EFFECT OF XUEBIJING COMBINED WITH THROMBOLYSIS ON PULMONARY EMBOLISM AND ITS EFFECT ON APELIN-13, INFLAMMATORY FACTORS AND HEMORHEOLOGY: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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ABSTRACT

Objective*: To observe the efficacy of Xuebijing combined with thrombolysis for pulmonary thromboembolism (PTE), and its effects on apelin-13, inflammatory factors and hemorheology.*

Methods*: 47 patients with high-risk PTE treated at the First People's Hospital of Changshu City from January 2013 to December 2019 were enrolled and divided into control group and observation group according to random number table. Both groups received thrombolysis using rt-PA. After its completion, unfractionated heparin sodium (UFH) was used for anticoagulant. On this basis, the observation group was treated with 100ml intravenous infusion of Xuebijing q12h for 7 days. The control group was treated with equal amount of normal saline. The two groups were compared before and at 3, 5, and 7 days after treatment in terms of oxygenation index, pulmonary arterial systolic pressure, apelin-13, TNF-α, IL-1, IL-6, IL-8, HMGB-1 levels and hemorheological indicators (low shear blood viscosity, high shear blood viscosity, RBC aggregation index, RBC deformation index, erythrocyte rigidity index, hematokrit, plasma viscosity and platelet aggregation rate). Also, APACHE-II score and incidence of bleeding events were compared between the two groups before and at 7 days after treatment.*

Results*: No such adverse reactions as allergies occurred in the two groups, and no difference was shown in bleeding events (P>0.05). In different time windows after treatment, oxygenation index, pulmonary artery systolic pressure, apelin-13, TNF-α, IL-1, IL-6, IL-8, HMGB-1 levels of the observation group were statistically different from the control group (P<0.05), and the observation group had a lower APACHE-II score than the control group on the 7th day after treatment, showing statistical difference (P<0.05). In terms of hemorheology, the two groups showed no significant difference over time in terms of RBC deformation index, erythrocyte rigidity index, hematokrit and plasma viscosity (P>0.05), showing no statistical difference (P>0.05), and the observation group was statistically different from the control group under the same time window in terms of low shear blood viscosity, RBC aggregation index and platelet aggregation rate (P<0.05).*

Conclusion*: Xuebijing can better improve clinical indicators of high-risk PTE by regulating apelin-13, inhibiting inflammatory factors and adjusting hemorheology without increasing the risk of bleeding, thus safe and reliable.*

Keywords: *Xuebijing, Pulmonary embolism, apelin-13, Inflammatory factors, Hemorheology.*

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Introduction

Pulmonary thromboembolism (PTE) is the most common type of pulmonary embolism (PE). Thrombus inducing PTE mainly derives from deep vein thrombosis of the lower limbs. PTE has a high incidence worldwide[(1)], showing an increasing trend with age[(2)]. PTE causes very high mortality rate and disability rate.

International registration studies in recent years indicate that its 7-day all-cause mortality rate is 1.9 -2.9%, and its 30-day all-cause mortality rate is 4.9 -6.6%[(3)]. PTE not only causes pulmonary artery stenosis or even occlusion by mechanical thrombus obstruction, thereby leading to a series of pathological changes.

Moreover, it is a result of imbalance of the coagulation and fibrinolytic system. Meanwhile, en-

dothelial cells are damaged by ischemia and hypoxia due to impaction of thrombus[4], thereby causing extensive inflammatory reactions under the action of neurohumoral factors, thus aggravating pathological changes of the lung.

Immediate thrombolysis is a major treatment for high-risk PTE at present, because it can rapidly dissolve some or all of the thrombus, restore lung tissue reperfusion, reduce pulmonary artery resistance, lower pulmonary artery pressure, improve right ventricular function, thereby lowering mortality. Multiple randomized clinical trials in Europe and the United States have confirmed that thrombolysis can quickly improve pulmonary hemodynamic indicators and increase early survival rate of patients[5-7]. So far, the mainstream thrombolytic drugs are recombinant tissue-type plasminogen agonists (rt-PA), which may dissolve thrombus faster. A Chinese study suggests that low dose (50mg rt-PA) has similar efficacy with FDA recommended dose (100mg rt-PA) while safety is improved[8].

