

Bon Secours Richmond
Pharmacy & Therapeutics Committees
Catheter Clearance Protocol
3/06

Recommendation(s):

- The initial dose of Cathflo will be the priming volume of the catheter lumen up to 1 ml (1 mg/ml). If the catheter volume is greater than 1 ml normal saline will be used to fill the remainder of the catheter. If catheter patency is not established in 60 minutes an equal volume of alteplase will be re-instilled, up to 1 ml (1mg/ml). The same vial will be used for the initial and follow up dose.
 - The policy for clearing occluded venous access device will be amended.
- When orders are written for CathFlo (alteplase) may repeat x1, the pharmacist will only send one 2 mg dose (2 mg/2ml). Nursing will call pharmacy if another vial is needed.

Findings:

- Catheter clearance rates increase with longer dwell times. The catheter should not be disturbed for a minimum time of 1 hour after instillation of the thrombolytic.
- Partial occluded catheters have a lower clearance rate than completely occluded catheters.
- Cathflo (alteplase) may be used for 8 hours following reconstitution when stored between 36-86 degrees F.
- The priming volume of most central venous is less than 1 ml resulting in alteplase wastage (see attached).
- 1 mg of alteplase is approximately equivalent to 36,000 units of urokinase.
- The minimum dose of alteplase required to open an occluded catheter has not been determined, but 0.5 mg is effective.
- The catheter lumen volume had no apparent impact on 1 mg alteplase dose success rate in permanent hemodialysis catheters.
- Protocol
 - Instill a volume of alteplase equal to the priming volume of the catheter, up to 1 mg (1 ml). If the catheter volume is greater than 1 ml, instill sufficient amount of NS to fill internal volume of each catheter.
 - Do not premix alteplase and normal saline.
 - Wait 60 minutes, then attempt to aspirate.
 - If catheter is still occluded repeat above steps.
- Definitions of catheter occlusion
 - Complete: inability to infuse fluid and to aspirate blood
 - Partial: ability to infuse fluids but not to aspirate blood

Cost Analysis For One Year							
	Dose	Cost per Dose	RCH	MRMC	SFMC	SMH	Totals
Cathflo 1 mg/ml-2 ml vial	2 mg	\$58.00	23	508	74	989	1594
			\$1,334.00	\$29,464.00	\$4,292.00	\$57,362.00	\$92,452.00

Lumens	Fink N=61	Haymond N=50	Eyrich N=63	Davis N=66	Package Insert N=150	Package Insert N=995
Reference	Annals of Pharmacotherapy 2004;38:351	Journal of Vascular Access 2005;6:76-82	American Journal of Health System Pharmacist 2002;59:1437-40	American Journal of Health System Pharmacist 2000;57:1039-45		
Study Type	Randomized, unblinded	Open label	Retrospective review	Open label dose escalation	Randomized double blind Placebo control	Open label single arm
Catheter Type(s)	Single, double, triple lumen tunneled catheters or implanted ports 33% Implanted ports 67% tunneled catheters	Hemodialysis permanent tunneled Central Venous Catheters, lumen >= 2 ml 78% 1.5-1.9 ml 20% < 1.5 ml 2%	Hemodialysis permanent and temporary tunneled central venous catheters	PICC 31 (53.5%) Tunneled 18 (31%) CVC 6 (10.3%) Implantable Port 2 Midline 1 <i>No hemodialysis catheters</i>		
Outcome Measure	Restoration of catheter function after 1 hour dwell time	Restoration of catheter function after 1 hour dwell, blood flow rate > 300 ml/min	Restoration of catheter function after 1 hour dwell, blood flow rate > 300 ml/min	Restoration of catheter function after 1 hour dwell time	Restoration of catheter function after 2 hour dwell	Restoration of catheter function at 0.5 and 2 hours post dose
Drug & Dose	Alteplase 1 mg/ml Alteplase 2 mg/2ml after one or two dose with a 1 hour dwell after each dose	Alteplase 1 mg/ml after one or two doses with a 1 hour or 48-72 hour dwell	Alteplase 1 mg/ml versus urokinase 5000 units/ml with a 1 hour dwell	Alteplase 0.5 mg Alteplase 1 mg Alteplase 2 mg with a 1 hour dwell, dose escalation if not functioning	Alteplase 2 mg after one or two doses with a 2 hour dwell	Alteplase 2 mg After one or two doses with a 2 hour dwell
Outcome				Alteplase 0.5 mg 86.2% (34/50) after 1 hour dwell		
Outcome 1ml of 1mg/ml tPA	Alteplase 1 mg 81.3%(30/37) after one dose at 1 hour 85.5% after one or two doses at 2 hours	Alteplase 1 mg 72%(35/50) after 1 dose at 1 hour 83% (40/48) after two doses at 2 hours	70% (30/43) 1 mg at 1 hour Repeat treatment required in 5%	Alteplase 1 mg 94.8% (47/50) after 1 hour dwell	N/A	N/A
Outcome 2 mg of 1 mg/1 ml tPA	Alteplase 2 mg 83.3% (20/24) after one dose at 1 hour 87.5% (21/24) after one or two doses at 2 hours	N/A	35% (7/20) Urokinase 5000 units at 1 hour P=0.13 Repeat treatment required in 15%	Alteplase 2 mg 96.5% (48/50) after 1 hour dwell	Alteplase 2 mg 1 st dose 67% (51/76) at 2 hours 2 nd dose 88% (112/127) at 2 hours	Alteplase 2 mg 1 st dose 52% (512/995) at 0.5 hour 75% (747/995) at 2 hours 2 nd dose 82% (817/995) at 0.5 hour 85% (844/995) at 2 hours

Definition of non-functioning catheters: inability to withdraw at least 3 ml of blood from the device or flow rates less than 300 ml/minute for hemodialysis catheters.

Definition of catheter occlusion in Davis article: *complete*, an inability to infuse fluids and to aspirate blood; *partial*, an ability to infuse fluids but not to aspirate blood.

[Pediatr Nephrol.](#) 2006 Feb;21(2):300. Epub 2005 Oct 27.

Tissue plasminogen activator for blocked peritoneal dialysis catheters.

[Krishnan RG](#), [Moghal NE](#).

Ward 10, Department of Paediatric Nephrology, Royal Victoria Infirmary, Newcastle upon Tyne, NE12 5BL, UK, raj.krishnan@nuth.nhs.uk.

Tissue plasminogen activator was used for a blocked peritoneal dialysis catheter in a child with no vascular access. The catheter was salvaged using tissue plasminogen activator and dialysis could be carried out without any difficulty.

PMID: 16252099 [PubMed - in process]

[Hemodial Int.](#) 2005 Apr;9(2):189-95.

Short and long alteplase dwells in dysfunctional hemodialysis catheters.

[Macrae JM](#), [Loh G](#), [Djurdjevic O](#), [Shalansky S](#), [Werb R](#), [Levin A](#), [Kiaii M](#).

Division of Nephrology, St Paul's Hospital, Univeristy of British Columbia, Vancouver, British Columbia, Canada. jmmacrae@hotmail.com

BACKGROUND: Hemodialysis catheter dysfunction (CD) is the inability to attain adequate blood pump speeds (BPS) and is attributed to thrombus or catheter malposition; alteplase (TPA) is often given in a variety of dwell times to treat CD. The purpose of this study was to determine if TPA dwell time affects short- or long-term catheter patency rates. **METHODS:** Sixty hemodialysis (HD) patients with CD, as defined by BPS of < 250 mL/min, were randomized to receive either 1- or > 48-hr (to subsequent HD run) TPA dwell. The primary outcomes were catheter patency (BPS of > 250 mL/min) at the subsequent HD run and catheter patency at 2 weeks. The secondary outcome was the time from study entry to the next catheter intervention (including subsequent TPA installation). **RESULTS:** After TPA installation, a 78% overall catheter patency rate was observed at the subsequent HD run, falling to 48% patency at 2 weeks. There is no statistically significant difference between the short and long TPA dwell groups for catheter patency at the subsequent HD run (76.9% vs. 79.4%) or at 2 weeks (42.3% vs. 52.9%). Multivariate analysis demonstrates that the use of TPA on two or more previous occasions is a predictor of TPA failure both at the subsequent HD run and at 2 weeks. TPA installation achieves a median catheter function time of only 14 days, after which CD reoccurs. **CONCLUSION:** This study demonstrates that although patency for the next HD run can be achieved with either short or long TPA dwell, neither is reliable in terms of long-term patency. Strategies that employ TPA for CD are temporary and allow a 2-week window during which more definitive therapies for HD access should be sought.

Publication Types:

- [Clinical Trial](#)
- [Randomized Controlled Trial](#)

PMID: 16191068 [PubMed - indexed for MEDLINE]

[EDTNA ERCA J.](#) 2005 Apr-Jun;31(2):75-8.

Analysis of rt-PA infusion in tunnelled dialysis catheters.

