Intravenous Thrombolytic Therapy for Deep Venous Thrombosis of the Lower Extremities

Jian YIN¹,a, Rui-Si XU²,b, Si-Qi ZHANG³,c*

¹Vascular Surgery, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.
²Endoscopy Center, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.
³Nephrology, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin Province, China.

a16407026@qq.com, bhrs-email@163.com, csiqi@jlu.edu.cn
*Corresponding author

Keywords: Venous thrombosis of the lower extremities, Filter, Catheter, Thrombolysis.

Abstract. Objective to investigate the efficacy and clinical application of catheter thrombolysis in the treatment of acute deep venous thrombosis of the lower extremities. Patients with acute lower limb DVT 2016 November 2013 year in November 50 cases as experimental group, June 2007 to 2010 December were acute lower extremity DVT patients 69 cases as control group. All patients were diagnosed by venography of lower extremity or Doppler by intravenous ultrasound, and symptoms such as pain or tenderness in the groin area, pain of the limb and so on. Results the clinical curative effect of 12 groups of test group 50 cases, 1 cases were lost, 13 cases were cured, 34 cases markedly effective in 2 cases, the total efficiency of 98% (49 /50); the control group of 69 cases, 11 cases were cured, 26 cases markedly effective, 5 cases effective, 27 cases ineffective, the total effective rate was 60.9% (42 /69).

Introduction

Deep vein thrombosis, referred to as DVT (hereinafter referred to as), DVT usually appears in the lower limbs, such as the thigh, lower leg and pelvis, is abnormal blood coagulation in the deep veins, is a lower extremity venous reflux disorder, the incidence of this disease Rate is high¹-², mainly due to slow blood flow, venous wall injury and hypervascular coagulation state. DVT pathogenesis, timely closure of occluded blood vessels, otherwise it will lead to the occurrence of pulmonary embolism, while the traditional anticoagulant, thrombolytic effect is not ideal, long treatment cycle, complications, trauma. In this study, intravenous catheter thrombolysis combined with inferior vena cava filter implantation DVT, are as follows.

Technology Survey

Catheter contact thrombolysis (CDT) is a method of interventional thrombolysis in which thrombolytic catheters are directly inserted into deep vein thrombosis under DSA fluoroscopy, which can improve the thrombus clearance rate and improve the drug the thrombolytic efficiency of rapid open blocked veins. The first was proposed by Semba et al³,
the rapid popularization and development of clinical in our country in the 90's, through the
catheterization of thrombolysis anticoagulant thrombolytic drugs continue bolus, direct
thrombus, thrombosis can quickly dissolve, less drug consumption, High utilization, can
reduce the complications of visceral hemorrhage, and can effectively protect the function of
deep venous valves in the lower extremities. In 2006, Vedanthan et al \cite{4} confirmed the
significant effect of CDT in the treatment of DVT based on the clinical data of 1046 patients.
The results showed that the success rate was 88%. CDT thrombosis complete dissolution rate
was 76% to 90%, the incidence of bleeding complications was 0. 3%~3.8%; and systemic
thrombolysis were 28%, 8% to 10% \cite{5}.

**CDT Indications**

(1) of acute iliofemoral venous thrombosis; (2) acute femoral popliteal vein thrombosis; (3)
the duration of less than 14 d.

**CDT Contraindications**

(1) using anticoagulant, thrombolytic drugs and contrast agents are taboo or allergy; (2)
Within the past 3 months there was a history of intracranial hemorrhage and surgery,
gastrointestinal and other visceral bleeding in one month and surgical history; (3) More
serious limb infection; (4) the pregnancy; (5) high blood and difficult to control pressure
(Systolic blood pressure>180 mm Hg, diastolic blood pressure>110 mm Hg);(6) the bacterial
endocarditis; (7)and a coagulation disorder;(8) Over 75 years of careful choice.

**The Operation Method and Path of CDT**

Preoperative preparation was diagnosed by medical history collection, physical
examination, color Doppler ultrasound or venography. Routine blood routine, clotting routine,
virus detection and electrocardiogram were examined to exclude operation taboos.

Inferior vena cava filter DSA patients with supine position, using Seldinger technology, the
contralateral femoral vein into first received contralateral iliac vein and inferior vena cava
angiography; such as the discovery of thrombosis of inferior vena cava, right internal jugular
vein puncture from inferior vena cava angiography to observe thrombosis, double renal vein
and inferior vena cava at the bifurcation of the opening position measuring the diameter of
inferior vena cava. The inferior vena cava filter is placed under the opening of the inferior
vena cava. If the implanted filter is recyclable, the inferior vena cava angiography is
performed before the thrombolysis catheter is removed. If there is no residual thrombus in the
inferior vena cava filter, it will be removed. If there is no residual thrombus, it will be placed
permanently. The indications for the insertion of the filter refer to the guidelines for the
diagnosis and treatment of deep venous thrombosis established by the vascular surgery group
of the foreign science branch of the Chinese Medical Association.

