Anticoagulant drugs in the elderly: the risks usually outweigh the benefits

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Elderly people are more susceptible to the side effects of drugs,¹ and anticoagulant drugs are no exception.²⁻⁷ Recommendations for using anticoagulant drugs in elderly patients mainly concern treating deep venous thrombosis and pulmonary embolism⁸⁻⁹ and preventing embolic stroke.¹⁰ As the adverse effects of anticoagulants may be fatal, evidence for their efficacy in elderly patients must be obtained from prospective randomised studies of patients older than 75 who are similar to those seen in everyday practice.

Pulmonary thromboembolic disease

The clinical diagnosis of deep vein thrombosis is more often wrong than right.¹¹ The diagnosis is best made by phlebography,¹²⁻¹³ but most studies use a radiolabelled fibrinogen technique that is significantly inaccurate and entails a delay of 24 hours.¹²⁻¹³ Either technique shows deep vein thrombosis in about 28-70% of patients with stroke¹⁴⁻¹⁵ and 30% of patients having abdominal or orthopaedic operations.¹⁶ The incidence of deep vein thrombosis increases with age,¹⁷⁻¹⁸ but only a very few thromboses cause pulmonary embolism.¹⁹

The incidence of pulmonary embolism is unknown, but most are small and asymptomatic.¹⁹⁻²⁰ Clinical diagnosis is difficult,²⁰⁻²¹ especially in elderly patients.⁹ The most accurate investigation is pulmonary angiography,²¹ which may not be generally available. Diagnosis is usually confirmed by isotope scanning of the lung, although scans giving false positive results are common.²¹⁻²²

No satisfactory placebo controlled trials of anticoagulant drugs in treating thromboembolism have been performed in patients of any age.²³ Reports from studies usually give little information about criteria for inclusion or exclusion and even less about the age of the patients concerned. Recruitment is often slow—for example, 51 patients over three years²⁴—which is surprising considering the high prevalence of the disease.¹⁴⁻¹⁶ Such highly selected patients are probably not representative of elderly patients who are routinely admitted.

The incidence of bleeding in trials of anticoagulant treatment for deep vein thrombosis has been reported to be as high as 20%, even with good control.⁶⁻²⁵⁻²⁶ The incidence of bleeding in elderly patients is likely to be even higher.²⁻⁷

Reasons for cautiousness when treating elderly patients with anticoagulants

- Increased sensitivity to the drugs
- Increased adverse reactions even with strict control
- Possibility of other diseases increasing the risk of haemorrhage
- Large risk of drug interactions
- Lack of controlled trials in elderly patients

There has been a recent review of the trials investigating the use of anticoagulants in preventing peri-operative deep venous thrombosis.¹⁶ Although only some of the studies were placebo controlled, there is evidence that subcutaneous heparin reduces the incidence of asymptomatic positive fibrinogen scans. Although mortality after operation was related to the age of the patients, no separate information was available about the benefits and risks of preventing deep vein thrombosis in elderly patients. The information on preventing postoperative pulmonary embolism at any age was less positive. This would probably require a study of up to 100 000 patients.¹⁶

Preventing embolic stroke

The prevalence of atrial fibrillation (mostly non-rheumatic) increases with age and is associated with stroke.²⁷ Despite a lack of any randomised controlled trials anticoagulant treatment is recommended to reduce the chance of cerebral embolism.¹⁰⁻²⁸ A two centre study, however, examined anticoagulant treatment in patients with stroke associated with non-rheumatic atrial fibrillation.²⁹ No difference was found in the rates of survival or recurrence between one group in The Netherlands, where anticoagulants were prescribed, and another in England, where they were not.

