Anticoagulation and atrial fibrillation

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Key points

How dangerous is atrial fibrillation?
Atrial fibrillation (AF) is an important risk factor for stroke. Stroke risk is increased 5-fold for patients with AF. Oral anticoagulation with vitamin K antagonists results in a 60–70% relative risk reduction of stroke compared with placebo [1]. Oral anticoagulation with an international normalised ratio (INR) of 2.0 to 3.0 prevents strokes in patients without cerebral vascular events (primary prevention) as well as in patients who have already had a transient ischemic attack (TIA) or ischemic stroke (secondary prevention).

What are the problems with vitamin K antagonists?
Oral vitamin K antagonists have a number of shortcomings. Genetic factors can influence metabolism and lead to situations in which it is difficult to keep the INR within the therapeutic range. Vitamin K antagonists have numerous interactions with food and other drugs. This requires frequent coagulation monitoring. Patient compliance with regular intake is poor. Warfarin has a long lead time until it becomes effective and a long time period after treatment termination until coagulation becomes normal.

Are antiplatelet drugs an alternative to warfarin in AF?
Acetylsalicylic acid (ASA) reduces the relative risk of stroke by 22% compared to placebo in patients with contradictions for oral vitamin K antagonists. The combination of aspirin plus clopidogrel is inferior to warfarin and carries a similar bleeding risk [2]. The combination of ASA and clopidogrel is more effective than ASA mono-therapy in reducing ischemic stroke but leads to significantly increased bleeding rates, which almost offset the therapeutic gain [3].

Are there alternatives to vitamin K antagonists?
A number of new drugs for oral anticoagulation are under investigation, which do not exhibit the disadvantages of vitamin K antagonists. These include factor Xa antagonists such as rivaroxaban, apixaban, betrixaban, LY317717, YM150 and DU-176b (edoxaban) or factor IIa inhibitors (direct thrombin inhibitors).

Are the new direct thrombin antagonists effective in stroke prevention in patients with AF?
Ximelagatran, a direct thrombin antagonist, was equally effective in stroke prevention in patients with AF as warfarin and had a somewhat lower rate of bleeding complications [4]. However, due to disturbances in liver function, the development of ximelagatran was subsequently abandoned. Dabigatran was not inferior to warfarin in a low dose and superior in terms of preventing stroke or systemic embolism in a higher dose, and resulted in significant fewer haemorrhagic strokes and intracranial bleeds [5]. Dabigatran is given in fixed oral doses and does not require coagulation monitoring.

Key words: atrial fibrillation; ischemic stroke; anticoagulation; antiplatelet drugs; secondary prevention

References

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