

PREVENTION OF AF RELATED STROKE – POSSIBILITIES OF PREVENTION

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Atrial fibrillation represents the most common, highly prevalent cardiac arrhythmia which is the strongest risk factor for ischemic stroke, affecting millions of people.

Effective anticoagulation therapy is associated with decreased stroke severity, improved functional outcome, and better survival in patients with AF admitted with acute brain ischemia.

Several risk stratification schemes such as CHADS₂ score, CHA₂DS₂-VASc score, or HAS-BLED are used.

Patients with AF <65 years of age and no other risk factors have a minimal benefit from warfarin as compared to no therapy, due to the low underlying risk of stroke. It is increasingly evident that treatment decisions have to be based on individual risk assessment.

Although we are all aware of devastating consequences of stroke, a large number of patients are still left untreated. On average 30% out of possible 60-70% of patients are treated with oral anticoagulation.

Because of the limitations of old oral anticoagulants, as well as parenteral anticoagulants which are not suitable for long-term therapy, our hopes are set towards new oral anticoagulants without the need for constant coagulation monitoring. New oral anticoagulants include oral thrombin inhibitors and oral factor Xa inhibitors. Among thrombin inhibitors we have dabigatranetexilate, a prodrug of dabigatran, which

reversibly inhibits the active site of thrombin. Peak plasma levels are reached 0.5 to 2 hours after administration of single dose. Dabigatran's half-life is 14 to 17 hours, which makes it suitable for once or twice daily administration and about 80% of the drug is secreted by kidneys unchanged.

Among oral factor Xa inhibitors, progressively investigated are rivaroxaban, apixaban, and edoxaban. Factor Xa inhibitors bind reversibly to active sites of fXa. Rivaroxaban is an active compound with oral availability of about 80%, with rapid onset of action and a half-life of 7 to 11 hours. Elimination of the compound can be prolonged in elderly patients.

Apixaban is an active drug, rapidly absorbed, reaching maximal plasma concentrations after 3 hours, and having a half-life of 8 to 14 hours. It is eliminated through multiple pathways, the hepatic metabolism via CYP3A4, renal and intestinal excretion.

Edoxaban is an active drug, rapidly absorbed, with a half-life of 9 to 11 hours. Approximately one third of the drug is eliminated through the kidney, while the rest is excreted by feces.

The need for anticoagulants which are simpler to administer than vitamin K antagonists, will soon be resolved by availability of new oral anticoagulants.