atrial fibrillation and found that many patients with chronic atrial fibrillation and no contraindications to anticoagulants were not prescribed warfarin.¹ We surveyed the use of warfarin by 50 randomly selected general practitioners working in this health district by means of a questionnaire presenting the different clinical features associated with atrial fibrillation in a 60 year old man with no contraindications to anticoagulation.² The table shows the results for the 42 general practitioners who replied.

Use of warfarin in chronic atrial fibrillation by 42 general practitioners

| | Occasionally | Never | No answer |
|-------------------------------------|--------------|-------|-----------|
| <i>Chronic atrial fibrillation:</i> | | | |
| Alone | 1 | 4 | 37 |
| With mitral valve disease | 9 | 8 | 24 |
| With transient ischaemic attack | 1 | 12 | 28 |
| With cerebral infarction | 2 | 10 | 28 |

After the survey we developed guidelines for the use of warfarin in atrial fibrillation and distributed them to physicians and general practitioners locally. Three months later we did not see any change in the rate of new referrals to this hospital's department of haematology for monitoring international normalised ratios.

Despite strong evidence, patients with atrial fibrillation and no contraindications to warfarin are not receiving anticoagulation. The reasons for this are unclear. Perhaps the message is not being put across sufficiently well; further progress might be possible if national organisations—for example, the British Cardiac Society, Stroke Association, or British Geriatric Society—championed this issue. Understandably, doctors may also be concerned that the complication rate for warfarin used in atrial fibrillation in the different trials does not reflect what is seen in clinical practice because all the trials excluded a high proportion of potential participants with atrial fibrillation and because those who participated were monitored closely.

Finally, Bath and colleagues state that warfarin is contraindicated in people over 80. In our guidelines we have not included age as a contraindication because the main determinant of complications from warfarin is the presence of underlying problems such as peptic ulcer disease, uncontrolled hypertension, or repeated falls. Increasing age is associated with greater sensitivity to warfarin, but this effect can be overcome as the dose is tailored to the international normalised ratio. The risk of an embolic event during atrial fibrillation increases with age; if people over 80 do not have any contraindications to warfarin they should be