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The new trend in laboratory assay of NOACs

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Abstract: New Oral Anti-Coagulants (NOACs) are becoming more and more popular now and overwhelming majority of patients are taking NOACs as thrombo-prophylaxis now. The merits of NOACs include wide therapeutic index and stable pharmacokinetics and hence there's no need for laboratory monitoring. However, there are some clinical circumstances that laboratory observance of NOACs is essential for patient's care; for instance, patients undergoing invasive procedures or patients affected by bleeding complications. Various principles of laboratory assay are available for measuring the drug level of dabigatran, rivaroxaban and apixaban. The measurement of rivaroxaban and apixaban are often done by anti-Xa assay and dilute thrombin time are often used to measure the extent of dabigatran. Some review articles mentioned that the worth of specific assay of NOACs is uncertain, mainly because the precision and accuracy of the precise assay isn't optimal, especially for low drug level. Nowadays, some companies provide kit with low-level calibrators to enhance precision of measurement of low drug level. In our research, we use the diluted thrombin time kits and anti-Xa kits from Werfen and Sysmex Company for assessing and estimating the drug assay of dabigatran and rivaroxaban. The precision, accuracy, linearity and limit of detection are acceptable for computing various levels of dabigatran and rivaroxaban, including low drug concentrations and therefore the performance of the kits provided by two companies are comparable. The relationship between the drug levels of NOACs with regime coagulation screening tests was also assessed. The issue of internal control and a few practical issues for implementation of the precise laboratory assay of NOACs also will be discussed.

Introduction: New oral anticoagulants (NOACs) are an alternative form for vitamin K antagonists (VKAs) to avert stroke in patients with non-valvular fibrillation (AF). Unlike VKAs, these anticoagulants do not require routine INR monitoring and possess favourable pharmacological properties. The lack of an efficient antidote, their cost, or reservations in patients with renal disorder may explain their slow rate of expansion. Safe and effective use of those new drugs will depend upon clinical experience amongst the medical profession. This review discusses the present NOACs, providing practical and easy-to-use algorithms for application within the clinical routine.

Vitamin K antagonists (VKAs) have been the major stone for the antithrombotic prevention in fibrillation (AF) for >60 years. Despite its unquestionable impact to avert strokes, medical profession need to affect significant limitations, such us common drug or food interactions, and therefore the necessity of normal monitoring to adjust doses, inter alia. In the last 5 years, oral anticoagulant therapy is now witnessing a revolution after the completion of huge phase III clinical trial clinical trials on the commonly termed the new oral anticoagulants (NOACs). Advantages of these new agents including the uses of fixed-dosing with no need for monitoring, few interactions, and a wider therapeutic window counteract with their current drawbacks. The lack of an efficient antidote, their cost, or reservations in patients with renal disorder may explain their slow rate of expansion.

After the unpreventable enthusiasm, it is the medical profession responsibility to make sure the present appropriate use of NOACs that considerably depends on the experience, and exhaustive knowledge of their indications and particularities in specific clinical scenarios.

Two classes of NOACs are currently available, the oral direct thrombin inhibitors (DTIs; e.g. dabigatran) and oral direct factor Xa inhibitors (e.g. rivaroxaban, apixaban, and edoxaban). Unlike VKAs, which block the formation of multiple active vitamin K-dependent coagulation factors (factors II, VII, IX, and X), these drugs block the activity of 1 single step in coagulation.

This review discusses the new anticoagulants such as dabigatran, edoxaban, rivaroxaban, and apixaban.

Dabigatran was the first approved NOAC; it was approved in 2008 by the EU and by the Food and Drug Administration (FDA) in 2010. A new oral, direct thrombin (FIIa) inhibitor that prevents the conversion of fibrinogen to fibrin and thus averts clot formation, dabigatran is designated to lower the risk of stroke and systemic embolism in patients with NVAF. Dabigatran is a synthetic small molecule, hirudin analog that display univalent binding to only one of the two key thrombin sites.

Rivaroxaban is the second NOAC approved in many countries, in 2008 by the European Medicine Agency and by the FDA. Rivaroxaban, an oxazolidinone derivative, is a selective direct inhibitor of FXa. Activated FXa plays a vital role in the coagulation cascade that eventually leads to hemostasis because it links the intrinsic and extrinsic coagulation pathways and acts as a rate-limiting step in thrombin formation.

Apixaban is the third NOAC that was approved by the FDA and by the European Medicine Agency, in 2011. Apixaban is a reversible direct Xa antagonist. It exerts a similar anticoagulant activity as rivaroxaban, by the direct inhibition of factor Xa, which is formed by both intrinsic and extrinsic coagulation pathways. This prevention of thrombin formation from prothrombin is needed to prevent the conversion of fibrinogen to fibrin.

Biography: Sin Chun Fung has obtained his Medical degree in 2008 and is a qualified Hematopathologist in Hong Kong. Currently he is working as a Clinical Assistant Professor in University of Hong Kong. He had been working as Physician in the past. He is interested in the work and research in various hematological malignancies and investigating the novel treatments. He is also passionate in the field of coagulating and hemostasis. With his experience and expertise in internal medicine, he had done work on the laboratory assay of new oral anti-coagulants, with the aim of improving the management of patients taking NOACs.