Clinical Guideline No.: CG335

Peripheral catheter directed thrombolysis (CDT) with alteplase Clinical Guideline

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Contents

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1. Introduction

Alteplase is a thrombolytic medication used for the dissolution of arterial or venous, thrombus or emboli. Peripheral catheter directed thrombolysis (CDT) is a procedure used to deliver the thrombolytic directly to the location of the thrombus/embolus.

2. Background

This guideline has been developed jointly by the Vascular Surgery Departments of SALHN and CALHN to assist in the safe administration and management of alteplase during peripheral catheter directed thrombolysis.
The use of alteplase for catheter directed thrombolysis is an 'off-label' indication. The following guideline has been developed based on primary literature, published guidelines, expert opinion and clinical experience.

3. Definitions

CDT: Catheter directed thrombolysis
TIA: Transient ischaemic attack
CPR: Cardiopulmonary resuscitation
FBC: Full blood count
EUC: Electrolytes, urea & creatinine
LFT: Liver function test
APTT: Activated partial thromboplastin time
INR: International normalised ratio
SBP: Systolic blood pressure
PE: Pulmonary embolus
SALHN: Southern Adelaide Local Health Network
CALHN: Central Adelaide Local Health Network

4. Principles of the standards

The following National Safety and Quality Health Service Standards apply:

Standard 1- Governance for Safety and Quality in Health Care
Create integrated governance systems that maintain and improve the reliability and quality of patient care, as well as improve patient outcomes.

Standard 4- Medication Safety
Ensure competent clinicians safely prescribe, dispense and administer appropriate medicines to informed patients and carers.

5. Safety, quality and risk management

National Safety and Quality Health Service Standards

 National Standard 1 Clinical Governance	 National Standard 2 Partnering with Consumers	 National Standard 3 Preventing & Controlling Healthcare-Associated Infection	 National Standard 4 Medication Safety	 National Standard 5 Comprehensive Care	 National Standard 6 Communicating for Safety	 National Standard 7 Blood Management	 National Standard 8 Recognising & Responding to Acute Deterioration
☒	☐	☐	☒	☐	☐	☐	☐

6. Pathway / Protocol

Decision for CDT will be made by the treating consultant vascular surgeon.

Informed consent must be obtained (on a standard consent form) and a patient information leaflet should be provided: http://www.anzsvs.org.au/patient-information/thrombolysis/

GENERIC NAME: Alteplase

SYNONYMS: Recombinant tissue plasminogen activator, tPA

TRADE NAME: Actilyse®

PRESENTATION:
10mg vial of powder for dilution. Supplied with diluent vial of water for injection.
50mg not required for CDT.

CLINICAL USES:
Decision for CDT will be made by the treating consultant vascular surgeon.
Peripheral arterial thromboembolism
Deep vein thrombosis

ACTION:
Thrombolytic agent. Activates plasminogen by converting it to plasmin to initiate fibrinolysis.

6.1 Contraindications/Precautions

CONTRAINDICATIONS:

Absolute contraindications	Relative contraindications
• Hypersensitivity to alteplase, gentamicin or to the excipients • Active internal bleeding or disseminated intravascular coagulopathy • Significant bleeding disorder at present or within the past 6 months • Cerebrovascular event (including TIA), neurosurgery (intracranial or spinal) or intracranial trauma within the last 3 months • History of intracranial haemorrhage or subarachnoid haemorrhage • Intracranial neoplasm or other neoplasm with increased bleeding risk • Gastrointestinal bleeding within 10 days • Presence/development of compartment syndrome • Absolute contraindication to anticoagulation	• Severe uncontrolled hypertension (>160 systolic or >90 diastolic) • Arterial aneurysms, arterial/venous malformations (including cerebral) • Gastrointestinal bleeding >10 days and <3 months • Major surgery, trauma or CPR within 14 days (caution within 3 months) • Recent internal haemorrhage, puncture of non-compressible artery or organ biopsy • Recent eye surgery (<3 months) • Diabetic haemorrhagic retinopathy • Gastrointestinal diseases with potential sources of bleeding • Patients currently receiving oral anticoagulants eg warfarin, apixaban, rivaroxaban or dabigatran • Blood coagulation defects or thrombocytopenia (platelets <100x10^9/L) • Severe hepatic insufficiency- decision made by treating consultant with consultation from liver specialist if required • Acute pancreatitis, pericarditis, bacterial endocarditis, sepsis or suspicion of septic emboli • Life expectancy < 1 year • Pregnancy or lactation

