An update on new anticoagulant drugs

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Current anticoagulant drugs include unfractionated heparin, low molecular weight heparin, or fondaparinux, and vitamin K-antagonists. These well established agents have, however, significant drawbacks. In the search for new agents to better fit the profile of an ideal anticoagulant, direct Factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban) and direct thrombin inhibitors (dabigatran etixelate) are in clinical development.

For the prevention of VTE, rivaroxaban was more effective than enoxaparin in patients undergoing knee or hip arthroplasty. Apixaban was superior to the European regimen of enoxaparin but did not meet the non-inferiority criterion compared with the North-American enoxaparin regimen. Concerning edoxaban, two phase II studies in the prevention of VTE in patients undergoing arthroplasty showed promising results. Dabigatran etexilate was as effective as the European regimen of enoxaparin for the prevention of VTE in patients undergoing hip or knee replacement but showed inferior efficacy to the North American enoxaparin regimen.

Rivaroxaban and apixaban are presently being tested in large phase III trials in patients with atrial fibrillation. Thus, a phase III RE-LY trial with dabigatran etexilate showed that 110 mg bid was non-inferior and 150 mg bid was superior to warfarin for the prevention of stroke and systemic embolism with similar or diminished bleeding rates, respectively.

Several phase II studies have been conducted with rivaroxaban, apixaban, and dabigatran for the treatment of venous thromboembolism showing promising results. Presently, phase III trials are ongoing with these agents and their results are eagerly awaited, while the RE-COVER study recently showed non-inferiority of non monitored dabigatran etexilate compared to INR monitored warfarin for treatment of established venous thromboembolism. The EINSTEIN-EXT study showed clear superiority of rivaroxaban (20 mg qd) over placebo in the indication of long-term secondary prophylaxis following an initial anticoagulant treatment period of at least 6-months.

Altogether, these data suggest that we have entered a new era with novel drugs that are closer than ever to the ‘ideal anticoagulant’ and that are likely to replace both heparin and vitamin K antagonists in the next years.