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Use of Tissue Plasminogen Activator in Catheters Used for Extracorporeal Renal Replacement Therapy

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Background: Intraluminal thrombosis of central venous catheters used for renal replacement therapy (RRT) decreases the ability to provide adequate treatment. Alteplase is a recombinant tissue plasminogen activator that has been used to improve the function of catheters used for RRT in humans.

Objectives: To retrospectively review alteplase instillation in dysfunctional catheters used for RRT in dogs and cats.

Animals: Seventeen dogs and 8 cats receiving RRT for kidney failure.

Methods: Medical records of patients in which alteplase was used for RRT catheter dysfunction from 2004 to 2012 were retrospectively reviewed to characterize reasons for use, improvement in function, increase in blood flow, and duration of improvement.

Results: Alteplase was instilled 43 times in 29 catheters, most commonly because of suspicion that the catheter would not provide sufficient flow on the next treatment (n = 21). The second most common reason was inability to start a dialysis treatment (n = 12). Catheter function improved after alteplase instillation in 34 of 43 treatments (79%). Median blood flow rate increased by 13% (18 mL/min) in the dialysis session after alteplase instillation. Seven of 29 catheters (24%) were treated with alteplase on >1 occasion (median time to second treatment, 8 days), and 1 catheter had to be replaced because of intractable dysfunction.

Conclusions and Clinical Importance: Alteplase is effective at improving function of central venous catheters used to provide RRT, but the results are short-lived.

Key words: Alteplase; Dialysis; Thrombosis.

Double-lumen central venous catheters are the predominant type of vascular access used for dogs and cats undergoing extracorporeal renal replacement therapy (intermittent hemodialysis and continuous renal replacement therapy).[1,2] These catheters are typically inserted into the external jugular vein by the Seldinger technique and can be used immediately after placement. Despite widespread preference for arteriovenous fistulas or grafts in human medicine, central venous catheter use is also common, although differences exist in the insertion vessels and catheter specifications compared with dogs and cats. An ideally functioning catheter will provide rapid continuous blood flow. In practice, however, catheter-related complications occur frequently in dogs and cats, as well as in humans.

Patient movement may cause a catheter to kink, abruptly stopping or curtailing blood flow, but flow is generally restored immediately when the catheter position is corrected. A relatively large catheter in relation to the diameter of the cranial vena cava may impair catheter blood flow if the catheter inlet or outlet holes are occluded by contact with the vessel wall. This phenomenon may be worsened by vascular constriction and intravascular volume depletion.

Abbreviations:

IQR	interquartile range
RRT	renal replacement therapy
tPA	tissue plasminogen activator

Although repositioning the catheter may temporarily resolve the problems described, additional catheter complications that are more difficult to resolve can occur. Vessel stenosis occurs in 10–50% of humans, depending on the anatomic location of the catheter.[3] Intraluminal thrombosis affects 17–33% of long-term hemodialysis catheters placed in people.[4] Dialysis catheter thrombosis includes several types of obstruction, including intraluminal thrombi, fibrin tails that extend from the distal tip of the catheter, fibrin sheaths that adhere to and encase the external surface of the catheter, and mural thrombi attached to the vessel or right atrial walls.[5]

Effects of catheter thrombosis include inadequate dialysis delivery, which may lead to decreased quality of life and increased mortality, and the need for inconvenient and potentially costly intervention.[5,6] Replacement of the catheter is frequently necessary, but not always effective at eliminating catheter dysfunction, and replacing the catheter incurs increased cost (especially for tunneled cuffed catheters) and the risk associated with sedation or anesthesia. In a study of central venous catheters placed in the intensive care unit (ICU) for acute RRT in humans, 10–11% of catheters were replaced because of dysfunction defined as a blood flow rate insufficient to continue or complete RRT.[7] In a follow-up study that evaluated the performance of replacement catheters placed at a different anatomic location, the incidence of catheter dysfunction increased to 23–26%.[8]

