IP Indian Journal of Neurosciences 5 (2019) 113–116

Content available at: iponlinejournal.com

IP Indian Journal of Neurosciences

Journal homepage: www.innovativepublication.com

Original Research Article

Oral anticoagulation in cerebral venous sinus thrombosis-Experience from a tertiary care hospital in Karnataka, South India

Pawan Raj Pulu Ishwara[1],*, BS Raghavendra[1]

[1]*Dept. of Neurology, Father Muller Medical College, Mangaluru, Karnataka, India*

ARTICLE INFO

Article history:
Received 25-06-2019
Accepted 27-07-2019
Available online 06-09-2019

Keywords:
Cerebral Venous thrombosis
Anticoagulation
Venous stroke

ABSTRACT

Aim: To study clinical features of Cerebral venous sinus thrombosis patients and to assess type of oral anticoagulant, efficacy and Clinical outcome at the end of 3 months.
Materials and Methods: Our study was a retrospective observational study. Patients presenting with clinical and imaging features of cerebral venous sinus thrombosis to Fr Muller Medical College hospital from January 2017 till March 2019 were included in the study. Clinical features and outcome was recorded at discharge and at follow up of 3 months. Type of oral anticoagulant used, any complications of therapy, any recurrence of thrombotic events during follow up were recorded.
Results: Total of 18 patients were studied. Common Presenting features were headache (83.3%), seizures (38.9%), motor weakness (33.3%) and visual disturbances (27.8%). All patients received therapeutic anticoagulation. Nine (50%) patients received warfarin, 5(27.8%) received dabigatran and 4(22.2%) received acenocoumarol during follow up. There were no complications during follow up period.
Conclusions : Vitamin K antagonists and Direct oral anticoagulants are equally effective in preventing recurrence of CVST in the short term.

1. Introduction

Cerebral Venous Sinus Thrombosis (CVST) is a disease with manifestations ranging from simple headache to life threatening disease with severe neurological impairment. This disease commonly affects young population and is an important cause of morbidity and mortality.[1] Although the disease is reported to be rare in Western population, Indian population has relatively higher incidence of CVST according to multiple case series and studies.[1–3]

Clinical features of CVST are diverse. Symptoms of headache, convulsions, visual loss, limb weakness, altered sensorium can be seen. Clinical signs vary from presence of papilledema, cranial nerve palsy and limb weakness. Diagnosis of cerebral venous sinus thrombosis can be established with the help of clinical symptoms and signs and neuro imaging with either CT or MR imaging of the brain with Venography.[4] Neuro imaging features of CVST in CT include Direct visualization of thrombus as a dense cord like hyperdensity in plain CT (cord sign) and contrast filling defect in the axial section (empty delta sign) and indirect signs such as hemorrhagic infarcts and juxtacortical hemorrhages. MR imaging has, in addition to the above signs, additional features of absence of flow voids in the sinus and visualization of thrombus in a variety of sequences. Contrast enhanced imaging is beneficial in demonstrating the size and extent of thrombus. CT venography and MR venography are useful in confirming the diagnosis evaluating severity and extent of the disease.[5]

Treatment of CVST consists of parenteral anticoagulation either with unfractionated or low molecular weight heparin in order to recanalize the occluded sinuses and veins and also to prevent progression of disease.[6] Patient with CVST may also require anti edema measures such as intravenous mannitol, anti epileptic drugs and decompressive craniectomy according to the severity of illness. Intrasinus thrombolysis is a newer modality of

* *Corresponding author*.
E-mail address: drpawanraj88@gmail.com (P. Raj Pulu Ishwara).

https://doi.org/10.18231/j.ijn.2019.016
2581-8236/© 2019 Published by Innovative Publication.

treatment being offered at higher centres for severe disease.[4]

Once the patient improves clinically, oral anticoagulation is started and continued for 3 to 6 months in CVST with treatable risk factors and for lifelong in CVST with thrombophilic states and in recurrent CVST. Vitamin K antagonists such as warfarin and acenocoumarol are commonly used and dosage is adjusted to achieve an international normalized ratio(INR) between 2 and 3.[4] Newer oral anti-coagulants are recently introduced drugs which act at specific sites in the coagulation pathway and have considerable advantage over vitamin K antagonists such as less interaction with food and absence of need for INR monitoring. Dabigatran is a direct thrombin inhibitor which has been used in multiple studies as an off label anticoagulant for CVST in recent past.[7–11] Apixaban and rivaroxaban are the other direct acting anticoagulants being tried in therapy of CVST.[12]

Our study aimed at analyzing clinical features of CVST patients admitted to Fr Muller Medical College Hospital and to assess type of oral anticoagulant used, complications, efficacy and Clinical outcome at the end of 3 months after discharge.

2. Materials and Methods

Our study was a retrospective observational study conducted at department of neurology in Fr Muller Medical College, Mangalore from January 2017 till March 2019. Patients admitted with a diagnosis of CVST i.e., Clinical features of headache, seizures, focal neurological deficits and MR imaging features of T2 mixed intensity parenchymal lesions, visualization of thrombus in sinuses and cortical veins and loss of flow signal in MR venography. Case records were reviewed and demographic details, clinical features were recorded into a structured proforma. Modified rankin scale was applied at the time of admission and at 3 months follow-up as an outcome measure. Type of oral anticoagulant used, any complications of therapy, any recurrence of thrombotic events during follow up were recorded.

