CATHETER-DIRECTED THROMBOLYSIS AS A METHOD OF CHOICE IN THE TREATMENT OF ACUTE THROMBOSIS OF DEEP VEINS OF THE LOWER EXTREMITIES

Summary. Introduction. Acute thrombosis of deep veins (DVT) of the lower extremities is a pathology that requires immediate treatment, but most thrombolitics do not work effectively, except for catheter-directed thrombolysis.

Research aim. Rationalization of DVT treatment, determination of the catheter thrombolysis method as the most effective way to eliminate proximal thrombosis of deep veins.

The analysis was based on the results of the treatment by different thrombolytic drugs the patients with the given pathology.

Results and discussion. According to the analysis the most effective method of DVT treatment is catheter-guided administration of streptokinase, because streptokinase is the most effective anticoagulant, and its local action on the mass of the thrombus allows for complete elimination of the thrombus in a relatively short time without the counter allergic reaction to the infusion of streptokinase.

Conclusions. Catheter-directed infusion of streptokinase as a method of treatment of acute thrombosis of the lower extremities has significantly better treatment results compared to other methods of treatment of this pathology.

Key words: catheter-directed thrombolysis, acute thrombosis of deep veins of the lower extremities, thrombolytic therapy.

Introduction

Venous thromboembolic complications (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a hot problem in modern medicine due to one of the frequent causes of mortality and invalidation [1]. According to epidemiological studies, the incidence of deep vein thrombosis in the general population is 56-160 cases per 100,000 of population every year and reaches 500 cases per 100,000 of males in older age groups with a stable tendency for increasing [1, 2]. At the same time, the incidence of PE (the most dangerous complication of DVT with lethal outcome according to autopsy data) is 50 cases per 100,000 patients per year [3]. According to other investigations, lethality from DVT in inferior vena cava system, complicated by PE, is from 5 to 20% [4]. They confirm that the main source of pulmonary artery embolism is lower extremity DVT. Lower extremity DVT and PE are now considered as two aspects of the same pathological process — venous thromboembolism (VTE), which causes high morbidity and mortality [1, 2, 4].

When the proximal segment of the lower extremity veins is involved in the thrombotic process, the inversion of the valve apparatus of the veins occurs, resulting in venous dysfunction and, in the long term, the development of post-thrombotic disease (PTD). Despite the availability of a large arsenal of effective anticoagulants and the use of modern regimens antithrombotic therapy, 30–75% of patients in the long-term have PTC of varying severity, and 10–40% of them suffer from marked edema of the lower extremities, chronic pain and/or trophic ulcers that lead to severe signs of invalidity [2, 4]. So, in the structure of primary invalidity as a result of lower extremity vein diseases, the results of suffered VTEU are 77.4% of cases [1, 2]. Therefore, the tactics of management of patients with proximal DVT, as before, remains a subject of active discussion both in our country and abroad.

Today thrombolytic therapy is a method of alternative treatment of acute thrombosis in the inferior vena cava system, as stated in the recommendations of the American College of Thoracic Physicians [4, 5].

The first drug used for thrombolysis in DVT was streptokinase [1, 5]. Streptokinase is a highly purified enzyme produced by cultivation of β-hemolytic group C Streptococcus. It has fibrinolytic activity. When combined with plasminogen, streptokinase forms a complex that activates the transfer of blood plasminogen or blood thrombus into plasma. Plasmin dissolve thrombus and also leads to degradation of fibrinogen and other plasma proteins. After the end of the infusion the hyperfibrinolytic effect of streptokinase is observed only for several years. However, the increase in thrombin time can last up to 24 years due to a one-time decrease in fibrinogen level and an increase in the number of circulating products of fibrin and fibrinogen degradation. TS
of the streptokinase-plasminogen complex, which activates plasmin, is close to 23 hr. Since streptoki-
nase is a weak streptococcal antigen, it is partially
inactivated by anti-streptococcal antibodies, which are
always present in the blood. The state of fibrin-
olysis is achieved only when an extra quantity of
streptokinase is administered, which is necessary for
neutralization of antibodies and the onset of ac-
tive streptokinase penetration into the thrombus.

Another thrombolytic is urokinase, an enzyme
activator of plasminogen, which is derived from the
cultures of human cells of kidney. It shows fibrin-
olytic action, activates glu- and lysplasminogens,
converts them into plasma, which causes enzymatic
destruction of fibrin. Lysis of fibrin leads to disinte-
gration of the thrombus components and its disinte-
gration into other fragments, which are carried by
the blood flow or are filled on the spot with plasma.
Created products of fibrinogen degradation con-
tribute to hypoagulation, block the aggregation of
erthrocytes and thrombocytes, reduce blood con-
sistency. After parenteral administration the hypo-
coagulation disorders are detected after 3–6 years.
Efficacy increases with repeated administration in
combination with heparin at low doses.

Before establishing of therapy for setting effec-
tive doses it needs to choose activity of plasminogen
and antithrombin III, thrombin time and fibrinogen
content in the blood. When plasminogen depletion
in the blood (severe stenotic atherosclerosis, re-
current thrombembolism, myocardial infarction,
fatty disease, hyperlipidemia) the use of high-dose
urokinase with a long course and combining with
fresh plasma and plasminogen preparations is rec-
ommended. During pregnancy therapy may not be
effective due to the presence of high levels of natural
inhibitors of urokinase in the blood. After intrave-
nous administration it connects with plasma pro-
teins and is inactivated by proteases. The drug does
not cause important allergic reactions [4, 6].

