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New Oral Anticoagulants (NOACS) For Cerebral Venous Thrombosis

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Cerebral venous thrombosis (CVT) is a relatively rare condition that results from thrombosis of the superficial or deep venous sinuses of the brain. The first ever reported case of the condition was back in 1825 and this was diagnosed at autopsy. It took more than 150 years before imaging modalities were developed that could diagnose cases earlier. With the advent of CT and MR venogram, the diagnosis has become much easier and is contributing to a larger number of cases being picked up. Despite that the incidence in Western literature stays low at 1.3-1.6 cases per 100,000 people. Middle Eastern and Asian countries seem to have a larger burden of CVT, possibly because of higher rates seen with infections and pregnancies.

CVT affects mostly young and middle aged adults and in this age group it tends to affect women much more than men. This is largely due to the cases seen during pregnancy and puerperium. Other transient or permanent factors predisposing to the condition are infections, use of oral contraception, acquired and inherited thrombophilia states, trauma and surgery.

Despite the presence of hemorrhagic strokes, the mainstay of treatment for these patients has always been anticoagulation. Often heparin, unfractionated or low molecular weight, is used followed by vitamin K antagonist, warfarin. A study conducted by Cundiff et al compared CVT patients who received heparin and warfarin to those who did not receive any treatment and found that this anticoagulation arm had a significantly lower mortality. This however, came at the cost of a higher risk of major and intracranial bleeding and heparin induced thrombocytopenia. In addition, fluctuations in INR and the requirement of frequent monitoring make this a cumbersome exercise for most patients.

Now with the advent of new direct oral anticoagulants (NOACs), there is a growing interest in expanding their use to other indications. These drugs have several advantages over vitamin K antagonists including rapid onset of action, predictable pharmacokinetic properties and few drug interactions. This precludes the need for frequent monitoring as is required for Warfarin. Several case reports and case series have been published over the past 5 years supporting the use of various NOACs in CVT patients and with good results. The three drugs reportedly used so far include Dabigatran (direct thrombin inhibitor), Apixaban and Rivaroxaban (factor Xa inhibitors).

One series by Geisbuch et al, reported on seven patients who were treated with Rivaroxaban. These were compared with nine cases that received vitamin K antagonist. The authors reported no major differences in terms of outcomes, recanalization on MR Angiograms, and bleeding complications at a median of 8 month follow up.

The largest series of NOAC use in CVT is by Mendonca et al. They reported on 15 cases of CVT treated with Dabigatran, four of which were switched from Warfarin because of adverse effects. 80% of the patients had recanalization and 87% had excellent outcomes at 19 months median follow up. Other case reports exist that report use of lower dose of Dabigatran (110mg twice daily) and shown similar good results.

Rao et al, recently published their case series of 3 CVT patients who were started on heparin and switched to Apixaban on discharge. All three patients had no therapy related complications and showed recanalization at follow up.

Despite this reported success, there are still uncertainties around the use of these agents for this particular indication. This niche will only be filled by well-designed randomized controlled trials with clear outcome definitions. The RESPECT CVT, TO-ACT, and EXCOA-CVT trials are currently underway and will hopefully provide robust evidence for use of NOACs in patients with cerebral venous thrombosis.

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Maria khan; concept, data collection, data analysis, manuscript writing, manuscript review
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