Advanced Care for Anticoagulation Therapy: Pharmacist Role

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ABSTRACT: *Anticoagulants are extremely helpful drugs, but when administered improperly or without the right medical care, they can potentially cause thromboembolic and hemorrhagic consequences. The intricate pharmacology and pharmacokinetics of anticoagulants contribute to their small margin of safety. Pharmacists are well-suited to help patients maintain safe and effective anticoagulation due to their special knowledge of pharmacology, pharmacokinetics, and interactions. There should be fewer instances of therapeutic failures and bleeding problems if anticoagulant therapy is successful. To supervise and manage oral and parenteral anticoagulants, the pharmacist managed anticoagulation management service was established. And use of anticoagulant alert card are helpful to manage anticoagulation treatment in patients and also to aid communication with other healthcare professionals and keeping patients safe.*
KEYWORDS: *Anticoagulant, Anticoagulant clinic, Bleeding, Thromboembolism, INR*

I. INTRODUCTION

Anticoagulant, any drug that, when added to blood, prevents it from clotting.. Anticoagulants comprise a chemically heterogeneous group of drugs acting at different steps within the coagulation cascade. Heparin and heparin-based anticoagulants are indirect anticoagulants that bind to antithrombin and enhance the inhibitory capacity of this natural anticoagulant. Coumarin derivatives (e.g., warfarin) interfere with the hepatic synthesis of coagulation factors (vitamin K antagonists). A third class comprises direct inhibitors of enzymes of the clotting cascade, primarily thrombin. Clinically, anticoagulants like unfractionated heparin and coumarins have some disadvantages. The pharmacokinetics of heparin are variable and unpredictable, requiring parenteral administration, resulting in serious adverse effects, and complicating the process of dose adjustment. The orally active coumarin derivatives have a narrow therapeutic window and multiple interactions with food and drugs, necessitating individualized dosing and monitoring.[1]

It is important to note that anticoagulant therapy carries substantial risks as well as substantial benefits (reduction in thrombus extension and fatal pulmonary embolism [PE] in acute illness and recurrent venous thromboembolisms [VTE] afterward) besides the substantial benefits (life-threatening bleeding complications).[2]

Pharmacist play an important role in management of anticoagulant. Strategies include for the management of optimal use of anticoagulants include initial anticoagulant dose selection ,drug-interaction management , international normalized ratio (INR) testing, INR recall interval selection , laboratory monitoring of the anticoagulant response, transitions between anticoagulants, the use of specialized anticoagulation-management services (AMSs) , structured patient education, efforts to improve adherence to anticoagulant medication regimens, invasive procedure management, excessive anticoagulation and bleeding management, anticoagulant resumption following bleeding and renal function monitoring[2]

Anticoagulant has wide variety indications .Parenteral anticoagulant used as Prophylaxis of ischemic complications in the setting of unstable angina or NSTEMI ,Treatment of atrial fibrillation with embolization ,Prophylaxis of peripheral arterial embolism, Prophylaxis of clotting in cardiac surgery, Prophylaxis or treatment of thrombosis in adult patients with HIT including during PCI procedures ,Extended treatment of symptomatic venous thromboembolism to reduce recurrence in patients ,Prophylaxis of postoperative VTE in patients undergoing abdominal surgery, hip replacement surgery, or knee replacement surgery, Prophylaxis of VTE in acutely ill medical patients with severely restricted mobility ,Extended treatment of symptomatic venous thromboembolism to reduce recurrence in patients with cancer. And oral anticoagulants used to Reduced risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation, Prophylaxis and treatment of embolic complications associated with atrial fibrillation or cardiac valve replacement ,Reduced risk of death, recurrent myocardial infarction, and stroke or systemic embolism after myocardial infarction ,Antiphospholipid syndrome, Venous thrombosis Prophylaxis of DVT and PE in patients who have undergone hip replacement surgery Treatment of DVT and PE ,Reduced risk of recurrent DVT and/or PE in patients at continued risk for

recurrent of VTE ,Reduced risk of recurrent DVT and/or PE in patients at continued risk for recurrent of VTE in cancer patients.[3]

The commonly used anticoagulant is Unfractionated heparin, low-molecular-weight heparin (LMWH) and the pentasaccharide fondaparinux and the direct oral anticoagulants DOACs dabigatran, rivaroxaban, apixaban, edoxaban and vitamin K antagonists (VKA)- warfarin, acenocoumarol. These medications are an important treatment modality for patients, yet they are considered high-risk medications that require careful attention. [4] In all healthcare settings, anticoagulants have been repeatedly identified as one of the drug classes most frequently associated with adverse drug events (ADEs), with bleeding being the most concerning ADE. The useful effect of anticoagulant drugs, vitamin K antagonists (VKAs) and direct oral anticoagulant (DOACs) is always counterbalanced by an increased risk of bleeding.[5] Major bleeding complications such as intracranial hemorrhage (ICH) or massive gastrointestinal bleeding deter many patients and physicians from initiating treatment with anticoagulants.[6]