Xuebijing (XBJ) injection is an intravenous preparation mainly prepared by extracting Chinese traditional medicines such as salvia miltiorrhiza, radix paeoniae rubra, carthamus tinctorius, szechuan lovage rhizome, angelica sinensis, etc. based on modern technology. Such main active ingredients as carthamin yellow A, salvianic acid, ferulic acid, paeoniflorin, ligustrazine are used as quality control standards to guarantee safety and stable efficacy of the injection. It has the effects of promoting blood and qi circulation, removing stasis and relieving pain, clearing away heat and toxic materials. According to function mechanism of traditional Chinese medicine, in this study, while using rt-PA to treat PTE, XBJ was used in combination to observe its therapeutic effect and its effects on adipokine apelin-13, inflammatory factors and hemorheology, and investigate function mechanism of XBJ in treating pulmonary embolism.

Patients and Methods

Study design and Settings

This study is a randomized controlled study approved by the hospital ethics committee. From January 2013 to December 2019, 47 patients with high-risk PTE admitted to emergency intensive care unit (EICU) and intensive care unit (ICU) in First People's Hospital of Changshu City were enrolled and divided into control group (thrombolysis) and observation group (thrombolysis + XBJ) according to random number table. All patients or their families participated on voluntary basis and signed informed consent.

Diagnostic criteria

According to the diagnostic method in "Guidelines on the diagnosis and management of acute pulmonary embolism" published by the European Society of Cardiology (ESC) in 2008, diagnostic criteria included clinical symptoms consistent with PTE, elevated D-dimer levels, right ventricular overload indicated by echocardiography, intrapulmonary thrombus indicated by CT pulmonary angiography (CTPA). Meanwhile, according to this guideline, risk stratification was performed based on whether hemodynamics was stable. Occurrence of hypotension or shock (defined as non-new-onset arrhythmia, hypovolemia, and sepsis-induced systolic pressure <90mmHg, or fall of blood pressure≥40mmHg for at least 15 minutes) is diagnosed as high-risk PTE.

Inclusion criteria:

• Patients meeting high-risk PTE diagnosis in "Guidelines on the diagnosis and management of acute pulmonary embolism";

• aged between 18~85 years old, no gender limitation

• Weight between 40~100 kg;

• Sign the informed consent.

Exclusion criteria:

• Patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), community-acquired or hospital-acquired pneumonia, active tuberculosis, bronchiectasis, sleep apnea syndrome, chronic pulmonary embolism and other lung diseases;

• patients with absolute contraindication to thrombus, including structural intracranial disease, history of hemorrhagic stroke, ischemic stroke within 3 months, active bleeding, recent brain or spinal surgery, recent head fracture trauma or head injury with bleeding tendency;

• patients with survival time after admission <7 days;

• patients with previous history of coagulopathy and taking anticoagulant drugs;

• patients with severe liver and kidney dysfunction (in multiple organ dysfunction score (MODS), single liver and kidney function scores 3 and above);

• patients with malignant tumor history;

• pregnant and lactating women;

• patient with uncontrollable hypertension (systolic pressure> 180mmHg);

• patients with blood diseases (such as polycythemia vera);

• those who have allergic reactions to XBJ and other proprietary Chinese medicine injections;

• patients judged unsuitable for the trial by the investigator (e.g. potential risk of medical disputes, post-organ transplantation event, etc.).

Withdrawal or dropout criteria:

• Loss of major data affects evaluation on efficiency of the main indicators;

• Due to condition changes or complications, the original treatment plan was changed or other treatment measures not appropriate for further study implementation were accepted;

• Those with allergies to XBJ during the treatment;

• Patients or family members voluntarily withdrew.

Methods

Trial treatment methods

Both groups were given conventional treatments such as oxygen inhalation or tracheal intubation, maintenance of internal environment stability and prevention of stress ulcers. Simultaneously, rt-PA was taken for thrombolysis. The method was continuous intravenous drip of rt-PA 50mg for 2 hours. After the end of rt-PA therapy, activated partial thromboplastin time (APTT) was measured every 2-4 hours. When the level was 2 times lower than the baseline value (or <80s), anticoagulation was performed with unfractionated heparin sodium (UFH). In the meantime, APTT was monitored every 4 hours and UFH dosage was adjusted to stabilize APTT value between 60-80s. On the basis of this treatment, while further using UFH for anticoagulation, the observation group received intravenous drip of 100ml XBJ injection (to be completed in half-hour) q12h for 7 days. The control group was additionally treated with saline under the same usage, dosage and treatment period as XBJ of observation group after UFH was started.