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To decrease the risk of intraluminal thrombosis, an anticoagulant is placed in the lumen of the catheter between intermittent RRT treatments. Unfractionated heparin (1,000–10,000 units/mL) is a common choice in humans,[5] although 4% trisodium citrate has been shown to be an effective intraluminal anticoagulant with antimicrobial properties as well.[9,10] In the interval between dialysis treatments, the anticoagulant diffuses out of the tip of the catheter, which not only predisposes the catheter to intraluminal thrombosis but also results in systemic anticoagulation of the patient (particularly when high concentrations of heparin are used).[11] Notwithstanding these efforts, catheter dysfunction related to intraluminal thrombosis seems to be common in both the human and the veterinary dialysis fields.[1,2]

Although techniques that address this problem, such as forceful flushing of the catheter lumen with sterile saline, dislodgement of an intraluminal thrombus with a guidewire, and reversal of catheter lines from the standard configuration, exist, they may not be successful.[1,2] The ports of the dialysis catheter are staggered, and the blood is generally withdrawn from the most cranial ports and returned through the distal ports. If the cranial ports are partially occluded, reversing this configuration may restore blood flow, although it increases the risk of recirculation of blood that was just returned from the dialysis machine, decreasing efficiency of clearance. Instillation of thrombolytic agents may be a suitable alternative for restoring catheter patency in veterinary patients. Tissue plasminogen activator (tPA) converts plasminogen to plasmin, which accelerates clot lysis by cleaving fibrin into fibrin degradation products. Recombinant DNA technology has enabled the creation of several compounds with tPA activity, including alteplase,[a] reteplase,[b] and tenecteplase.[c] Alteplase was approved by the Federal Drug Administration for use in thrombosed central venous catheters in people in 2001. Although not specifically approved for thrombolytic use in hemodialysis catheters, alteplase has been commonly used for this purpose. Tissue plasminogen activator products have replaced the use of urokinase and streptokinase in the United States. This retrospective study describes the use of alteplase in central venous catheters used for RRT in dogs and cats.

Materials and Methods

Records of dogs and cats that received extracorporeal RRT (including intermittent hemodialysis, continuous renal replacement therapy, and prolonged intermittent renal replacement therapy) at the Animal Medical Center from 2004 to 2012 were retrospectively reviewed for the use of alteplase to treat dialysis catheter dysfunction. Any catheter used for RRT was considered for inclusion, including cuffed and noncuffed catheters, tunneled and nontunneled catheters, and those used in any anatomic location. The use of alteplase was based on subjective assessment of dialysis catheter performance and clinician discretion. Species, type of renal disease prompting RRT (acute kidney injury, chronic kidney disease, or acute exacerbation of chronic disease), and outcome were recorded.

Alteplase is provided as lyophilized powder. Standard protocol for use is to reconstitute it with sterile water immediately before use to create 2 mL of a 1 mg/mL solution. In most cases, the catheter lumen was filled with a volume of alteplase solution identical to the priming volume of the catheter lumen. If the catheter lumen volume exceeded 2 mL (or if both lumens were being treated and the combined lumen volumes exceeded 2 mL), saline was used to advance the alteplase to the catheter tip. In the early part of the study, the alteplase was occasionally reconstituted with a volume of sterile water equal to the volume of the catheter lumens, leading to concentrations that varied from 0.7 to 1.3 mg/mL. As this observation was rarely recorded in the medical record, it is not reported. In the early part of the study, when alteplase was instilled before or after the RRT treatment, aspiration was attempted on each treated lumen every 30 minutes, until the lumen aspirated easily. In the later part of the study, the protocol was the same when instilled before RRT, but for the majority of use immediately after RRT, alteplase was instilled as a catheter-locking solution without attempts to aspirate the lumen until the next day or the next dialysis treatment. The duration of time alteplase remained in the catheter lumen (dwell time) was recorded. If alteplase was not used as a catheter-locking solution, from 2004 to 2008, unfractionated heparin (500–5,000 units/mL) was used as the anticoagulant catheter-locking solution between dialysis treatments. From 2009 to 2012, 4% trisodium citrate was used as the locking solution.