Catheter thrombolytic approach and method of anterograde approach: (1) the
catheterization of the small saphenous vein is suitable for the central and mixed lower
extremity DVT. Take the prone position, limb lateral malleolus and the Achilles tendon at the
middle longitudinal skin and about 2 cm, exposure of small saphenous vein; via the small
saphenous vein implanted 4~5 F catheter sheath, select the side hole length 20~40 cm 4~5 F
thrombolysis catheter limb iliac vein. (2) The catheterization of the great saphenous vein is
suitable for the central and mixed DVT of the lower extremities, and is also suitable for patients with fractures that cannot be reversed. During the initial part of the medial malleolus saphenous vein cut the skin and subcutaneous tissue, direct puncture in the path under the assistance of the guidewire through the popliteal vein communicating branch implantation via femoral vein to the inferior vena cava. The popliteal venous catheter: central type DVT for thrombosis confined to the iliac vein, while patients without limitation of limbs. The patient in the prone position, ultrasound guided or via dorsal vein angiography shows the location of popliteal vein puncture of popliteal vein catheter sheath, the rest of the operation. Anterograde approach cannot be inserted into the canal. Retrograde route can be chosen: (1) by jugular vein catheterization: the right neck vein is inserted into the catheter sheath, and the thrombolytic catheter is placed through the jugular vein into the iliac femoral vein of the affected limb, and the catheter tip is placed at the distal end of the femoral vein as far as possible. (2) femoral vein catheterization: puncture the healthy side femoral vein into catheter sheath, with the help of co-bra catheter, the guide wire was placed in the iliac femoral vein of the affected limb and finally switched to the thrombolysis catheter. The head of the thrombolysis catheter was placed at the distal end of the femoral limb.

The use of heparin for anticoagulant thrombolytic drugs is a common anticoagulant drug, which can be treated by subcutaneous injection or intravenous drip. After the injection of heparin, it can take effect immediately, reach its peak quickly, and then decrease its function. Its half-life in the body is 90 min and the effect of 2~3 h disappears. Low molecular weight heparin is mostly subcutaneous injection, and its half-life time is longer (12 h). Urokinase, recombinant tissue type plasminogen activator (t-PA) and streptokinase are currently clinically available thrombolytic drugs. Because streptokinase hypersensitivity and bleeding with restricted risk and other reasons, and because of the characteristics of urokinase and recombinant t-PA had good thrombolytic effect, low bleeding rate become the clinical treatment of DVT preferred, but because of the high cost, to make more use of urokinase clinical popularization. There is no uniform standard for the dosage and method of urokinase. We recommend catheter thrombolysis first 250 thousand units of urokinase plus 50 m saline L disposable thrombolysis catheter injection, then the use of high-pressure pump pulse injection of urokinase thrombolysis catheter, 60~80 /24 h million units, 2 times of administration, each within 1 h after injection. Injection of urokinase during intermittent period, heparin 100 ~ 150mg/24 h was injected through catheter. (2) continuous infusion of urokinase (24 h total 60~80 units) and continuous subcutaneous injection of low-molecular-weight heparin 5000 units, 12 h/times, and 7 d continuous application. In the process of anticoagulant and thrombolysis, it is necessary to check the index of coagulation daily. Anticoagulant therapy should be monitored: (1) clotting time: when heparin is used for therapeutic purposes, the time required for coagulation is prolonged 2~3 times, that is, 20~30 min; when the clotting time is less than 12 min, the dosage of heparin should be increased, and the dosage of heparin should be reduced when clotting time is 30 min. The activated partial thromboplastin time (APTT): normal values for the laboratory vary, heparin to extend 1.5~2.5 times. The concentration of serum heparin could be monitored to reach 0.3 ~ 0.5 g /m L. The indicators that should be monitored in thrombolytic therapy include: (1) prothrombin time: normal value of 11~13 s and >25 s as abnormal. (2) plasma fibrinogen: the normal value is 2~4 g/L, and plasma fibrinogen <1.5 g/L needs to reduce the dosage of urokinase, and continue monitoring, such as fibrinogen level <1 g/L, then discontinue immediately. (3) thrombin time: the normal value is 16~18 s, and the thrombolytic period should not exceed 3~4 times normal, and 60 s is
ideal. Each of the 48 h after thrombolysis for deep venous catheter angiography, if the display side hole section of thrombus most or all dissolved according to the length of the catheter thrombolysis can go back 20~30 cm. In the case of 7 d, the thrombolytic catheter was pulled out at 4~5 d after operation, and the history of the disease was prolonged to 6~8 d at 7~14 D.

**Treatment**

A total of 60 patients with acute lower extremity DVT admitted to our hospital from November 2013 to November 2016 were selected as the experimental group and 79 patients with acute lower extremity DVT admitted from January 2009 to June 2012 as control group. All patients were diagnosed by venography of lower extremity or Doppler by intravenous ultrasound, and symptoms such as pain or tenderness in the groin area, pain of the limb and so on. There was no significant difference in age, sex and thrombus location between the 2 groups (P>0.05), which was comparable.