[Davies J](#), [Casey J](#), [Li C](#), [Crowe AV](#), [McClelland P](#).

Renal Unit, Wirral Hospital NHS Trust, Merseyside, UK.

Urokinase and streptokinase are commonly used thrombolytic agents for obstructed central venous catheters. Although proven to be efficacious, these agents have the potential to induce fibrin breakdown and streptokinase cannot be used repeatedly due to its allergenic nature. Documented evidence suggests that urokinase is safe and effective (> 70% efficacy for catheter installation) however further evidence points to tissue-type plasminogen activator (rt-PA) achieving as much as 98% success. This study reports on the safety and efficacy of alternative catheter thrombolysis, namely rt-PA and evaluates the efficacy of rt-PA. 20 patients required 57 infusions in 38 lumens between 01/01/02 to 01/09/03. For completely blocked lines rt-PA was infused at 2 mg/hr for 4 hours achieving 85% success rate. For inadequate flow (< 250 mls/min) rt-PA was infused at 1 mg/hr for 4 hours achieving 88% success rate.

PMID: 16180551 [PubMed - indexed for MEDLINE]

[Pediatr Nephrol.](#) 2005 Jul;20(7):989-93. Epub 2005 Apr 21.

Recombinant tissue plasminogen activator infusion for hemodialysis catheter clearance.

[Bamgbola OF](#), [del Rio M](#), [Kaskel FJ](#), [Flynn JT](#).

Department of Pediatrics, Division of Pediatric Nephrology, Oklahoma University Health Science Center, 940 NE 13th Street, Oklahoma, OK 73104, USA. Fatai-Bamgbola@OUHSC.edu

Hemodialysis (HD) catheter occlusion is a common cause of poor blood flow and inadequate dialysis. In order to address this problem in our pediatric dialysis unit, we elected to use short (2-h) infusions of low-dose recombinant tissue plasminogen activator (rtPA) for thrombolysis of occluded catheters. Catheters meeting diagnostic criteria for thrombosis were infused with 2.5 mg rtPA in 25 ml 0.9 normal saline over 2 h prior to dialysis. Retrospective data collection was carried out to assess the success of this procedure. Variables assessed included blood flow (Qb), transmembrane pressure (TMP) and venous pressure (VP) before and after rtPA infusion. Seven catheter thromboses in six patients were successfully treated with rtPA; there were significant improvements in Qb ($p < 0.01$), TMP ($p < 0.01$), and VP ($p < 0.02$). At 32 weeks after rtPA therapy, Kaplan-Meier survival analysis showed a 60% probability of primary catheter patency. At the end of the study, 85% of catheters had adequate function as defined by a Qb > 200 ml/min. No adverse events were observed. Low-dose rtPA infusion is safe and effective for catheter thrombolysis in outpatient pediatric HD patients. It may serve as an alternative method of administration to local instillation and may be used to restore patency before resorting to surgical revisions.

PMID: 15843999 [PubMed - indexed for MEDLINE]

[CANNT J.](#) 1999 Fall;9(4):25-8.

Tissue plasminogen activator (t-PA) efficacy in the restoration of hemodialysis catheter function.

[Meers C](#), [Toffelmire EB](#).

End Stage Renal Disease Care Services, Kingston General Hospital, Ontario.

Thrombus formation within hemodialysis catheters contributes to inadequate dialysis and adverse patient outcomes. A thrombolytic agent may be required to restore patency and improve blood flow. This study evaluates the efficacy of instilling low dose (1 mg/ml) t-PA in catheter lumens to restore patency in malfunctioning catheters. t-PA was utilized to treat suspected catheter thrombus over a four-month period. Seventeen patients with 21 catheters (12 temporary, 9 permanent) received 40 doses of t-PA. Catheter function was restored in 39 of 40 cases (97.5%). Significant improvement in blood flow was confirmed by paired t-test ($p < 0.001$). Sustained improvement in blood flow was confirmed by ANOVA ($p < 0.001$). The mean primary patency of all catheters was 29.7 days (SD = 27.0 days). No adverse patient effects were noted. These results demonstrate that t-PA can safely and effectively restore blood flow and extend patency in hemodialysis catheters.

PMID: 15714785 [PubMed - indexed for MEDLINE]

[J Clin Pharm Ther.](#) 2004 Dec;29(6):517-20

Restoration of flow following haemodialysis catheter thrombus. Analysis of rt-PA infusion in tunnelled dialysis catheters.

[Davies J](#), [Casev J](#), [Li C](#), [Crowe AV](#), [McClelland P](#).

Wirral Hospital NHS Trust, Arrowe Park Hospital, Upton, Wirral, Merseyside, UK.

PROBLEM: Urokinase and streptokinase are commonly used thrombolytic agents for obstructed central venous catheters. Although proven to be efficacious, these agents have the potential to induce fibrin breakdown and streptokinase cannot be used repeatedly because of its allergenic nature. Published evidence suggests that Urokinase is safe and effective ($> 70\%$ efficacy for catheter installation) and that Tissue-type plasminogen activator (rt-PA) can achieve as much as 98% success. **OBJECTIVE:** To describe our experience with and our protocol for the use of rt-PA as an alternative agent for catheter thrombolysis. **DESIGN:** Investigation of a cohort of haemodialysis patients with tunnelled central venous catheter (SPCVC) placed between December 2001 to August 2003 and who developed catheter thrombus (female, $n = 8$; male, $n = 12$). Each patient was given an infusion of between 1 and 2 mg rt-PA/h for 4 h. The dose was dependent on partial or total line

obstruction. The technical success of rt-PA is defined as returning catheter blood flow to >250 mL/min for a 4-h period. FINDINGS: Twenty patients required 57 infusions in 38 lumens between 01/01/02 to 01/09/03. For completely blocked lines rt-PA was infused at 2 mg/h for 4 h achieving 85% success rate. For inadequate flow (<250 mL/min) rt-PA was infused at 1 mg/h for 4 h achieving an 88% success rate. CONCLUSION: Rt-PA administered at 2 mg/h for blocked lines effectively restores haemodialysis catheter patency, and at 1 mg/h for sluggish lines is also effective in restoring blood flow through catheters.

PMID: 15584939 [PubMed - indexed for MEDLINE]

[Am J Health Syst Pharm.](#) 2004 Sep 15;61(18):1922-4.

Establishing an alteplase dosing protocol for hemodialysis-catheter thrombosis.

[Nguyen TV, Dikun M.](#)

Holy Name Hospital, 718 Teaneck Road, Teaneck, NJ 07666, USA. nguyen@mail.holyname.org

PMID: 15487882 [PubMed - indexed for MEDLINE]

[Nephrol Nurs J.](#) 2004 Mar-Apr;31(2):199-200.

The use of tissue plasminogen activator infusion to re-establish function of tunneled hemodialysis catheters.

[Dowling K, Sansivero G, Stainken B, Siskin G, Dolen E, Ahn J, Mitchell N.](#)

Albany Medical College, Vascular Institute for Health and Disease, Albany, NY, USA.

PURPOSE: To evaluate the safety and efficacy of the recombinant tissue plasminogen activator alteplase in the clearance of poorly functioning tunneled hemodialysis catheters. METHODS: We retrospectively reviewed the outcomes of 25 patients who presented with poorly functioning hemodialysis catheters and were treated with alteplase. After confirming fluoroscopically the need for thrombolytic therapy, alteplase was administered over 2 hours as a 2.5-mg/hour/catheter lumen infusion (total 10 mg). Treatment was considered a clinical success if a flow rate of 250 mL or more per minute was established. RESULTS: Clinical success was achieved in each of 25 patients (100%). There were no thrombolytic-related complications. Catheter survival was extended 30 days in 54% of patients and 45 days in 33% of patients. CONCLUSION: Alteplase is a safe and effective means of producing clearance of blocked tunneled catheters.

PMID: 15114800 [PubMed - indexed for MEDLINE]

[Nephron Clin Pract.](#) 2004;96(2):c39-42.

The efficacy and safety of reteplase for thrombolysis of hemodialysis catheters at a community and academic regional medical center.