Based on notes in the dialysis record, the reason for intervention was retrospectively categorized as (a) catheter performance (based on ease of aspiration) was judged to be insufficient for dialysis, (b) involuntary dialysis interruption and unable to restart without intervention, (c) voluntary dialysis interruption because of impending crisis (eg, progressively decreasing flows, imminent circuit clotting), (d) voluntary dialysis interruption because of an inability to reach clearance goals without intervention, (e) suspicion that the next treatment would be problematic, or (f) the presence of a thrombus in the catheter associated with catastrophic clotting of the extracorporeal circuit. The severity of malfunction at the time that alteplase treatment was initiated was retrospectively scored on a scale of 0–4 (Table 1). The effect of treatment was determined during the subsequent dialysis treatment and retrospectively scored using the same scale. Each lumen was scored separately. A posttreatment score of 3 or 4 was considered a successful treatment. If both lumens were treated simultaneously, both had to be scored 3 or 4 to be considered a successful treatment. The average blood flow speed (calculated by dividing the liters of blood processed by the dialysis treatment time) during the treatment before intervention and during the treatment after the intervention was recorded. For treatments performed on the Gambro Phoenix[d] intermittent hemodialysis machine, the blood pump speed was used for determining blood flow rates instead of the compensated blood flow rate, to conform to measurements available on the CenturySystem 3[d] and PrismaFlex[d] dialysis equipment.

The number of dialysis treatments performed after alteplase intervention was counted until either another intervention was performed (subsequent use of alteplase or mechanical clot disruption with a guidewire), or the catheter was removed.

Table 1. Severity of catheter malfunction.

Score	Description
0	Not Functional
1	Insufficient function for dialysis
2	Poor function, inadequate dialysis likely
3	Adequate function
4	Excellent function

No attempt was made to evaluate for potential adverse events related to alteplase (eg, intracranial hemorrhage, major bleeding, embolic events, thrombosis, catheter-related bloodstream infection, or catheter-related complications).

Results were reported as median (interquartile range [IQR] or range). Categorical data were reported as frequencies and percentages. The blood flow speed and pre- and posttreatment severity scores were compared with the Wilcoxon matched pairs test. Alteplase dwell time was categorized as 30–60 minutes or 18–72 hours, and groups were compared by the Fisher's exact test. P values of <.05 were considered statistically significant. GraphPad InStat was used for statistical analysis.[e]

Results

During the study period, 43 alteplase treatments were performed in 76 catheter lumens. In 33 treatments, alteplase was infused into both lumens. In 9 treatments, alteplase was infused only into the proximal lumen, and in 1 treatment, it was infused only into the distal lumen. These 43 treatments were performed on 29 catheters in 25 patients (17 dogs and 8 cats). Thus, 7 patients (6 dogs and 1 cat) were given multiple treatments. No patient was treated with RRT for >1 temporal episode of kidney disease. The median weight for the dogs was 30.6 kg (range 6.7–44.9 kg) and 4.25 kg (range 3.0–8.8 kg) for the cats. The etiology of kidney disease prompting RRT was acute kidney injury in 17 patients (68%), chronic kidney disease in 6 patients (24%), and an acute exacerbation of chronic disease in 2 patients (8%). Of the patients with acute or acute-on-chronic disease, 9 recovered and 10 died or were euthanized. All of the patients with chronic end-stage kidney disease eventually died.

Seventeen types of catheters that varied by brand, French size, and length were used during the study (Table 2). All were inserted into the right or left external jugular vein. The majority (65.5%; 19 of 29 catheters) were noncuffed, nontunneled catheters. Ten catheters (34.5%) were cuffed and were inserted into the vein after being tunneled SC. The median weight of the patients with an 8 Fr catheter was 5.3 kg (range 3.0–12.9 kg, n = 2 dogs and 8 cats); 34.4 kg (range 9.1–42.1 kg, n = 6) for dogs with an 11.5 Fr catheter; and 30.6 kg (range 10.1–41.0 kg, n = 7) for dogs with a 14 Fr catheter. The 2 cats with 7 Fr catheters weighed 3.3 and 3.4 kg, and the 2 dogs with Quinton Permcath weighed 40.2 and 44.9 kg.