Drugs

XBJ injection, 10ml/tube, was produced by Tianjin Hongri Pharmaceutical Co., Ltd., with Chinese medicine permission number Z20040033. Alteplase (rt-PA, Actilyse), 50mg/tube was produced by Boehringer Ingelheim Pharmaceuticals, Germany, with imported drug registration number S20110051.

Outcome measures

Efficacy evaluation indicators include oxygenation index, pulmonary arterial systolic pressure and APACHE-II score. Where, changes in oxygenation index and pulmonary arterial systolic pressure need to be observed before and at 3, 5, and 7 days after treatment. APACHE-II score shows changes before and at 7 days after treatment. At the same time, apelin-13 levels, inflammatory factors TNF-α, IL-1, IL-6, IL-8, HMGB-1 and hemorheological indicators (low shear blood viscosity, high shear blood viscosity, RBC aggregation index, RBC deformation index, erythrocyte rigidity index, hematokrit, plasma viscosity, platelet aggregation rate) were detected. These indicators need to be detected and recorded for the two groups before and at 3, 5, 7 days after treatment.

When detecting apelin-13, TNF-α, IL-1, IL-6, IL-8 and HMGB-1 indicators, 3 ml venous blood was drawn in the morning on an empty stomach in the observation time window, which was centrifuged at 4 °C at 3000 r/min for 20min to collect the supernatant. Kit of Shanghai Biological Technology Co., Ltd. Enzyme Research (article number: ml028068) was used uniformly. Enzyme-linked immunosorbent assay (ELISA) was performed in strict accordance with the instructions to reduce test error. For hemorheology test, send the drawn blood sample to Changshu clinical test center, and the designated collaborators perform test using SA-7000 hemorheology analyzer (Succeeder Technology Co., Ltd., Beijing, China) based on standard procedure.

Pulmonary arterial systolic pressure was measured by the same experienced ultrasound physician (working for more than ten years) using Mindray M9cv portable color Doppler imagining (Mindray Biomedical Electronics Co., Ltd., Shenzhen, China) based on consistent method. Pulmonary arterial systolic pressure is calculated as: 4 × (maximum tricuspid regurgitation velocity) 2+ right atrial estimated pressure. Where, the right atrial pressure is estimated at 5mmHg for mild tricuspid regurgitation, 10 mmHg for moderate tricuspid regurgitation and 15 mmHg for severe tricuspid regurgitation.

APACHE-II score covers body temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, arterial pH, sodium, potassium, creatinine, hematokrit, white blood cell count, Glasgow

coma score, age, chronic disease and surgical status. The score range is 0 to 71 point[9].

Evaluation of Side Effects of XBJ Injection

Evaluation of adverse reactions to XBJ injection is mainly to observe bleeding events, including skin mucous membrane, digestive tract, urinary tract and intracranial bleeding. Other parameters include changes in vital signs (heart rate, blood pressure), presence or absence of allergic reactions (rash, asthma, shock), neurological symptoms (epilepsy), whole blood cell count, liver function (alanine aminotransferase, aspartase aminotransferase, total bilirubin, direct bilirubin), renal function (serum creatinine, urea nitrogen), blood glucose and electrolytes.

Statistical Analysis

All data in this study were comprehensively calculated and analyzed by SPSS 13.0 statistical software (SPSS Co., Ltd., Chicago, Illinois, USA). Measurement data for normal distribution are expressed as mean ± standard deviation ($\bar{x}\pm s$). If the measurement data are normally distributed with uniform variances, t test or one-way analysis of variance is taken for comparison. In the case of non-normal distribution or uneven variance, comparison between the two groups was analyzed by Mann-Whitney U test, and the binary data were analyzed by Fisher's exact test.