Parenteral anticoagulant has the following adverse drug reactions;
- Bleeding due to overdose is the most serious complication of heparin therapy. Since heparin (and other anticoagulants) interfere with secondary hemostasis, bleeding from deeper organs is more common. Hematuria is generally the first sign; other sites are GI tract, brain, joints, muscles.
- Heparin-induced thrombocytopenia (HIT) is another common problem. Generally, it is mild and transient; occurs due to aggregation of platelets. Occasionally serious thromboembolic events result. In some patient's antibodies are formed to the heparin-platelet complex and marked depletion of platelets occurs- heparin should be discontinued in such cases. Even low molecular weight (LMW) heparins are not safe in such patients, and they should be treated with a direct thrombin inhibitor.
- Transient and reversible alopecia is infrequent. Serum transaminase levels may rise.
- Osteoporosis may develop on long-term use of relatively high doses.
- Hypersensitivity reactions are rare; manifestations are urticaria, rigor, fever and anaphylaxis. Patients with allergic diathesis are more liable

Oral anticoagulant has following ADR

Bleeding as a result of extension of the desired pharmacological action is the most important problem causing ecchymosis, epistaxis, hematuria, bleeding in the GIT, intracranial or other internal hemorrhages may even be fatal. Bleeding is more likely if therapy is not properly monitored, or when the International normalized ratio (INR) exceeds 4, or interacting drugs/contraindications are present.[7]

Oral anticoagulation (OAC) is prescribed for the prevention and therapy of thromboembolic diseases with either vitamin K antagonists (VKA) or non-vitamin K antagonist oral anticoagulants (NOAC), also called direct oral anticoagulants. Warfarin, as the most commonly used oral anticoagulant in clinics, has been used for half a century. Warfarin is widely used in the treatment of cardiovascular diseases such as cardiac valvular disease, cardiac valve replacement, atrial fibrillation, deep venous thrombosis and pulmonary embolism. Warfarin is characterized by a narrow range of effective blood concentrations, complex factors affecting anticoagulant effect and obvious individual differences in efficacy, making it difficult for clinicians to master the dosage of warfarin in the implementation of anticoagulant therapy. The effectiveness and safety of long-term warfarin anticoagulant therapy have also become the main factors affecting the quality of life of patients after operation. Therefore, it is necessary to closely monitor the international normalized ratio (INR) for a long time to adjust the dosage of warfarin in order to achieve both effective prevention and treatment of thrombosis, but also to reduce the occurrence of adverse reactions. Therefore, the long-term management of warfarin after discharge has become particularly important.[8]

There has been a shift to non-vitamin K antagonist oral anticoagulation (NOAC) over vitamin K antagonist oral anticoagulation (VKA) due to the improved efficacy, safety, practicability, and fewer drug-drug and drug-food interactions that NOAC offers. Despite this, strict adherence to VKA and NOAC dosage is required to achieve optimal therapeutic outcomes. The main benefit of NOACs over VKAs is that they permit the use of a fixed-dose regimen without the requirement of ongoing coagulation monitoring. Treatment with NOACs is therefore especially beneficial for patients who, despite strong compliance, frequently experience significant INR fluctuations when taking VKAs, have drug-drug interactions with VKAs, or for whom regular INR monitoring is logistically challenging.[9]

INTERNATIONAL NORMALIZED RATIO (INR)

The PT with international normalized ratio (INR) is measured daily in hospitalized patients and starting on or around day 3 in healthy outpatients. The prothrombin time (PT) measures the time it takes plasma to clot when exposed to tissue factor, which assesses the extrinsic and common pathways of coagulation.

The PT test is performed by recalcifying citrated patient plasma in the presence of tissue factor and phospholipid and determining the time it takes to form a fibrin clot. The formation of a fibrin clot is detected by

visual, optical, or electromechanical methods. The result is measured in seconds and reported along with a control value and/or an INR.

The normal range for the PT varies by laboratory and reagent/instrument combination, and local institutional ranges should be used. In most laboratories, the normal range is approximately 11 to 13 seconds.

The INR is dimensionless. It is calculated as a ratio of the patient's PT to a control PT obtained using an international reference thromboplastin reagent developed by the World Health Organization (WHO), using the following formula:

$$INR = [Patient\ PT \div Control\ PT]^{ISI}$$

The control value for the PT is the mean normal PT for the laboratory determined from ≥30 fresh, normal plasmas handled identically to patient material. The ISI (international sensitivity index) is based on an international reference thromboplastin reagent; however, it is useful to have the ISI value confirmed within each laboratory for each PT reagent and instrument to account for effects of handling and equipment performance.