Table 2. Catheters used.

# Used	Brand	French Size	Cuff
6	MedComp[f]	8	Yes
6	MedComp	11.5	No
3	Arrow[g]	8	No
3	MedComp	14	No
2	Arrow	7	No
2	Quinton[h]	Permcath	Yes
1	Arrow	14	No
1	Arrow Split Tip	14	Yes
1	MedComp	8	No
1	MedComp	9	No
1	MedComp	14	Yes
1	MedComp	16	No
1	Undetermined		No

Alteplase was used immediately before the dialysis treatment in 12 of 43 instances (28%) because catheter performance based on ease of aspiration was judged to be insufficient for dialysis. Alteplase was used during a treatment interruption in 6 of 43 instances (14%; 2 instances resulting from involuntary dialysis interruption with inability to restart without intervention, 3 instances resulting from voluntary dialysis interruption because of impending crisis, and 1 instance resulting from voluntary dialysis interruption because of inability to reach clearance goals). In 20 of 43 instances (46.5%), alteplase was instilled immediately after treatment (2 after premature termination of treatment because of catheter dysfunction, 16 because of suspicion that the next treatment would be problematic, and 2 because of the presence of a thrombus in the catheter associated with catastrophic clotting of the extracorporeal circuit). Alteplase was used 5 of 43 times (11.5%) between dialysis treatments because of suspicion that the next treatment would be problematic. Seven of the 29 (24%) catheters were treated with alteplase on >1 occasion. For 3 catheters (7%), 2 alteplase treatments were administered; for 2 catheters (5%), 3 treatments were administered; and 1 catheter each received 4 and 5 treatments. The median time from catheter placement to the first intervention with alteplase was 8 days (IQR 2, 19 days; range 1–82 days; n = 29) and the median time between the first and second alteplase treatment was 8 days (IQR 6, 12 days; range 4–42 days, n = 7) in the 7 catheters receiving >1+ alteplase treatment.

There was a statistically significant improvement in the median severity score (Table 1) after treatment with alteplase (median 4 [excellent function]; IQR, 3, 4; range 0–4), compared with before the treatment (median 1 [insufficient function for dialysis]; IQR, 1, 2; range 0–3; n = 65 lumens; $P < .001$). In 34 of 43 treatments (79%), improvement was sufficient to complete the next dialysis treatment without prolonging the initial prescribed dialysis time (severity scores 3 or 4). Five treatments (12%) were unsuccessful, of which 3 showed no improvement and 2 had insufficient improvement to dialyze (severity scores 0, 1 or 2). Response to alteplase treatment was not assessed after 4 treatments because the catheter was not used again (n = 3) or because of missing data (n = 1).

After instillation of alteplase, the median intraluminal dwell time was 60 minutes (IQR 45, 1,080 minutes; range 30–8,640 minutes; n = 74). For 1 treatment in which both lumens of the catheter were treated, alteplase was administered as a constant rate infusion over 3 hours. In all other treatments, alteplase was instilled and allowed to dwell in the catheter lumen with intermittent aspiration (30–120 minutes, n = 29), or as a locking solution without intermittent aspiration attempts (18–144 hours, n = 13). Although there was a higher proportion of successful treatments with a longer dwell time (18–72 hours, 10 of 10 evaluable

treatments were successful, 100%) compared with a shorter dwell time (30–60 minutes, 18 of 23 were successful treatments, 78.3%), we were unable to demonstrate a statistically significant difference between groups in this small sample ($P = .29$). The median number of dialysis treatments after intervention was 1 (IQR, 1, 3.5; range 0–61; n = 43). Of the 43 treatments, 16 (37%) were followed by a subsequent intervention with alteplase (14 treatments), insertion of a guidewire to dislodge a thrombus (1 treatment), or both (1 treatment). In 3 cases, a different catheter was placed (1 case was because of inadvertent removal, 1 case was a scheduled replacement with a tunneled catheter, and 1 case was because of inability to continue dialysis despite alteplase instillation). No further intervention was required after alteplase instillation in 20 treatments (47%). Neither the success of alteplase instillation nor the need for further catheter intervention could be assessed for 4 catheters because these catheters were not used for RRT after instillation.

