

Local Intrasinus Thrombolysis for Cerebral Venous Sinus Thrombosis

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Abstract

Background—Cerebral venous strokes due to cerebral venous sinus thrombosis (CVST) have varied presentation and clinical outcome. Despite aggressive medical treatment with optimal anticoagulation, some patients develop progressive neurologic deterioration causing significant morbidity and mortality. The aim of the present series is to analyze the safety and efficacy of *in situ* thrombolysis in patients with cerebral venous sinus thrombosis in severe clinical grade and refractory to conventional medical management.

Materials and methods—Twenty-nine patients with cerebral venous thrombosis who received *in situ* thrombolysis during a 3-year period (April 2013 to April 2016) were included in the study. Tissue plasminogen activator (tpa) was used in all the patients. The lytic agent was infused into the sinus via the micro catheter. Data regarding demographic, clinical, and radiologic features were analyzed in all the patients.

Results—Recanalization of the affected sinuses was achieved in all the cases. Twenty-four patients had good outcome (mRs 0 or 1) and three patients had mild deficits (mRs 2). One patient had moderate disability (mRs 3). One patient succumbed due to increased hematoma causing midline shift and transtentorial herniation. At 3 months follow-up, 26 patients were asymptomatic and two patients had minor symptoms.

Conclusion—Local intrasinus thrombolysis (LIST) is safe and effective method in patients with poor clinical grade and the present study highlights the benefit of thrombolysis, particularly in patients unresponsive to anticoagulation. The improved efficacy of this therapy depends on early recognition of worsening symptoms and timely intervention.

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) accounts for 0.5% to 1% of all strokes and more common in young population [1,2]. Incidence of CVST is more common in Indian subcontinent accounting for 10% to 20% of all young strokes [3]. The mortality in these patients is highly variable between 5% and 30% [4,5]. In patients with encephalopathy or with impending encephalopathy the mortality is up to 53% [2,6].

Endovascular intrasinus lysis give better outcome in patients with patients with rapidly progressing clinical deficits, posterior fossa lesions, and deep venous system involvement [7,8,9]. Identifying the patients with severe clinical grade at an early stage and endovascular lysis in this subgroup yields good results and favorable outcome. We present our series of 29 patients, who received LIST in our institution which is a tertiary care center,

analyzed the results by comparing with previous studies in the literature.

MATERIALS AND METHODS

Twenty-nine patients (17 males and 12 females) with CVST underwent treatment with LIST at our institution from April 2013 to May 2016. The age group of the patients ranged from 19 to 54 years. Anticoagulation with conventional heparin was started in all the patients with a dosage of heparin 1 u/kg. The grading of CVT was done using the criteria proposed by INR, King Edward Memorial Hospital (KEM), Mumbai, India (Table 1). Patients in grade 4 and grade 5 and patients in grade 3 with no response to systemic heparinization or worsening despite of heparin underwent LIST. Nine patients in grade 3, 13 patients in grade 4 and seven patients in grade 5 were treated in the present study.

Table 1. KEM INR criteria for local thrombolysis for cerebral venous sinus thrombosis [9].

Grade	Clinical criteria	DSA grading
Grade 1.	Symptom free	Partial thrombosis of dural sinus with no restrictive venous outflow
Grade 2	Minor Symptoms (headache, vomiting, diplopia, seizures)	2 Dural sinus occlusion with no restrictive venous outflow.
Grade 3	Major neurological deficit but fully responsive	Dural sinus occlusion with restrictive venous outflow
Grade 4	Impaired state of alertness but capable of protective or adaptive responses to noxious stimuli (GCS 8–10)	Deep venous system occlusion
Grade 5	Poorly responsive, but with vital signs (GCS 5–7)	Dural sinus and deep vein occlusion with restrictive venous outflow
Grade 6	Not responsive to shaking, nonadaptive response to stimuli and progressive instability of vital signs. (GCS 3–4)	