Results

Baseline Characteristics of Patients

47 patients with high-risk PTE were enrolled in this study, with 23 and 24 cases randomly assigned to the control group and the observation group, respectively. During the treatment, 1 patient in the control group was excluded due to intracranial hemorrhage. Finally, 22 patients in the control group and 24 patients in the observation group fulfilled the experimental research. The two groups have no statistical differences in baseline characteristics such as age, gender and BMI based on Table 1 ($P>0.05$). No significant difference is shown in Apelin-13, inflammatory factors, hemorheological indicators, oxygenation index, pulmonary arterial systolic pressure and APACHE-II score before the treatment ($P>0.05$).

Outcome Measures of Curative Effect

Both groups have improved oxygenation index after treatment, and the observation group has a higher improvement than the control group under the same time window, showing statistical difference ($P<0.05$). Both groups have decreased pulmonary arterial systolic pressure after treatment, and the observation group has larger decrease than the control group under the same time window, showing statistical difference ($P<0.05$). APACHE-II score has greater decrease in the observation group than in the control group on the 7th day after treatment, showing statistical difference according to Table 2 ($P<0.05$).

	Control group (n=22)	Observation group (n=24)	*P*
Age (years)	69.1±10.3	68.67±9.1	0.557
Male (n, %)	10(45.24)	11(45.83)	0.421
BMI	21.89±3.01	22.57±2.87	0.162
Apelin-13(ng/mL)	66.14±9.32	65.57±10.04	0.180
TNF-α(ng/L)	33.03±10.98	32.22±11.01	0.240
IL-1(ng/L)	22.93±9.97	23.14±9.34	0.113
IL-6(ng/L)	46.72±13.53	47.13±12.96	0.312
IL-8(μg/L)	42.14±10.98	41.83±11.02	0.108
HMGB-1(μg/L)	11.98±0.75	12.13±0.69	0.38
Hemorheology			
Low shear blood viscosity (mPa•s)	25.63±1.89	24.99±2.11	0.191
High shear blood viscosity (mPa•s)	4.78±0.87	4.69±0.92	0.055
Plasma viscosity	1.45±0.10	1.41±0.12	0.293
Platelet aggregation rate (%))	70.4±2.87	71.1±2.21	0.061
RBC aggregation index	6.45±0.87	6.52±0.56	0.083
RBC deformation index	0.71±0.23	0.76±0.26	0.091
Erythrocyte rigidity index	4.11±1.03	4.20±1.21	0.110
Hematokrit	0.43±0.04	0.44±0.03	0.345
Oxygenation index	132(71-216)	129(70-221)	0.113
Pulmonary artery systolic pressure (mmHg)	44.78±8.93	45.13±7.91	0.216
APACHE-II score	22.15±2.98	21.87±3.12	0.612

Table 1: Baseline characteristics of patients.

Group	Time	Oxygenation index	Pulmonary arterial systolic pressure	APACHE-II
Control group (n=22)	3d after treatment	182(99-242)[a]	38.13±8.02[a]	
	5d after treatment	199(124-258)[ab]	35.98±7.56[ab]	
	7d after treatment	231(159-325)[ac]	33.44±9.12[ac]	8.14±1.58[a]
Observation group (n=24)	3d after treatment	195(123-284)[ad]	36.11±7.24[ad]	
	5d after treatment	240(208-317)[abd]	32.75±8.85[abd]	
	7d after treatment	261(187-398)[acd]	29.81±7.47[acd]	6.12±2.01[ad]

Table 2: Comparison of oxygenation index, pulmonary arterial systolic pressure and APACHE-II score between the two groups at 3, 5, and 7 days after treatment.
Note: Compared with the same group before treatment, [a]P<0.05; compared with the same group 3 d after treatment, [b]P<0.05; compared with the same group 5 d after treatment, [c]P<0.05; compared with the control group in the same period, [d]P<0.05.