Sufficient data were available to assess changes in blood flow rate during dialysis treatments before and after alteplase administration for 32 alteplase treatments. The median change in average blood flow, comparing the treatment before with the treatment after alteplase instillation, was 13% (IQR, 0%, 38%; range −31% to +100%). In absolute terms, the median increase was 18 mL/min (IQR, 0, 36 mL/min; range −69 to +143 mL/min; $P = .002$). This calculation excludes measurements taken when alteplase was instilled during a dialysis treatment because measurements were not available. Twenty-four of the 32 (75%) treatments in which the average blood flow rate could be assessed before and after treatment had an increase in average blood flow rate. The blood lines were attached to the catheter ports in a reversed configuration at some point during 13 of 38 (34%) dialysis treatments performed after alteplase.

Sixteen of 29 catheters (55%) were removed when the patient died or was euthanized, and 8 catheters (28%) were removed when the patient recovered renal function and no longer required dialysis. Three catheters were removed inadvertently (2 were replaced and 1 was not); 1 catheter was removed and replaced with a larger bore, tunneled catheter; and 1 catheter was removed and replaced because of obstruction unresponsive to alteplase treatment. The median time each catheter remained inserted in the patient was 16 days (IQR, 8, 40; range 2–292; n = 29). Twenty-one of the 29 catheters (72%) were removed within 14 days of the first alteplase treatment, but only 1 removal was because of catheter dysfunction.

Discussion

Various parameters may indicate catheter dysfunction, and routine monitoring is recommended. In a patient with a set dialysis prescription over several dialysis treatments, a progressive decrease in the average blood flow rate, a decrease in blood flow rate of >10% while the blood pump is generating a fixed access pressure (eg, −200 mmHg), a lower than expected clearance, an access pressure <−250 mmHg, or a return pressure of >250 mmHg could indicate catheter dysfunction.[5] Although these parameters can be monitored quickly and noninvasively, many of them are not well suited for monitoring in the first week of RRT, when each dialysis prescription, and thus the required blood flow rate, is likely to vary from the previous prescription. In veterinary medicine, differences in catheter length, luminal diameter, design, and position, as well as patient size, conformation, and position impact expected blood flow rates, further complicating standardization of catheter performance evaluation. In many instances, it is difficult to determine whether poor catheter performance is the result of intraluminal thrombosis, formation of a fibrin sheath, malpositioning of the catheter (eg, in the right auricle), or malpositioning of the patient (eg, ventroflexion of the neck causing catheter kinking). All of these factors may occur in isolation or simultaneously, affecting recorded blood flow rates and perceived catheter performance.

When catheter dysfunction occurs and intraluminal thrombosis is suspected to be a contributing factor, there are few interventions that reliably restore catheter patency. A typical interventional algorithm in veterinary medicine includes forceful flushing of the catheter lumen with sterile saline, followed by reversal of catheter lines from the standard configuration. This reversed configuration increases the amount of blood returning from the dialysis circuit that is taken up by the access port, and this recirculation of blood decreases the efficiency of solute clearance during RRT. If the reversal allows a faster blood flow rate or decreases the amount of time the circuit is stopped because of pressure alarms, the decrease in efficiency may be overcome. Reversing the configuration of the dialysis lines incurs no additional expense and can be performed rapidly during a dialysis treatment. If blood flow cannot be maintained in a conventional or reversed configuration, both catheter lumens are likely affected by thrombosis or malpositioning, presuming that the catheter lumens are sized to provide adequate blood flow. There are a small number of reports in human and veterinary medicine describing use of a guidewire or brush inserted in the lumen to dislodge an intraluminal thrombus.[12–14,16] Despite concerns that the dislodged thrombus will become a clinically relevant pulmonary embolus, respiratory compromise has not been noted after this procedure.

