Evaluation of Alteplase 1 mg for the Restoration of Occluded Central Venous Access Devices in a Tertiary Care Hospital

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Abstract

Background: *Alteplase is a recombinant tissue plasminogen activator that is approved for the treatment of occluded central venous access devices (CVADs) and is commercially available as a 2 mg/2 mL dose. Due to the increasing price of 2 mg/2 mL alteplase vials, our institution switched to using a 1 mg/1 mL dose for certain CVADs. The purpose of this study was to evaluate the use, effectiveness, and cost of a maximum of 2 doses of 1 mg/1 mL alteplase for the restoration of an occluded catheter.*

Methods: *A report was generated to identify patients who were administered 1 mg alteplase during the period May 2016 through July 2016. A chart review was performed on each patient identified to collect the data needed, such as documentation of a dysfunctional lumen and documentation of patency after alteplase 1 mg was given. To determine the cost of waste, expired 1-mg syringes returned to the pharmacy were collected.*

Results: *In total, there were 524 1-mg alteplase doses administered during the 3-month time frame. The effectiveness after the first and second dose was 88% and 80%, respectively. Thirty-four doses were wasted, resulting in a cost of around $2,200. It is estimated that the 1-mg syringes provided the institution with $136,000 in annualized savings.*

Conclusions: *It is beneficial to use 1 mg alteplase for occluded CVADs. The cost of waste is nominal compared with the cost savings for the institution. The next step is to analyze other doses of alteplase to find additional areas of cost savings.*

Keywords: *alteplase 1 mg, occlusion, cost-savings, intraluminal volume-based, central venous access device*

Central venous access devices (CVADs) are used in both inpatient and outpatient settings for patients undergoing intravenous therapies.[1] CVADs can be used for withdrawing or administering blood, delivering fluids, and administrating medications such as chemotherapy or antibiotics.[2] Among the most common CVAD complications is catheter occlusion,[2] which can occur in about 30% of catheter placements.[3] To prevent treatment delay and complications as a result of the occlusion,[2,4] catheter function is assessed before each infusion by flushing the catheters and aspirating for a blood return.[5] Replacing a dysfunctional CVAD is expensive and uncomfortable for patients, so it is essential to prevent or resolve thrombotic occlusions to salvage the device.[4] Studies have found that using alteplase in occluded catheters results in savings to hospitals compared with complete catheter replacement.[6,7]

Alteplase is a recombinant tissue plasminogen activator and is the only Food and Drug Administration (FDA)-approved product indicated for the restoration of function to CVADs as assessed by the ability to withdraw blood. Alteplase is instilled into the catheter lumen and allowed to dwell up to 120 minutes.[8] Although there are studies to show that the standard alteplase dose of 2 mg/2 mL is effective for the restoration of function to CVADs in both adult and pediatric patients,[9-11] administering any volume of alteplase sufficient to completely fill the occluded line should be noninferior to the 2 mg dose. Furthermore, the intraluminal volume of most commercially available peripherally inserted central catheter (PICC) lines is <0.8 mL,

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meaning that approximately half of each standard alteplase dose is wasted as it enters a patient's systemic circulation.[12]

Alteplase is included in the top-25 drugs based on drug expenditure in nonfederal hospitals in 2016.[13] The price of 2-mg vials has been rising each year. It is currently about 40% more costly to obtain the vials at our institution than in 2013. Despite the increased cost, there are minimal studies showing the efficacy or effectiveness of a reduced dose of alteplase. Gilarde et al[1] found that a mean dose of about 1 mg alteplase can successfully resolve catheter occlusions. Whigham et al[14] determined that 93% of occlusions can be cleared with 1 mg alteplase. Fink et al[15] showed that a 1-mg dose of alteplase resulted in about 81% patency, which is comparable to 83% patency with using the 2-mg dose.[15] Plohal et al[16] found that a reduced dose of alteplase restored patency in non-hemodialysis CVADs.[16] There are also studies showing the efficacy of 0.5-2 mg alteplase doses for the treatment of thrombus-related venous catheter occlusion in pediatric patients as well as neonates.[17-19]

As a cost-reduction strategy, our institution decided in 2014 that alteplase doses will be based on intraluminal volume. A protocol was created to assign an occluded CVAD to either a 1-mg dose or a standard 2-mg dose. Due to minimal information in the primary literature regarding the 1-mg dose, the purpose of this project was to describe and assess 1 mg alteplase use, effectiveness, and cost.

Methods

This was a retrospective study that evaluated the use, effectiveness, and economic benefit of using 1 mg alteplase in occluded CVADs. No safety data were collected during this evaluation because a dose lower than the FDA-approved dose was used. Per institutional protocol, patients with a confirmed catheter occlusion were recommended to receive an alteplase dose based on the catheter volume to minimize waste. Devices with lumen volumes > 1 mL received the full 2-mg vial of alteplase. Devices with lumen volumes ≤ 1 mL received 1 mg/mL syringes drawn up using 2-mg vials or 50-mg vials (Table 1). The computerized physician order entry (CPOE) system prompted the nurse or prescriber on which dose of alteplase to order depending on the type of CVAD that was occluded. The nurse or prescriber did have the ability to choose a different dose from what the protocol suggested. For example, based on clinical judgment, a nurse could decide to order 2 mg instead of the suggested 1 mg for a particular line or order 1 mg instead of the suggested 2 mg.

Table 1. **Alteplase Dose Based on Device**

Type of device	Alteplase dose/volume
Peripherally inserted central catheter	1 mg/1 mL syringe per lumen
Triple lumen	
4 lumen	
5 lumen	
Tunneled catheter	
Hemodialysis	2 mg/2 mL vial to fill lumen
Ports	
Hickman	

Table 2. **Terms and Definitions**

Term	Definition
Lumen dysfunction	No blood return or not able to flush
Effectiveness after first dose	Documentation of lumen dysfunction via flowsheet or notes before alteplase dose AND documentation of functional lumen ≥ 2 hours after dose
Effectiveness after second dose	Documentation of lumen dysfunction after first dose of alteplase given via flowsheet or notes AND documentation of functional lumen after second dose given 2-8 hours after first dose

The facility policy for declotting a CVAD recommends that a nurse instill an alteplase dose and allow up to 30-60 minutes of dwell time. The catheter function is then reassessed by attempting to aspirate blood. If the catheter remains occluded after a total of 120 minutes of dwell time, a second dose of alteplase is instilled. If patency is not restored—as evidenced by a positive blood flow return—the CVAD must be evaluated further for position and possibility of replacement or removal. In this evaluation, it was assumed the nurses followed proper line care steps before ordering alteplase, such as establishing whether the line is still needed, making sure the catheter did not have mechanical issues, and repositioning the patient.

The end points for use included number of doses used, use by inpatient unit, and CVAD type. The effectiveness end points included patency after the first dose and second dose. Lumen dysfunction was defined as no blood return or not being able to flush the line (Table 2). To determine effectiveness after the first dose, documentation must have stated that there was lumen dysfunction before the alteplase dose was given and documentation that the lumen was functional after 2 or more hours if only 1 dose was given. If the first dose did not result in patency, then there had to be documentation that the lumen was still not functional and a second dose was administered. For it to be considered effective after the second dose, there must have been documentation that the lumen was functional after the second dose was given 2-8 hours after the first dose. This time frame was chosen because 2 hours is the minimum amount of time required before a second dose should be administered according to the FDA labeling of 2 mg alteplase. Eight hours was chosen as the maximum time because it would allow adequate time for