




Evaluation of Short-Term and Long-Term Effects of Fibrinolytic Drug Alteplase on Catheters Dysfunction in Dialysis Patients

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ABSTRACT

Background and Aim: Despite the tendency to important infectious and mechanical complications, central venous catheters have become a common means of vascular access worldwide for patients requiring hemodialysis. In some studies, the use of fibrinolytic drugs is effective in the treatment of catheter function problems. In this study, the effects of Alteplase (a fibrinolytic drug) on catheter function was investigated.

Methods: This study was performed on 100 dialysis patients in the dialysis ward of Imam Reza Hospital in Kermanshah (Iran) who had a catheter dysfunction. After confirmation by the nephrologist, in case of catheter dysfunction and failure to resolve it with the usual methods, one milligram of Alteplase with normal saline was added to each lumen of the catheter and left in place for one hour. After aspirating the lacquered solution, the rate of blood outflow was assessed by aspiration, and catheter function was evaluated.

Results: The mean age was 60.31 ± 11.67 years. 52 patients were male and 48 patients were female. In terms of catheter implantation time, 20 patients were less than 3 months, 12 patients were between 3 to 6 months and 68 patients were more than 6 months. The duration of proper catheter function after injection was less than 3 months in 11 patients, between 3 to 6 months in 31 patients, and more than 6 months in 58 patients. Only 6 out of 100 cases received 2 mg and others received 1 mg of the drug. 25 patients had the insufficient effect of the drug on catheter function in terms of blood flow velocity, and in 75 patients this effect was good. Only 8 patients had inoperable lock catheters. Out of 100 patients studied, 7 had temporary catheters and 93 had permanent catheters.

Conclusion: Alteplase is safe and effective on catheter function in hemodialysis patients.

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INTRODUCTION

There are about 40,000 dialysis patients in Iran and this number increases by about 12% every year. In these patients, the kidneys are unable to maintain metabolic functions and the balance of fluids and electrolytes. Renal activity less than 15% of normal leads to a dangerous uremic condition (1). Hemodialysis is one of the main treatments for these patients (2). In hemodialysis, there are three main ways to access blood. A venous catheter, an arteriovenous fistula and a

synthetic graft. They will be selected based on the patient's condition, the condition of the arteries, and the type of kidney failure. All three methods require surgical intervention to perform. In more than 80% of dialysis patients, this access is through a central venous catheter (CVC). Although CVC has many advantages, including ease of injection and immediate access, it also has significant disadvantages. Significant mortality and disability due to CVC use have been well reported (3, 4). There are more than 500 patients undergoing



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hemodialysis in Kermanshah province, and the vascular path of more than 70% of these patients is through a permanent or perimeter CVC.

Catheter dysfunction is caused by problems with the catheter implanting and its position, or by mechanical disruption of the catheter, or due to the material and quality of the catheter (5). By implanting a catheter, vascular endothelium is damaged and the inflammatory and coagulation process begins. Regular blood contact with catheters, lines, chambers, and smooth membranes may result in the activation of platelets, leukocytes, and coagulation cascades and finally, clots are formed (6-9). Also, decreased blood flow, high rate of ultrafiltration, blood transfusion or lipid compounds can all play a role in accelerating clot formation (1, 10-12). Acute catheter dysfunction requires immediate therapeutic intervention. Thrombosis is the cause of 30 to 40% of dysfunction (13). Thrombolytic agents may be needed if initial efforts such as flush saline and inversion of arterial and venous lines are not effective. To improve catheter function, lacquer solutions are slowly injected into the catheter between hemodialysis treatments. Sodium citrate (4%) or concentrated heparin solution (1000 unit / ml) are the most common solutions (14). Streptokinase, urokinase, and Alteplase are also used to remove clots (15). There are different types of thrombolytic agents, some of which work better than heparin. The best of these is tissue plasminogen activator (tPA), which is more specific for fibrin binding, activating the fibrinolytic system through the release of plasminogen, activating plasmin and causing fibrin degradation, and includes Alteplase, reteplase, and tenecteplase (16). Various studies have shown the effectiveness of Alteplase in eliminating catheter dysfunction and the effective dose and duration of the treatment in the catheter (16-21). The duration of the effect of the drug on the performance of catheters in studies is from 14 to 30 days (17). Therefore, in this study, it is intended to use Alteplase (fibrinolytic drug) in dialysis patients who have catheter dysfunction to determine its effect in resolving catheter dysfunction.

METHODS

The study was an interventional type. By selecting 95% confidence level and 80% power for non - parametric two - domain test and effect size equal to 15% (average effect size based on Cohen's equation) and using G power software version 3.1.9.2, the number of samples for this study was calculated 90 people and 100 people were studied to deal with the possible loss of samples.

