

Short-Term Continuous Infusion Thrombolytic Therapy for Occluded Central Venous Dialysis Catheters

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Abstract

The necessity of maintaining a strict schedule of dialysis treatments in patients with chronic renal failure dictates that occluded access catheters be restored to full function in a timely and cost-effective manner. The records of 22 consecutive patients receiving outpatient treatment for occluded hemodialysis catheters at Osteopathic Medical Center of Texas were reviewed by the authors. Each patient had 100,000 units of urokinase in 50 ml normal saline instilled over 30 minutes through the occluded catheter. In most instances the dose was divided to allow 35 ml to the proximal port and 15 ml to the distal port. The maximum sustained blood flow rate on dialysis was recorded for each patient. The mean maximum sustained blood flow rate improved from 150 ml/min \pm 79 ml to 261 ml/min \pm 62 ml. Following infusion, improvement was obtained in 19 of 22 patients, with 14 catheters delivering blood flow greater than 250 ml/min. The total cost per treatment was \$316. No adverse events were experienced. Thrombotic occlusion of extended use hemodialysis catheters can be rapidly and safely relieved in a cost-effective manner with little delay in scheduled dialysis treatments.

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Percutaneous venous catheters for hemodialysis have been in use for more than 30 years.¹ The later introduction of dual lumen catheters greatly simplified securing venous-venous access, reducing reliance on peripheral arteries that frequently are compromised by low flow and vasopressors.² While thrombosis is inevitable with these short term catheters,

they can readily be exchanged until long term access is established, which suffices in acute care settings. In the ambulatory patient, extended use catheters (eg, Vas-Cath [Bard, Salt Lake City, UT] and Perm-Cath [Quinton, Seattle, WA]) are widely used.³ Many centers rely on these catheters for prolonged periods while awaiting fistula maturation or if peripheral sites are unavailable. These catheters are subject to thrombotic occlusion similar to that experienced with short term catheters.^{4,5} Additionally, over time, fibrin sheaths occur along their surface due to long term irritation of the endothelial lining of the host vessel and deposition of fibrin, associated with foreign body reaction.^{6,7} Multiple side holes further enhance the likelihood of thrombus and fibrin deposition that may require treatment beyond simple flushing. Current continuous infusion protocols for catheter thrombolysis may be efficacious; however, dialysis must be delayed until sufficient clearance is established to allow resumption of adequate flow rates. Here we describe a protocol that provides expedient and cost-effective catheter clearance, allowing timely resumption of dialysis in patients presenting with catheter occlusion.

... MATERIALS AND METHODS ...

The records of 22 consecutive patients for whom complete and reliable data could be obtained were retrospectively reviewed by the authors. Each had presented to Osteopathic Medical Center of Texas for catheter thrombolysis after blood flow rates greater than 250 ml/min could not be maintained in the outpatient dialysis center. In each instance, attempts at catheter clearance performed in the ambulatory dialysis center by saline irrigation or filling the catheter lumens with urokinase (Open-Cath, Abbott Laboratories, Abbott Park, IL) by methods previously described^{7,8} failed to significantly improve catheter function. Both catheter lumens were initially tested for patency by simple saline irrigation and aspiration.

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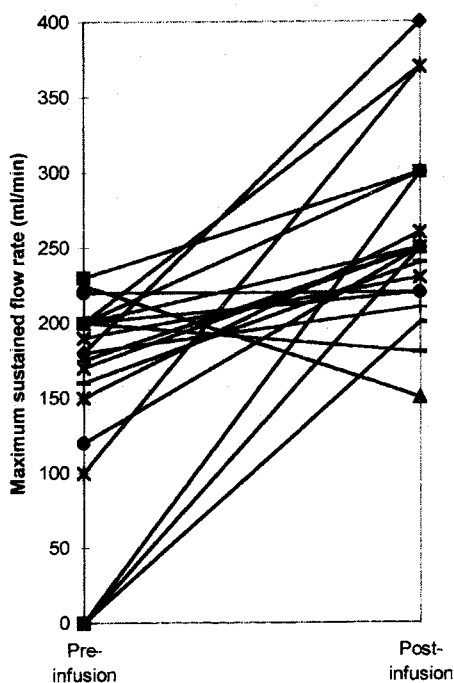
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Table 1. Patient Blood Flow Rates

Patient no.	Preinfusion Flow rate*	Postinfusion Flow rate*
1	0	300
2	0	250
3	190	230
4	150	260
5	120	250
6	175	250
7	0	300
8	160	240
9	200	220
10	200	300
11	225	150
12	170	250
13	200	370
14	220	220
15	180	210
16	0	200
17	200	180
18	180	400
19	230	300
20	200	250
21	200	250
22	100	370

*Maximum sustained rate (ml/min)

Figure 1. Change in Blood Flow Rate Following Thrombolysis (no of patients = 22)



If saline could not readily be infused or no blood could be aspirated, a 0.035 hydrophilic guide wire (Medi-tech, Boston Scientific, Natick, MA) was inserted into the catheter. In all instances, this resulted in achieving adequate patency to allow thrombolytic infusion. A solution of 100,000 U of urokinase in 50 ml normal saline was infused at a rate of 100 ml/h through the proximal (outflow) port. After 35 ml was infused, the proximal port was aspirated. If blood flowed freely, the lumen was irrigated with normal saline (no urokinase) and locked. The remaining 15 ml was infused at the same rate through the distal (return) port. If any resistance to aspiration through the proximal port was encountered, the remaining 15 ml was infused through this channel. Both channels were then irrigated with saline and filled with 2.5 ml of 1000 U/cc heparin. Patients so treated then returned to the ambulatory dialysis center. Blood flow rates were determined every 15 minutes during dialysis. Maximum sustained blood flow rates were recorded for each treatment (maximum sustained blood flow rate is the highest volume per minute rate that could be maintained throughout treatment).

