Current Indian Scenario on the Use of Oral Anticoagulants

Introduction

In the present scenario it is imperative to use oral anticoagulants (OAC) to combat life-threatening conditions like cardioembolism and venous embolism. The various indications of OAC therapy are as follows:

- **Prophylaxis** of cardiac thromboembolism in atrial fibrillation (AF), severe left ventricular (LV) dysfunction, mechanical heart valves, bioprosthetic heart valves (first 3 months), intracardiac thrombi, heart valve disease with AF, large left atrial (LA) or history of embolism clot.
- **Treatment** of deep vein thrombosis (DVT), pulmonary thromboembolism, and prevention of recurrence.
- Prophylaxis for prevention of venous thromboembolism (VTE) in high-risk patients, e.g., post-orthopaedic surgery
- Stroke prevention in non-valvular atrial fibrillation (NVAF).
- Embolic peripheral arterial disease

Issues Peculiar to India

In India, the vitamin K antagonist (VKA) are the most popular choices due to a comfort level developed by the physicians after years of its usage and lot of relevant data is available to support its efficacy. But there are certain issues with the use of VKAs specific to India.

- Indians have a different dietary intake as compared to the western community. Inconsistent consumption of green leafy vegetables like cabbage, cauliflower, spinach, and other foods rich with vitamin K in the Indian diet would prevent the achievement of target international normalised ratio (INR) on patients with VKA and cause problem in INR values.
- **Over-the-counter** (OTC) drugs (nonsteroidal anti-inflammatory drugs [NSAIDs], alternative herbal products like garlic and fenugreek) increase the OAC action of the VKA and may cause haemorrhage. Certain antipyretics like paracetamol (PCM) and antituberculous drugs can cause over or under coagulation in India.
- Monitoring is a major issue as Indian hospitals lack laboratories with standardised measurement of prothrombin time (PT)/INR. Several Indian studies have shown that outpatient anticoagulant control was generally poor with inadequate pretherapeutic assessment, an unacceptably high proportion of subtherapeutic PT/INR values and high complication rates; unsatisfactory knowledge base of clinicians for OAC targets; irregular PT monitoring in 25% patients. 1-3
- Genetic factors affect the clinical outcomes of OAC therapy; this has been established by recent pharmacogenetics findings. Warfarin has reported to have large inter-individual and ethnic variations in drug response. 4 The three single nucleotide polymorphisms identified help to determine:
  - The dose of warfarin required to produce a therapeutic INR (typically 2-3)
  - The risk of bleeding or of producing supratherapeutic INR (> 4)
  - The time required to achieve a stable therapeutic dose

Since this information is utmost crucial in the initial phase of OAC treatment the US Food and Drug Administration (FDA) in 2010 made specific recommendations for dosage range initiation in carriers of the CYP2C9 and VKORC1 variants as determined by genotyping test. Such advanced tests are yet not available
in India very easily and hence there is no such aid in deciding the dose of warfarin.5

- There is very minimal evidence on the VKA dosing and risk benefits. In a small study it was concluded that in Asians the starting average dose requirement was 3.4 mg vs 5 mg in Whites, which was also recognised by US FDA while labeling warfarin. Moreover, there is no current data for relation of ethnicity and risks of warfarin therapy as the larger trials established an INR range of 2-3 to balance the benefits with the risks of warfarin therapy that were conducted exclusively in Whites. Whereas, some studies from China and Japan have documented that Asians might need lower INR for protection from thromboembolism and might have higher risk of bleeding at lower INR.6 The anticoagulation consensus guidelines relating specially to warfarin also do not mention the influence of ethnicity on the typical warfarin maintenance dose.7-10

- In India it is very common to detect pregnancy late in the first trimester and hence increasing the chances of continuous warfarin use as there is lack of early briefing on the teratogenic effects due to warfarin usage during conception and pregnancy. It is extremely difficult to implement the guidelines suggesting low molecular weight heparin (LMWH) once daily prior to conception in India.11

**Current Usage of Oral Anticoagulants in India**

Vitamin K antagonists like warfarin, acenocoumarol, etc., are the most frequently prescribed drugs for managing blood coagulation in patients with AF, rheumatic valvular disease,12 heart valve replacement (HVR), DVT, pulmonary embolism, and after orthopaedic surgery. Warfarin is very popularly prescribed in the US whereas in India acenocoumarol is the drug of choice.13 A report suggests that in North India acenocoumarol is widely used in place of warfarin.14 Recently, with the advent of new OACs many questions have risen as to will the new agents replace the older OACs and are they much more effective than the older OACs. The use of newer agents in India is reduced due to higher cost, poor compliance, minimal monitoring facilities, no specific antidote available, and serious bleeding in renal impaired patients and elderly > 80 years.15

**Conclusion**

Appropriate patient education and physician update is mandatory in order to achieve better patient compliance and target INR values as per the recommended OAC guidelines. While prescribing OACs in India it is very necessary that the practitioner considers the cost of the drug, compliance, and the dietary patterns of the patient. The present scenario supports the usage of the VKAs as the efficacy of the newer agents needs to be studied in greater detail in the Indian population.

**References**