[Hyman G, England M, Kibede S, Lee P, Willets G.](#)

New Hanover Regional Medical Center, Wilmington, NC, USA. ghyman@ec.rr.com

In occluded hemodialysis catheters, thrombolytic agents are used to dissolve fibrin clots, reestablish blood flow and allow the patient to continue with hemodialysis treatment. Prior to 2001, urokinase was the indicated fibrinolytic for hemodialysis catheter thrombolysis. However, when urokinase became unavailable in the United States, New Hanover Regional Medical Center developed and implemented a protocol for the use of another fibrinolytic, reteplase, to lyse catheter occlusions. The purpose of this retrospective analysis was to assess the safety and efficacy of reteplase in opening occluded catheters in a series of patients receiving hemodialysis. Between January 1 and June 30, 2002, 59 patients could not complete dialysis, because of either poor arterial blood flow or elevated venous resistance. Reteplase, 0.4 U, was administered to the lumen of occluded catheters. After 30 min dwell times, the lumens were aspirated. If flow could not be sufficiently reestablished, a second reteplase dose was administered. Efficacy endpoints were defined as the ability to complete hemodialysis and achieve flow rates of > or =250 ml/min. Safety endpoints were defined as the occurrence of allergic reactions or bleeding. Eighty-five percent (50/59) of the patients were able to complete their hemodialysis session following reteplase administration, with 70% (41/59) able to sustain blood flow rates of > or =250 ml/min. Of the 50 patients who successfully completed dialysis, 66%

(33/50) required only one 0.4-unit dose of reteplase per lumen while 34% (17/50) required a second dose. No instances of bleeding or allergic reactions were noted. Copyright 2004 S. Karger AG, Basel

PMID: 14988596 [PubMed - indexed for MEDLINE]

[Clin Nephrol.](#) 2004 Jan;61(1):47-53.

Efficacy of reteplase in poorly functioning hemodialysis catheters.

[Falk A](#), [Samson W](#), [Uribarri J](#), [Vassalotti JA](#).

Department of Radiology, Division of Nephrology, The Mount Sinai-NYU Medical Center, New York, NY, USA.
abigailfalk123@pol.net

AIM: This is a retrospective study of reteplase efficacy for restoration of flow in occluded and poorly functioning hemodialysis catheters. PATIENTS AND METHODS: From May 1, 2001 to December 31, 2001, all hemodialysis patients seen at our university dialysis center with occluded or poorly functioning (< 200 ml/min blood flow) catheters treated with reteplase were included in the study. All catheters had been in place for more than 48 hours. Reteplase 0.4 U was instilled into each port; dwell time was 30 minutes. If aspiration had not been possible, reteplase had remained in the catheter for an additional 30 minutes. If flow was established (> 200 ml/min), the catheter was used for dialysis. If flow was not adequately established after 1 hour, the patient was referred for catheter exchange. RESULTS: Reteplase (0.4 U) was used in 50 instances to restore or improve blood flow rates in a total of 23 catheters in 19 patients. Reteplase was effective in establishing adequate blood flow rates during the current and next dialysis session in 44/50 (88%) cases; 6 cases required 1-hour dwell time. Six cases (in 5 patients) required catheter exchange; in these, an anatomic or pathologic complication was responsible for catheter malfunction. No adverse events were related to reteplase instillation during the study. CONCLUSION: Data suggest that reteplase is safe and effective in restoring flow to malfunctioning hemodialysis catheters. Results are comparable to those achieved with alteplase.

PMID: 14964457 [PubMed - indexed for MEDLINE]

[Ann Pharmacother.](#) 2003 Jan;37(1):27-33.

Alteplase versus urokinase for occluded hemodialysis catheters.

[Zacharias JM](#), [Weatherston CP](#), [Spewak CR](#), [Vercaigne LM](#).

Department of Internal Medicine, Section of Nephrology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.

BACKGROUND: The use of central venous catheters as a source of vascular access in patients undergoing hemodialysis may be complicated by thrombosis. Frequently, thrombolytics are used in an attempt to reestablish blood flow through partially or completely occluded catheters. OBJECTIVE: To compare the efficacy of alteplase (recombinant tissue plasminogen activator) versus urokinase in reestablishing adequate blood flow through partially or completely occluded vascular catheters. METHODS: Part 1 of the study prospectively investigated the effect of alteplase in reestablishing adequate blood flow through partially or completely occluded vascular catheters in 30 hemodialysis patients. Part 2 of the trial compared the efficacy of alteplase with that of urokinase in 14 of 30 patients who had also previously received urokinase. A 30-minute push-protocol was used to administer thrombolytics in both parts of the study. The primary endpoint was the proportion of patients with partially or completely occluded catheters achieving post-thrombolytic blood flow of > or =200 mL/min. RESULTS: Part 1 showed a large proportion of partially or completely occluded catheters achieving post-alteplase blood flows > or =200 mL/min (70/76, 92.1% vs. 34/40, 85%, respectively). In Part 2 of the study, the proportion of partially occluded catheters achieving post-thrombolytic blood flows > or =200 mL/min was not significantly different between the alteplase and urokinase groups, (36/41, 87.8% vs. 21/28, 75%, respectively; p = 0.205). The proportion of completely occluded catheters achieving post-thrombolytic blood flows > or =200 mL/min was significantly better with alteplase compared with urokinase (15/17, 88.2% vs. 6/14, 42.8%, respectively; p = .018). CONCLUSIONS: Alteplase, administered via the 30-minute push-protocol, is an effective thrombolytic for restoring hemodialysis catheter patency. In our study sample, alteplase was generally more effective than urokinase in restoring blood flow through catheters, especially those that were completely occluded.

PMID: 12503929 [PubMed - indexed for MEDLINE]

[Nephrol Nurs J.](#) 2002 Aug;29(4):355-60; quiz 361-2.

Lytic therapy in central venous catheters for hemodialysis.

[McFarland HE](#), [Dinwiddie L](#), [Ferrell J](#), [Forloines-Lynn S](#).

Nephrology Department, UNC School of Medicine in Chapel Hill, NC, USA.

Over the past 2 decades the use of central venous catheters (CVCs) for hemodialysis has become commonplace. While these devices have provided much needed temporary access to the bloodstream, they often become thrombosed and require procedures to restore patency. This article examines the lytic enzymes that are currently available and focuses on the assessment and treatment of thrombosis.

Publication Types:

- [Review](#)

PMID: 12224368 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol](#). 2002 Aug;13(8):775-84.

Alteplase for hemodialysis access graft thrombolysis.

[Sofocleous CT](#), [Hinrichs CR](#), [Weiss SH](#), [Contractor D](#), [Barone A](#), [Bahramipour P](#), [Brountzos E](#), [Kelekis D](#).

Department of Radiology, UMDNJ-New Jersey Medical School, Newark, New Jersey 07103, USA. constant@pol.net

PURPOSE: To evaluate the efficacy and safety of alteplase, a recombinant tissue plasminogen activator, in hemodialysis access graft thrombolysis. **MATERIALS AND METHODS:** From November 1999 to May 2001, 68 episodes of occlusion in 50 grafts (in 49 patients) were included in the study. Occlusion was treated with pulse-spray (n = 41) or lyse-and-wait (n = 27) thrombolysis with use of alteplase. Balloon angioplasty of all identified stenoses was performed. The arterial plug was mobilized with the Fogarty maneuver. **RESULTS:** Procedural success was achieved in 64 of 68 episodes (94%) with a dose of 2-10 mg (mean = 4.13 mg) of alteplase, allowing successful hemodialysis within 24 hours. Failures (6%) were the result of PTA perforation (one of 68), nonnegotiable outflow occlusion (one of 68), delayed bleeding (one of 68), and balloon bursting and shearing becoming occlusive within the graft (one of 68). Primary and secondary patency rates were 72% and 87% at 30 days, 57% and 80% at 90 days, and 44% and 72% at 180 days, respectively. Arterial emboli (two of 68) were treated by Fogarty balloon retrieval and alteplase infusion locally over the course of 20 minutes. One of two PTA perforations was controlled by balloon tamponade. **CONCLUSION:** Alteplase can be used successfully for hemodialysis graft thrombolysis.

PMID: 12171980 [PubMed - indexed for MEDLINE]

[Am J Health Syst Pharm](#). 2002 Aug 1;59(15):1437-40.

Alteplase versus urokinase in restoring blood flow in hemodialysis-catheter thrombosis.

[Eyrich H](#), [Walton T](#), [Macon EJ](#), [Howe A](#).

Department of Pharmacy and Drug Information, Grady Health System, 80 Jessie Hill Jr. Drive, Atlanta, GA 30303, USA.

The effectiveness of alteplase and urokinase in restoring adequate hemodialysis blood-flow rates was examined. A retrospective review of the medical records of hemodialysis patients with central venous catheters receiving alteplase or urokinase for presumed catheter thrombosis between June 1997 and December 2000 was conducted. Patients received 1 mL of alteplase 1 mg/mL or 1 mL of urokinase 5000 units/mL in each catheter port. The choice of the thrombolytic agent was left to the prescriber. Effectiveness of thrombolysis was defined as achieving a posttreatment hemodialysis blood-flow rate of > 300 mL/min, maintained for at least 30 minutes during the dialysis session. Inclusion criteria included adherence to the thrombolytic protocol and the inability to achieve a hemodialysis blood-flow rate of > 300 mL/min during the first 60 minutes of the hemodialysis session despite at least one attempt to reposition the catheter. Both thrombolytic agents significantly increased the hemodialysis blood-flow rates. Patients with alteplase-treated catheters were twice as likely to achieve hemodialysis blood-flow rates of > 300 mL/min (p = 0.0134) and were more likely to complete hemodialysis during that session (93% versus 70%, p = 0.0234). The percentage of functioning catheters at a subsequent hemodialysis session did not significantly differ between groups (p = 0.0806). The majority of patients in both treatment groups required no further interventions. Hemodialysis blood-flow rates increased after either alteplase 1 mg/mL per port or urokinase 5000 units per port was used to clear presumed catheter thrombosis. Alteplase was more likely than urokinase to result in a hemodialysis blood-flow rate of > 300 mL/min.