Statistical Analysis

The difference between the pre- and post-thrombolytic infusion blood flow rates was determined using the Mann-Whitney test. Contingency analysis (2 x 2) using two rows (blood flow rates 250 ml/min versus blood flow rates < 250 ml/min) and two columns (preinfusion versus postinfusion) was performed using Fisher's exact test. All tests were two tailed. Alpha was set at 0.05. All analyses were performed using Instat 2.01 (Graphpad, San Diego, CA).

... RESULTS ...

The preinfusion and postinfusion maximum sustained blood flow rates are shown in Table 1. The mean (\pm standard deviation) pre- and postinfusion blood flow rates (ml/min) were 150 ± 79 and 261 ± 62 , respectively. The median pre- and postinfusion blood flow rates (ml/min) were 180 [P(115<M<185) 95%] and 250 [P(234<M<289) 95%], respectively. The pre- and postinfusion group blood flow rates were significantly different (Mann-Whitney test, two tailed, $P < 0.0001$). Improved blood flow rates were obtained in 19 of 22 patients, with 14 patients dialyzed at blood flow rates of

≥ 250 ml/min postinfusion (Fig. 1). Attaining blood flow rates of 250 ml/min or greater was contingent upon urokinase infusion (Fisher's exact test, two sided, $P < 0.0001$). No complications of this procedure were experienced. The total cost was \$316 per treatment.

... DISCUSSION ...

The past several years have seen a steady growth in the chronic dialysis population.^{9,10} This has placed increasing demand on the resources available to treat these patients. All centers in our region operate 3 shifts, 6 days per week with little space available to accommodate patients other than at their scheduled treatment times. This has placed a considerable burden on those responsible for creating and maintaining access sites to return patients quickly to the ambulatory centers when revisions and declotting become necessary.

Several protocols published in the past several years have been designed to achieve durable patency of otherwise nonfunctional access catheters.^{7,8,11-16} Many of these evolved from the demands of the chemotherapy units that merely require infusion capability and occasional blood sampling. In this setting, mechanical declotting by forced irrigation coupled with thrombolysis by catheter filling will suffice. It has been our experience, however, that these methods do not address the problems of retained distal thrombus seen with multi-side-hole catheters. Frequently there is insufficient clearance of clot and, perhaps, fibrin distal to the catheter tip to permit aspiration and return of blood at a rate that will adequately support dialysis. Toward this end, a blood flow rate of at least 300 ml/min is desirable with recent trends suggesting rates of 400 ml/min to 500 ml/min.¹⁷ While we have been unable to routinely attain blood flow rates greater than 400 ml/min with catheter access, we have been able to satisfactorily clear volume and solutes (electrolytes and acid) at blood flow rates of at least 250 ml/min. This allows the opportunity to establish and mature conventional long term access (arteriovenous fistula).

It is our belief that the problem does not lie in the lumen of the catheter. Silicone catheters do not allow firm adherence of clotted blood and can be readily cleared by the simple mechanical means described above. Consequently, catheter filling techniques, while maximizing clearance of the catheter lumen, have not generally resulted in improved blood flow rates in our experience. Continuous thrombolytic infusion, however, will duplicate the intraluminal clearance while possibly

providing the added benefit of distal clearance at and immediately beyond the catheter tip.

Thus far, the attempt to dissolve fibrin sheaths by long-term infusion techniques has not been fruitful. We speculate that mechanical disruption of the fibrin matrix by guide wires, balloon catheters, and forceful irrigation may expose sufficient plasmin binding sites to aid in partial lysis of these sheaths. This has yet to be convincingly demonstrated in vivo but further study is warranted. In any event, prolonged infusion demands greater nursing and facility time.^{8,15} Ultimately this results in greater cost and prevents early return to the dialysis unit for treatment (Table 2). The short term infusion protocol described here allows rapid patient turnaround.

... CONCLUSION ...

Short term, continuous infusion thrombolytic therapy is an effective method of providing sufficient clearance of occluded hemodialysis catheters, permitting resumption of adequate blood flow rates to support dialysis. We describe here a cost-effective protocol that allows rapid catheter clearance and prompt return of the patient to the ambulatory center for dialysis.

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Table 2. Cost Comparison of Selected Infusion Techniques

Reference	Infusion Time	Comparative Cost*
Haire et al ⁸	12 h	\$626
Haire et al ¹⁵	6 h	\$316
Wachs ⁷	30 min/dose (up to 3 doses)	\$96-\$288
Peska et al (present study)	30 min	\$316

*Costs were derived by applying current product costs at our institution to published protocols.

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