INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

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Review Article

Recent Advances And Emergency Trends In Anticoagulant Therapy

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ARTICLE INFO

Received: 17 April 2024
Accepted: 21 April 2024
Published: 03 May 2024
Keywords:
vitamin K antagonists, direct oral anticoagulants, anticoagulant therapy, thromboembolism, pharmacokinetics
DOI:
10.5281/zenodo.11109662

ABSTRACT

Anticoagulant therapy plays a pivotal role in the management of various thromboembolic disorders, including venous thromboembolism (VTE), atrial fibrillation (AF), and acute coronary syndromes (ACS). Over the years, significant advancements have been made in anticoagulant therapy, leading to improved efficacy, safety, and patient outcomes. This research article aims to review the recent advancements and emergency trends in anticoagulant therapy. In recent years, direct oral anticoagulants (DOACs) have emerged as a promising alternative to traditional vitamin K antagonists (VKAs) such as warfarin. DOACs, including dabigatran, rivaroxaban, apixaban, and edoxaban, offer several advantages over VKAs, including predictabe pharmacokinetics, fewer drug interactions, and no need for routine monitoring. Clinical trials have demonstrated the non-inferiority or superiority of DOACs compared to VKAs in preventing stroke and systemic embolism in patients with AF, as well as in the treatment and prevention of VTE. Ongoing research focuses on optimizing anticoagulant therapy in special populations, including patients with renal impairment, obesity, or cancer-associated thrombosis.

INTRODUCTION

Anticoagulant therapy stands as a cornerstone in the management of various thrombotic disorders, ranging from atrial fibrillation to venous thromboembolism. Over the years, relentless efforts have been made to enhance the efficacy and safety profile of anticoagulant agents, aiming to alleviate the burden of thrombotic events while minimizing the risk of bleeding complications. This article delves into the latest advancements and emerging trends in anticoagulant therapy, shedding light on the imperative need for continual innovation in this vital therapeutic domain. Recent years have witnessed the advent of anticoagulant agents with innovative mechanisms of action, diversifying the armamentarium available to

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

clinicians. From direct thrombin inhibitors to factor Xa inhibitors, these agents offer targeted and potent inhibition of coagulation pathways, presenting promising alternatives to traditional therapies.

NEED FOR NEW ORAL ANTICOAGULANTS

New oral anticoagulants (NOACs) have more efficacy than vitamin K antagonists (VKA). The vitamin K antagonists have limitations, like the slow onset of action, Prominent care should be given to achieve desired Anticoagulation and the anticoagulant effect is uncertain. The VKA associated dietary precautions, monitoring and dosing adjustment to maintain the international normalized ratio within the therapeutic range and bridging therapy [3]. These factors were difficult for the patient; this may result in inappropriate VKA therapy. This can cause increased bleeding risk or reduced anticoagulation and increased risk of thrombotic events. These side effects lead to the rise of NOACs. The NOACs have single targets in the coagulation cascade. They have more predictable pharmacokinetics. They do not require regular monitoring like VKA. They can be given in fixed doses [8]. They are associated with significantly less intracranial bleeding than conventional anticoagulants. The onset of action of NOACs is rapid compared with VKA therapy. NOACs have no interactions with food but the traditional anticoagulants have. So the patient can have any food during NAOCs therapy. They have wider therapeutic window compared with traditional oral anticoagulants [10]. So, the disadvantages of conventional oral anticoagulants and the advantages of novel oral anticoagulants show the need of novel oral anticoagulants.

