The Heart Health Centre
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New Anticoagulants for Non-Valvular Atrial Fibrillation

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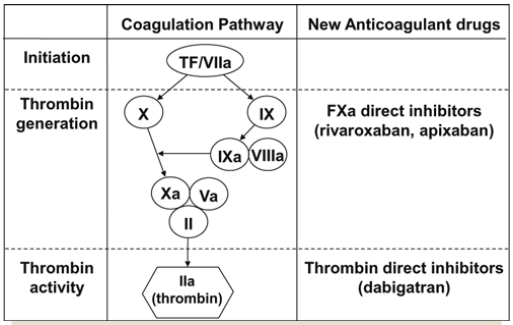
In the last 2 years, two new anticoagulants have become available clinically for use as alternatives to warfarin, with more likely to be approved soon. They offer the advantage of a more rapid onset of action within a few hours compared to days, uniform dosing without the need for laboratory monitoring, and a lower likelihood for drug interaction.

The first of these agents approved was dabigatran (Pradexa). It is a direct, selective Factor IIa (thrombin) inhibitor. The maximal anticoagulant effects are present 2 hours after administration, it has a half-life of 12-14 hours; 80% of the drug is excreted by the kidneys and 20% by the liver; 35% is protein-bound and has bid dosing. The RE-LY study was a non-inferiority study of approximately 18,000 patients who were randomly assigned to a fixed dose of dabigatran or warfarin. Stroke or systemic embolism occurred at a rate of 1.69% per year in patients receiving warfarin and 1.11% per year in those treated with 150 mg dabigatran (RR versus warfarin 0.66; 95% CI 0.53–0.82; P < 0.001). With regard to safety, the rate of major bleeding was 3.36% per year in the warfarin group, versus 3.11% per year in the 150 mg dabigatran group (RR 0.93; 95% CI, 0.81– 1.07; P = 0.31).

The second agent approved was rivaroxaban (Xarelto). Rivaroxaban is a selective, direct inhibitor of Factor Xa. The maximal anticoagulant effects are present 2-4 hours after administration, it has half-life of 9-13 hours; 1/3rd is renal excretion, 1/3rd is renal excretion as an inactive metabolite and the remaining 1/3rd is excreted by the biliary system; 90% is protein-bound and has a once a day dosing. The ROCKET-AF study was a multi-center, randomized, double-blind trial with approximately 14,000 patients with AF were randomly assigned to receive fixed-dose rivaroxaban 20 mg qday (or 15 mg qday in patients with a CrCl of 30-49 mL/min) or adjusted-dose warfarin. Primary outcome events (stroke or systemic embolism) occurred at a rate of 1.7% per year in the rivaroxaban group and 2.2% per year in the warfarin group (HR 0.79; 95% CI 0.66–0.96; P < 0.001 for non-inferiority). Rates of major bleeding were not different in the rivaroxaban and warfarin treated patients (3.6% and 3.4%, respectively); the rates of major and clinically relevant non-major bleeding were also similar in the two groups (14.9% and 14.5% per year).

These new agents have several characteristics that are appealing when compared to warfarin - they have a relatively short half-life, an acceptable therapeutic window, a predictable dose-response without need for regular laboratory monitoring and dose adjustment. However, there are several important factors to be considered. Firstly, these agents are excreted to different degrees by the kidneys and doses need to be reduced when the CrCl falls below 30-50 and should not be used with a CrCl <15. Secondly, reversing their anticoagulant effects is problematic. At this time there is no agent that can be administered to reverse the effects of dabigatran; the effects of rivaroxaban can be reversed with prothrombin complex concentrate. The higher cost of the newer agents can also be barrier to their use.



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September 6th -8th Dr. Saeed
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September 20th-22nd Dr. Rivas-Gotz
(Nuclear Stress Testing and Stress Echocardiography Available)

September 27th-29th Dr. Kosiborod
(Stress Echocardiography Available)

September 29th World Heart Day

For additional information refer to http://bloodjournal.hematologylibrary.org/content/119/13/3016.full.html and follow manufactures' instructions when prescribing these medications.

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