PMID: 12166043 [PubMed - indexed for MEDLINE]

[Am J Kidney Dis](#). 2002 Jan;39(1):86-91.

A longitudinal study of the repeated use of alteplase as therapy for tunneled hemodialysis catheter dysfunction.

[Little MA](#), [Walshe JJ](#).

Department of Nephrology and Transplantation, Beaumont Hospital, Dublin, Ireland.

When hemodialysis catheters allow only poor or no blood flow, it has become established practice in many centers to instill a thrombolytic agent in an attempt to clear the catheter. The catheter survival advantage gained by repeated use of such treatment is not known. In a prospective study, we analyzed all uses of alteplase in the setting of inadequate catheter blood flow in a cohort of 570 catheters over a 2(1/2)-year period. The time from alteplase instillation to the next episode in which it was required or catheter removal for nonfunction or thrombosis was recorded. Survival analysis was used to estimate the additional catheter survival afforded by each treatment. After censoring for elective catheter removal, the overall catheter half-life was 10.2 months. Catheter malfunction or thrombosis was the most common indication for catheter removal (36.3% of all catheters removed). Alteplase instillation was necessary in 2.77% of dialysis sessions. The median time from the first to second treatment or catheter removal for nonfunction or thrombosis was 27 days (95% confidence interval, 15.7 to 32.3). Additional median survival advantage gained from each subsequent treatment ranged from 10 to 18 days. Treatment of recurrent catheter malfunction with alteplase allows for a median of only five to seven additional dialysis sessions before the treatment must be repeated or the catheter must be exchanged. Although associated with minimal disruption to the dialysis schedule, the ultimate clinical benefit and cost-effectiveness of such treatment is doubtful. Copyright 2002 by the National Kidney Foundation, Inc.

PMID: 11774106 [PubMed - indexed for MEDLINE]

[AJR Am J Roentgenol](#). 2001 Aug;177(2):317-8.

A rapid low-cost uncrossed sheath method for clearing thrombosed hemodialysis grafts.

[Strauss EB](#), [Delman BN](#), [Maitem A](#).

Department of Diagnostic Radiology, Section of Interventional Radiology, Norwalk Hospital, Maple St., Norwalk, CT 06856, USA.

PMID: 11461852 [PubMed - indexed for MEDLINE]

[J Thromb Thrombolysis](#). 2001 Apr;11(2):127-36.

Thrombolysis for restoration of patency to haemodialysis central venous catheters: a systematic review.

[Clase CM](#), [Crowther MA](#), [Ingram AJ](#), [Cina CS](#).

Division of Nephrology, Dalhousie University, Halifax, Nova Scotia, Canada. catherine.clase@dal.ca

Urokinase, previously used to restore patency to thrombosed haemodialysis catheters, is now unavailable in North America. We performed systematic reviews of four questions related to the safety and efficacy of alternative agents for catheter thrombolysis, searching Medline and the Cochrane Controlled Clinical Trials Register. In dialysis patients, large case series have documented that urokinase is safe and effective (>70 % efficacy for catheter instillation, and >80 % for systemic lysis). Experience with streptokinase is limited and allergic complications develop with repeated use. Studies of catheter instillation with 1--2 mg of tPA per lumen reported short-term success in 83--98 % of uses. One non-peer-reviewed study described 44--59 % success using systemic tissue plasminogen activator (tPA), 2.5 mg through each of 2 lumens, over 1 h. Meta-analysis of randomized comparisons of urokinase and tPA as full-dose thrombolytic agents suggested that 1 mg tPA was likely equivalent in thrombolytic potency to 36,000 units urokinase. In nondialysis populations, four case series suggested that catheter instillation with 0.5--2 mg tPA was effective and safe in reestablishing patency, and a randomized controlled trial found 2--4 mg tPA more effective than 5,000--10,000 units urokinase. No complications have been reported in any patient treated with systemic or local tPA for catheter thrombolysis. In studies of fistula thrombolysis with 5--50 mg tPA major complications occurred in one episode in 130 patients treated. This review suggests that 1--2 mg/lumen tPA is a suitable dose for catheter instillation and likely to be more effective than 5000 units/lumen urokinase. Systemic lysis with 5--10 mg tPA is likely to be safe and effective in suitably selected patients. Further studies are needed.

Publication Types:

- [Meta-Analysis](#)

PMID: 11406727 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol](#). 2001 Jun;12(6):711-5

Treatment of hemodialysis catheter-associated fibrin sheaths by rt-PA infusion: critical analysis of 124 procedures.

[Savader SJ](#), [Ehrman KO](#), [Porter DJ](#), [Haikal LC](#), [Oteham AC](#).

Department of Radiology, Methodist Hospital, Indianapolis, Indiana, USA. ssavader@clarian.com

PURPOSE: To prospectively evaluate the efficacy of a low-dose, 3-hour infusion of recombinant tissue plasminogen activator (rt-PA) for the treatment of hemodialysis catheter (HDC)-associated fibrin sheaths. This report expands the authors' experience with this technique over that previously reported. **MATERIALS AND METHODS:** Fifty-five patients with end-stage renal disease (38 women, 17 men) undergoing catheter-directed hemodialysis treatment were evaluated for 124 episodes of HDC dysfunction. This patient group had a mean age of 57 years and an age range of 23-92 years. Radiographic contrast studies and/or clinical evaluation were consistent with the presence of a fibrin sheath on the arterial and/or venous port in all cases. Each patient underwent a thrombolytic infusion consisting of 2.5 mg rt-PA in 50 mL normal saline at 17 mL/h (3-hour infusion) per port. All infusions were performed in the interventional radiology recovery room on an outpatient basis. Patients were followed prospectively for technical success, complications, catheter patency, and long-term outcome. **RESULTS:** The technical success rate, defined as return of effortless manual aspiration and infusion capability from both ports followed by at least one successful dialysis session, was 91%. No patient was excluded from rt-PA therapy because of contraindications, and the procedure-related complication rate was zero percent. A Kaplan-Meier survival analysis yielded primary patency rates at 30, 60, 90, and 120 days of 0.55, 0.36, 0.25, and 0.15 (SE <.10), respectively; secondary patency rates at 60, 120, 180, and 240 days were 0.70, 0.46, 0.30, and 0.27 (SE <.10), respectively (P < 001). At the end of the study period, all 52 surviving patients continued to undergo catheter-directed hemodialysis and 34 (65%) were using the same catheter present at the time of entrance into the study. Of the 18 patients (35%) requiring catheter exchange, 16 (89%) did for persistent malfunction after rt-PA therapy, one (5.5%) for infection, and one (5.5%) for a fractured hub. **CONCLUSION:** Thrombolytic therapy with use of a 2.5-mg rt-PA infusion through each port over a 3-hour period would appear to be a safe method for treating HDC-associated fibrin sheaths. Immediate return of catheter function is achieved in most patients, obviating more invasive techniques. Primary patency rates are relatively short, but catheters that fail can be retreated, resulting in secondary patency rates that are substantial and significantly improved.

[J Vasc Interv Radiol](#). 2001 Mar;12(3):305-11.

Thrombolysis of clotted hemodialysis grafts with tissue-type plasminogen activator.

[Falk A](#), [Mitty H](#), [Guller J](#), [Teodorescu V](#), [Uribarri J](#), [Vassalotti J](#).

Department of Radiology, The Mount Sinai-NYU Medical Center, New York 10029-6574, USA.

PURPOSE: To evaluate prospectively the efficacy of treating thrombosed hemodialysis arteriovenous polytetrafluoroethylene (PTFE) grafts using tissue-type plasminogen activator (tPA) and percutaneous transluminal angioplasty (PTA). **MATERIALS AND METHODS:** Forty-two sequential thrombosed PTFE dialysis grafts in 33 patients presented for declotting. All 42 grafts were treated with a modified lysis and PTA technique with use of 2 mg tPA and 3,000-5,000 U heparin in a total volume of 5 mL, administered into the graft via an angiocatheter. The elapsed time from tPA injection until completion was recorded. Prospective data collection included demographic information, technical details of the procedure, immediate outcomes, complications, and patency rates. **RESULTS:** Technical success, defined as complete graft recanalization with a palpable thrill after treatment plus successful hemodialysis, was achieved in all cases, except five. These five cases were deliberate graft closures due to inadequacy of the outflow veins to support an arteriovenous graft after successful lysis. Mean lysis time was 40.8 minutes and mean room procedure time after the lysis period was 65.4 minutes. Eight procedure-related complications occurred (two major and six minor). The follow-up period was 4-241 days, with an estimated mean of 157 days. The 30-day and 90-day primary patency rates were 57% and 50%, respectively. **CONCLUSIONS:** Treatment of thrombosed PTFE dialysis grafts with use of 2 mg tPA and 3,000 U of heparin is safe and effective. Use of this modified lysis and PTA technique allows an expeditious procedure in the angiography suite. However,

this technique precludes imaging of the outflow veins before treatment, so that grafts entering diffusely diseased veins may need to be closed after successful lysis.