The control group was treated with conventional anticoagulant or system thrombolytic therapy. The experimental group was implanted into VCF under the protection of the small saphenous vein catheter thrombolysis methods: implantation of inferior vena cava filter: 40 cases, implantation of permanent filter Recyclable filter implantation in 20 cases, Recyclable filter after 10~15 D, 19 of which were removed successfully 1 because there were a large thrombus together, give out. (2) implantation of catheterization: ultrasound examination and evaluation of the location and scope of thrombus, determine the position and length of the catheter. The limb of small saphenous vein section start routine disinfection and local anesthesia, patients in the lateral malleolus and the Achilles tendon at the midpoint of 1 cm small incision, exposing the initial segment of the small saphenous vein, insert 4F sheath, the wire along the small saphenous vein directly into the popliteal vein through the catheter sheath, upward inserted through the proximal head, through the guide wire the internal thrombolytic catheter implantation of conventional fixed thrombus. (3) thrombolytic therapy: daily dosage of urokinase 400 thousand U / time, 2 times / D, autolysis catheter catheter injection, about 60 min / times; Conventional heparin 125000 U + saline 60 m L for 24 h, to remove catheter. Ultrasonic monitoring, when the thrombus was completely dissolved, after the venous blood flow recovered, the thrombolytic catheter was retreated by about 15 cm, and the treatment period was 3~5 D.

Clinical observation of the index of 2 groups were observed, compared to the average treatment time, the dosage of urokinase, recurrent thrombosis, pulmonary embolism and bleeding complications such as index, postoperative follow-up of 12 months, according to the Villalta score standard[6], record the Villalta score of the 2 groups.

Invalid outcome: lower limb swelling and pain still exists, did not alleviate imaging of venous thrombosis dissolved, venous blood flow; effective: lower extremity swelling and swelling significantly reduced, there is still residual thrombus imaging examination of deep vein recanalization, and occlusion small proportion in 50%; lower limb swelling significantly reduced markedly: pain, decreased or disappeared, imaging of deep vein patency, but still remains part of thrombosis and recanalization / occlusion ratio greater than 50%; the cure: lower limb swelling and pain disappeared, lower extremity deep vein imaging blood stream recanalization, or have a little residual thrombus.
Results

Clinical curative effect of 2 groups of test group 60 cases, 1 case lost to follow-up, 17 cases cured, 37 cases markedly effective, 5 cases effective, the total efficiency of 98% (59/60); the control group of 69 cases, 1. Cases were cured, 28 cases markedly effective, 7 cases effective, 31 cases ineffective, the total effective rate was 60.7% (48/79). The total effective rate of the experimental group was significantly higher than that of the control group (P<0.01).

Compared with the control group compared with 2 groups of general detection index and Villalta score of experimental group, the average treatment time and the dosage of urokinase and bleeding complications were reduced, the difference was statistically significant (P < 0.05 or P<0.01); recurrent thrombosis and pulmonary embolism is reduced, but the difference was not statistically significant (P > 0.05); comparison with before treatment, after treatment, the Villalta scores of the 2 groups were significantly decreased, and the experimental group than the control group, the difference was statistically significant (P<0.05).(See Table 1)

Table 1. Comparison of 2 groups of general testing indicators and Villalta score [n( %)].

<table>
<thead>
<tr>
<th>index</th>
<th>test group(n=60)</th>
<th>Control group(n=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Billalta score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>21.4±4.7</td>
<td>22.8±3.3</td>
</tr>
<tr>
<td>After treatment</td>
<td>11.7±3.2*#</td>
<td>17.6±5.6#</td>
</tr>
<tr>
<td>Mean treatment time/d</td>
<td>4.5±1.1**</td>
<td>7.7±3.1</td>
</tr>
<tr>
<td>Urokinase dosage/U</td>
<td>360.1±40.3*</td>
<td>420.5±80.4</td>
</tr>
<tr>
<td>Thrombosis relapse</td>
<td>1(2.0)</td>
<td>7(10.1)</td>
</tr>
<tr>
<td>Bleeding complications</td>
<td>0**</td>
<td>17(24.6)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>3(4.3)</td>
</tr>
</tbody>
</table>

Discussion

Most of the DVT treatments were thrombolytic with acute phase urokinase impact therapy. Urokinase thrombolysis in the activation of plasminogen can also cause systemic fibrinolysis hyperfunction, resulting in skin and mucosa or intracranial hemorrhage and a series of bleeding complications, especially intracranial hemorrhage is the most serious, causing brain compression symptoms, the severity and the dosage of urokinase is proportional to the. In this study, urokinase was directly delivered to thrombus through catheter thrombolysis, which significantly increased the concentration of urokinase and increased the utilization rate of urokinase, and the dosage of urokinase in the experimental group was significantly lower than that in the control group (P<0.05). It is proved that VCF protected thrombolysis via small saphenous vein catheter for acute lower limb DVT, which not only reduces the dosage of urokinase, effectively dissolves thrombus, but also reduces severe bleeding complications caused by excessive urokinase.

Acknowledgement

This study was the outcome of the “establishment and experimental study of the mouse deep vein thrombosis model” of Jilin University.
References