Unlike the PT, the results of the INR will be similar on a blood sample tested in any laboratory using any thromboplastin reagent/instrument system when calibrated correctly. This allows comparison of the patient's testing performed at different times and/or locations, which is of great benefit for Warfarin and other VKAs monitoring". Use of the INR is also extremely valuable for research studies because it allows investigators to compare the degree of anticoagulation of patients from different institutions.

Clinical uses of the PT include the evaluation of unexplained bleeding, diagnosing disseminated intravascular coagulation, obtaining a baseline value prior to initiating anticoagulation, monitoring warfarin therapy ,assessment of liver synthetic function

ADVANCED CARE SETTINGS IN HOSPITALS

Anticoagulant monitoring clinics/services

Anticoagulant monitoring Clinics specialize in the care of patients receiving anticoagulant therapy. They can be set up as a division of a thrombosis center's multifunctional services, which offer clinical and laboratory experts who can provide thromboembolic illness diagnosis, treatment, and prevention, or they can operate independently. Currently, ACs primarily manage patients on vitamin K antagonists, but over the past few years, the patient population has changed due to an increase in treatments with other anticoagulant medications, such as low molecular weight heparin (LMWH) or pentasaccharide, which require different management systems.

Following are the service provided by the anticoagulant clinics:

Choose the optimal medication based on the clinical patient profile, assess any potential pharmacological interactions, especially in the elderly, and determine the proper clinical indications for anticoagulant treatment. control drug compliance, which for VKAs is confirmed by laboratory testing, choose the best laboratory test for each molecule to support clinical and therapeutical activities, define a follow-up program, define educational programs to increase adherence, manage patients undergoing surgical interventions or invasive procedures, manage patients with bleeding and thrombotic complications during anticoagulant treatment, and manage patients with concurrent diseases.[10]

pharmacist-managed anticoagulation clinic, to find out patients' perceptions of pharmacist involvement with anticoagulation services, it was indicated that majority of patients were comfortable with pharmacists providing monitoring and dosage adjustments of anticoagulant. During the course of anticoagulation therapy, a variety of health-care professionals are involved in patient care. The pharmacist's role is multifactorial and can include monitoring, dosing and provision of drug information, patient education, drug interaction screening and research. Pharmacist guided anticoagulation clinics play an important role in managing anticoagulation therapy for both hospitalized patients and outpatients. These pharmacists evaluate and manage essentially all hospitalized patients treated with warfarin, as well as most patients treated with full dose heparin or low molecular weight heparin. The pharmacists give the attending physicians and house-staff important information about potential drug interactions, in addition to daily dosing recommendations.

The pharmacist working in the clinic is responsible for teaching patients about proper dietary habits with a focus on vitamin K content and modifying warfarin medication dosage as necessary. Also, potential drug interactions are examined, and after consulting with the designated physician, modifications are made.[11]

Anticoagulant alert card

Anticoagulants are now being used more often. Anticoagulants are dangerous drugs. When used incorrectly, they carry a higher risk of substantial harm and are commonly blamed for avoidable injuries and hospital admissions. The most extensively used and well-known vitamin K antagonist (VKA) is warfarin, however newer direct acting oral anticoagulants (DOACs) may not be identified as anticoagulants, which has led to a number of medication errors. Individuals who are receiving anticoagulant medication should always have a

standard yellow alert card on them, the size of a credit card, to let healthcare professionals know they are taking an anticoagulant. The use of patient held anticoagulation alert cards used to assess compliance with national alert recommendations including monitoring requirements for warfarin and explore the role of pharmacists in anticoagulant safety[12]

When then patients start taking oral anticoagulant, an alert card is given to patients. This explains their treatment. There's also a section to write down and keep a record of their anticoagulant dose. Always take alert card during the visit to doctor for consultation. It tells healthcare professionals that the particular taking an anticoagulant. This can be useful for them to know in case of a medical emergency. If the patients need any medical or dental treatment, show anticoagulant alert card to the nurse, doctor or dentist beforehand. This includes before the patients have vaccinations and routine sessions with the dental hygienist.

II. CONCLUSION

Due to the complexity of anticoagulant management, potentially-inappropriate prescribing and drug related problems are common. Multidisciplinary collaborative projects including review and consultation by clinical pharmacists are an effective method of improving management of patients on anticoagulant. clinical pharmacist in anticoagulation therapy leads to proper use of anticoagulant which can be useful while physician prescribes anticoagulant. Education of patients by a pharmacist improved patient understands of use of anticoagulants and as a result a greater percentage of patients had their INR within recommended therapeutic range. The pharmacist can efficiently manage anticoagulation and provide optimal care, it is recommended that major hospitals should consider providing pharmacist managed anticoagulation service or clinic for the benefits of patients.

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