TRADITIONAL ANTICOAGULANTS VS NEW ORAL ANTICOAGULANTS

For the past several decades Warfarin is the mostly prescribed effective anticoagulant, because of its side effects (adherence of the patient, unwillingness of physician, therapeutic index), the traditional oral anticoagulants such as warfarin are prescribed only for few patients who have adherence to warfarin and only few patients maintain the plasma concentration within the therapeutic range. The traditional anticoagulants do not work well without side effects and regular monitoring of coagulation [16]. Prevention of thromboembolic outcome requires Prophylactic anticoagulation therapy is required to prevent the thromboembolic diseases [14]. Apart from the side effects and adherence challenges of the patient, warfarin is the gold standard for anticoagulation therapy. Main limits of traditional anticoagulants are bleeding risk, regular laboratory monitoring coagulation, adjustment of dose and drug or food interactions. The metabolism of the traditional anticoagulants was affected by diet and other medications. They were effective but have number of side effects and expensive also. The advantages of novel oral anticoagulants are more than the traditional anticoagulants. The onset of action and offset of action of the novel oral anticoagulants is rapid. The new oral anticoagulants such as Dabigatran, Rivaroxaban, Apixaban, and Edoxaban were newly designed to overweigh the side effects of traditional anticoagulants. So nowadays these modern oral anticoagulants are prescribed[18]. Compared VKA with these NOACs, anticoagulant responses are predictable, and it is effective in the treatment of venous thromboembolism and in the prevention of systemic stroke and pulmonary embolism in patients with non-valvular atrial fibrillation. The novel anticoagulants are administered in fixed doses. NOACs are known as direct oral anticoagulants or target anticoagulants because they direct inhibit thrombin activation and X factor. They have single target in the coagulant cascade[8]. Avoiding of food products are not required because they did not affect the efficacy of the drug as traditional oral anticoagulants. Regular

monitoring of coagulation regularly is not necessary like traditional coagulants.

CLASSIFICATION OF NAOCs

The NAOCs are classified into two categories [26]. The oral direct factor Xa inhibitors (e.g., rivaroxaban, Apixaban, and Edoxaban) and oral direct thrombin inhibitors (DTIs; e.g., dabigatran).

RIVAROXABAN

Rivaroxaban is an oral Xa factor inhibitor used for treating and managing venous thromboembolism for the patient undergone orthopaedic surgery. It is also used in preventing stroke in patients who have non valvular atrial fibrillation. Rivaroxaban is prescribed to treat deep vein thrombosis and preventing the recurrence of blood clots. As a Xa factor inhibitor, it inhibits the prothrombinase activity and prolongs the time of blood clot. It is orally administered. The half-life of this drug is 5-9 hours; In geriatric patients the half period is longer. The recommended dose is from 2.5 mg twice a day to 20 mg once a day and it does not require regular laboratory monitoring. It should be taken with food. It has several benefits over warfarin.

APIXABAN

Apixaban is a direct oral anticoagulant. It can be orally administered. It inhibits both free and clot bound Xa factor. It has been approved for treating various thromboembolic disorders such as venous thromboembolism and pulmonary embolism. It is reversible and highly selective inhibitor of Xa factor. The dose available of Apixaban is 5mg, 10 mg. It is absorbed rapidly. The half-life of this drug is 12 hours [17]. The recommended dose of this drug is 5mg twice a day in the patient who have non valvular atrial fibrillation, so it reduces the risk of systemic embolism and stroke. The peak plasma concentration is 3-4 hours after administered orally. It has the predictable pharmacokinetics and pharmacodynamics properties. It has onset of action is fast, less chance for food and drug interactions [5].

EDOXABAN

Edoxaban is one of the direct oral anticoagulants and it is recommended in treating of pulmonary embolism, venous thromboembolism and the risk of stroke and systemic embolism are reduced in the patient with mitral valve stenosis. The U. S. Food and Drug Administration approved this drug to treat venous thromboembolism and pulmonary thromboembolism. It directly, selectively, and reversibly inhibits factor Xa. It has the advantages of fewer requirement of monitoring, lower risk of substantial bleeding, and infrequent drug interactions. The half-life of the drug is 10-14 hours [28]. It has rapid onset of action. The dose available is 15mg, 30mg, and 60mg. The dosage form available is as film-coated tablets. Recommended dosage of this drug is 60 mg once daily for NVAF. It also has several advantages over warfarin [18].

