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Progress in the Study of Drugs for Thrombolytic Therapy of Acute Myocardial Infarction

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Abstract: Acute myocardial infarction has become a serious disease that affects the quality of contemporary human survival, and improved efficacy and risk avoidance can be achieved through the upgrading of thrombolytic drugs and precise intervention. This article takes the development of three generations of thrombolytic drugs as the main line, and combs through the development of thrombolytic drugs from the era of urokinase and streptokinase to Alteplase and single-chain urokinase-type fibrinogen activator and their respective advantages and disadvantages. The advantages of three generations of tissue-type fibrinogen kinase derivatives, Reteplase, and tenecteplase, are compared and described in this article.

Keywords: Acute myocardial infarction; Thrombolytic therapy; Urokinase; Teneplase

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1. Introduction

Acute myocardial infarction belongs to the problem of cardiovascular blood supply disorders, which is classified as an acute and critical disease in cardiovascular medicine, and the priority of carrying out therapeutic interventions is higher, which needs to be realized as soon as possible to achieve effective interventions. Because the occurrence of this disease is more closely related to coronary atherosclerosis, when the hospital finds that patients have similar problems, it is necessary to carry out targeted measures promptly to help patients solve the problem [1]. With the continuous improvement of medical standards and the promotion of advanced treatment experience worldwide, the difficulty of treating acute myocardial infarction is decreasing, and the assessment of the actual type of acute myocardial infarction condition has been completed. According to the degree of occlusion of coronary artery thrombus, those completely close to occlusion are acute ST-segment elevation myocardial infarction, and the rest of the cases are categorized as non-ST-segment elevation myocardial infarction. According to relevant statistical data, the current myocardial infarction group is expanding, the incidence rate of rural middle-aged and elderly groups is increasing year by year, and the proportion of patients with ST-segment elevation type is getting bigger and bigger. Therefore, organizing the case data of patients with acute myocardial infarction, seeking more reliable treatment methods, and vigorously

carrying out research on thrombolytic therapy drugs are still the focus of current medical work.

Thrombolytic therapy is one of the recommended ways to solve coronary artery occlusion, which not only has a relatively long history of application and research but also has a more ideal practical application effect. It can open the relevant blood vessels, restore the blood supply to the patient's myocardial tissues promptly, lift the risk of death from ischemic heart disease, and together with percutaneous coronary intervention, emergency coronary artery bypass grafting and other techniques, form an emergency coronary artery embolism treatment plan to save the patient's life [2]. After nearly half a century of exploration, thrombolytic drugs have gone through many iterations and have accomplished three fruitful and significant changes, and have achieved the division of whether or not they act on fibrin (proteins), expanding the population for which thrombolytic drugs can be used to cope with, and pushing for a more diversified therapeutic approach. The important content of this article is to organize and summarize the existing research on thrombolytic drugs for acute myocardial infarction and complete a brief description of the relevant content as follows.

2. Mechanism of thrombolytic therapy for acute myocardial infarction

The work of the heart and the life activities of cardiomyocytes are dependent on blood transportation. When acute myocardial infarction occurs, the coronary arteries are basically in the situation of not being able to transport, at this time, the cardiomyocytes can only be maintained for no more than half an hour, and after that, they will be necrotic and lose their functions [3]. Once the degree of necrosis increases, it causes a regional chain reaction, an effect that is difficult to undo once it occurs, and a succession of life-threatening complications. According to the existing data show that in the coronary artery blockage will appear at several key time points, for example, at about 20 minutes, there will be necrotic cardiomyocytes; at more than 3 hours, myocardial cell necrosis will be more than half of the area; at more than 6 hours, cardiac myocardial tissue necrosis will be approximately 80%. Some scholars pointed out that when myocardial cell damage exceeds 40%, serious complications will begin to appear. The golden period of thrombolytic drug treatment in the infarction is within three hours; once the condition is delayed for more than three hours, the thrombolytic effect will be less than the expected results, but there is still a positive effect. Currently, some studies have also demonstrated the pain-relieving effect of thrombolytic therapy and found that even in patients with severe myocardial infarction, the adverse effects can still be reduced by thrombolytic therapy.