If these maneuvers fail, catheter replacement in the same vessel, using a guidewire to facilitate the exchange, is a simple alternative technique. Although the procedure can be performed without sedation in some patients, patient movement increases the risk of inadvertent dislodgement before the new catheter is positioned and secured, and increases the risk of contamination. Replacing the catheter in another vessel is limited to the contralateral external jugular vein in most veterinary patients, because the 2 external jugular veins are typically the only vessels sufficiently large enough to accommodate the luminal diameter of

dialysis catheters. If a fibrin sheath is present, a catheter exchange may not resolve the dysfunction unless the sheath is simultaneously disrupted. Balloon dilatation of the sheath during catheter exchange or fibrin sheath stripping (typically using the femoral vein to introduce a snare that then is placed around the catheter and fibrin sheath) has been described.[17,18] Both techniques involve a risk of pulmonary thromboembolism, in addition to the added expense of the balloon or snare, fluoroscopy, and anesthesia.

In most catheter treatments (77%) reported in our study, alteplase was instilled in both lumens simultaneously, typically because adequate blood flow could not be obtained from either lumen despite blood line reversal. In some cases, the second lumen was treated as a prophylactic measure if the reconstituted volume of alteplase was larger than the priming volume of the affected catheter lumen. Being able to start or continue dialysis with or without the lines reversed was considered a successful alteplase treatment in this study.

Unfortunately, the precise concentration and dose administered per lumen were not recorded in all cases included in this study, although no more than 2 mg (the contents of 1 vial) was administered in any case. The most common dose of alteplase used in people is 2 mg per lumen (4 mg per treatment episode), but several studies have found a lower dose of 1 mg/lumen to be effective.[19–21]

Many protocols for use of alteplase in the treatment of central venous catheters in people have been published. Various dwell times (30 minutes to several days) have been evaluated,[22] with no difference in success with a 1-hour dwell compared with 48- to 72-hour dwell times, as was seen in our study.[23] A continuous infusion of a low dose (eg, 5 mg over 3 hours) has been used,[24] as has a "push" protocol, in which the catheter lumen is filled with alteplase, and 0.1 mL of saline is injected every 10 minutes to "push" the alteplase to the catheter tip, replacing the drug that has diffused out of the lumen.[25] This latter protocol was shown to have comparable results to a 30- to 120-minute dwell time, but could be completed in only 30 minutes.[25] Our report includes treatments using all of these protocols except the "push" protocol. We excluded treatments using streptokinase and urokinase. Streptokinase is associated with immunologic reactions that have limited its use in humans,[26,27] and alteplase had superior performance compared with urokinase in several studies of human.[21,28,29] Other thrombolytic agents, such as reteplase, tenecteplase, recombinant urokinase, and alfimeprase, have been evaluated, but the lack of studies directly comparing these agents makes it difficult to judge relative merit.[26]

Our 79% primary success rate (defined as adequate function to complete the next treatment; Table 1) was similar to reports in the human medical literature. In a recent systematic review of studies in human patients evaluating thrombolytic therapy for hemodialysis dysfunction, Hilleman reported a success rate of 81 $\pm$ 37% in 12 studies of alteplase use for hemodialysis catheter dysfunction.[20] Common primary efficacy endpoints in the studies of humans include a sustained blood flow rate of >200–300 mL/min, an increase in blood flow rate of at least 25 mL/min, or both.[22,30] Despite the relatively smaller size of dogs and cats, we achieved a median increase of 18 mL/min after treatment. This increase in blood flow rate results in a clinically relevant increase in the liters of blood processed during a treatment, relative to the body weight of our patients. The liters of blood processed relative to body weight is the primary determinant for prediction of treatment efficacy in veterinary patients.[31] We used a scoring system to assess the severity of catheter dysfunction. The median result score after treatment of 4 (excellent flows established) also demonstrated improvement, compared with the pretreatment severity score of 1.