DABIGATRAN

Dabigatran was the first novel oral anticoagulants and USFDA approved. It is the reversible oral inhibitor of thrombin. On the active site of the thrombin molecule, it binds and prevents the coagulation factor activation. The Thrombin can be inactivated by this drug and reduce the fibrinolysis inhibition. It increases the fibrinolysis. The indication is identical to warfarin in preventing venous thromboembolism [4]. The RE-LY trial is compared Dabigatran is compared with warfarin in a RE-LY trial; it showed that it is better than warfarin in the prevention of ischaemic stroke. It has predictable pharmacokinetics than traditional oral anticoagulants; dabigatran does not require routine close Regular laboratory monitoring of coagulation is not necessary like warfarin. Dabigatran has several important benefits than warfarin [4].

CONTRAINDICATIONS

The contraindications of the novel anticoagulants are active bleeding, coagulopathy, recent major surgery and major trauma. The Pregnant Patient,

babies and paediatric patients should avoid the use of NOACs. NOACs should be avoided to the patients who have mitral valve issues. They are not prescribed to the patients with malignant disease, Hypercoagulability state and Phospholipid syndrome. The patient who have liver or kidney disease are not given with NOACs .because 80% of active component of dabigatran , Only less amount of active component of rivaroxaban and apixaban is eliminated via kidneys[5] .The drug dabigatran is not recommended to the patient with chronic kidney disease because most of the active component of dabigatran is eliminated through kidneys[4]. With dose adjustment and care ,the drugs apixaban and rivaroxaban are given can be given with caution and dosage adjustment is required, especially in elder patients. So, renal function assessment is necessary to the patient with chronic kidney disease and elder patients. The short half lives of NOACs IS disadvantage at some conditions. It causes risk to the patient misses the dose of the drug .In the special populations such as geriatric and pregnant patients the drug should be given with caution. Rivaroxaban was not prescribed for VTE prophylaxis for the renal failure patient. Also It was not recommended for the hepatic impaired patients [29]. Also it should not be used in the patient under the age of 18. It should not be taken before 24 hours of a surgery. According to the International Society on Thrombosis and Haemostasis (ISTH) 2016 guideline suggests avoid the taking rivaroxaban in the population with body weight under 40kg and above 120kg. It causes severe hypersensitivity, prolonged bleeding also occurs. These are the some of the contraindications of Rivaroxaban. Edoxaban was not prescribed for patients who have non valvular atrial fibrillation. It should be avoided in the hepatic and renal impairment. Pregnant and lactating patient should not take Edoxaban. It is not recommended for children. It was contraindicated for patients who have massive and pathological bleeding. It is not indicated for patients with underlying valvular pathologies or those who have mechanical heart valves [18].

ACKNOWLEGEMENT

We extend our sincere appreciation to Arulmigu Kalasalingam College of Pharmacy for their invaluable support. Special thanks to the authors of the source articles for their invaluable contibution.

CONFLICT OF INTEREST

The authors declare no conflicts of interest regarding the publication of this article.

CONCLUSION

The recent advancements in anticoagulant therapy, particularly the introduction of DOACs and reversal agents, have revolutionized the management of thromboembolic disorders. Understanding these advancements and emerging trends is crucial for healthcare professionals to make informed decisions and optimize patient care in both routine and emergency settings. Ongoing research focuses on optimizing anticoagulant therapy in special populations, including patients with renal impairment, obesity, or cancer-associated thrombosis. Tailoring anticoagulant regimens based on individual patient characteristics and risk factors is essential to maximize efficacy and minimize adverse events.

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HOW TO CITE: Julliyan Dilleban A., Bhavani Suba Niranjana M., Deephiha E., Balakrishnan K., Recent Advances And Emergency Trends In Anticoagulant Therapy, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 5, 119-124. https://doi.org/10.5281/zenodo.11109662