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Three new alternatives to warfarin for atrial fibrillation - which to choose?

I have written on this matter intermittently in the last year or two as new alternatives to warfarin have become available for patients with atrial fibrillation. The question now is which anticoagulant is best or are they all the same?

The backdrop to this is that atrial fibrillation is the commonest change in heart rhythm, increasing in frequency with age. Atrial fibrillation significantly increases the risk of clot formation within the heart, which can lead to stroke should the clot, or part of it, travel to the brain and block an artery. These types of stroke are typically severe and with less chance of recovery. For decades warfarin has been the only available drug which significantly reduces the risk of clot formation and therefore stroke, but is disliked by patients for a number of good reasons; it requires regular blood tests in order that the dose can be adjusted as necessary, and it can interact with a number of drugs, which may increase or reduce its effectiveness. Warfarin is also affected by many food substances, which can be irritating and limiting for some patients, and alcohol intake has to be regulated and moderated. These negative aspects have led to the development of new alternatives, the first being dabigatran (Pradaxa), followed by rivaroxaban (Xarelto) and now apixaban (Eliquis). Termed novel or new oral anticoagulants, or NOACs, they are a truly welcome alternative to warfarin for this condition and are also being studied in other conditions where warfarin would normally be advocated. It should be noted that although these drugs are new in atrial fibrillation they have been used for some time in other conditions, for example, to prevent leg clots (deep vein thrombosis) after orthopaedic procedures.

Broadly speaking the benefits of NOACs over warfarin are that there is no need for regular blood monitoring, there are no apparent food interactions, and interactions with other drugs are fewer than with warfarin. However, on the down side they are more expensive (because they are new) and there is no clear reversal agent should a patient suddenly bleed, for example after trauma or from a bleeding stomach ulcer. Dabigatran is a twice daily medication, like apixaban, whereas rivaroxaban is taken once daily. Dose reduction is recommended with increasing age and with impaired kidney function for all drugs. All three have been shown to be as effective or better than warfarin at reducing the risk of stroke in atrial fibrillation.

So, is one NOAC better than another? It is not particularly easy to answer this question since there has been no head to head comparison between them, instead they have simply been compared to warfarin. However, in most patients the NOACs have a greater clinical benefit over warfarin in patients at higher risk of stroke, measured by the CHA2DS2-VASc scoring system, regardless of the bleeding risk. Because of the greater cost of NOACs there is pressure to limit prescription of these drugs to patients in the higher risk categories. Similarly, if a patient is very stable on warfarin the case to switch to a NOAC is less.

All three NOACs reduce the risk of stroke due to bleeding (haemorrhagic stroke) compared with warfarin. Dabigatran and apixaban cause less major and minor bleeding ,whereas rivaroxaban predisposes to more major bleeds from the gut, as does the higher dose of dabigatran, all compared with warfarin. Older patients are often denied treatment with warfarin to reduce stroke due to a higher risk of bleeding with increasing age. In them the NOACs could be preferred due to a lower risk of bleeding into the brain with a similar reduction in stroke compared with warfarin. Although there is little to choose between them, overall apixaban takes the lead on currently available evidence, and was approved by NICE only last month.