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INTRODUCTION AND DEFINITION

Thrombolysis (fibrinolysis) is the phenomenon by which preformed thrombi are lysed by a complex series of events, the most important of which involves the local action of plasmin confined within the substance of the thrombus. The procedure involves the infusion of fibrinolytic agents to activate plasminogen to plasmin thereby converting insoluble fibrin into soluble fibrin degradation products. Initial clinical experience involved high-dose intravenous infusions of fibrinolytic agents for the purpose of lysing thrombi or thromboemboli that usually were remote from the site of infusion. Local or catheter directed thrombolysis involves the infusion of thrombolytic agents into the clot. Advantages over systemic therapy include:

- (A) reduced dose and faster action because the drug is released within the clot (the drug is in the thrombus),
- (B) decrease infusion times,
- (C) decreased dosage of fibrinolytic agent,
- (D) delay of onset of hazardous systemic lytic state,
- (E) fewer haemorrhagic complications and
- (F) less cost. Currently available fibrinolytic agents include: streptokinase, urokinase, and tissue plasminogen activator (tPA).

RADIOLOGIST QUALIFICATIONS

That Physicians involved in the performance, supervision and interpretation of regional thrombolysis should be Diagnostic Radiologists and must have a Fellowship or Certification in Diagnostic Radiology with the Royal College of Physicians and Surgeons of Canada and/or the Collège des médecins du Québec. Also acceptable are foreign Specialist qualifications if the Radiologist so qualified holds an appointment in Radiology with a Canadian University.

As new imaging modalities and interventional techniques are developed additional clinical training, under supervision and with proper documentation, should be obtained before radiologists interpret or perform such examinations or procedures independently. Such additional training must meet with pertinent provincial/regional regulations. Continuing professional development must meet with the requirements of the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

INDICATIONS AND CONTRAINDICATIONS

INDICATIONS

The use of fibrinolytic agents for arterial or venous thrombosis is undergoing constant revision as further experience and results of the technique become available. As with any interventional procedure, the indication for lytic treatment is based on the clinical status of the patient, the potential risk of lytic therapy versus alternative (surgical) treatment, and estimates of the potential for success. The following is a list of indications generally accepted by experienced interventional radiologists as of 1995.

- acute arterial thrombosis of native artery or venous bypass graft
- post angioplasty or catheter-induced thrombosis
- acute peripheral emboli not easily assessed by surgery
- pre-angioplasty (ulcerative plaques)
- bypass graft thrombosis 4 weeks after implantation
- recent thrombosis of dialysis grafts
- acute thrombosis in large veins (SVC, IVC, brachycephalic, axillary, and iliac veins).
- massive pulmonary embolism

- pharmacangiography: in diagnosis of occult gastrointestinal hemorrhage refractory to routine angiographic detection

CONTRAINDICATIONS

Absolute

- active internal bleeding
- signs of irreversible limb ischemia
- recent stroke (6 hr - 2 months)
- intercranial neoplasm or recent (2 months) craniotomy

Relative

- recent surgery (10 days) including biopsy
- recent gastrointestinal bleeding
- recent trauma
- recent cardiopulmonary resuscitation
- severe uncontrolled hypertension (diastolic > 125 mm/mercury).
- subacute bacterial endocarditis
- coagulopathy
- pregnancy
- severe cerebrovascular disease
- non-hemorrhagic stroke less than 6 hrs. old
- when there is risk of distal e.g. occluded left subclavian artery origin
- diabetic haemorrhagic retinopathy

APPROACH AND METHODS

Local thrombolytic therapy should be approached as a cooperative effort with a vascular surgeon. Two important considerations regarding potential for successful lysis include getting the catheter into the clot and the ability to cross the occluded segment with a guidewire. The supervising interventional radiologist must be available at all times and be informed of any change in the patient's status. The patient should be closely observed in an intensive care unit or other high intensity nursing unit for evidence of local or remote bleeding, maintenance of the arterial line, function of the infusion pumps, and changes in coagulation factors. Patients are re-evaluated angiographically at 4 to 12 intervals. The use of concomitant intravenous heparin remains controversial but it is used to prevent pericatheter thrombosis and extension of the thrombus. PTT levels are kept at 2 to 2.5 times normal. Baseline laboratory studies required include the following: haemoglobin and haematocrit, platelet count, prothrombin time and partial thromboplastin time, serum fibrinogen, BUN and creatinine. PT, PTT, fibrinogen levels and fibrin split products are obtained when appropriate. The fibrinolytic agent should be reduced in amount or discontinued if hemorrhagic complications ensue or fibrinogen levels fall below 100mg/%.

CHOICE OF AGENT

Tissue plasminogen activator is currently an investigational drug and is not approved for use in non-coronary thrombolysis. The two agents commonly available are streptokinase and urokinase. Because of the disadvantages of streptokinase (antigenicity, unpredictability of action, high incidence of haemorrhage and complications) urokinase is preferred.

CATHETERIZATION AND INFUSION TECHNIQUES

- requires high quality diagnostic angiogram
- placement of catheter into thrombus until antegrade flow is established
- infusing length of thrombus with multiside hole or co-axial catheter system
- with long segment occlusions, start proximally and advance catheter distally monitoring the patient with arteriography
- endpoint: lysis of clot; re-establishment of flow; treatment of any underlying stenosis by surgery/angioplasty; major complication, lytic stagnation defined as prolonged lack of progression
- continued anticoagulation - ? appropriate anticoagulation

DOSES

The literature is replete with various doses and regimens for administration of intraclot urokinase. Low-dose infusions (60-100,000 units/hour) are considered for venous clot or intraarterial clot when patients are at low risk for tissue infarction.

High-dose infusions (250,000 units/hour x 4 hours decreased to 60-100,000 units/hour until complete lysis) are considered when more rapid lysis is desired. Infusion times can vary from 4 to 48 hours. the longer the infusion, the higher the dose and the more likely the onset of the systemic lytic state. Another approach is pulsed spray pharmacomechanical thrombolysis using special catheters with split holes. The end hole is

occluded with a wire and via a side hole adaptor concentrated urokinase is forcibly injected into the thrombus until complete clot lysis is obtained.

COMPLICATIONS

The most common complication of regional thrombolysis is hemorrhage. Major hemorrhage (defined as bleeding requiring transfusion, surgical intervention, or discontinuation of thrombolytic infusion) is seen in approximately 7% of cases and usually occurs locally at the catheter insertion site or in the region of infusion. In one-fourth of the cases, clinically significant bleeding occurred at a remote site, including 0.55% intracranial bleeding.

An additional 6% of patients developed minor bleeding, usually requiring only local compression for control. Death related to thrombolytic infusion occurred in 0.8% of cases and was usually always related to either remote bleeding or the re-perfusion syndrome. The following table lists complications in 1787 reported cases and compiled by Gardiner and Sullivan and represents the expected rate of complication.

Complication Incidence

- major bleeding 6.6%
- minor bleeding 6.3%
- embolization 5.2%
- thrombosis 3.1%
- death 0.8%
- re-perfusion syndrome 0.7%
- vessel wall dissection 0.6%
- acute renal failure 0.3%
- sepsis 0.2%
- myocardial infarction 0.2%
- myoglobinuria

References

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4. LeBlang SD, Becker GJ, Benenati JF, Katzen BT, Sallee SS. Low-dose urokinase regimen for the treatment of lower extremity arterial and graft occlusions: Experience in 132 cases. J. Vascular Interventional Radiol. 1992; 3:475-483
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