Despite the utility of alteplase treatments for restoration of catheter function, the benefits appear to be short-lived. In multiple studies of human patients, 35–62% of catheters required a second alteplase treatment a median of 13–27 days after the first treatment.[19,22,32] In our study, a second alteplase treatment was administered to 24% of patients a median of 8 days after the first treatment. The lower number of second and subsequent treatments may be confounded by the acute nature of kidney injury in most of our patients, in that patient recovery or death may have precluded further need for dialysis treatments. The low number of dialysis treatments completed after alteplase instillation was affected by the high rate of recovery or death within 2 weeks of the first episode of thrombolytic therapy. Although adverse events were not specifically reported here, patient deaths that occurred were attributed to the primary renal disease in most cases and were not suspected to be related to alteplase use.

Our study did not attempt to evaluate the reason for catheter dysfunction, and may have included alteplase treatments performed because of intraluminal thrombosis, extraluminal fibrin sheath, and vessel stenosis. Some studies exclude cases with dysfunction arising from fibrin sheath and vessel stenosis. Contrast angiography was performed to further evaluate catheter dysfunction in only 2 patients in this study. In 1 dog, a fibrin sheath was documented. A 3-hour infusion of alteplase improved function, but the duration of improvement could not be assessed because the dog died during the next dialysis treatment. A study of human patients evaluated the effectiveness of alteplase infusion for restoration of catheter patency after a diagnosis of a fibrin sheath. The diagnosis was made with angiography or if infusion but not aspiration was possible through 1 or both catheter ports. A 3-hour alteplase infusion allowed for aspiration in 100% of affected catheters. Median catheter patency was 25 days.[24] More recent studies, however, have shown that when thrombolytic therapy with tPA fails, both fibrin sheath stripping and catheter exchange with or without balloon dilatation of the fibrin sheath are viable options.[15,33]

There are many difficulties in interpreting these data. Because of the retrospective nature of this study, data in many categories are incomplete. Furthermore, there was no standard protocol for deciding when to use

alteplase. In prospective studies in people receiving chronic intermittent hemodialysis through a central venous catheter, common indications for intervention include inability to achieve a blood flow rate >250 or 300 mL/min, a blood flow rate >25 mL/min below the prescribed blood flow rate, or both.[5,19,23,25,30,34] In this study, the decision to use alteplase was based on clinician preference, and may have been performed with early or mild dysfunction or may have been withheld until severe or persistent dysfunction.

This retrospective description of the use of alteplase provides preliminary information that may be useful in veterinary practice. Alteplase appeared effective in restoring sufficient function to catheters refractory to repositioning, saline flushes, and reversal of the lines from the standard configuration in 79% of treatments, and the average blood flow rate was increased in 75% of the 32 treatments in which it was evaluated. The benefit of treatment, however, must be weighed against the financial cost, because the estimated cost of alteplase is currently $107 per 2 mg vial. Controlled evaluation that includes more rigorous catheter function monitoring and more extensive assessment of the cause of dysfunction may help identify a subset of situations in which tPA therapy (alteplase or alternative products) provides maximum benefit. Prospective comparison of tPA with other interventions also may be helpful in managing catheter dysfunction. Despite the short duration of improvement, tPA use can restore function to catheters used for RRT until other interventions can be scheduled.

Footnotes

[a] Cathflo Activase; Genetech, San Francisco, CA
[b] Retavase; PDL BioPharma, Inc, Fremont, CA
[c] TNKase; Genentech
[d] Gambro, Lakewood, CO
[e] GraphPad Software Inc, La Jolla, CA
[f] MedComp Medical Components, Inc, Harleysville, PA
[g] Teleflex, Research Triangle Park, NC
[h] Covidien, Mansfield, MA

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