PMID: 11287506 [PubMed - indexed for MEDLINE]

[Int J Artif Organs](#). 2000 Oct;23(10):668-9.

Alteplase (TPA) for clotted dialysis catheters.

[Hathiwala SC](#), [Hristea I](#), [Khalili V](#).

Publication Types:

- [Editorial](#)

PMID: 11075895 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol](#). 2000 Oct;11(9):1131-6.

Hemodialysis catheter-associated fibrin sheaths: treatment with a low-dose rt-PA infusion.

[Savader SJ](#), [Haikal LC](#), [Ehrman KO](#), [Porter DJ](#), [Oteham AC](#).

Department of Radiology, Methodist Hospital, Indianapolis, IN 46202, USA. ssavader@clarian.com

PURPOSE: To prospectively evaluate the efficacy of a low-dose, 3-hour recombinant tissue plasminogen activator (rt-PA) infusion for the treatment of hemodialysis catheter (HDC)-associated fibrin sheaths. **MATERIALS AND METHODS:** Seventeen patients with end-stage renal disease (female, n = 11; male, n = 6), who were undergoing catheter-directed hemodialysis, were evaluated for 28 episodes of HDC dysfunction. This patient group ranged in age from 25 to 92 years (mean, 57 years). Radiographic contrast and/or clinical evaluation were consistent with the presence of a fibrin sheath on either the arterial and/or venous port in all cases. Patients subsequently underwent a thrombolytic infusion consisting of 2.5 mg rt-PA in 50 mL normal saline at a rate of 17 mL/h (3-hour infusion) per port. All infusions were performed in the interventional radiology recovery room, on an outpatient basis. Patients were followed-up prospectively for technical success, complications, catheter patency, and long-term outcome. **RESULTS:** The immediate technical success rate, defined as return of manual aspiration and infusion capabilities to both ports, was 100%. No potential patients required exclusion from thrombolytic therapy secondary to contraindications, and no procedure-related complications occurred. The arithmetic mean and median catheter patency at the end of the study was 41 and 25 days, respectively (range, 1-116 days). A Kaplan-Meier survival analysis yielded a 30-, 60-, and 90-day probability of patency of 0.67, 0.61, and 0.51, respectively. At the end of the study period, all 17 patients remained on catheter-directed hemodialysis and 13 (76%) were utilizing the same catheter present at the time of entrance into the study. **CONCLUSION:** Thrombolytic therapy utilizing a 2.5-mg rt-PA infusion through each port during a 3-hour period would appear to be a safe, efficient method for treating HDC-associated fibrin sheaths. Three-month patency rates are comparable to those reported for other methods of restoring function to HDC catheters, including new catheter placement, catheter exchange over a guide wire, thrombolytic infusions with urokinase, and percutaneous fibrin sheath stripping.

PMID: 11041468 [PubMed - indexed for MEDLINE]

Comment in:

- [Am J Kidney Dis](#). 2001 Feb;37(2):453-4.

[Am J Kidney Dis](#). 2000 Jul;36(1):75-9.

Efficacy of tissue plasminogen activator administration on patency of hemodialysis access catheters.

[Daeiagh P](#), [Jordan J](#), [Chen J](#), [Rocco M](#).

Departments of Internal Medicine and Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC 27157-1053, USA.

Patients with end-stage renal disease use hemodialysis catheters for either temporary or permanent blood access. Recurrent thrombosis and fibrin sheath formation are common causes of poor or inadequate blood flow rates that require intervention. We studied the effect of tissue plasminogen activator (tPA) in reestablishing adequate blood flow rates through nonfunctional vascular catheters in 22 consecutive chronic hemodialysis patients. From January 1, 1999, to May 20, 1999, there were 56 instances in which tPA was used in an attempt to improve blood flow rates. In all instances, 2 mg of tPA was infused into each port of a dual-lumen internal jugular catheter. Dwell time ranged between 2 and 96 hours (median, 24 hours), and patient follow-up ranged between 47 and 140 days (median, 133.5 days). tPA was effective in establishing adequate blood flow rates (≥ 200 mL/min) during the next dialysis session in 49 of 56 cases (87.5%). Seven additional interventions were required because of early or late tPA failure (one fibrin sheath stripping, one catheter replacement for kinking, one catheter replacement for central venous stenosis, and four catheter replacements for persistently poor blood flow rates), and eight catheters were replaced for infection. Thus, further interventions to achieve adequate blood flow rates were required in 12.5% of the cases because of early or late tPA failure. tPA appears to be as effective as urokinase for reestablishing adequate blood flow rates through hemodialysis catheters that are thrombosed or have low blood flow rates.

PMID: 10873875 [PubMed - indexed for MEDLINE]

[Nephron](#). 1993;64(3):468-70.

Use of tissue plasminogen activator for reopening of clotted dialysis catheters.

[Paulsen D](#), [Reisoether A](#), [Aasen M](#), [Fauchald P](#).

Medical Department B, National Hospital of Norway, Oslo.

The use of central venous catheters as permanent vascular access in chronic hemodialysis is complicated by clotting. We have tried a nonallergenic thrombolytic agent, tissue plasminogen activator (t-PA), to dissolve catheter luminal thrombosis. Eight patients, 7 in chronic hemodialysis and 1 treated by immune adsorption had 18 treatments with locally applied t-PA (2 mg/2 cm³). Fifteen out of 16 treatments with longer bolus dwell than 60 min were successful. No side effects occurred. t-PA dissolves clot formation efficiently and safely, the drug is nonallergenic and can therefore be given repeatedly.

PMID: 8341396 [PubMed - indexed for MEDLINE]

[Nephron](#). 1991;59(3):517-8.

Thrombolysis of blocked hemodialysis catheter using recombinant tissue-type plasminogen activator.

[Hannah A](#), [Buttimore AL](#).

Publication Types:

- [Case Reports](#)
- [Letter](#)

[Nephron](#). 1993;64(3):468-70.

Use of tissue plasminogen activator for reopening of clotted dialysis catheters.

[Paulsen D](#), [Reisoether A](#), [Aasen M](#), [Fauchald P](#).

Medical Department B, National Hospital of Norway, Oslo.

The use of central venous catheters as permanent vascular access in chronic hemodialysis is complicated by clotting. We have tried a nonallergenic thrombolytic agent, tissue plasminogen activator (t-PA), to dissolve catheter luminal thrombosis. Eight patients, 7 in chronic hemodialysis and 1 treated by immune adsorption had 18 treatments with locally applied t-PA (2 mg/2 cm³). Fifteen out of 16 treatments with longer bolus dwell than 60 min were successful. No side effects occurred. t-PA dissolves clot formation efficiently and safely, the drug is nonallergenic and can therefore be given repeatedly.

PMID: 8341396 [PubMed - indexed for MEDLINE]

[Nephron](#). 1991;59(3):517-8.

Thrombolysis of blocked hemodialysis catheter using recombinant tissue-type plasminogen activator.

[Hannah A, Buttimore AL.](#)

Publication Types:

- [Case Reports](#)
- [Letter](#)

[Am J Health Syst Pharm](#). 2000 Jun 1;57(11):1039-45.

Activity and dosage of alteplase dilution for clearing occlusions of venous-access devices.

[Davis SN, Vermeulen L, Banton J, Schwartz BS, Williams EC.](#)

Department of Pharmacy, University of Wisconsin Hospital and Clinics, Madison 53792, USA.

The activity and sterility of reconstituted alteplase solution and the effectiveness of an alteplase dose-escalation protocol for the clearance of midline-catheter and central-venous-access device occlusions were studied. Reconstituted alteplase solution was stored at -70, -25, or 2 degrees C at concentrations of 0.5, 1, or 2 mg/mL. Durations of storage in the freezer were 0, 7, and 14 days, and durations of storage in the refrigerator were 0, 48, and 72 hours and 7 and 14 days. Samples were also assayed and cultured without prior freezing after refrigeration at 2 degrees C for 0, 48, and 72 hours and 7, 14, and 28 days. Fifty-eight pediatric and adult patients were enrolled in a separate study in which catheter clearance was initiated with alteplase 0.5 mg, and the dose was escalated to 1 and 2 mg sequentially until the catheter was cleared. The primary endpoint was restoration of catheter patency, and the secondary endpoint was the occurrence of bleeding episodes within 24 hours of alteplase administration. Catheter removal due to failure to restore patency was also documented. The activity and sterility of alteplase were maintained under all conditions studied. Fifty catheters (86.2%) were cleared with alteplase 0.5 mg, 5 (8.6%) after dose escalation to 1 mg, and 1 (1.7%) after escalation to 2 mg. The alteplase solution did not clear the occlusion in 2 catheters (3.4%): 1 had a mechanical obstruction and 1 cleared two hours after the 1-mg dose was deemed a failure. None of the six catheter removals was due to recalcitrant clots. Bleeding observed was not considered to be the result of alteplase administration. For use in clearing occlusions of venous-access devices, alteplase 0.5, 1, and 2 mg/mL retained sufficient fibrinolytic activity when stored for up to 14 days at 2 degrees C (28 days for the 0.5-mg/mL dilution) and when stored for 14 days at -70 or -25 degrees C followed by up to 14 days at 2 degrees C. The dose-escalation protocol was effective.