PRECAUTIONS:

- Access site complications are common during/after thrombolysis
  - Recommend care with arterial/venous access (ultrasound guidance recommended)
  - Manual compression of puncture site ≥30 minutes after cannula removal
  - Regular access site observations after compression
- Inability to tolerate prolonged arterial catheterisation eg unable to lie flat for a prolonged period of time (>12 hours) ie back pain, heart failure
- Severe renal impairment increases the risk of contrast induced acute kidney injury
  - Alteplase dose is unchanged in renal impairment[3]

6.2 Preparation

PREPARATION:

- Reconstitute 10mg vial with 10mL of the diluent provided. Add the diluent using the transfer cannula provided or a large bore needle (18 gauge). Swirl gently until completely dissolved. DO NOT SHAKE vigorously. Allow to stand for several minutes to dissipate large bubbles[1].
- The 10mg/10mL solution should be diluted in 500ml of 0.9% sodium chloride[2]
- Label bag as per labelling guidelines.

Resultant concentration 0.02mg/mL[2]

STABILITY:
Up to 24 hours at room temperature[2]

COMPATIBILITY:
0.9% Sodium chloride
Limited information. No other medication should be added to the prepared infusion solution[1].

BASELINE TESTS (prior to treatment):
Full blood count (FBC)
Coagulation studies (coags)
Group and save
Electrolytes, urea & creatinine (EUC), liver function tests (LFTs)
Observations- vascular, neurological, vital signs, temperature, pain score

6.3 Procedure

Preparation for CDT:

Prior to commencement of CDT

1) Ensure the shift coordinator of the receiving ward is aware of the planned CDT to arrange staffing allocation/requirements
2) IDC and 2 large bore IV lines to be placed

After CDT catheter placement in angiography suite

3) Catheter and sheath side arm to be labelled as per labelling guidelines in the angiography suite upon placement of lines
4) Vascular or interventional radiologist team performing procedure to prescribe alteplase infusion
5) Infusions to be connected in angiography recovery by the vascular surgeon, registrar or interventional radiologist and a senior nurse in concert with receiving ward nurse prior to transfer to the ward
6) Use only threaded lock cannula connections

Prior to transfer to receiving ward

7) Document medications to be withheld while patient receiving thrombolysis
8) Stress ulcer prophylaxis (eg pantoprazole 40mg daily, oral or IV) should be prescribed at initiation of thrombolysis and continued until discharge.

6.4 Dosage

CATHETER (intra-arterial or intra-venous)
Alteplase bolus:
5mg bolus, may repeat if required.
Maximum bolus of 20mg (ie 4x5mg bolus).

Alteplase infusion:
See 'Preparation' section on page 6 for preparation
Run at **25mL/hour** of diluted solution (=0.5mg/hour)
Rate may be increased to a maximum of 50ml/hr of diluted solution (=1mg/hr) at the discretion of the treating surgeon.

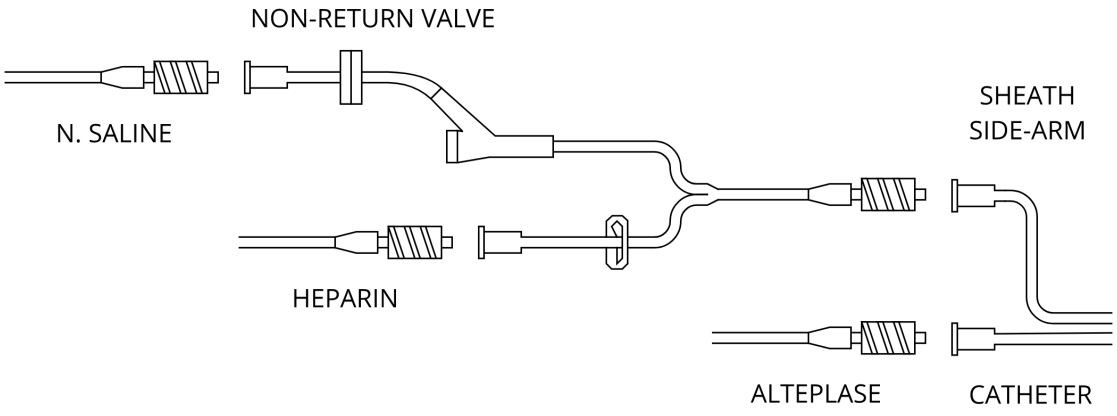
Note: Treatment for venous thromboembolism may require the higher dosing regimen at the discretion of the treating surgeon.

