Non vitamin K oral anticoagulant

Non vitamin K oral anticoagulant (NOACs) are termed direct oral anticoagulants or target anticoagulants due to their direct inactivation of thrombin (FIIa) and factor Xa.

Disadvantages with traditional anticoagulants (vitamin K antagonists and heparinoids) have led to the development on non-vitamin K oral anticoagulants.

The nonvitamin K antagonist oral anticoagulants (NOACs) dabigatran, rivaroxaban, apixaban, and edoxaban are associated with an equal or lower incidence of stroke and systemic embolism and a much lower incidence of intracranial hemorrhage and hemorrhagic stroke than warfarin is, without the need for routine laboratory monitoring.

But this only applies for patients with atrial fibrillation or venous thrombo-embolism, and not for carriers of mechanical heart valves [1].

Indications

These drugs have been approved for the prevention of venous thromboembolism VTE in patients after elective hip or knee arthroplasty in the European Union (EU) and many other countries worldwide [2].

Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (NVAF) [3] [4].

In phase III clinical trials and meta-analyses, the NOACs were at least as effective as vitamin K antagonists (VKAs) and were associated with a similar or lower incidence of major bleeding, including consistent and significant decreases in intracranial bleeding, although with an increase in gastrointestinal bleeding for some agents compared with VKAs. Subsequent real-world evidence supports these outcomes.

Their predictable pharmacokinetics and pharmacodynamics allow for a fixed oral dosing without the need for anticoagulation monitoring.

Monitoring

Although superior to vitamin K antagonists and heparinoids in several aspects, NOACs retain the ability to cause haemorrhage and, despite claims to the contrary, may need monitoring [5].

Reversal

A major concern is the lack of a readily available antidote to reverse their anticoagulation effect in case of life-threatening bleeding or need for emergent surgery.

The specific reversal agents idarucizumab, which is a monoclonal antibody against dabigatran; andexanet alfa, a recombinant human factor Xa decoy for Xa inhibitors; and PER977, a small synthetic molecule for reversal of both Xa and thrombin inhibitors, are currently under development. These agents will facilitate the clinical management of NOAC-associated hemorrhagic stroke and other severe bleeding [6].

The prothrombin complex concentrates, activated prothrombin complex concentrates and recombinant activated factor VII are hemostatic agents that have been assessed in reversing NOACs. Preclinical studies with hemostatic agents report variable results and there is only limited clinical data available to date. While evidence-based recommendations cannot be definitively provided for management of DOAC-related bleeding events at present, several targeted reversal agents are currently in development, and hold promise for solving this important clinical problem [7].

Aripazine is a universal anticoagulation reversal agent. Preclinical studies show promising results and these agents are already in different stages of clinical development. Phase I and II clinical trials demonstrate efficacy in reversing NOACs without major side effects. Until these agents become commercially available, management of patients receiving NOACs who present with major bleeding or require emergent surgery should focus on (a) immediate discontinuation of NOACs, (b) supportive measures or postponing surgery for 12-24 h after the last NOAC dose, and/or © consideration of hemostatic agents [8].

see direct thrombin inhibitor

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