Discussion on Curative Effect and Safety of Small-dosage Alteplase Combined with Urokinase in Treatment of Acute Pulmonary Embolism

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Abstract: Objective: to discuss curative effect and safety of small-dosage alteplase combined with urokinase in treatment of acute pulmonary embolism. Method: the inclusion time bucket of the objects of this study was from January 2017 to March 2018. Random number table was used to choose 64 patients with acute pulmonary embolism received in our hospital. Then, single blind method was used to classify them into control group and observation group. Each group included 32 cases. The control group received pure urokinase treatment, while the observation group received the treatment by small-dosage alteplase combined with urokinase. The clinical data of both groups were sorted, compared and analyzed in detail. Results: the improvement degree of pulmonary artery systolic pressure and arterial partial pressure of oxygen in the observation group was better than that in the control group. Total effective rate of clinical treatment was 93.75%, higher than that of control group (75.00%), $P<0.05$. Bleeding rate of observation group was 6.25%, while the bleeding rate of control group was 3.13%, without comparison difference, $P>0.05$. Conclusion: small-dosage alteplase combined with urokinase has the better clinical effect and higher safety for the patients with acute pulmonary embolism.

Since endogenous and exogenous emboli of the patients with acute pulmonary embolism block pulmonary artery and its branches, pulmonary circulation disorder occurs. Any carelessness will make patients lose life[1]. At present, many drugs can be used to treat pulmonary artery embolism clinically, but the clinical effect differs. To further improve clinical treatment effect of pulmonary artery embolism, the objects were classified into two groups, and different treatment schemes were provided for them to discuss clinical effect and safety of small-dosage alteplase combined with urokinase in the treatment of acute pulmonary embolism.

1. Data and Method

1.1 General data

In this study, 64 patients with acute pulmonary embolism who were received in our hospital from January 2017 to March 2018 were chosen as the objects with random number table method. Then, single blind method was used to classify the objects into control group and observation group. Each group included 32 cases. In the control group, the proportion of male and female patients was 18:14, and the age was 23-80, with the average age of 53.74±5.07. The duration from onset to acceptance of treatment was 6h-13d, with the average time of (10.50±1.30)h. In the observation group, the proportion of male and female patients was 19:13, and the age was 25-81, with the average age of 53.91±5.55. The duration from onset to acceptance of treatment was 7h-12d, with the average time of (10.43±1.07)h. The clinical data of both groups were entered in SPSS 20.0 statistical software, and the analysis results had no difference, P>0.05. The research content conformed to medical ethics and also gained the approval of Ethics Committee of the hospital.

Inclusion criteria: (1) the disease of patients was verified by clinical pathology and imageology, with typical clinical symptoms, including chest pain, dyspnea or polypnea, syncope, hemoptysis and hyoxemia etc.; (2) accompanied by shock, systolic pressure≤90mmHg, duration > 15min, pulmonary artery high pressure and (or) right cardiac insufficiency; (3) the disease time did not exceed 14d; the family members knew the research content and signed the informed consent form.

Exclusion criteria: (1) combined with other major organ diseases or functional insufficiency; (2) cerebral apoplexy and intracranial hemorrhage occurred within 3d after the onset; (3) retinal hemorrhage; hemorrhage in other parts; blood platelet count did not exceed 100×10^9/L; (4) incomplete clinical data; those who could not cooperate with clinical treatment and research.

1.2 Method

Observation group: thrombolytic therapy was implemented for the patients in the first day when the patients were hospitalized. 20mg alteplase (S20110051, Boehringer Ingelheim) and 600,000U urokinase (GYZZ H20113006, Techpool Bio-Pharma Co., Ltd.) were chosen. From the second day to the fifth day, 600,000U urokinase was given every day.

Control group: 40,000U/kg urokinase was given for the patients in the first day when the patients were hospitalized, and was intravenously injected within 30min. Later, 1,200,000U thrombolytic therapy was carried out. From the second day to the fifth day, 600,000U urokinase was given every day.

After thrombolysis was completed in the first day of treatment, patients' activated partial thromboplastin time (APTT) was closely monitored. If the value is lower than the normal value, low molecular heparin should be given for the patients (0.1ml /10kg) by subcutaneous injection. The drug was injected for the patients at the interval of 12h. After continuous injection of 5d, warfarin started to be given. If international normalized ratio of prothrombin time is2-3 times higher than the normal value, low molecular heparin should stop giving at once. The patients should take warfarin for 12 consecutive months[2].

1.3 Evaluation criteria of curative effect

Clinical effect judgment criterion evaluation is referred to in Literature [3]: patients' clinical

symptoms are improved significantly or disappear, and pulmonary artery embolism has been improved obviously or recovered, promoting the curative effect is significant. Patients' clinical symptoms are improved slightly or relieved, and degree of pulmonary artery stenosis does not exceed 50% or thrombus has been dissolved, promoting the curative effect is good. Patients' clinical symptoms do not change obviously, and degree of pulmonary artery thrombolysis does not exceed 25%, or no obvious change is seen, promoting the treatment fails. Patients' clinical symptoms are exacerbated, and the coloboma number of pulmonary artery embolism segment increases, promoting disease exacerbation. Obvious effect + effect = total effect, expressed with %.

