Cerebral venous thrombosis: local thrombolysis

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Although local thrombolysis, both pharmacological and pharmacomechanical, seems to restore flow more frequently and more rapidly than heparin alone in cerebral venous sinus thrombosis, there are no data confirming better clinical outcome. Systemic intravenous thrombolytics have been tried with mixed success and are seldom currently used[1–6]. Assessment of treatments is made difficult by the rarity of the disease and the frequency of spontaneous recovery[7–10]. A particular difficulty in evaluation of local thrombolysis is that heparin, generally considered beneficial[7,10–12] and safe[7,10,11,13], is part of that treatment and not readily separated.

TECHNIQUES

Local pharmacological thrombolysis was first reported by Scott *et al.*[14] in 1988, who infused urokinase directly into the superior sagittal sinus over 11 hours via a midline frontal burr hole. The patient, at first decerebrate, improved rapidly over three days and was only mildly dysphasic with short-term memory difficulties at four weeks.

Currently, local thrombolysis of the cerebral venous sinuses is usually performed via the femoral route in a fully heparinized patient. A guide catheter is advanced into the jugular bulb and a microcatheter and wire are coaxially manipulated retrogradely through the guide catheter to the site of thrombus. Thrombolytic agent, either urokinase or recombinant tissue-type plasminogen activator (rt-PA), is delivered directly into the clot after some inevitable mechanical disruption of the clot by catheter and microguide wire. Either bolus hand injections or infusions are used. The objective in most cases is complete recanalization but unpublished experience in my own institution suggests that complete recanalization is not necessary for a good outcome. Heparin is usually continued post-procedure and the patient is subsequently anticoagulated with warfarin.

Pharmacomechanical thrombolysis combines pharmacological thrombolysis with mechanical fragmentation of the clot to increase the surface area exposed to thrombolytic agent. This is achieved with a balloon catheter or microsnare device; the latter is a microcatheter with a wire loop at the end which can be extruded and retracted, so macerating the thrombus. The technique may be painful and theoretically increases the risk of complications; perforation of the sinus could be catastrophic.

Catheter-mediated thrombectomy with a saline jet vacuum device has been described in two case reports and is used in conjunction with local pharmacological thrombolysis[15,16]. This device, originally marketed for management of thrombosed dialysis grafts, has also been used in coronary thrombectomy. A clinical trial to evaluate its use in carotid artery occlusion is underway. It consists of a double-lumen 5F catheter tapering to 3.5F: its size alone creates potential difficulty in navigating the catheter to the site of thrombus. Once it is in place, high-velocity saline jets are directed through one lumen, connected to a bag of heparinized saline. A Venturi effect breaks up the thrombus and the debris is directed down the other lumen and collected in a bag. This device theoretically has the advantage of eliminating larger volumes of thrombus more quickly but preclinical evaluation suggests that it can result in mild focal injury to blood vessels.

EVALUATION

Thrombolytic agents are plasminogen activators converting plasminogen to plasmin, which dissolves fibrin in blood clots, producing soluble fibrin degradation products. At our institution we use rt-PA in preference to urokinase because it has a greater affinity for plasminogen bound to fibrin than to circulating plasminogen and thus has less systemic effect. It has a short half-life of 4–5 minutes, is not antigenic and produces fewer fibrinogen degradation products than other thrombolytic agents. Fibrinogen degradation products themselves have an anticoagulant effect. Recanalization is also faster with rt-PA than with urokinase[17].

There are several case reports[18–28] and small series (involving 5–18 patients)[29–34] reporting encouraging results. However, the variability of disease and absence of controlled trials make the efficacy of local thrombolysis impossible to assess. Entry criteria for thrombolysis range from coma, on the one hand, to headaches and papilloedema with normal brain parenchyma on the other. Duration of symptoms varies from under 1 hour[31] to six months[29]. The thrombolytic agent may be delivered by

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bolus injections only, bolus plus infusion or a pulse spray technique via side-hole catheters. Sometimes the thrombus is additionally macerated. Infusions into the thrombosed dural sinus have continued for as long as 244 hours[29] and the dose of thrombolytic agent varies enormously: quantities of rt-PA administered range from 23 to 300 mg and urokinase from 470 000 to 13 790 000 iu. The endpoint in most cases has been complete clot lysis but good outcomes have been achieved with only partial recanalization at the time of the procedure[11,13,20,22].

Local pharmacological thrombolysis is not always successful. I have personal experience of a patient in whom the microcatheter and wire could not be navigated through the thrombus, presumably because of its age and degree of organization. This patient had a good outcome after ventriculoperitoneal shunting and anticoagulation. Others have reported similar cases[31,34,35]: 2 patients were successfully managed with anticoagulation[34,35] but a third died of pulmonary embolism[31].

In other types of thrombosis we know that the older the clot the more difficult it is to lyse. In patients with myocardial infarction, the best chance of recanalization occurs within 3 hours. The response of pulmonary emboli to urokinase delivered into the central veins is most dramatic within a few days after embolism, before the clot adheres to the vessel wall and acquires surface endothelium[36]. Of the 10 patients I have treated, 7 had a good outcome but 3 died despite thrombolysis. The 2 who died had been diagnosed late and were comatose on arrival with extensive thrombosis involving the deep and cortical veins and cerebral oedema. One had haemorrhagic venous infarction. If there is extensive involvement of the cortical veins, thrombolysis of the major dural sinuses is presumably futile. Might infusion of thrombolytic agent into the internal carotid arterial circulation be of more benefit in these patients? The third patient, confused and very drowsy before thrombolysis, had a rethrombosis 15 hours post-procedure and became comatose with extensive haemorrhagic venous infarction. Others have reported rethrombosis following thrombolysis[15].

COMPLICATIONS

Minor bleeding at the femoral puncture site and transient haematuria are complications of the technique. More serious systemic complications include retroperitoneal haemorrhage[31,32] and intracranial haemorrhage[34]. I have seen intracranial haemorrhagic changes post-thrombolysis in 3 patients. In one there was no clinical change and she made a good recovery. The other 2, in coma, died from venous infarction and severe extensive venous sinus thrombosis unresponsive to local thrombolysis. Presumably in these the haemorrhagic changes were secondary to venous infarction. A fatal pulmonary embolus is also reported[31], and at my institution one patient has complained of pleuritic pain post-procedure.

CONCLUSION

Heparin remains first-line therapy for cerebral venous sinus thrombosis and thrombolysis should be considered only if there is neurological deterioration despite adequate anticoagulation. Cerebral oedema and haemorrhagic venous infarction are not contraindications. The optimal method is not known, and I urge fellow neuroscientists to participate in the International Study on Cerebral Vein and Dural Sinus Thrombosis, headed by Professor Jose Ferro at the Hospital Santa Maria, Lisbon. It is hoped that 70–100 centres will recruit 500 patients by the end of the year 2000 and thus obtain reliable data on natural history, risk factors, prognostic factors, current treatment, complications and outcomes and subsequently to identify a subset of patients at risk of incomplete recovery—a target population for future therapeutic trials.

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