Maximum total dose: 50mg (including bolus doses)

SHEATH side arm
Heparin infusion, to prevent peri-catheter thrombus formation:
25,000units/50ml unfractionated heparin syringe (=500units/mL)
Run **heparin** at **1mL/hour** (=500units/hour)
'Piggy back' 500mL bag of 0.9% sodium chloride onto heparin syringe. (See instructions below)
Run saline at 10mL/hour
THIS IS A SUBTHERAPEUTIC INFUSION. APTT SHOULD **NOT** BE THERAPEUTIC.
Reduce rate if APTT>60 seconds (consult vascular registrar)
This heparin infusion must be prescribed on a variable dose infusion chart or fluid chart.
Do not use "heparin infusion chart for systemic anticoagulation".
Therapeutic anticoagulation is not recommended while using alteplase CDT for venous thromboembolism[16,20,45,47]

Instructions for set up of heparin syringe with saline 'piggy back':

1. Attach heparin syringe and prime microbore line
2. Attach microbore line to interlink extension with non- return valve on the non-valve/clamp side
3. Prime interlink extension to y-site with heparin
4. Prime pump line with 0.9% sodium chloride
5. Attach pump line to interlink extension with non-return valve on the valve side
6. Finish priming extension with sodium chloride
7. Attach distal end of pump line to the sheath side arm
8. Commence heparin and sodium chloride infusions



Note:

- Alteplase and heparin are incompatible via the same access device due to precipitation.
- Do not give oral anticoagulants (warfarin, apixaban, rivaroxaban or dabigatran) or low molecular weight heparin (enoxaparin or dalteparin) while running CDT due to the increased risk of haemorrhage.
- Do not give IM injections while undergoing CDT and for 24 hours after cessation.

6.5 Observations

Monitoring during CDT infusion:

1) Nurse to patient ratio is 1:1 for the first 4 hours then reassess for potential 1:2 ratio for duration of infusion
2) Ensure baseline tests have been performed- see 'Preparation' section on page 6
3) Check patient identification, infusion program and lines on return to ward- 2 nurse check
4) Rate changes and reference ranges under direct supervision of the vascular registrar on call.
5) All rate and bag changes to be checked by 2 nursing staff
6) Blood pressure to be taken manually
7) Patient must rest in bed and lie flat while catheter/sheath are in place.
8) Strict 2-3 hourly pressure area care, keeping affected limb with catheter in situ as straight as possible. Consider a pressure reducing mattress
9) Mobility orders after removal of catheter as per vascular team
10) Fluid balance chart

Observation	Frequency
Neurovascular observations of affected limb Monitor catheter insertion site for bleeding/haematoma Check all line connections	Every 15 minutes for 2 hours then every 30 minutes for 4 hours then if stable hourly
Blood pressure (manual), pulse, temperature, respiratory rate, neurological observations, pain score, sedation score	Hourly for 4 hours then if stable 4 hourly
Blood tests: EUC, FBC, APTT*, INR and fibrinogen level**	4 hours after return to ward and then daily (or as ordered by MO)

*If APTT therapeutic (>60sec) decrease rate of heparin infusion
**If fibrinogen <1g/L consider FFP, reducing dose or stopping thrombolysis

Complication	Action
Major bleeding or haemodynamic or neurologic instability	STOP INFUSION and notify vascular registrar immediately
Haemorrhage/haematoma at access site	Apply local pressure (no sandbag) and notify medical officer and vascular registrar immediately
Deteriorating neurovascular observations or increased pain in either limb	Notify vascular registrar
Tachycardia (pulse>100), hypertension (SBP>160mmHg) or headache	Notify vascular registrar

FOLLOW UP ANGIOGRAPHY:
Patient will require follow up angiography within 24 hours of thrombolysis initiation
Repeat check angiography every 24 hours while CDT continues
Check with registrar or consultant for hydration protocol
Patient to be fasted from solids for 2 hours prior (can have clear fluids) or as advised
Routine post angiography observations

6.6 Adverse reactions

Very Common: Haemorrhage (puncture site and wound)

Common: Haemorrhage (including intracerebral, gastrointestinal), haematuria, fever, chills, nausea, vomiting

Uncommon: epistaxis, hypotension, urticaria, bronchospasm
Rare: hypersensitivity/anaphylaxis (refer to local Anaphylaxis management guideline for treatment)

Unknown incidence: cholesterol embolism, embolism formed through thrombus degradation (including PE)

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8. Document Ownership & History

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