3. Results

Total of 18 patients were admitted with the diagnosis of CVST during the study period. Among them 14(77.8%) were male and 4(22.2%) were female. Mean age of patients was 37.7±14.95 years. Among the risk factors, Alcohol use was seen in 6(33.3%), Hyperhomocysteinemia was seen in 5(27.8%) tobacco smoking in 2(11.1%), connective tissue disease in 2, Puerperal CVST was seen in one(5.5%) and Oral contraceptive induced CVST was seen in one patient. Two patients had past history of venous thrombosis. Headache was seen in 15(83.3%), seizures in 7(38.9%), motor weakness in 6(33.3%) and visual disturbances were observed in 5(27.8%) patients. Mean Modified Rankin Scale (mRs) score at admission was 3.5±1.2, at discharge mean mRs reduced to 1.22±0.94 and at 3 months mean mRs score was 0.33±0.59. All patients received parenteral anticoagulation during admission and were on oral anticoagulation at the time of discharge and during follow up. Nine (50%) patients received warfarin, 5(27.8%) received dabigatran and 4(22.2%) received acenocoumarol. None had recurrence of CVST during the follow up period. One patient had a seizure recurrence. Complications of anticoagulant therapy such as bleeding gums, hematoma formation, intracranial bleeds were not observed during the study period. International normalized ratio values were available for 13 patients. Eight (44.4%) patients had INR values between 1-2, 3(16.7%) had INR values 2-3 , one (5.6%) patient had INR value above 3 and one patient (5.6%) had INR value below 1.

4. Discussion

Cerebral venous sinus thrombosis is a devastating disease which can affect any age group. Previously the disease was more common in females especially during puerperium, however currently many studies are showing reversal of trends and increasing incidence in Men.[1,3] Our study also showed increased incidence of the disease in males compared to females. Among men alcohol abuse was commonly observed. Alcohol abuse leads to vitamin B12 deficiency, dimorphic anemia and hyperhomocystienemia which is a prothrombotic state. This combined with state of dehydration is thought to be causative agent for CVST in such patients.[13] Among women oral contraceptive pill(OCP) use, ,especially combined OCP use is associated with increased incidence of CVST. Prothrombotic effect of estrogen along with coexisting anemia are suspected to be the causative factors for CVST in this subgroup of patients.[14,15]

Headache was the most common symptom in our study followed by seizures, motor weakness and visual disturbances. Similar incidence was found in multiple national and international studies.[3,16,17] Clinical features occur as a result of hemorrhagic infarction, raised intracranial tension and brain edema.[1] After treatment with parenteral anticoagulation, antiepileptic drugs and anti edema therapy, patients clinical status gradually improved as shown by their modified rankin scores.

Anticoagulation is an effective treatment for CVST as mentioned by various guidelines and our study also reiterates the same.[4,7] Oral anticoagulation is advised for a variable duration after the initial illness as per international guidelines.[4] Warfarin is a compound which inhibits the action of vitamin K epoxide reductase and prevents gamma carboxylation of glutamate in various clotting factors such as II, VII, IX, X and leads to delay in clotting. The dose is started at 2.5mg/day and can be titrated upto 10mg /day based on desired range of International Normalized

Ratio (INR) values for Prothro mbin Time (PT). Warfarin absorption is affected by dietary factors and the drug has multiple drug-food and drug-drug interactions and needs regular INR monitoring during therapy. Commonly used drugs in neurological patients such as anti epileptics, antibiotics, anti inflammatory medcations have significant drug interactions with warfarin.[18] Dabigatran is a newer directly acting oral anticoagulant which inhibits factor IIa. It has rapid onset of action and does not need INR monitoring. Dabigatran has minor drug and diet related interactions and has been shown to be effective in preventing venous thromboembolism. Recently several case series have demonstrated efficacy of dabigatran in CVST.[7–11] Bleeding complications can occur during oral anticoagulant therapy. Minor bleeding complications such as bleeding gums were observed in upto 9% and major bleeding episodes such as gastro intestinal or intracranial hemorrhages in 3% of patients receiving warfarin.[19] Incidence of major bleeding in dabigatran use found to be 2.7% per year in RE-LY trial.[20]

In our cohort majority of patients received vitamin K antagonists (72.2%) as compared to direct oral anticoagulant dabigatran (27.8%). There were no bleeding complications or recurrence of thrombosis in either group during follow up. As dabigatran has lesser drug interactions and does not need INR monitoring, it may become preferred anticoagulant especially for short duration.

In patients receiving Vitamin K antagonists INR values during follow up were significantly lower than the recommended value of 2-3. However lack of recurrence of thrombosis in these patients may suggest that lower dosages of anticoagulants are effective for preventing disease recurrence.

5. Conclusion

Cerebral venous sinus thrombosis is a treatable disease which responds to therapeutic anticoagulation. Patients who receive appropriate therapy improve significantly and maintain improvement during follow up. Variety of oral anticoagulants are prescribed to prevent recurrence after recovery. Vitamin K antagonists are time tested drugs which have limitations of drug interactions and the need for therapeutic monitoring. Our study suggests lower dosages of anticoagulants may be sufficient to prevent CVST recurrence during follow up. Direct oral anticoagulant such as dabigatran are also equally effective in preventing the recurrence of thrombosis in short term. Further studies are needed to understand the dose and duration of oral anticoagulation in CVST patients after the acute event.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Pawan Raj Pulu Ishwara Assistant Professor

BS Raghavendra Associate Professor

Cite this article: Raj Pulu Ishwara P, Raghavendra BS. Oral anticoagulation in cerebral venous sinus thrombosis-Experience from a tertiary care hospital in Karnataka, South India. *Indian J Neurosci* 2019;5(3):113-116.