Which agent for which patient? Individual profiling of NOACs

Novel anticoagulant drugs (NOACs) constitute an important alternative for vitamin K antagonists (VKAs) to prevent stroke in patients with non-valvular atrial fibrillation (AF). Although different trials have shown the equivalence or superiority of NOAC versus VKA, the question arises whether the NOACs are also equivalent to each other. They are named as one group, but constitute molecules with different molecular actions (direct factor IIa or Xa inhibition), dosing schemes (once or twice daily), absorption, metabolism and bio-availability, elimination, and potential for drug-drug interactions. The question therefore is legitimate in how far the choice of NOAC should depend on clinical characteristics of the AF patient. Indirect comparison of trial results are difficult because of differences in the populations studied. For secondary prevention (i.e. after a previous stroke), the overall efficacy of dabigatran (110 and 150 mg), rivaroxaban and apixaban seems similar, but dabigatran 150 mg may be more efficacious to prevent ischemic strokes. If overall bleeding is of concern, dabigatran (especially 110 mg) may be preferred, or apixaban (especially if gastro-intestinal bleeding is feared). There remains some concern about the potentially higher myocardial infarction rate with dabigatran compared to factor Xa inhibitors, although this does not seem to impact on the overall ischemic event rate or net clinical effect. In patients with a low CHA2DS2-VASc profile, apixaban seems to be a better alternative for aspirin given its similar overall bleeding profile. Although renal function will impact plasma levels of all NOACs, dabigatran is most sensitive to further deterioration of renal function in patients with an already low creatine clearance (between 30 and 50 ml/min). Also other medications and patient factors may impact the NOAC plasma levels, and hence should be evaluated in global in every patient: combined effects could render a given NOAC unattractive, or require dose reduction. Unfortunately, for some drugs the quantitative impact on NOAC plasma levels is still unknown, making physicians somewhat unsure on how to titrate the NOAC dose in particular cases. Last but not least: the effect of NOAC therapy will only be predictable if the drug is taken. Whether adherence is dependent on the dosing scheme, and whether once or twice daily dosing is the best guarantee for a continuous antithrombotic coverage, should be a topic of urgent scientific studies. In some cases, a proven stable INR may be better than blind belief in the predictable NOAC effect in an unpredictable patient...

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