PMID: 10876745 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol](#). 2002 Dec;13(12):1199-205.

Treatment of occluded central venous catheters with alteplase: results in 1,064 patients.

[Semba CP, Deitcher SR, Li X, Resnansky L, Tu T, McCluskey ER; Cardiovascular thrombolytic to Open Occluded Lines Investigators.](#)

Department of Vascular Medicine, Genentech, South San Francisco, CA 94080, USA. cpsemba@gene.com

PURPOSE: Thrombosis of central venous access devices (CVADs) is a relatively frequent complication. Alteplase (tissue plasminogen activator) has been used to salvage dysfunctional devices. The purpose of this study was to analyze the safety and efficacy of alteplase after administration of a maximum of two 2-mg/2-mL doses to thrombosed CVADs. **MATERIALS AND METHODS:** A combined analysis was performed of two pivotal prospective phase-III clinical trials (Cardiovascular thrombolytic to Open Occluded Lines [COOL] Trials) involving 80 centers enrolling patients from November 1999 through December 2000. Patients 2 years of age or older (with body weights >10 kg) with dysfunctional nondialysis CVADs were eligible, including those with peripherally inserted central catheters, apheresis catheters, and ports. Alteplase (2 mg/2 mL) was instilled into the lumen of the central venous catheter and allowed to dwell for as long as 120 minutes. For patients with body weights of 10-30 kg, 110% of the internal lumen volume of alteplase (2 mg/2 mL) was administered. If the device was still occluded after a maximum of 120 minutes, a second alteplase dose was given and allowed to dwell for as long as 120 minutes. The primary efficacy endpoint was designated as restored function after a maximum of two doses. The primary

safety endpoint was intracranial hemorrhage (ICH) within 5 days. RESULTS: A total of 1,064 patients (465 men, 599 women; mean age, 50.7 y; range, 2-91 y) with dysfunctional catheters were treated. After alteplase administration, function was restored in 798 patients (75.0%; 95% CI: 72.3%, 77.6%) after one dose and 905 (85.1%; 95% CI: 82.8%, 87.2%) after two doses. Efficacy rates were similar among catheter types (single-, double-, and triple-lumen catheters, and ports). Serious adverse events monitored within 30 days of treatment included ICH (0.0%), embolic events (0.0%), gastrointestinal bleeding (0.3%), thrombosis (0.3%), and sepsis (0.4%). One event (fever) was attributed to the study drug. Efficacy was independent of age, sex, body weight, and catheter type. CONCLUSION: A regimen of as many as two 2-mg doses of alteplase is safe and effective for restoring flow to occluded central venous access devices.

Publication Types:

- [Clinical Trial](#)
- [Clinical Trial, Phase III](#)
- [Multicenter Study](#)

PMID: 12471182 [PubMed - indexed for MEDLINE]

Comment in:

- [J Pediatr Hematol Oncol. 2003 Jul;25\(7\):589; author reply 589.](#)

[J Pediatr Hematol Oncol. 2003 Jan;25\(1\):38-45.](#)

Recombinant tissue plasminogen activator (alteplase) for restoration of function to occluded central venous catheters in pediatric patients.

[Shen V](#), [Li X](#), [Murdock M](#), [Resnansky L](#), [McCluskey ER](#), [Semba CP](#); [COOL Investigators](#).

Children's Hospital of Orange County, 455 S. Main Street, Orange, CA 92868, USA. vshen@choc.org

PURPOSE: To evaluate the safety and efficacy of alteplase for restoring function to occluded central venous catheters in a pediatric population. PATIENTS AND METHODS: A phase III, open-label, single-arm, multicenter trial was performed in 995 adult and pediatric patients with dysfunctional nondialysis catheters and ports. This report is a subset analysis of subjects between 2 and 18 years of age (N = 122) who were enrolled in the study. Alteplase (2 mg/2 mL) was instilled into the dysfunctional catheter lumen and assessed at 30 and 120 minutes. Subjects weighing > or =30 kg received 2 mL of alteplase; subjects <30 kg received 110% of the internal lumen volume (not exceeding 2 mL). Alteplase dosing was repeated once after 120 minutes if the catheter remained dysfunctional. The primary safety endpoint was the rate of intracranial hemorrhage (ICH) within 5 days of treatment. RESULTS: The overall efficacy following up to two instilled doses of alteplase was 87%. In 70 patients (57%), restoration of catheter flow occurred by 30 minutes following a single dose of alteplase. Restoration of function was related to the duration of occlusion (P = 0.04). For catheters with occlusions of 0, 1 to 14, and >14 days duration, the efficacy was 91%, 78%, and 60%, respectively. Success was independent of the patient's age, sex, body weight, CVC type, or catheter age. There were no cases of death, ICH, major bleeding episodes, or embolic events attributable to treatment. CONCLUSIONS: An alteplase regimen of up to two 2-mg doses is safe and effective for restoration of function to occluded central venous catheters in a pediatric population.

Publication Types:

- [Clinical Trial](#)
- [Clinical Trial, Phase III](#)
- [Multicenter Study](#)

PMID: 12544772 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol. 2001 Aug;12\(8\):951-5.](#)

Recombinant tissue plasminogen activator (alteplase) for restoration of flow in occluded central venous access devices: a double-blind placebo-controlled trial--the

Cardiovascular Thrombolytic to Open Occluded Lines (COOL) efficacy trial.

[Ponec D](#), [Irwin D](#), [Haire WD](#), [Hill PA](#), [Li X](#), [McCluskey ER](#); [COOL Investigators](#).

Division of Radiology, Tri-City Medical Center, Oceanside, California, USA.

PURPOSE: Central venous access devices (CVADs) are a mainstay of current medical therapy but often become occluded by thrombus. Tissue plasminogen activator (alteplase), at a dose of 2 mg per 2 mL, has been shown to be effective in restoring flow to catheters proven by radiographic contrast injection to be occluded by thrombus. The purpose of this double-blind placebo-controlled multicenter trial was to determine the efficacy of alteplase in occluded catheters without earlier contrast injections or radiographic examinations. **MATERIALS AND METHODS:** Patients were eligible for inclusion if blood could not be withdrawn from their catheter after a period of normal function of at least 48 hours. Single or multiple catheters, peripherally inserted central catheters, catheters with valves, and implanted ports were eligible; catheters used for hemodialysis were not included. Patients were randomly assigned to one of two groups. In one group, patients received a first dose of 2 mg alteplase followed, if needed, by a second dose of 2 mg alteplase and a third dose of placebo. The other group received placebo first followed by one 2-mg dose of alteplase and then a second, if needed. Each dose was allowed to dwell for 2 hours and ability to withdraw blood from the catheter was reassessed. The endpoint was restoration of the ability to withdraw and infuse through the catheter. One hundred forty-nine patients were randomized: 74 received placebo first, 75 received alteplase first. **RESULTS:** After the first 2-hour treatment, function was restored to 74% in the alteplase arm and 17% in the placebo arm ($P < .0001$ compared to placebo). After one or two treatments, function was restored in 90% of patients. There were no serious study-drug-related adverse events, no intracranial hemorrhage, no major hemorrhage, and no embolic events. **CONCLUSION:** Infusion of alteplase appeared to be safe and effective in restoring flow to occluded catheters without need for pretreatment radiographic evaluation.

Publication Types:

- [Clinical Trial](#)
- [Multicenter Study](#)
- [Randomized Controlled Trial](#)

PMID: 11487675 [PubMed - indexed for MEDLINE]

[J Clin Oncol](#). 2002 Apr 1;20(7):1918-22.

Safe and cost effective use of alteplase for the clearance of occluded central venous access devices.

[Timoney JP](#), [Malkin MG](#), [Leone DM](#), [Groeger JS](#), [Heaney ML](#), [Keefe DL](#), [Klang M](#), [Lucarelli CD](#), [Muller RJ](#), [Eng SL](#), [Connor M](#), [Small TN](#), [Brown AE](#), [Saltz LB](#).

Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA. timoneyj@mskcc.org

PURPOSE: To determine whether cryopreserved solutions of the thrombolytic agent alteplase could be used as a safe, effective, and economically reasonable alternative to urokinase in patients presenting with occluded central venous access devices (CVADs). **MATERIALS AND METHODS:** Alteplase has been reported as an efficacious alternative to urokinase for treatment of occluded CVADs. However, the practicality of using alteplase as the thrombolytic of choice for this indication remained conjectural. To make this approach economically feasible, alteplase was diluted to 1 mg/mL and 2.5-mL aliquots were stored at -20 degrees C until use. A need to confirm that the cryopreserving and thawing of the reconstituted solution did not compromise the safety and efficacy reported from prior trials was recognized. A quality assessment initiative was undertaken to concurrently monitor the safety and efficacy of this approach. Patients presenting with occluded CVADs received a sufficient volume of the thawed alteplase solution to fill the occluded catheter(s). Data, including efficacy, adverse reactions, dwell time, and catheter type, were collected over a 5-month period. **RESULTS:** One hundred twenty-one patients accounting for 168 attempted clearances were assessable for safety and efficacy. One hundred thirty-six (81%) of the 168 catheter clearance attempts resulted in successful catheter clearance (95% confidence interval, 74% to 86%). No adverse events were reported. **CONCLUSION:** Cryopreserved 1-mg/mL aliquots of alteplase are safe and effective in the clearance of occluded CVADs when stored at -20 degrees C for 30 days. The ability to cryopreserve alteplase aliquots makes it an economically reasonable alternative to urokinase in the setting of CVAD occlusion.

PMID: 11919252 [PubMed - indexed for MEDLINE]

[J Infus Nurs.](#) 2004 May-Jun;27(3):171-4.

The use of alteplase for restoring patency to occluded central venous access devices in infants and children.

[Fisher AA](#), [Deffenbaugh C](#), [Poole RL](#), [Garcia M](#), [Kerner JA Jr](#).

Lucile Packard Children's Hospital, Palo Alto, California 94305, USA.

A 21-month retrospective review was completed at the Lucile Packard Children's Hospital to assess the experience of 22 infants and children who received alteplase for the clearance of occluded central venous access devices. After the first dose, 86% (n = 19) of the catheters cleared. Two additional catheters cleared with a second dose. With alteplase treatment, 95% (n = 21) of the catheters cleared. No adverse events were noted within 24 hours after the alteplase was received. Infusion of alteplase appeared to be safe and effective in restoring patency to occluded central venous access devices in infants and children.

PMID: 15118455 [PubMed - indexed for MEDLINE]

[J Pediatr Hematol Oncol.](#) 2003 Nov;25(11):864-7.

Safety, dose, and timing of reteplase in treating occluded central venous catheters in children with cancer.

[Terrill KR](#), [Lemons RS](#), [Goldsby RE](#).

Department of Pharmacy, Primary Children's Medical Center, University of Utah School of Medicine, Salt Lake City, USA. kelly.terrill@ihc.com

OBJECTIVES: Recombinant tissue plasminogen activator, alteplase, began to be commonly used to restore the patency of occluded central venous catheters (CVCs) as urokinase production was halted in the late 1990s. However, alteplase often requires an extended dwell time to restore patency to occluded CVCs. In adults, reteplase, a newer thrombolytic agent, has been reported to restore patency to CVCs in 30 minutes. The authors prospectively evaluated the safety and efficacy of reteplase in restoring patency to occluded CVCs in children with cancer. **METHODS:** This was a dose escalation trial. The dose of reteplase was initiated at 0.1 units and increased by increments of 0.1 units to a maximum dose of 0.4 units. Each dose was tested on at least three participants. Time to patency after reteplase administration was recorded by nurses caring for the patients. Attempts to access the line occurred every 15 minutes for 1 hour. CVCs that remained occluded after 1 hour were treated with alteplase. **RESULTS:** Reteplase was administered to 15 clotted CVCs. Twelve of the 15 were cleared with an average dwell time of 38 minutes. The time to patency did not appear to correlate with the dose. No adverse events were reported. **CONCLUSIONS:** Reteplase can restore patency to occluded CVCs in a pediatric population. Reteplase appears to have comparable efficacy with alteplase, but reteplase may require shorter dwell times. A prospective, randomized, clinical trial is warranted to determine whether reteplase is as effective as alteplase in restoring patency to occluded CVCs.

Publication Types:

- [Clinical Trial](#)

PMID: 14608195 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol.](#) 2004 Jan;15(1 Pt 1):45-9.

Alteplase for treatment of occluded peripherally inserted central catheters: safety and efficacy in 240 patients.

[Ng R](#), [Li X](#), [Tu T](#), [Semba CP](#).

University of California San Francisco School of Medicine, USA.

PURPOSE: Peripherally inserted central catheters (PICCs) have dramatically improved intravenous therapy, but thrombotic occlusion remains a common problem. Despite the popularity of PICCs, there are few prospective data on the use of fibrinolytic agents to salvage these particular devices. The purpose of this study was to evaluate the efficacy and safety of alteplase treatment. **MATERIALS AND METHODS:** A subgroup analysis was performed from a phase IIIB prospective, multicenter trial of 995 patients evaluating the use of alteplase to restore function in occluded venous catheters. Two hundred forty patients (126 men; mean age, 53.5 years; range, 2-90 y) with occluded single-lumen (n = 104) or double-lumen (n = 136) PICCs were identified and constitute the study population. Dysfunction was defined as the inability to withdraw 3 mL of blood. Alteplase (2 mg/2 mL) was instilled into the dysfunctional lumen and assessed at 30 and 120 minutes. If the lumen remained occluded, a second alteplase dose was instilled and assessed at 30 and 120 minutes. Patency was defined as the ability to withdraw 3 mL blood and infuse 5 mL of saline solution. The primary efficacy endpoint was the cumulative restored patency rate after a maximum of two doses of alteplase. The primary safety endpoint was the incidence of intracranial hemorrhage within 5 days of treatment. Serious adverse events were recorded for 30 days after treatment. **RESULTS:** The primary efficacy endpoint was 92.9% (95% CI: 88.8%, 95.8%). Cumulative efficacy 30 and 120 minutes after first and second doses were 59.4%, 81.1%, 89.1%, and 92.9%, respectively. The primary safety endpoint was 0.0%. One major hemorrhage was reported: a patient with acute flare of ulcerative colitis experienced hematochezia 3 days after treatment. One serious adverse event (fever) was attributed to study drug. **CONCLUSIONS:** Treatment with use of a maximum of two doses of alteplase is safe and effective in restoring function to occluded PICCs.

Publication Types:

- [Clinical Trial](#)
- [Clinical Trial, Phase III](#)
- [Multicenter Study](#)

PMID: 14709686 [PubMed - indexed for MEDLINE]

[Int J Artif Organs](#). 2000 Oct;23(10):668-9.

Alteplase (TPA) for clotted dialysis catheters.

[Hathiwala SC](#), [Hristea I](#), [Khalili V](#).

Publication Types:

- [Editorial](#)

PMID: 11075895 [PubMed - indexed for MEDLINE]

[Ann Pharmacother](#). 2002 Feb;36(2):272-4.

Alteplase use for prevention of central line occlusion in a preterm infant.

[Lee EK](#).

Pharmacy Department, Naval Medical Center, 34800 Bob Wilson Dr., Ste. 113, San Diego, CA 92134-1113, USA.
EdeeRx@aol.com

OBJECTIVE: To report the use of alteplase for catheter clearance in a neonate of 27 weeks' gestation at day 50 of life. **SETTING:** Neonatal Intensive Care Unit, Naval Medical Center. **CASE SUMMARY:** At day 50 of life, a neonate boy of 27 weeks' gestation had a clotted peripherally inserted central catheter line. He required central access to complete a 28-day course of amphotericin B. An alteplase dose of 0.3 mg/0.3 mL was instilled into the catheter, for an indwelling time of 1 hour. The initial attempt was successful, and the patient was able to finish the course of amphotericin B. **DISCUSSION:** When a catheter becomes occluded, the cause must be determined initially; then an appropriate treatment option can be initiated. Hydrochloric acid and ethanol are some of the pharmacologic agents available, with their use dependent on the precipitating cause of the occlusion. Thrombolytic agents, such as streptokinase and urokinase, have also been used in catheter clearance. The potential risk of anaphylactic reactions with streptokinase and the unavailability of urokinase have clinicians searching for other pharmacologic alternatives. Alteplase, a synthetic tissue plasminogen activator, has been shown

to be a promising alternative agent. There are various reports of alteplase use in pediatric patients for catheter clearance, with different suggested doses ranging from 0.25 to 2 mg. To minimize the risk of bleeding events, initiation with low doses from the suggested range is recommended. CONCLUSIONS: Alteplase was shown to be safe and effective for clearance of an occluded central line in a preterm infant.

Publication Types:

- [Case Reports](#)

PMID: 11847948 [PubMed - indexed for MEDLINE]

[J Vasc Interv Radiol](#). 2005 Mar;16(3):379-83.