Anticoagulant drugs are contraindicated in cerebral haemorrhage. Five per cent of unselected patients with stroke and up to a fifth of those with proved large ischaemic strokes will deteriorate if given such drugs.³⁰ Computed tomography is therefore essential before anticoagulant treatment of patients with stroke.³¹ Unfortunately, computed tomography is not widely enough available in the United Kingdom even to conduct a study of anticoagulant treatment, stroke, and atrial fibrillation.³¹

Conclusion

Good reasons exist for being extremely cautious before prescribing anticoagulant drugs to elderly patients. The risk of bleeding with heparin may be as high as half in women over the age of 60; the anticoagulant response to warfarin is greater³²; and the risk of serious adverse reactions exists even with efficient monitoring of the response to the drugs.⁷⁻³³

The decision to use anticoagulants in elderly patients depends on the individual opinion of the doctor. Many factors have to be considered, including the presence of diseases that may increase the risk of haemorrhage and other drugs that may interact.³⁴ The patients may

Conditions potentiating anticoagulants³⁴

Alcoholism
Cardiac failure
Cholestasis
Diarrhoea (enteritis)
Fever
Gastrocolic fistula
Hypoalbuminaemia
Liver damage
Malnutrition
Renal impairment
Thyrototoxicosis

Drugs expected to potentiate oral anticoagulants³⁴

Alcohol (dose dependent)	Feprazone
Allopurinol	Glucagon
Anabolic steroids	Ketoprofen
Aspirin and its analogues (in large doses)	Mefenamic acid
Azaproprazole	Metronidazole
Chloramphenicol	Naproxen
Chlorpromazine	Neomycin
Cimetidine	Oxymetholone
Clofibrate	Oxyphenbutazone
Co-trimoxazole	Phenylbutazone
Danazol	Phenylramidol
Dextrothyroxine	Quinidine
Disulfiram	Salicylates (see aspirin)
Ethacrynic acid	Thyroxine
	Triclofos sodium

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simply forget instructions about the dose and the risks. Access to anticoagulant clinics may be difficult, especially as most elderly patients need to be taken in an ambulance. Consideration should be given to alternative treatment such as mobilisation and wearing compression stockings for deep vein thrombosis.

The common practice of diagnosing deep vein thrombosis and pulmonary embolism on clinical evidence alone³⁵ is unacceptably inaccurate.^{9 11 20 21} If, however, an elderly patient is suspected of having a massive pulmonary embolism there is certainly an argument to give anticoagulant drugs initially, if there are no contraindications. The diagnosis should then be confirmed by angiography or less invasively by a lung scan, preferably with ventilation enhancement.^{19 23} Anticoagulants should be discontinued when a scan shows negative results. In patients whose scans show a positive or even equivocal result continuing anticoagulant treatment depends on clinical judgment. If warfarin is prescribed there seems to be no advantage in continuing for longer than four weeks³⁶ and probably not after discharge from hospital.

With the increased risk of bleeding with anticoagulants in the elderly there is a clear ethical need for fully reported studies of the prevention and treatment of thromboembolism and embolic stroke.

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ANY QUESTIONS

How effective is laser endarterectomy, and how widely used is the technique?

Lasers have been used in arterial surgery experimentally and in clinical practice, principally in techniques with microvascular anastomosis and recanalisation of atherosclerotic vessels. In microvascular anastomosis spot welds can be made joining small vessels of 1 mm or less in diameter or by coagulating collagen or blood around the weld to act as a support.

With blocked arteries in arteriosclerosis it has been shown that atherosclerotic plaque can be vaporised with various lasers, a technique that is especially effective when the plaque is mainly composed of cholesterol. Calcified plaque is more difficult to remove. The technique differs from endarterectomy, when plaque and occluding thrombus are removed surgically.

Several clinical studies have been made using neodymium yttrium aluminium garnet (YAG) or argon lasers to recanalise occluded femoral

arteries. The failure rate seems higher than that of surgical methods either because of failure to vaporise calcified plaque or because of immediate thrombosis. Perforation of the artery is the main complication; the effect of vaporised plaque debris on the peripheral vascular bed seems to be minimal but may depend on the quantity of plaque treated.

So far the results do not compare favourably with established methods of treatment by surgery or, indeed, by balloon angioplasty. There may, however, be a place for a combination of percutaneous laser treatment with balloon angioplasty, with the obvious advantage that patients do not need to have surgery. — JOHN M EDWARDS, consultant surgeon, Surrey

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