$P=0.44$), with significant reductions in intracranial haemorrhage (0.5% vs 0.7%, $P=0.02$) and fatal bleeding (0.2% vs 0.5%, $P=0.003$) in the rivaroxaban group.

Conclusion: In patients with AF, rivaroxaban was non-inferior to warfarin for the prevention of stroke or systemic embolism. There was no significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group.

2. **Apixaban versus warfarin in patients with atrial fibrillation.** Granger CB, Alexander JH, McMurray JJ, ARISTOTLE Committees and Investigators. *N Engl J Med* 2011;365:981–92. doi: 10.1016/S0019-4832(12)60030-3

Background: Vitamin K antagonists are highly effective in preventing stroke in patients with atrial fibrillation (AF), but have several limitations. Apixaban is a novel oral direct factor Xa inhibitor that has been shown to reduce the risk of stroke in a similar population in comparison with aspirin.

Methods: In this randomised, double-blind trial, we compared apixaban (at a dose of 5 mg twice-daily) with warfarin (target international normalised ratio [INR], 2.0–3.0) in 18,201 patients with AF and at least one additional risk factor for stroke. The primary outcome was ischaemic or haemorrhagic stroke or systemic embolism. The trial was designed to test for non-inferiority, with key secondary objectives of testing for superiority with respect to the primary outcome and to the rates of major bleeding and death from any cause.

Results: The median duration of follow-up was 1.8 years. The rate of the primary outcome was 1.27% per year in the apixaban group, as compared with 1.6% per year in the warfarin group (hazard ratio with apixaban, 0.79; 95% confidence interval [CI], 0.66–0.95; $P<0.001$ for non-inferiority; $P=0.01$ for superiority). The rate of major bleeding was 2.13% per year in the apixaban group, as compared with 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60–0.80; $P<0.001$), and the rates of death from any cause were 3.52% and 3.94%, respectively (hazard ratio, 0.89; 95% CI, 0.80–0.99; $P=0.047$). The rate of haemorrhagic stroke was 0.24% per year in the apixaban group, as compared with 0.47% per year in the warfarin group (hazard ratio, 0.51; 95% CI, 0.35–0.75; $P<0.001$), and the rate of ischaemic or uncertain type of stroke was 0.97% per year in the apixaban group and 1.05% per year in the warfarin group (hazard ratio, 0.92; 95% CI, 0.74–1.13; $P=0.42$).

Conclusion: In patients with AF, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality.

Perspective

Atrial fibrillation is the most prevalent sustained arrhythmia affecting aging population. One of the most important aims of managing AF is to prevent embolic stroke. Oral anti-coagulation with vitamin K antagonist has been shown to be very effective in achieving this goal and has been used for long time now. Although very effective, this needs frequent monitoring and dose adjustment. Besides the drug and food interactions are very common, making the dose adjustments very important. Bleeding complications related to oral anti-coagulation in addition to the above mentioned difficulties make physicians extremely cautious while prescribing these very important drugs especially elderly in India. With limited high quality pathology laboratory set up in the semi-urban and rural India physicians many a time refrain from prescribing oral anti-coagulants for AF. Advent of oral Xa inhibitors mark a new era in management of patients requiring oral anti-coagulation. These drugs are given in fixed dose, have shorter half-lives and have limited interactions with other drugs and food. The two recent studies ROCKET AF and ARISTOTLE done with rivaroxaban and apixaban indicate the potential of these drugs. Both studies included large number of patients treated with either of the drug and followed up for approximately 2 years. Most importantly, both these studies used the established therapy, i.e. warfarin as the comparator drug. This puts both the studies on a very high pedestal. ROCKET AF study showed non-inferiority of rivaroxaban to warfarin in preventing strokes and systemic embolism. Incidence of bleeding was same although intracranial bleeding and fatal bleeding was less with rivaroxaban. In ARISTOTLE, apixaban reduced strokes and bleeding compared to warfarin when tested in >18,000 patients for mean 1.8 years. Both these studies usher in a new era of drugs for stroke prevention in AF. The beauty of these drugs lies in fixed drug dose requiring no monitoring of the drug effect as against warfarin. Frequent international normalised ratio (INR) monitoring with dose adjustment has been the main hurdle in using warfarin especially in countries like ours. The only question for us would be the cost of the new drugs as the therapy is long-term. If the industry can offer factor Xa inhibitors at a cost which is feasible for long-term use in most of the patients; stroke prevention in AF can change from dream to reality. However, a word of caution is that these drugs are predominantly excreted through kidneys and therefore one has to be careful while prescribing to patients with chronic kidney disease (CKD).

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