Alteplase as a catheter locking solution: in vitro evaluation of biochemical stability and antimicrobial properties.

[Weck S](#), [Cheung S](#), [Hiraoka-Sutow M](#), [Patapoff T](#), [Semba CP](#).

Department of Pharmaceutical Research and Development, Genetech, South San Francisco, USA.

PURPOSE: To reduce potential complications of fibrin deposition to catheter surfaces, there is increasing empiric use of alteplase as a catheter lock solution. The purpose is to evaluate the properties of alteplase when reconstituted in sterile water (SW) or bacteriostatic water (BW) for prolonged periods. **MATERIALS AND METHODS:** Alteplase in glass vials was reconstituted (1 mg/mL) with SW or BW (0.9% benzyl alcohol) in duplicates and stored at 37 degrees C. Biochemical assays were performed at days 0 and 7 and included optical clarity, protein concentration, percent protein monomer, and in vitro clot lysis activity. Microbiologic assays were performed on days 7 through 28 with use of a standardized antimicrobial effectiveness test (pass/fail) and pour-plate methods incubated at 22.5 degrees C (fungus, 3-7 days) or 32.5 degrees C (bacteria, 3-5 days). Organisms tested included Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, and Aspergillus niger. **RESULTS:** Biochemical assay results were as follows: on day 0, all samples were clear/colorless; protein concentrations were 1.10 mg/mL +/- 0 in SW and 1.11 mg/mL +/- 0 in BW; percent protein monomer was 8.2% +/- 0.07 in SW and 98.6% +/- 0.07 in BW; and in vitro clot lysis activity (in percent of relative activity) was 100% in all samples. On day 7, all samples were clear/colorless, protein concentrations were 1.11 mg/mL +/- 0.07 in SW and 1.11 mg/mL +/- 0.07 in BW; percent protein monomer was 97.4% +/- 0.21 in SW and 96.1% +/- 0.21 in BW; and in vitro clot lysis activity (relative activity compared with day 0) was 91% +/- 2.8 in SW and 90% +/- 2.8 in BW. Microbiologic assays (US Pharmacopeia [USP] antimicrobial effectiveness test) yielded a failing result for alteplase reconstituted in SW and a passing result for alteplase reconstituted in BW. **CONCLUSIONS:** Alteplase reconstituted with SW or BW remains relatively stable with retained bioactivity when stored at 37 degrees C for as long as 7 days. Despite the biochemical similarities of the two solutions, only alteplase in BW met USP criteria as an effective antimicrobial solution. Further clinical evaluation is warranted.

PMID: 15758134 [PubMed - indexed for MEDLINE]

[J Clin Oncol](#). 2002 Jan 1;20(1):317-24.

Safety and efficacy of alteplase for restoring function in occluded central venous catheters: results of the cardiovascular thrombolytic to open occluded lines trial.

[Deitcher SR](#), [Fesen MR](#), [Kiproff PM](#), [Hill PA](#), [Li X](#), [McCluskey ER](#), [Semba CP](#); [Cardiovascular Thrombolytic to Open Occluded Lines-2 Investigators](#).

Cleveland Clinic Foundation, Cleveland, Ohio, USA.

PURPOSE: To evaluate the safety and efficacy of alteplase (TPA) for restoring function to occluded central venous catheters (CVCs). **PATIENTS AND METHODS:** The study design was a phase III, open-label, single-arm multicenter trial. Subjects with occluded, nondialysis CVCs were enrolled. All subjects received a 2-mg dose of TPA within the dysfunctional catheter lumen that was allowed to dwell for 30 to 120 minutes. Functionality was tested at 30 and 120 minutes. If the CVC remained obstructed at 120 minutes, a second 2-mg TPA dose was allowed to dwell for 30 to 120 minutes. The primary safety end point was the rate of intracranial hemorrhage (ICH) within 5 days of treatment, and serious adverse events were recorded up to 30 days. **RESULTS:** Nine hundred ninety-five patients received treatment (female, 562; male, 433; mean age, 50.7 years; range, 2 to 91 years). CVCs treated were as follows: single (26%), double (39%), or triple (6%) lumen catheters or ports (29%). The primary end point was 0% ICH within 5 days. There were no cases of death, major bleeding episodes, or embolic events attributable to treatment. Flow was successfully restored in 52% and 78% of CVCs at 30 and 120 minutes after one

dose, and 84% and 87% at 30 and 120 minutes after a second dose, respectively. Restoration of flow was 86%, 93%, 90%, and 79%, for single, double, and triple lumen catheters and ports, respectively. Estimated 30-day catheter patency was 74%. CONCLUSION: A regimen of up to two 2-mg doses of tPA is safe and effective for the restoration of flow to occluded central venous catheters.

Publication Types:

- [Clinical Trial](#)
- [Clinical Trial, Phase III](#)
- [Multicenter Study](#)

PMID: 11773185 [PubMed - indexed for MEDLINE]

[Cardiovasc Intervent Radiol.](#) 2002 Nov-Dec;25(6):513-6. Epub 2002 Oct 24.

Venous port salvage utilizing low dose tPA.

[Whigham CJ](#), [Lindsey JI](#), [Goodman CJ](#), [Fisher RG](#).

Baylor College of Medicine, Department of Radiology, One Baylor Plaza-MS 360, Houston, Texas 77030-3487, USA.
cliffw@bcm.tmc.edu

This study was performed to evaluate the efficacy of low dose tPA for catheter salvage in cases of fibrin sheath formation in patients with venous access ports. Prospective evaluation was accomplished in patients who had venous ports with catheter malfunction. There were a total of 50 patients and 56 occlusive events. Each patient had a catheter injection documenting a fibrin sheath. Patient population included 45 for chemotherapy and 5 for antibiotics. A low dose tPA regimen was instilled into the port and upon successful return of function, a completion venogram was accomplished. Fifty patients were enrolled in the study with the average time between placement and dysfunction of 99 days. Five patients had a second occlusive event (38.5 days) and one had a third event (27 days). All patients had a venogram confirming a fibrin sheath as the cause of catheter malfunction. The average dose of tPA was 2.29 mg (range 1 mg-4 mg). Success was achieved in 52 of the 56 occlusive events (92.9%). There were no bleeding complications. Catheter occlusion is a common complication of long-term venous access ports. Aggressive therapy with low-dose tPA can salvage function. It provides safe and effective therapy for venous port malfunction secondary to fibrin sheath.

PMID: 12391517 [PubMed - indexed for MEDLINE]

[J Pediatr Hematol Oncol.](#) 2002 Nov;24(8):653-6.

Use of tissue plasminogen activator (rt-PA) in young children with cancer and dysfunctional central venous catheters.

[Chesler L](#), [Feusner JH](#).

Department of Hematology/Oncology, Oakland Children's Hospital, 747 52nd Street, Oakland, CA 94609-1809, USA.

PURPOSE: To determine the efficacy and safety of low, nonescalating dose tissue plasminogen activator (rt-PA) in restoring the patency of occluded central venous access devices (CVCs) in children with cancer who weigh less than 30 kg. **PATIENTS AND METHODS:** A single-center review of the use of rt-PA (0.5 mg indwelling for 30 minutes in the CVC) was conducted in 42 cancer patients with large bore central venous access devices implanted over a 2-year period. All patients weighed less than 30 kg. None had been previously treated with a thrombolytic agent. The efficacy for restoring function to CVCs was measured and correlated with patient age, weight and CVC lumen size. Propensity to rethrombose following an initial occlusion and treatment was also determined. **RESULTS:** Of 235 doses of rt-PA administered in a 2-year period, 55 doses administered to 42 patients met the eligibility criteria as outlined. Twenty-nine patients (69%) had function restored with a single dose; 8 patients (19%) required 2 doses, and 5 patients (12%) failed 2 doses; for an overall success rate of 88%. No significant adverse events occurred. Of the 37 cleared CVCs, 14 (38%) reoccluded within 1 month. A higher proportion of patients initially treated with one rt-PA (71%) experienced another CVC dysfunction within 1 month, compared with 29% CVC dysfunction in those requiring >1 dose. **CONCLUSIONS:** This article describes the use of rt-PA (0.5 mg, without dose escalation) to lyse CVC-associated thrombi specifically in small children with cancer, a patient population in which it is particularly desirable to minimize the degree of fibrinolysis. One dose of 0.5 mg rt-PA, with an additional dose if necessary, is as safe and effective as previously reported escalating dose regimens for CVC clot lysis. There is no statistically significant correlation of treatment failure with patient age, weight, or catheter lumen size, and no significant propensity for

rapid rethrombosis following a single dysfunction and treatment. Patients initially treated with a single dose of rt-PA appear to have more subsequent dysfunctions in the month after treatment, an observation that warrants further study.

Publication Types:

- [Review](#)

PMID: 12439038 [PubMed - indexed for MEDLINE]