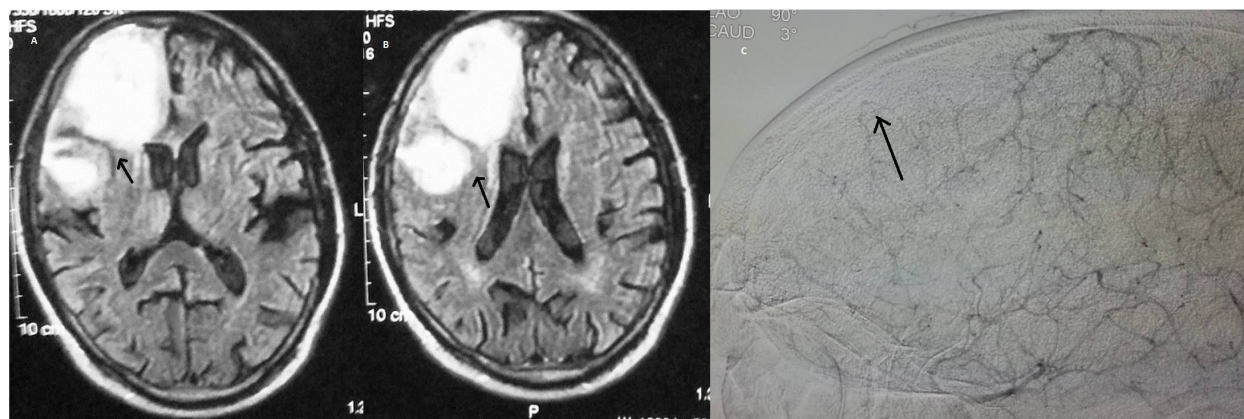


Figure 1. A 54-year-old male presented in grade 4 with MRI showing right frontal venous infarct (A, B arrows). Digital subtraction angiogram (c) in venous phase showing no flow in superior sagittal sinus corresponding to the region of infarcts (arrow).

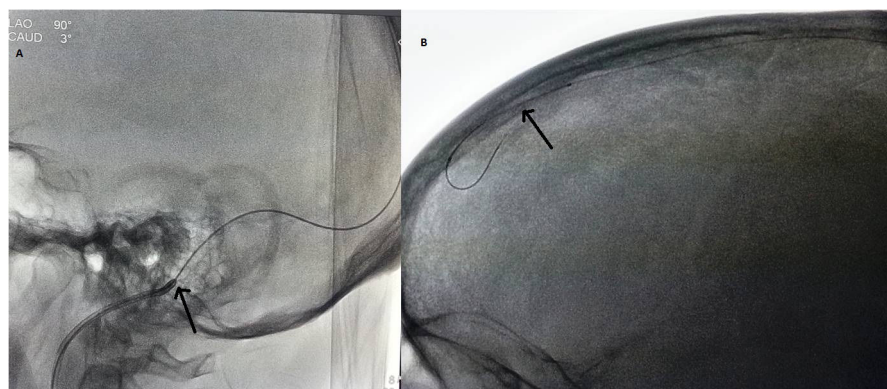


Figure 2. Envoy guiding catheter is placed in jugular as shown by the arrows in A. Micro catheter over micro wire (arrows in B) placed in superior sagittal sinus.

MRI (magnetic resonance imaging) and MRV (MR venogram) were done in all the patients prior to the treatment. All the patients had hemorrhagic venous infarcts. Patients with genitourinary bleed or gastrointestinal bleed (<2 weeks), intracranial aneurysms, and AVMs or bleeding diathesis and platelets count of <100,000 were excluded from the study. One patient with CVST who underwent emergency decompression

(without opening the dura) was treated with LIST after 48 hours due to worsening clinical status.

Informed consent for LIST is taken from all the patients. Clinical outcome was measured using modified Rankins score with scale 0, normal; 1, no significant disability; 2, slight disability (look after own affairs without assistance); 3, moderate disability (need help, able to walk

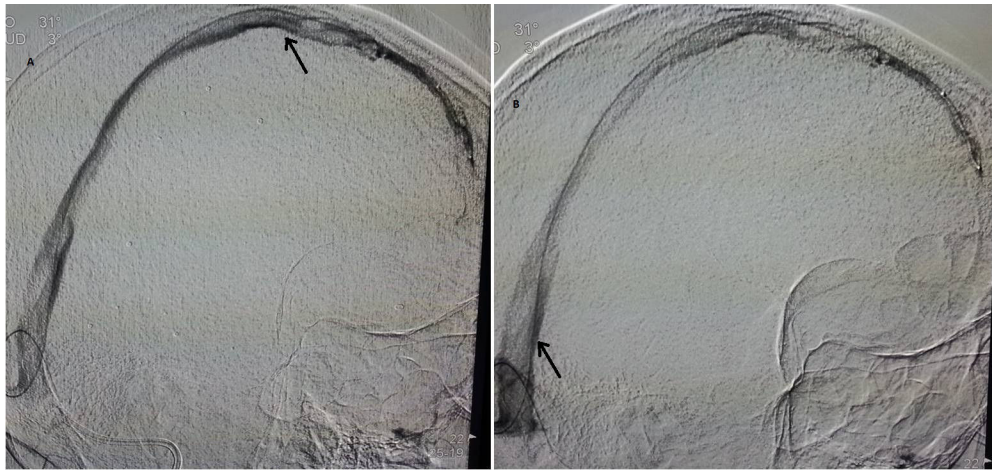


Figure 3. Post-LIST venograms showing recanalized supersagittal sinus (arrows in A,B)