This study was performed on dialysis patients in the dialysis ward of Imam Reza Hospital (Kermanshah, Iran), who have catheter dysfunction. After confirmation by a nephrologist,

patients who have undergone dialysis through catheter tunnel due to chronic kidney disease and have catheter dysfunction in the form of decreased blood flow speed during dialysis were included in this study. In these patients, the usual procedures, which include injecting saline into the catheter lines or inverting the arterial and venous lines, did not effective. In this study, patients with catheter infection, hypertension, coagulopathy disorders such as recent Cerebral Vascular Disease, systemic infections such as bacterial endocarditis, or who had received fibrinolytic drugs in the past 21 days, or admitted to the ICU were excluded. 1 mg of Alteplase ampoule with normal saline was brought to the volume indicated on each lumen of the catheter and the lumen was sealed with it so that the drug did not enter the systemic circulation and was left in place for an hour, then the solution was aspirated and the function of the catheter was checked by the speed of blood out of the lines. If the catheter function did not improve, the injection was repeated. Patient information includes the time from catheter insertion to the onset of dysfunction in less than 3 months, between 3 to 6 months and more than 6 months, and the number of times it is necessary to inject Alteplase, which was 1 dose or 2 doses, were checked.

This study was approved by ethics committee of Shahid Beheshti University of Medical Sciences (Ethics code IR.SBMU.MSP.REC.1399.305). Also, the written informed consent from participants was obtained.

RESULTS

Demographic findings

The mean age of patients was 60.31 ± 11.67 . The youngest patient was 5 years old and the oldest patient was 85 years old. The median age of patients was 62 years. Regarding the sex distribution of patients, 52 patients were male and 48 patients were female.

Catheter implantation time

In terms of catheter implantation time, patients were divided into three groups. 20 patients were less than 3 months, 12 patients were between 3 and 6 months and 68 patients were more than 6 months.

Duration of Alteplase effect

The patients were divided into three groups in terms of the duration of effect of Alteplase (proper function of catheter after injection). In 11 patients this time was less than 3 months, 31 patients between 3 to 6 months, and 58 patients more than 6 months.

Alteplase dosage

Only 6 out of 100 people received 2 mg and 94 others received 1 mg of the drug.

The effect of the drug on the performance of the catheter

Out of 100 patients, 25 had the insufficient effect of the drug on catheter function in terms of blood flow velocity, and in 75 patients this effect was good.

Impact of catheter lock

Out of 100 patients, only 8 patients had inoperable catheters lock and 92 patients had a function.

Catheter type

Out of 100 patients, 7 had a temporary catheter (Shaldon) and 93 had a permanent catheter.

The reason for the lack of effect of Alteplase on catheter dysfunction

80% of the cases of the lack of effect of Alteplase on catheter dysfunction were due to Superior venacava or Inferior venacava stenosis. The remaining 20% was due to catheter torsion or the formation of fibrin sheaths. A very small percentage of these cases were due to chelates that did not respond to Alteplase.

DISCUSSION

Our study investigated the effect of fibrinolytic agent (Alteplase) on catheter dysfunction in dialysis patients. The results showed that Alteplase has a positive effect in terms of the proper function of the catheter after injection.

Catheters are considered the main long-term permanent blood access in dialysis centers for aged patients. In addition, they are usually used while patients are waiting for the maturation of an autogenous fistula or artificial transplant (22, 23). Nevertheless, infection, thrombosis, and / or insufficient flow rate are significant factors limiting the long - term use of central venous dialysis catheters.

Recent examinations revealed that the success of topical fibrinolysis with urokinase is only 40 to 50% for the treatment of inadequate flow or clotting. Also, this success rate was achieved only a few days or weeks after implantation in the catheters and was less successful in catheter problems that occurred weeks or months after implantation. The success rate was raised by more aggressive approaches utilizing high-dose urokinase between dialysis sessions as well as during it (up to a maximum of 250,000 U three times). Blood flow improved to 81% after the first injection and 99% after the third injection (24).

Alteplase showed a better effect in clearing obstruction than urokinase in a small randomized trial. Side effects associated with the use of these thrombolytic agents are very rare. There are no serious bleeding events associated with any thrombolytic therapy (25).

Our study showed that in 75 out of 100 patients (75%) the attempt to clean the catheter resulted in proper function after one or two doses of Alteplase and only 25% were

unsuccessful. 80% of the cases of lack of effect of Alteplase on catheter dysfunction was due to Superior venacava or Inferior venacava stenosis. The remaining 20% is due to catheter torsion or the formation of fibrin sheaths. A very small percentage of these cases were due to chelates that did not respond to Alteplase. No side effects were seen in our study.

Therefore, the use of Alteplase to improve catheter dysfunction in dialysis patients can be done as a treatment protocol in centers that have neurology centers and nephrology centers at the same time. Alteplase is an expensive drug. In university centers where there are neurology and nephrology centers, we can take the remnants of the Alteplase vial used by the neurology department for patients who have had a stroke, keep them in dialysis wards, and use them for catheter dysfunction. It will be very good financially. Catheter replacement requires financial costs, time, and hospitalization of patients. On the other hand, by performing this surgery, there is a possibility of complications such as arrhythmia, pneumothorax, hemothorax, and catheter infection for the patient. So, sometimes this approach can even save the patient's life. Also, hospitalization and the stress of reoperation can affect the mental state of patients. By using Alteplase, the patient can be relieved of the mentioned problems. The most important limitation of this work was the lack of control group and non-comparison with other drugs. Further studies in this field are suggested.

CONCLUSION

We concluded that 1 mg and 2 mg Alteplase are safe and effective in clearing blocked central venous catheters for hemodialysis patients and have beneficial long - term effects.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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