

OPINION/OPINIE

Atrial fibrillation — an old problem and an old solution

ATRIAL fibrillation (AF) is a common arrhythmia affecting approximately 0,4% of the adult population. Prevalence rises to 2 - 4% in individuals over 60 years of age.^{1,2} There are many causes of AF, rheumatic heart disease being one of the more prominent. The combination of rheumatic heart disease and AF is associated with a 17-fold increase in the rate of cerebrovascular accidents compared with the rate in those individuals who do not have valvular disease and who are in sinus rhythm.³ The association between AF from other causes and strokes is not clear. The Framingham study reported a 5-fold increase in strokes in patients with chronic non-rheumatic AF compared with patients in sinus rhythm.⁴ However, Kopecky *et al.*⁵ were unable to demonstrate any association between strokes and lone AF. AF due to thyrotoxicosis and hypertension has been associated with an increased incidence of stroke.⁶⁻⁸ Autopsy studies⁹ suggest that patients with AF and ischaemic heart disease have a greater chance of suffering from systemic emboli than patients with ischaemic heart disease in sinus rhythm. Clinical findings do not support this observation, however.³

Not all strokes in patients with AF are due to emboli. Clinical and radiological examination cannot distinguish with certainty between thrombi and thrombo-emboli¹⁰ and even autopsy studies are not always conclusive.¹¹ This has generated much controversy and it has been suggested that the majority of strokes in AF patients are due to atherosclerosis and that the AF itself is simply a manifestation of this disease.¹² Further unresolved problems are those of asymptomatic cerebral infarction in patients with chronic AF and its role in the aetiology of multi-infarct dementia.

Computed tomography studies suggest that asymptomatic infarcts are more common in patients with AF compared with age-matched controls in sinus rhythm.¹³ These findings have not been confirmed, and glucose intolerance may be a more important risk factor.¹⁴

The value of anticoagulation in patients with AF and rheumatic heart disease is generally accepted. During the 1950s and 1960s trials were conducted in an attempt to assess its worth in cerebrovascular disease. Anticoagulant therapy failed to provide any benefit to patients and the incidence of side-effects was high. In retrospect, these trials were poorly designed from the point of view of defining end points and exclusion criteria. They also attempted to cover too many areas at once.¹⁵⁻¹⁷

However, three recent trials,¹⁸⁻²⁰ all involving large numbers of patients and statistically well planned, have clearly demonstrated the advantages of anticoagulation in patients with non-rheumatic AF. Two trials^{19,20} compared the effects of warfarin to those of placebo or aspirin. Warfarin reduced the incidence of mortality from vascular and thrombo-embolic events in both trials (overall mortality rates were 1% v. 5%¹⁹ and 2,2% v. 5,9%²⁰). In the Scandinavian trial,¹⁹ using conventional levels of anticoagulation (target INR: 2,4 - 4,2), haemorrhagic side-effects reached 7% (compared with 2% in the controls). In the Boston trial,²⁰ where the target INR was 1,7 - 2,5, major haemorrhagic side-effects were similar in both arms, but there was an impressive reduction in strokes (0,41% per year compared with 2,98% in the control

group). The third report concerned the ongoing 'stroke prevention in AF' study.¹⁸ This work is more difficult to interpret, being a preliminary report which showed that warfarin or aspirin separately were superior to placebo. The two study arms remained blinded and as yet no differences have been detected between the two agents.

As might be expected, these trials also raised a number of questions. Two trials^{18,19} had arms involving aspirin; in one¹⁹ aspirin failed to reduce the incidence of thrombo-embolic events. In the second,¹⁸ aspirin was shown to be of benefit, but this trial is ongoing and the results are not conclusive. Aspirin may be expected to have a beneficial effect in patients with AF; estimates of embolic episodes resulting in strokes range from 19% to 75% in these patients.²¹ A second unresolved issue is that of age, and the benefits of using anticoagulants in patients over 75 is an unresolved issue.

The Boston anticoagulation trial was notable for the low dose of warfarin used, an INR of 1,5 - 2,7 being considered therapeutic. Two strokes were recorded in the warfarin group of 212 patients compared with 13 strokes in the control group of 208 patients. These findings are in line with several other reports which indicate that anticoagulation at a low level is effective,^{22,23} and no doubt further trials will pinpoint just what the optimum dosage of anticoagulant is. Nevertheless, the message is clear: if a patient has AF and if there are no significant risk factors, then one has a good reason for administering anticoagulants.

