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Stroke Management by Anticoagulant Therapy in Atrial Fibrillation

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Abstract

Stroke is a fundamental cause of many cardiac disorders, and formation of Blood clots or thrombi (embolus) in the arterial circulation can lead to unstable angina, myocardial infarction, or ischemic stroke. Anticoagulant therapy is extensively used with establish benefit to prevent ischemic stroke and thromboembolic events in patients with atrial fibrillation (AF). Atrial fibrillation causes a major trouble on heart patients and CVS. Risk of stroke is increase in case of AF. The main goals of Anticoagulant therapy are to improve symptoms, reduce morbidity, mortality and chances of stroke. The results of many studies emphasize the importance of effective oral anticoagulant therapy in patients with moderate-to-high risk for stroke and superiority of dabigatran, an oral direct thrombin inhibitor, over warfarin in the prevention of stroke. Novel anticoagulants in developments may overcome some of limitations of vitamin k antagonist and address their underuse and safety concerns. : Atrial Fibrillation, Cardio vascular system.

INTRODUCTION

Atrial Fibrillation (AF and A-fib) the rapid, irregular, and Unsynchronized contraction of muscle fibres in upper Heart Chambers (Fig-1A). It is the most common cardiac arrhythmia in which P wave is absent it may cause no symptoms, but it is often associated with palpitations, fainting, chest pain, or congestive heart failure¹.