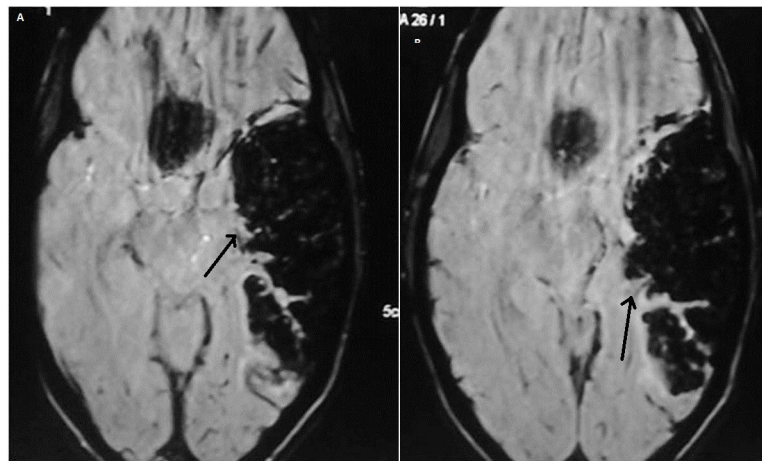


Figure 4. A 29-year-old presented in grade 3 developed right hemiparesis despite anticoagulation. MRI showing the hemorrhagic venous infarct in the left temporoparietal region (arrows in A, B)

when assisted); 4, moderately severe disability (unable to walk unassisted); 5, severe disability (unable to ambulate, altered mentation); 6, death. Treatment response was assessed as good improvement (MRS 0, 1, 2), partial improvement (MRS 3, 4), or poor outcome (MRS 5, 6).

Endovascular technique

All procedures were performed on Axiom Artis Zee, Siemens, Germany. Digital subtraction angiogram with late venous phase was done in all the patients. Six French guiding catheter is placed in the jugular bulb. Mechanical maceration of the clot is done with 0.038 glide wire (Terumo) in all the cases. Microcatheter

(echelon, progreat) over 0.014 wire was negotiated into the thrombosed sinus. Microcatheter injection confirmed the accurate position in the thrombus and 2 mg bolus is then given. tpa infusion was started at rate of 1 mg per hour and periodic check venograms were done. Infusion was continued until significant clinical improvement or partial recanalization of the sinus with good outflow is seen.

Postprocedure, systemic heparin, and subsequent oral anticoagulation with warfarin was given to all the patients for 6 months. Thrombophilic profile workup was done in all the patients to decide about long-term anticoagulation.



Figure 5. MR venograms time of flight images showing the thrombosis of the left transverse sinus (arrows in A and B)

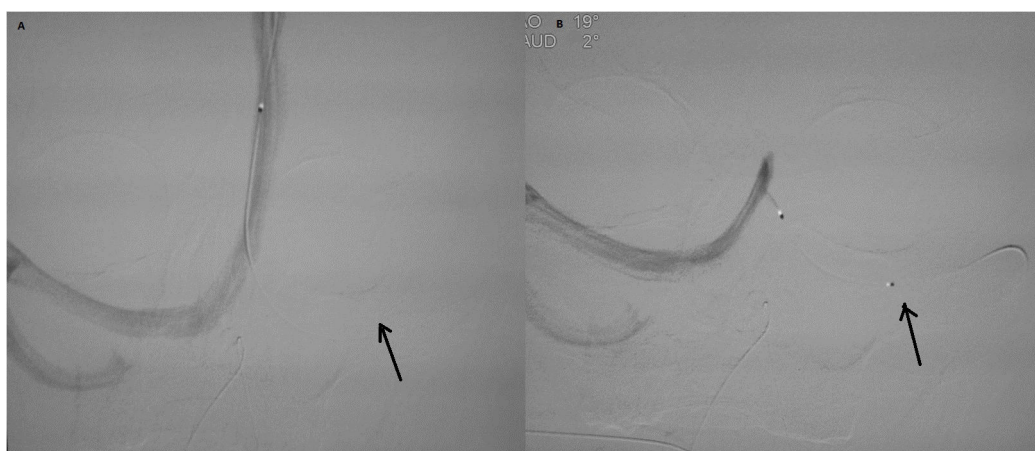


Figure 6. Microcatheter venograms (A, B) showing the thrombosed left transverse sinus (arrows) with no outflow.

Table 2. Causes or risk factors.