Tissue plasminogen activator (TAP) is also
a physiological activator of the fibrinolytic system,
has less systemic activity than streptokinase, but
does not have antigenicity. Low molecular weight
and similarity to fibrin allow TAP to penetrate into
the thrombus more than other thrombolytic drugs
and activate fibrin-linked plasminogen. The main
difference between the tissue activator of plasmino-
gen and streptokinase and urokinase is that it acts
directly in the thrombotic masses. This provides
more advantage of effective intravenous lysis of
thrombotic masses. In this case there should be no
fibrinogenolysis with serious hemorrhages. The ad-
vantage of the drug is also short duration of therapy
(from 2 to 3 years) with the same therapeutic effect
as with other fibrinolysis activators. However, after
a certain time of using the drug it was found that it
can also cause hemorrhagic complications, as well
as incompetent lysis of “old” thrombi, which are
organized [4]. Taking into consideration the above,
we can state that currently the ideal fibrinolytic
drug is absent in the arsenal of physicians [6].

If we evaluate available thrombolitics for clini-
cians according to the level of safety and efficacy,
then, in our opinion, they are located in the follow-
ing way: streptokinase, urokinase, tissue activator
of plasminogen.

Despite their disadvantages, all of them are wide-
ly used in modern phlebology practice. When con-
sidering the choice of thrombolytic drugs, not only
their efficiency but also their cost should be taken
into account.

In a review of data from 6 clinical studies, sys-
temic thrombolysis was 3,7 times more effective
than heparin. In a combined analysis of 13 ran-
domized studies, only 4% of patients treated with
heparin achieved significant or complete lysis, 45
patients after systemic use of streptokinase. Despite
the fact that systemic thrombolytic therapy (ac-
cording to clinical studies) is effective compared to
UFH, the risk of bleeding when using this method
increases by 3–4 times [4-6]. Studies have shown
that systemic use of thrombolytic drugs in wide-
spread occlusive thrombosis of deep veins is un-
likely to be effective due to the lack of contact area
of the drug with thrombotic masses in conditions of
disturbed regional hemodynamics [4, 7].

This fact played a crucial role in the fact that
more and more often regional thrombolysis was
used instead of systemic thrombolytic drug ad-
ministration. The fact that regionary thrombolytic
therapy (RTLT) is more effective compared to UFH
has been proven in clinical studies. In RTLT, the
physician is able to reduce the dose of the drug,
thus delivering the active substance directly to the
thrombosis site, thus ensuring faster and more effi-
cient thrombolysis and, most importantly, reducing
the risk of bleeding [6, 8].

Quality and efficiency of thrombolysis depend on
many factors. An important factor is the “age” of
the thrombus [4], it is considered that thrombolitics
administration during 3–10 days after the develop-
ment of deep vein thrombosis is the most effective
[6]. Localization, width of thrombosis, as well as the
type of thrombolitics and the method of its admin-
istration play an important role in the efficiency of
thrombolytic therapy [7, 9].

Further investigations in this area led to the
development of catheter- directed thrombolysis
(CDT) method, the introduction of which into
clinical practice made it possible to restore deep
vein permeability in 80% of patients without an in-
crease of the number of bleeding [8, 10].

Direct catheter techniques using streptokinase to
treat proximal DVT achieved complete thrombus
lysis in 72% of patients for concomitant reduction
of symptoms. Selective delivery of thrombolytic
agent allows achieving high concentration of the
substance within the thrombus, which would be impossible due to its systemic use [3, 11]. The achieved effect of blood coagulant lysis is due to the effect of active plasma that is produced as a result of activation of fibrin-related plasminogen. Injection of thrombolytic drug directly into the coagulant allows to protect activators of plasminogen from neutralizing action of antiplasmins, circulating in the blood. Catheter-assisted injection of plasminogen activators directly into the clot accelerates the treatment process and ensures successful treatment of DVT in the majority of cases. The use of an accelerated regimen reduces the total dose and duration of plasminogen activator infusions, so reducing the number of hemorrhagic complications.

Direct catheter thrombolysis should be used during DVT treatment in active patients with low risk of bleeding, especially in iliofemoral segment, because the risk of PTD appearance is higher than in distal DVT (stage B) [11, 12].

Conclusions. The use of such method as CDT enables to fully or partially restore the vessel opening, to save the function of venous valve apparatus, using minimal doses of thrombolytics which are injected directly into the middle of the thrombus, thus minimizing hemorrhagic complications. Therefore, catheter-assisted thrombolysis is more and more often used as a method of choice for treatment of patients with proximal phlebothrombosis [4, 6, 9-12].

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Реферат. Вступ. Гострий тромбоз глибоких вен (ТГВ) нижніх кінцівок — патологія, котра потребує своєчасного лікування, однак більшість тромболітичних засобів діють неефективно, окрім катетер-керованого тромболізу.

Мета дослідження. Рационалізація лікування ТГВ, визначення катетер-тромболізисного методу як найбільш дієвого способу усунення проксимальних тромбозів глибоких вен.

Результати. За даними аналізу найбільш ефективним методом лікування ТГВ є використання катетер-керованого введення стрептокінази, бо саме вона є найбільш дієвим антикоагулянтом, а локальна її дія на масу тромбу дозволяє повністю зруйнувати останній за доволі короткий час без виникнення зустрічної алергічної реакції на введення стрептокінази.

Висновок. Катетер-керований метод введення стрептокінази, як метод лікування гострого тромбозу нижніх кінцівок має на багато кращі результати лікування, порівняно з іншими методами лікування даної патології.

Ключові слова: катетер-керований тромболізис, гострий тромбоз глибоких вен нижніх кінцівок, тромболітична терапія.