

Commentary

Role of anticoagulation in neurological practice

Stroke is a common neurological disorder causing significant mortality and morbidity. The burden of stroke is much more in developing nations, particularly in India due to widely prevalent risk factors like hypertension, diabetes, smoking, metabolic syndrome and sedentary lifestyle¹. The stroke burden can be reduced by taking care of modifiable risk factors and administration of preventive medications. Cardioembolic stroke (CES) is one of the subtypes of stroke occurring due to embolization from heart to intracranial vasculature. The common cardiac conditions are non-valvular atrial fibrillation (NVAF), prosthetic heart valve (PHV), dilated cardiomyopathy (DCMP), left atrial appendage thrombus and left atrial myxoma. Of all cases of cerebral infarctions, the cardioembolic stroke accounts for 14-30 per cent cases². The prevalence of atrial fibrillation (AF) increases with age and it is around 10 per cent at 80 yr of age. AF leads to five-fold increase in risk of stroke and it causes more severe, lethal strokes due to high clot burden in major vessels and causes substantial morbidity and mortality³.

It is not only the irregular heart but other risk factors such as hypertension, congestive heart failure, diabetes, previous stroke/TIA which increase the vulnerability of stroke⁴. CHADS₂ and CHA₂DS₂-VASc scales help clinicians to understand the predisposition of stroke in cardioembolic strokes due to atrial fibrillation and also predict bleeding complications⁵. The strategies to reduce the incidence of stroke in NVAF are to restore the rate/rhythm and antithrombotic agents. The literature does not show trend in favour of significant reduction in incidence of stroke after restoration of rhythm, although rate control mechanism seems to be more effective⁶.

The antithrombotic agents prescribed in ischaemic stroke are antiplatelet agents and anticoagulants. The anticoagulants are of various types. Injectables like

unfractionated heparins and low molecular weight heparins have multimodal mechanism of action on coagulation pathway. These drugs have time tested evidence of efficacy in cardioembolic strokes. The problematic issue is bleeding complications which can be both intracranial and extracranial in nature. These can be life threatening situations. There should be regular monitoring of prothrombin time and International normalized ratio (INR) to predict the bleeding complications⁷.

The oral anticoagulant warfarin, a vitamin K antagonist has been prescribed for many decades. Warfarin reduces the risk of stroke up to 65-68 per cent vs placebo⁸. Warfarin should be administered with certain precautions in patients with concomitant illness like hypertension, liver dysfunction and renal disorders. Also due precaution is to be taken of diet and other drugs with administration of vitamin K antagonist. The strict monitoring of prothrombin time/INR is required to assess the efficacy and anticipate haemorrhagic complication⁷.

There is a need of new anticoagulant drugs which should be efficacious, with minimal bleeding complications and no requirements of laboratory monitoring. The novel oral anticoagulants; rivaroxaban, apixaban and dabigatran are now available. The evidence for these new anticoagulants is based on RELY⁹, ROCKET-AF¹⁰ and ARISTOTLE¹¹ trials. These anticoagulants have been proven to be efficacious in terms of reducing the incidence of stroke in CES. The evidence is predominantly based on patients with NVAF. These are direct acting drugs on coagulation cascade (thrombin inhibitors). The laboratory monitoring is not required. Though various trials have proved the efficacy of these drugs, but bleeding complications are reported to be in the same frequency as compared to warfarin particularly with dabigatran¹².

There are many unresolved questions. Whether it is prudent to use in early CES? It was advocated to start after two weeks¹³. This was justified as haemorrhagic infarction commonly occurs within a span of two weeks. On the contrary, in immediate post-stroke period the stroke recurs. Further studies are required to get the answer of correct timing of anticoagulation in post-stroke phase.

It is well proven that anticoagulants are indicated in CAS. But in real clinical practice, many patients, in whom anticoagulants are indicated, are deprived of this therapy. Many physicians are scared of administering anticoagulants because of bleeding complications¹⁴.

In cortical venous thrombosis, the utility of anticoagulation has been established, based on weak clinical evidence. No randomized clinical trial has been done. In this situation, the anticoagulants are effective even in presence of haemorrhagic infarction. The cochrane review of two trials which were not randomized of unfractionated and low molecular weight heparin did not reveal significant reduction in mortality [pooled relative risk of death-0.33 (95% confidence interval 0.08 –1.21)]¹⁵.

Singh *et al*¹⁶ have conducted a study at tertiary care center of north India to understand the quality of anticoagulation practices in various neurological disorders. The emphasis was on monitoring of oral anticoagulant drugs. They found that frequent monitoring of international normalized ratio/prothrombin time was required for stable dosage of oral anticoagulants. The diet and concomitant drugs should be considered when administering oral anticoagulants. The limitation of the study was addition of retrospective design in which PT/INR reports were not validated and small sample size¹⁶.

In our country, valvular heart disease particularly associated with rheumatic fever, is quite rampant¹⁷. The role of newer anticoagulants has not been established as no literature is available in this clinical setting. So this aspect should be resolved by Indian scientist as our population should not be deprived of this novel therapy.

The mainstay of treatment in cardioembolic stroke due to atrial fibrillation is anticoagulant agent. The newer oral anticoagulants have been proved to be efficacious with no requirement of monitoring but are expensive. The patients must receive anticoagulants while taking due precautions for bleeding complications. The

physicians should apply validated scales (HAS BLED) and scores for predicting bleeding complications.

Rajesh Verma

Department of Neurology
King George's Medical University (KGMU)
Shah Mina Road, Chowk
Lucknow 226 003, Uttar Pradesh, India
drrajeshverma32@yahoo.com

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