3. Thrombolytic therapy for acute myocardial infarction

Some studies have indicated that in the case of appropriate intervention methods, the thrombolytic time window of the patient will be expanded, which is more conducive to the recovery of the patient. Therefore, when carrying out thrombolytic drug therapy, it is necessary to flexibly use thrombolytic therapy to play the best therapeutic effect according to the situation. Intravenous thrombolytic therapy is the most common. According to the relevant research comparative report, intravenous thrombolytic therapy has obvious advantages, simple operation, and high acceptance by patients, so thrombolytic therapy is widely promoted. It mainly uses the upper limb channel as a medium to add thrombolytic drugs into the patient's blood circulation to achieve the effect of dissolving the thrombus. Secondly, arterial thrombolysis is relatively complex. The process is accomplished with the aid of direct imaging. The principle is to utilize a multilaterally perforated thrombolytic catheter to directly dissolve the thrombus. Studies have shown that this method is precise, less harmful, more targeted, and has a relatively high rate of revascularization, and intracoronary thrombolysis is one of the more effective types [4]. However, regardless of thrombolytic treatment methods, attention to the thrombolytic catheter

location, drug dose, and other key issues are required to maximize the control of bleeding risk.

4. Thrombolytic drug research

Research on thrombolytic drugs begins with understanding the composition of thrombus. Acute myocardial infarction patients' thrombus is generally composed of fibrin and other substances, and relevant studies have shown that dissolving fibrin can better complete the blood vessel opening. Therefore, most thrombolytic drugs follow the basic principle of activating fibrous enzymes to degrade fibrin. However, it is difficult to standardize the physical condition of patients, and it is impossible to achieve standardized treatment, so non-specific fibrinogen activators and specific fibrinogen activators are needed to cope with different conditions.

4.1. First-generation thrombolytic drugs

The first generation of thrombolytic drugs all belong to the non-specific fibrinogen activator fluid, whose important branches are two kinds of urokinase and streptokinase. Urokinase is a synthetic drug substance, which is named urokinase because it needs to be extracted with the help of urine or related tissue fluids to extract the necessary double-chain serine protease. According to research reports, it stimulates the thrombolytic zymogen in the blood, accelerates its conversion and functioning, and the substance has a certain antithrombotic coagulation effect, which partially facilitates the elimination of blood clots and accelerates the therapeutic process. The results of its use show that the drug is not targeted by the body as an antigen, the loss of potency and safety are guaranteed. As a more targeted drug, it also has the property of low cost, which was once chosen and sought after by the market. However, with the expansion of the scale of use, the drug gradually reflected the shortcomings of non-specific fibrinogen, that is, consuming excess fibrin, resulting in bleeding symptoms. Therefore, when using generation urokinase for treatment, it is required to try to maintain in the appropriate window period, intravenous thrombolysis not more than 6h, and need to confirm the status of the blood vessel after stopping the drug, to observe the effect, to prevent re-occlusion, and also need to control the time of drug use, to avoid the danger. Relevant research data show that with the improvement of pharmacological management, personnel quality, and other objective factors, as well as the reasonable improvement of urokinase, patients receiving urokinase after the vascular recanalization rate, from about 70% to nearly 83%; bleeding and other adverse conditions statistics are also reduced from more than 10%, and the overall quality of treatment continues to improve [5].

Streptokinase is an effective thrombolytic substance extracted from the culture fluid of hemolytic streptococci, and according to the results of the controlled study, it is pointed out that the drug, as non-specific fibrinogen activating fluid, has a similar action effect to streptokinase, and the manufacturing cost meets the market requirements, but the generalization of this drug is relatively poor in comparison with that of urokinase because the probability of this drug being regarded as an antigen by the human body during its use is that it will cause allergy, fever, and the safety coefficient is relatively low, hence leading to rare utilization of this drug in current clinical practice.