Risk factor	Number of patients
Oral contraceptives	8
Postpartum	3
Infection	4
Iron deficiency anemia	3
Hyperhomocysteinemia	5
Dehydration	3
No risk factor	4

RESULTS

Twenty-nine patients, 17 males and 12 females, were treated with a mean age of 36.5 years [19–54]. Risk factors of the patients were listed in the Table 2.

The Glasgow coma scale of the patients ranged from 5 to 11 (mean of 8) in the series.

All the patients presented with headache vomiting and altered sensorium. Eleven patients had seizures at presentation. Nine patients had neurological deficits (monoparesis in 2, hemiparesis in 3 and hemiplegia in 4)

because of underlying venous infarcts. Duration of presentation varied between 12 to 72 h. Superior sagittal sinus (sss) was the commonest sinus involved. SSS alone was affected in six patients, transverse sinus (TS) alone in four patients, SSS with unilateral TS in 15 patients and SSS and straight sinus (ss) was involved in four patients.

Mean duration of infusion was 13.5 h (11–16 h).

Technical success was 100 % with good recanalization seen in all the cases. Good improvement is seen in 24 patients, partial improvement is seen in three patients and one patient succumbed because of edema causing increased midline shift and transtentorial herniation. LIST was done as a last therapeutic option in this patient.

At one month follow-up, 24 patients has MRS of 0 or 1, three patients had MRS of 2 and one patient had MRS of



Figure 7. Post-LIST venograms showing the recanalized left transverse sinus (arrow in A) with good outflow into the jugular (arrow in B).

3 (residual limb weakness). At 6 months follow-up, 26 patients were asymptomatic and two patients had minor subjective symptoms. All the patients received oral anti-coagulation for 6 months.

DISCUSSION

Cerebral venous strokes due to CVST, unlike in arterial strokes, are more common in younger population with an incidence of less than 1% [1,2].

LIST was first reported by Scott et al., where they infused urokinase into superior sagittal sinus via frontal burr hole [10]. Later, many studies were reported describing the use of endovascular thrombolysis using urokinase in CVST with good outcome [7,8,9,10,11]. In our present series, we used tpa as the thrombolytic agent in all the patients after initial mechanical maceration of the thrombus.

The criteria of choosing patients were based on INR KEM criteria as described in Table 1 [9]. Our institution is a tertiary care center. All the patients were already on systemic heparinization when they came to our center. LIST is immediately advocated in grade 4 and grade 5 patients. In mild grade patients, LIST is advocated if there is deterioration despite heparin (e.g., development of fresh neurological deficit, stupor, and coma)

Early therapeutic intervention is important especially in severe grade patients, since there may be difficult in the navigation of microcatheter as encountered by several authors [7,9]. Mechanical laceration favored progression of microcatheter through the clot in our experience. Thrombus disruption also increased the surface of thrombus exposed to the drug and rapid recanalization. Mechanical suction with angiojet, rheolytic thrombec-

tomy, and penumbra aspiration catheters were described by few authors [12,13].

Occlusion of venous drainage in these patients causes back pressure effect resulting in venous infarcts and raised intracranial pressure (ICP) due to failure of CSF absorption by arachnoid villi. Longstanding high ICP leads to irreversible brain damage. Unlike in arterial stroke, there is no correlation between extent of recanalization and clinical outcome. Even partial recanalization resulting increased venous outflow decreases ICP and causes significant clinical improvement.

The concentration of the lytic agent reaching the clot by intravenous thrombolysis is very low as compared to the direct sinus infusion, which increases the efficacy of the drug treatment thus favoring rapid action and clot lysis. We used tpa in our study, which was well tolerated by all the patients. It is associated with fewer bleeding complications when compared with urokinase due to clot selectiveness and shorter half-life. Kim et al., and Frey et al., used tpa in a series of nine and 122 patients [14,15]. A mean total dose of 135 and 46 mg was used in these series and total recanalization was aimed in their studies.

Intracranial hemorrhage is a known complication of LIST. None of our patients had new hemorrhage because of thrombolysis. Mechanical laceration favored use of lower dose of tpa as compared to other studies and recanalization is faster when compared to urokinase. One patient (grade 5) who succumbed despite thrombolysis had increased edema because of pre-existing hemorrhagic infarct and developed transtentorial herniation.

Rapid and sustained recovery is seen in majority of our patients with LIST. Our study highlights the benefit of thrombolysis and mechanical clot laceration, particularly

in severe grade patients, and in patients unresponsive to anticoagulation. There are no randomized controlled series in the literature comparing the efficacy of endovascular therapy versus systemic anticoagulation. Our series is a retrospective analysis which is a major limitation of the study.

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