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- Örndahl G, Thulesius O, Hood B. Incidence of persistent atrial fibrillation and conduction defects in coronary heart disease. *Am Heart J* 1972; 84: 120-131.
- Ostrander LD, Ralph L, Marcus O, Frederick H. Electrocardiographic findings among the adult population of a total natural community, Tecumseh, Michigan. *Circulation* 1963; 31: 888-898.
- Wolf PA, Dawber TR, Thomas HE, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. *Neurology* 1978; 28: 973-977.
- Wolf PA, Kannel WB, McGee L, Meeke SL, Bhaducha N, McNamara PM. Duration of atrial fibrillation and imminence of stroke; the Framingham study. *Stroke* 1983; 14: 664-667.
- Kopecky SL, Gersh BJ, McGoon MD, *et al.* The natural history of lone atrial fibrillation. A population-based study over three decades. *N Engl J Med* 1987; 317: 669-674.
- Petersen P. Thromboembolic complications in atrial fibrillation. *Stroke* 1990; 21: 4-13.
- Flegel KM, Shipley MJ, Rose G. Risk of stroke in non-rheumatic atrial fibrillation. *Lancet* 1987; i: 526-529.
- Flegel KM, Hanley J. Risk factors for stroke and other embolic events with nonrheumatic atrial fibrillation. *Stroke* 1989; 20: 1000-1004.
- Hinton RC, Kistler JP, Fallon JT, Friedlich AL, Fisher CM. Influence of etiology of atrial fibrillation on incidence of systemic embolism. *Am J Cardiol* 1977; 40: 509-513.
- Hart R. Atrial fibrillation and the diagnosis of cardioembolic stroke. *Stroke* 1985; 16: 1043.
- Britton M, Gustafsson C. Non-rheumatic atrial fibrillation as a risk factor for stroke. *Stroke* 1985; 16: 182-187.
- Scheinberg P. Controversies in the management of cerebral vascular disease. *Neurology* 1988; 38: 1609-1616.
- Kempster PA, Gerraty RP, Gates PC. Asymptomatic cerebral infarction in patients with chronic atrial fibrillation. *Stroke* 1983; 14: 955-957.
- Kase CS, Wolf PA, Chodosh EH, *et al.* Prevalence of silent stroke in patients presenting with initial stroke: the Framingham study. *Stroke* 1989; 20: 850-852.

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15. Report of the Veterans' Administration Cooperative Study of Atherosclerosis, Neurology Section. An evaluation of anticoagulant therapy in the treatment of cerebrovascular disease. *Neurology* 1961; **11**: 132-144.
16. Fisher CM. Anticoagulant therapy in cerebral thrombosis and cerebral embolism. A national cooperative study, interim report. *Neurology* 1961; **11**: 119-129.
17. Baker RN, Fang HC, Groch SN *et al*. Anticoagulant therapy in cerebral infarction. *Neurology* 1962; **12**: 823-830.
18. Stroke Prevention in Atrial Fibrillation Study Group Investigation. Preliminary report of the Stroke Prevention in Atrial Fibrillation Study. *N Engl J Med* 1990; **322**: 863-868.
19. Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B. Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. *Lancet* 1989; **1**: 175-179.
20. 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**: 1505-1511.
21. Halperin JL, Hart RG. Atrial fibrillation and stroke: new ideas, persisting dilemmas. *Stroke* 1988; **19**: 937-941.
22. Hirsch J, Levine M. Therapeutic range for the control of oral anti-coagulant therapy. *Arch Neurol* 1986; **43**: 1162-1164.
23. Sauer JN, Sieck JO, Mamo LDR, Gallus AJ. Trial of different intensities of anticoagulation in patients with prosthetic heart valves. *N Engl J Med* 1990; **322**: 428-432.

MEDICOLEGAL

Lessons from the investigation into intravenous fluid-related neonatal deaths

It is a matter of record that during 1990 several neonates died unexpectedly at three Johannesburg clinics. Cases were reviewed by the Attorney-General of the Transvaal and an inquest was ordered, the purpose of which was to establish whether there was criminal negligence on the part of any of the parties concerned. The inquest examined 13 deaths which were temporally related, were associated with positive blood cultures or a clinical syndrome compatible with septicaemia, and which occurred in neonates who had received one of two proprietary intravenous fluids as part of their management.

While it was acknowledged that the intravenous fluids from two or possibly three batches were found to be contaminated, under the circumstances of an epidemic within intensive care units (ICUs) or high-care areas, the Court found it impossible to determine whether individual deaths might have been caused by an injection of contaminated fluid or as a result of nosocomial infection. The Court found in respect of all but two of the deaths that there was no evidence of any act or omission on the part of any person amounting to an offence which caused the death, and in the case of the remaining two deaths, the Court made an open finding. As regards the source of the contamination of the intravenous fluids, the Court was unable to find negligence on the part of the manufacturer and was satisfied that internationally accepted procedures and standards had been applied.

The epidemic created anguish on the part of the parents and the doctors caring for the babies and, with increasing intensity as the months went by, prompted searches for the source of infection and reviews of infection control procedures by the clinics and the manufacturer concerned. At various times some of the ICU facilities were closed in an attempt to eradicate the infections, and ultimately, when it became apparent that some IV solutions were contaminated, the manufacturer permanently closed the admixture unit in which the solutions had been prepared.

It is worth considering that the health care team in a situation like this includes doctors, nurses, dispensaries, clinic administrators and the manufacturer. What are the lessons the health care team can learn from this unfortunate episode, which has been so costly in terms of lives, time and money?

Accountability to parents

Perhaps on an emotional note, the first lesson is for the clinic administrators and the manufacturer. Quite obviously, where there was a threat of litigation neither party was prepared to accept responsibility for the deaths, leaving grieving parents with a sense of abandonment. While this aspect might be inevitable legalistically, it is nevertheless extremely distressing for families.

Frustration was added to the families' sense of abandonment by another legal inevitability, the time required for investigation by the Attorney-General. In this regard the health care team can do little other than respond timeously and adequately to requests for clinical details and affidavits.

Relationship between the manufacturers and the health professionals

Historically, the preparation of the two products under investigation was undertaken by the manufacturing firm in its admixture unit as a service to the medical profession. Prior to this, the products were mixed by individual hospitals and clinics, often in less than ideal circumstances.

Thousands of units of fluid were prepared by the manufacturer over several years and used without incident by facilities in the private and academic sectors. Unfortunately, the communication which was established when the services of the admixture unit were engaged lapsed somewhat as the years passed. This is probably not surprising because there was apparently