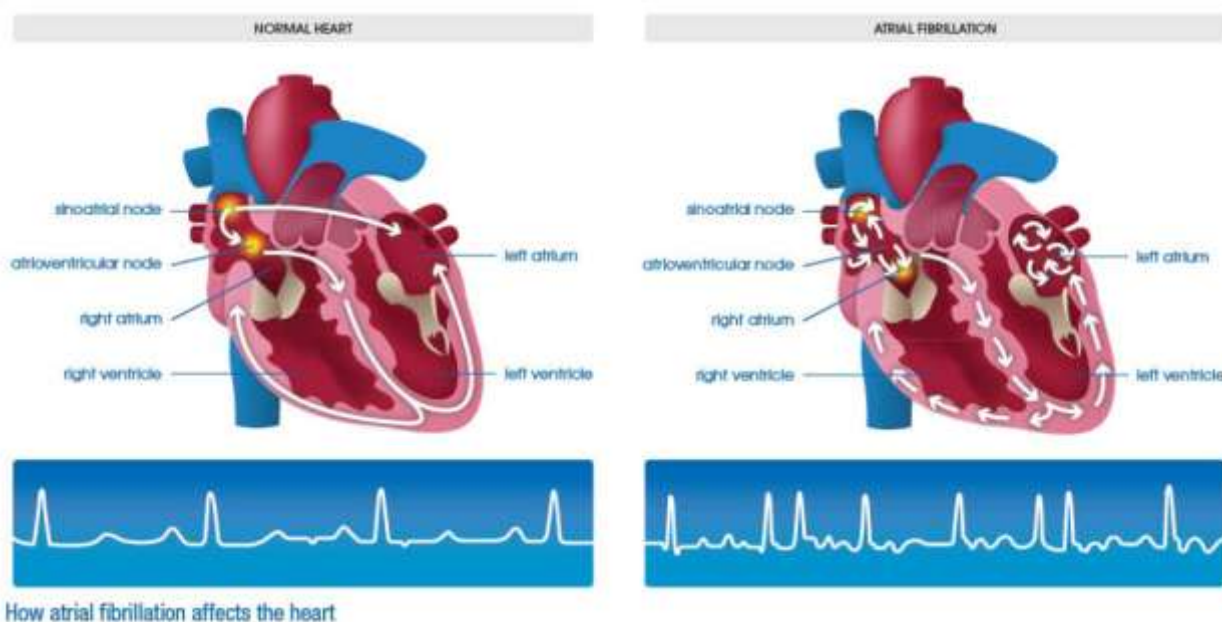
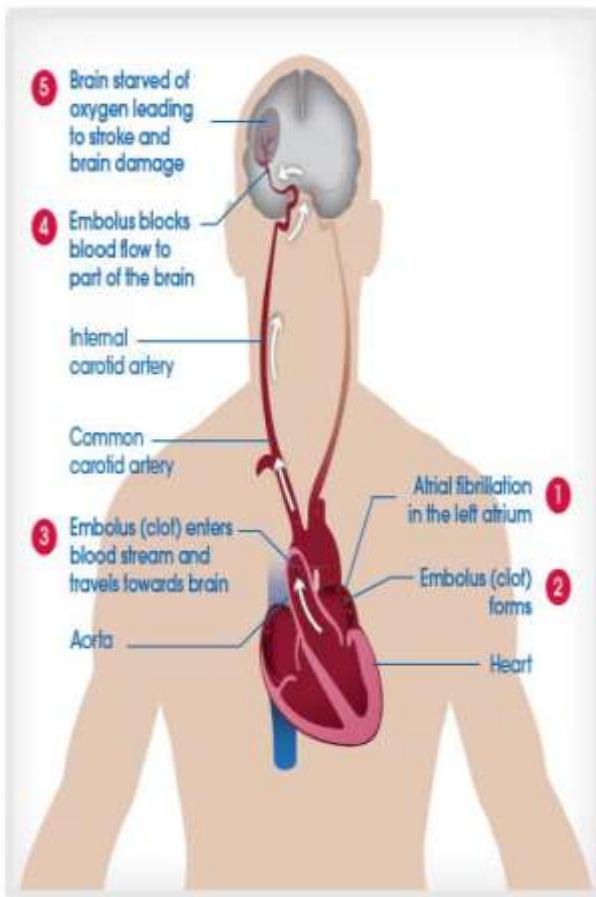
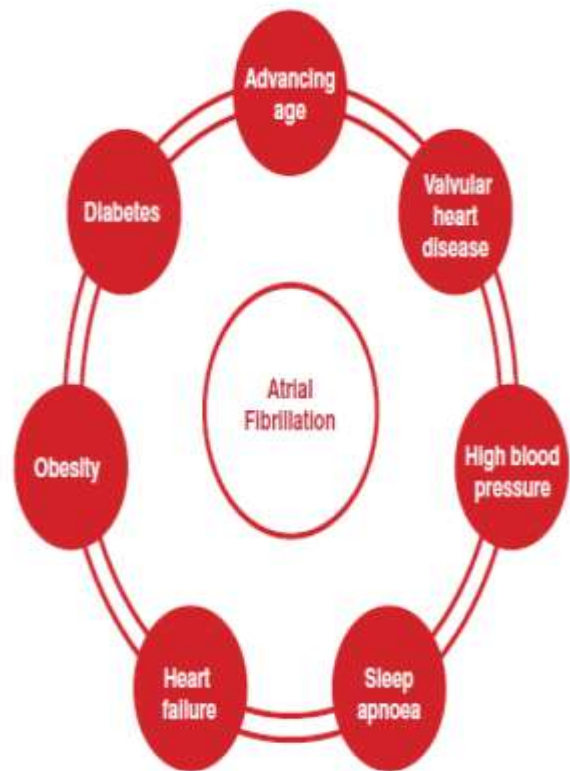


Figure 1. States of Heart in Normal and A.F condition²

Atrial fibrillation (AF) is associated with several serious consequences (Fig-2B). The rapid and irregular atrial activity in AF reduces the efficiency with which blood is pumped from the atria to the ventricles. Blood clots (thrombi) can form in the atria following the pooling of blood (stasis) that can dislodge and travel in the bloodstream, potentially blocking blood vessels in the brain and leading to ischaemic stroke³ (Fig-2A).



(A)



(B)

Figure 2. How A.F leads Stroke(A)and risk factors for A.F (B)

ANTICOAGULANTS THERAPY ⁴⁻¹⁷

Anticoagulants are a type of drug that reduces the body's ability to form clots in the blood. They do this by inhibiting the production of vitamin K in the liver. This increases the time your blood takes to clot. Although they are sometimes called blood thinners, they do not actually thin the blood¹. This type of medicine will not dissolve clots that already have formed, although it will help to stop an existing clot from getting larger.(antithrombics, fibrinolytic, and thrombolytics) are a class of drugs that work to prevent the coagulation (clotting) of blood.⁴⁻⁷ (Fig-3).