1.4 Statistical method

SPSS 20.0 statistical software was used to analyze clinical data. Measurement data were expressed with $\bar{x} \pm s$, and tested with t test. Enumeration data were expressed with %, and tested with chi-square test. Statistical software analysis showed P＜0.05, with statistical significance.

2. Results

2.1 Comparison of pulmonary embolism improvement before and after treatment

Before the treatment, the comparison of pulmonary arterial systolic pressure and arterial partial pressure of oxygen in both groups had no difference, P>0.05. After the treatment, pulmonary arterial systolic pressure and arterial partial pressure of oxygen in both groups were not improved, but the improvement degree of pulmonary arterial systolic pressure and arterial partial pressure of oxygen in the observation group was better than that in the control group, P ＜0.05, as shown in Table 1.

Table 1 Pulmonary embolism improvement of both groups before and after treatment ($\bar{x} \pm s$, mmHg)

Group	Pulmonary arterial systolic pressure			Arterial partial pressure of oxygen		
	Treatment for 1d	Treatment for 3d	Treatment for 5d	Treatment for 1d	Treatment for 3d	Treatment for 5d
Observation group	41.19±9.07	33.95±8.64	30.71±6.78	83.90±7.98	86.42±8.05	89.97±9.50
Control group	55.63±9.15	48.15±9.02	45.35±6.85	69.36±8.02	72.15±8.37	75.04±9.32
t value	6.3402	6.4311	6.6304	7.2700	6.9512	6.3461
P value	0.0467	0.0416	0.0409	0.0365	0.0412	0.0438

2.2 Comparison of clinical treatment effect

Total effective rate of observation group was 93.75%, higher than that of control group (75.00%), P＜0.05, as shown in Table 2.

Table 2 Comparison of clinical treatment effect (%, n)

Group	No.	Significant effect	Effective	Ineffective	Exacerbation	Total effective rate (%)
Observation group	32	21	9	2	0	30(93.75%)
Control group	32	11	13	7	1	24(75.00%)
X^2 value	-	-	-	-	-	4.2267
P value	-	-	-	-	-	0.0389

2.3 Comparison of hemorrhage rate

Hemorrhage occurred to 2 patients in the observation group (6.25%), while hemorrhage occurred to 1 patient in the control group (3.13%). Hemorrhage rate of observation group was 6.25%, while that of control group was 3.13%, without comparison difference, X^2=0.3497, P=0.5543>0.05.

3. Discussion

For the patients with pulmonary artery embolism, thrombus blocked their pulmonary artery and branches, thus leading to continuous rise of pulmonary circulation resistance. As a result, pulmonary artery pressure continued to rise, and the load of right ventricle expanded, thus leading to right cardiac insufficiency or dysfunction. After embolism, returned blood volume of patients decreased, thus cardiac output reduced and blood pressure dropped. As time went on, patients' life safety would be threatened [4-6]. Niu Hongxia et al.[7] indicated that, the state of pulmonary embolism is dangerous, pathogenesis is complex and clinical manifestations are not typical, so misdiagnosis and missed diagnosis cannot be avoided. The fatality rate can reach 20%-30%. Thus, seeking a scientific and effective treatment scheme has the favorable reference value for clinical treatment of acute pulmonary embolism.

At present, thrombolytic therapy is often used to treat pulmonary embolism. This method can achieve certain effect, and it is easy and safe to operate. However, the common thrombolytic drug urokinase can easily cause Extensive fibrinogen consumption, and patients may thus bleed[8]. Alteplase is a plasminogen activating agent, and has very excellent specificity. It can be combined with fibrous protein in the body to active plasminogen and transform it into plasmin. When plasmin flows to the thrombus with blood, the obvious thrombolysis effect can be seen. The drug can work rapidly. Except rapid thrombus dissolution, it can also promote improvement and recovery of lung tissue reperfusion and obviously improve right cardiac insufficiency[9]. Multiple research results show that, large-dosage alteplase can increase patients' hemorrhage rate[10]. Thus, the patients in the observation group were treated by small-dosage alteplase (20mg) combined with urokinase. The results showed that, pulmonary embolism improvement of the observation group was significant. The improvement degree of pulmonary arterial systolic pressure and arterial partial pressure of oxygen in the observation group was better than that in the control group. The total effective rate of clinical treatment in the observation group was higher than that in the control group (75.00%). Only 6.25% patients bled. Thus, small-dosage alteplase combined with urokinase has obvious effect. It can fully improve the disease, and well control bleeding risk.

In conclusion, small-dosage alteplase combined with urokinase has high clinical effect in the treatment of acute pulmonary embolism. Besides, it will not increase hemorrhage rate, and it is safe.

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