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Clinical Guide - Thrombolytic Therapy in Children (Reviewed 2006)

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INDICATIONS

Systemic thrombolytic therapy is indicated for arterial occlusions, massive pulmonary embolism, pulmonary embolism not responding to heparin therapy and threat of organ or limb viability. It may also be indicated for acute, extensive deep vein thrombosis.

In neonates less than 6 months of age with arterial occlusion following cardiac catheterization, thrombolytic therapy must be used with caution. Begin unfractionaled heparin as per protocol. If possible perform a head CT or cranial ultrasound prior to initiating lytic therapy. If avulsion or dissection of the vessel in question is diagnosed consult cardiovascular/plastic surgery immediately. If the viability of the limb is in doubt then all investigations and consultation should be expedited. Modifications for individual clinical circumstances may be necessary.

Thrombolytic therapy in children should be initiated and monitored by Medical Services or individuals with expertise in this area.

CONTRAINDICATIONS

Contraindications for thrombolytic therapy include active bleeding, significant potential for local bleeding (e.g. tumour surrounding vessel with clot), general surgery within the previous 10 days, neurosurgery within the previous 3 weeks, hypertension, AV malformations, and recent severe trauma. However in some patients, the need for thrombolytic therapy necessitates treatment despite the contraindications.

PRECAUTIONS

No intramuscular injections during therapy.

Minimal manipulation of the patient ie. no bathing, physiotherapy.

Avoid concurrent use of warfarin or antiplatelet agents.

No urinary catheterization, rectal temperatures, or arterial punctures.

Blood samples from a superficial vein or indwelling catheter. If blood sampling is difficult, insert an indwelling catheter for blood samples prior to thrombolytic therapy.

PREPARATION FOR INFUSION

CBC, platelet count, INR, APTT, fibrinogen. Cross and type for 1 unit of PRBC.

Admit to the pediatric intensive care unit or a designated floor identified for thrombolytic therapy.

Consider sedation depending on the child and clinical circumstances.

Sign for head of bed indicating patient is receiving thrombolytic therapy.

Have the following available in case of localized bleeding: compresses (4x4).

Notify blood bank to ensure factor VIIa FFP and cryoprecipitate are available.

Ensure good venous access for drug administration and for monitoring purposes. Consider central venous line placement prior to initiating therapy.

THROMBOLYTIC THERAPY

a) Tissue Plasminogen Activator (tPA) Dose

Use heparin at 10 U/kg/hr during tPA infusion. If patient is not already on heparin, start infusion but do not give a bolus dose. Administer FFP 10-20 mL/kg i.v. q 8-12 hours as a plasminogen source either before starting lytic therapy or simultaneously if thrombus is threatening of life, organ viability or limb viability.

Give t-PA as an infusion at a rate of 0.5 mg/kg/hr intravenously for 6 hours.There are small non controlled studies in the literature suggesting that lower doses of t-PA may be effective.

Re-evaluate radiographically following 6 hours of tissue plasminogen activator infusion (for arterial thrombi use the return of pulses and BP to pre-investigation values).

b) Recombinant Urokinase may be effective but controlled studies have not been done in children to determine dosing, safety or efficacy. Please check with hospital Pharmacy.

c) Streptokinase is not recommended in children.

MONITORING

Monitor the response to thrombolytic therapy by the PT/INR, APTT, and fibrinogen level 4 hours following the onset of the infusion and every 6-8 hours thereafter. If possible measure the plasminogen level at the end of the 6 hour infusion and/or prior to proceeding to another course of therapy.

Expect the fibrinogen concentration to decrease by at least 20-50%; maintain the fibrinogen concentration at approximately 1.0 g/L or higher by infusions of cryoprecipitate (1U/5kg) or fibrinogen concentrate.

If the fibrinogen concentration is less than 1.0 g/L and the patient is still receiving an infusion of tissue plasminogen activator, decrease the dose of the thrombolytic agent by 25%.

If there is no change in the fibrinogen concentration, check D-dimer to ensure that a thrombolytic state has been established.

Maintain the platelet count greater than $100x10^9$/L.

If a patient has received thrombolytic therapy for more than 6 hours, consider treating with heparin alone for 24 hours before reinstituting thrombolytic therapy. There may be ongoing thrombolysis even in the absence of continued administration of the thrombolytic agent.

HEPARIN THERAPY

Concurrent heparin therapy is recommended for all thrombolytic agents.

Use 10 u/kg/hr of heparin during t-PA infusion and increase to therapeutic dose when t-PA infusion is discontinued.

If heparin administration was discontinued during thrombolytic therapy, restart heparin infusion whenever thrombolytic therapy is stopped and the fibrinogen concentration is greater than 1.0g/dL. Do not give a bolus and aim for prolongation of the aPTT as per the heparin protocol (see heparin protocol).

COMPLICATIONS OF THERAPY

Bleeding may occur in 30-50% of patients - usually this is oozing from a wound or puncture site and should be treated with local pressure and supportive care.

If severe bleeding, stop the infusion of thrombolytic agent and heparin. Consider administration of factor VIIa (discuss with Hematology). Administer cryoprecipitate (usual dose of 1 unit/5 kg) to increase the fibrinogen concentration. Fresh frozen plasma may also be indicated in the presence of severe bleeding if factor VIIa is not administered.

If life threatening bleeding: stop the infusion of thrombolytic agent, strongly consider administration of factor VIIa. If factor VIIa is not administered infuse cryoprecipitate as above, and reverse the lytic process by infusing tranexamic acid (Cyklokapron) 10 mg/kg IV bolus. The administration of croprecipitate and tranexamic acid can be repeated q 8 hours. Protamine sulfate may be required to reverse the heparin.

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