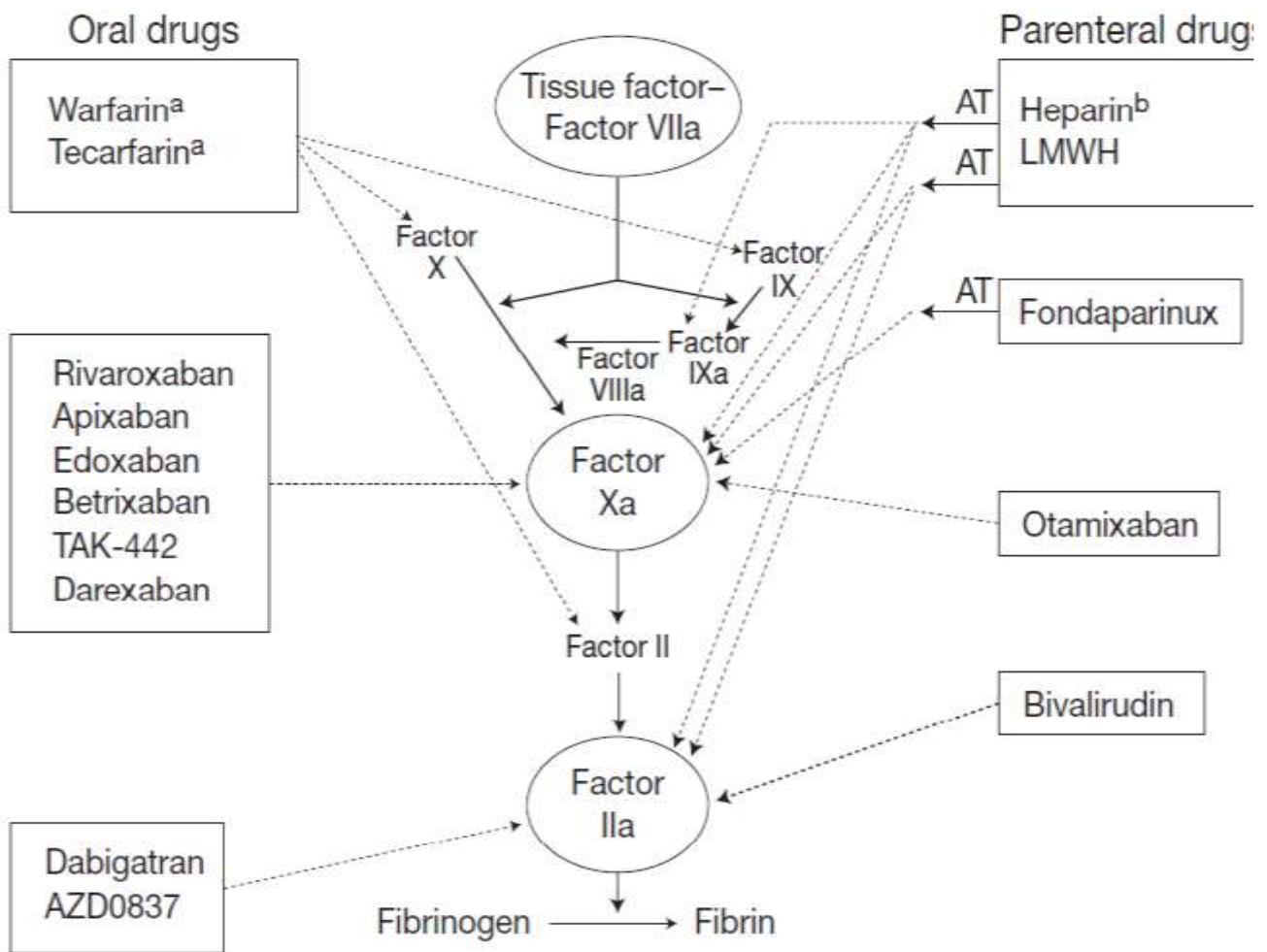


Figure-3 Pharmacologic targets (arrows with dotted lines) for anticoagulant therapy in the clotting cascade (pathways indicated by arrows with solid lines). AT = antithrombin; LMWH = low-molecular-weight heparins. A Other targets for warfarin and tecarfarin are factor VII, protein C, and protein S. bOther targets for heparin are factors VII, XIa, and XIIIa. ⁸