4.2. Second-generation thrombolytic drugs

The manufacture of second-generation thrombolytic drugs cannot be separated from the progress of related genetic engineering technology. To upgrade and improve the drug to avoid complications caused by non-specific thrombolytic zymogen, the type of second-generation drug is mainly a tissue-type fibrinogen activator that can complete specific thrombolysis. A representative one is Alteplase. The therapeutic effect of this drug relies on the 527 amino acids it carries, and in actual treatment, it can selectively activate the fibrinogen in the

thrombus to break down the fibrin in the thrombus and complete thrombolytic treatment. The specificity of the drug can help patients eliminate the risk of systemic fibrinolysis. Because the drug has a relatively short half-life, the effect is not sufficiently sustained. During application, Alteplase is used in relatively large doses and requires the completion of short periods of administration of large quantities of the drug. Relevant institutions recommend the use of intravenous thrombolysis, according to 15 mg, 20 mg, and 35 mg gradient injection, and according to the actual situation to control the dosing interval. Authoritative organizations on the drug dosage of the control demonstration concluded that the dose halved, but the efficacy of the difference is not obvious. However, compared with the first generation of drugs, in the second generation of drugs, the thrombolytic recanalization rate increased significantly, the mortality rate decreased to less than 1.2%, and the reinfarction rate after the realization of segmental administration was significantly lower than that of the first generation of drugs [6,7]. At the same time, some studies have emphasized the possibility of alteplase to prevent microvascular re-occlusion and put forward related ideas, but the practical verification of this idea is still divided.

Single-chain urokinase-type fibrinogen activators are representative of the better-performing second-generation agents. It has a relatively small number of amino acids and retains the dual properties of zymogen and enzyme. These properties allow it to perform thrombolysis in a way that ensures that the thrombus is dissolved relatively completely and that the fibrin in the plasma is not affected. Bleeding is relatively low and patients are less likely to develop allergic reactions. Studies have demonstrated the safety and efficacy of this drug.

4.3. Third-generation thrombolytic drugs

The main types of third-generation drugs are tissue-type fibrinogen kinase derivatives, of which Reteplase and Teneplase are used relatively frequently.

Reteplase itself is a genetically engineered and retooled derivative of Alteplase. Reteplase retains the potent effect of thrombolysis while reducing its specific receptor-binding properties through modified amino acid fragments to fully extend the drug's half-life cycle and improve therapeutic efficacy. It should be noted that Reteplase requires continuation of intravenous access and is used alone. Mixed administration with other drugs is prone to unpredictable trouble. Foreign research comparing Reteplase and Alteplase efficacy showed that the observation group of Reteplase had superior effectiveness, showing higher blood flow levels and significantly lower vascular re-infarction rates as compared to the observation group of Alteplase. Several medical institutions have given positive comments on this new type of drug [8,9].

Teneplase is a mutation product, as its effectiveness prolongation relies on multiple point mutations to achieve. According to relevant research, Teneplase not only prolongs the half-life cycle to 11–20 minutes but also has a nearly 14-fold enhancement of its fibrin specificity [10]. Both laboratory results and statistical data from medical unit studies demonstrated the superiority of Teneplase. Comparative results also found that when Teneplase was used in elderly female patients, it was able to reduce the incidence of cerebral hemorrhage and reduce blood transfusions. Additionally, the drug can realize thrombolysis through a single intravenous injection, which is more timely and convenient for acute patients. At present, China's production of Teneplase has been listed and put into use, and all the experimental data are relatively excellent. In the application field of elderly patients, the research of this drug is being supplemented, but there have been experiments to prove that after halving the dose, the safety and effectiveness of the drug are worth recognizing. However, the clinical aspect should continue to promote thrombolytic drug research, which will further amplify the therapeutic effect.

5. Conclusion

In summary, the continuous evolution of third-generation drugs has improved the effectiveness and safety of thrombolytic therapy, allowing patients to better cope with acute myocardial infarction. Moreover, the use of third-generation drugs has become the mainstream of treatment, the prolongation of its half-life is convenient for patient treatment, and the maintenance of specificity makes thrombolytic therapy more targeted. However, the clinical side should continue to optimize the treatment process, refine the details of drug therapy, more targeted control of drug dosage and timing, and rationally deal with the prognosis of the risk, thereby further enhancing the therapeutic efficacy of the drug itself and eliminating acute myocardial infarction issues in patients.

Disclosure statement

The author declares no conflict of interest.

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