Warfarin

Warfarin is an anticoagulant, which means it stops the blood from clotting. There is an increased risk of bleeding in people who take warfarin, but this small risk is usually outweighed by the benefits of preventing a stroke. It's important to take warfarin as directed by the doctor. If you notice any of the following symptoms when taking anticoagulants, seek medical attention immediately: passing blood in your urine or faeces (stools), passing black faeces, prolonged nosebleeds, bleeding gums, blood in your vomit or coughing up blood, in women, heavy or increased bleeding during your period, or any other bleeding from your vagina⁸.

Unfractionated Heparin (UFH)

UFH is indicated for numerous conditions including the treatment and prophylaxis of venous thromboembolisms (VTE), thrombus prophylaxis in atrial fibrillation, and treatment of disseminated intravascular coagulation. Unlike warfarin, UFH is administered parenterally, both subcutaneous for its prophylaxis use and as a continuous intravenous infusion when used therapeutically. UFH has much faster onset of action as compared to warfarin; when used intravenously, therapeutic efficacy

occurs almost immediately, while therapeutic efficacy is reached within 20–60 minutes when administered subcutaneously. UFH has a shorter half-life than warfarin, and does not require dosage adjustment in renal failure⁹.

New Anticoagulants

Among the new anticoagulants that are currently being investigated are oral direct thrombin inhibitors like dabigatran, oral direct factor Xa inhibitors like apixaban (currently being investigated in the ARISTOTLE and AVERROES studies) and rivaroxaban (ROCKET-AF study is ongoing), and parenteral long-acting indirect factor Xa inhibitors like biotinylated idraparinux¹⁰.

K Antagonist

Vitamin K antagonists have long been the mainstay of stroke prevention therapy in atrial fibrillation (AF), however, vitamin K antagonist therapy is difficult to use because of its narrow therapeutic window, the need for coagulation monitoring, and its interactions with diets and medications¹¹.

Rivaroxaban

Rivaroxaban a direct Factor Xa inhibitor, is a new oral anticoagulant indicated for the prevention of stroke and systemic embolism in at-risk patients with non-valvular atrial fibrillation (AF). Rivaroxaban is a once-daily tablet that can be used to help prevent strokes in people with a heart condition called atrial fibrillation. Rivaroxaban reduces the tendency of blood to clot and, therefore, the risk of having a stroke¹².

Apixaban¹³⁻¹⁵

A recent New England Journal of Medicine article, Apixaban versus Warfarin in Patients with Atrial Fibrillation, reported on ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation), an international multicenter trial that compared the effectiveness of apixaban and warfarin. Apixaban is a “direct factor Xa (pronounced 10a) inhibitor”, which means that it prevents clotting by a different method than Vitamin K antagonists such as warfarin. Apixaban is a third warfarin alternative. Dabigatran (Pradaxa) was approved by the FDA for stroke prevention in patients with afib one year ago on the strength of the RE-LY trial, a study demonstrating that patients taking dabigatran suffered fewer strokes than those taking warfarin.

1. Apixaban is an oral anticoagulant with a twice-daily dosing regimen. It inhibits factor Xa and is PBS listed for stroke prevention in patients with non-valvular atrial fibrillation (NVAf) who meet certain criteria.
2. Apixaban reduced the incidence of stroke and systemic embolism in people with NVAf.
3. Long-term safety and efficacy
4. There is no antidote for apixaban

CONCLUSION

Newer anticoagulants show early promise of reducing stroke and bleeding events when compared with warfarin, and apixaban shows safety and efficacy in patients who are not candidates for warfarin. However, further studies are required for key clinical scenarios involving anticoagulation use and procedures, switching or bridging therapies, and when to start anticoagulation after a hemorrhagic event.

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