Other Outcome Measures

Apelin-13 and inflammatory factors TNF-α, IL-1, IL-6, IL-8, HMGB-1 decrease in both groups at 3, 5, and 7 days after treatment, but the observation group has more obvious decrease than the control group under the same time window, showing statistical difference based on Table 3 ($P<0.05$). In terms of hemorheological indicators, both groups have decreased low shear blood viscosity, RBC aggregation index and platelet aggregation rate after treatment,

and the observation group has lower measured value than the control group under the same time window (P<0.05). High shear blood viscosity decreases over time, showing statistical difference (P<0.05), but no significant difference is found between the two groups under the same time window (P>0.05). No significant changes are observed in RBC deformation index, erythrocyte rigidity index, hematokrit and plasma viscosity over time (P>0.05), and no statistical difference is found between the two groups (P>0.05) (Tables 4 & 5).

Group	Time	Apelin-13	TNF-α	IL-1	IL-6	IL-8	HMGB-1
Control group (n=22)	3d after treatment	50.24±8.87^{a}	27.18±8.65^{a}	19.51±9.64^{a}	38.11±7.53^{a}	36.02±5.69^{a}	9.18±0.22^{a}
	5d after treatment	34.91±6.93^{ab}	23.02±7.47^{ab}	16.19±8.32^{ab}	31.84±6.34^{ab}	32.25±4.96^{ab}	6.45±0.32^{ab}
	7d after treatment	25.36±4.62^{ac}	20.52±7.94^{ac}	13.85±6.04^{ac}	23.34±4.27^{ac}	25.61±4.12^{ac}	4.18±0.35^{ac}
Observation group (n=24)	3d after treatment	45.35±9.12^{ad}	26.96±8.17^{ad}	16.01±8.57^{ad}	33.51±7.12^{ad}	35.24±6.27^{ad}	7.34±0.25^{ad}
	5d after treatment	31.57±7.83^{abd}	21.42±7.67^{abd}	12.89±5.94^{abd}	27.96±6.56^{abd}	28.46±7.03^{abd}	4.87±0.31^{abd}
	7d after treatment	21.25±5.34^{acd}	15.86±6.98^{acd}	10.17±5.32^{acd}	19.16±5.41^{acd}	21.14±5.23^{acd}	2.23±0.42^{acd}

Table 3: Comparison of Apelin-13 and inflammation indicators at 3, 5 and 7th days after treatment.
Note: Compared with the same group before treatment, $^{a}P<0.05$; compared with the same group at 3 d after treatment, $^{b}P<0.05$; compared with the same group at 5 d after treatment, $^{c}P<0.05$; compared with the control group in the same period, $^{d}P<0.05$

Group	Time	Low shear blood viscosity	High shear blood viscosity	Plasma viscosity	Platelet aggregation rate
Control group (n=22)	3d after treatment	20.21±1.45^{a}	3.71±0.21^{a}	1.46±0.09	55.5±2.7^{a}
	5d after treatment	16.39±1.76^{ab}	3.49±0.15^{a}	1.45±0.11	40.3±3.0^{ab}
	7d after treatment	15.47±1.01^{ac}	2.98±0.11^{ab}	1.48±0.08	33.8±2.6^{ac}
Observation group (n=24)	3d after treatment	18.14±0.98^{ad}	3.68±0.19^{a}	1.39±0.13	50.8±3.1^{ad}
	5d after treatment	15.69±1.13^{abd}	3.42±0.21^{a}	1.42±0.08	35.3±2.5^{abd}
	7d after treatment	12.65±1.83^{acd}	2.87±0.14^{ab}	1.46±0.11	28.3±2.2^{acd}

Table 4: Comparison of hemorheological indicators between the two groups at 3, 5, and 7 days after treatment (1).
Note: Compared with the same group before treatment, $^{a}P<0.05$; compared with the same group at 3 d after treatment, $^{b}P<0.05$; compared with the same group at 5 d after treatment, $^{c}P<0.05$; compared with the control group in the same period, $^{d}P<0.05$

Group	Time	RBC aggregation index	RBC deformation index	Erythrocyte rigidity index	Hematokrit
Control group (n=22)	3d after treatment	5.51±0.41^{a}	0.72±0.21	4.13±1.21	0.42±0.03
	5d after treatment	5.12±0.36^{a}	0.73±0.18	4.22±1.18	0.42±0.04
	7d after treatment	4.98±0.32^{ab}	0.72±0.29	4.16±1.09	0.43±0.02
Observation group (n=24)	3d after treatment	5.01±0.38^{ad}	0.74±0.20	4.18±1.36	0.44±0.02
	5d after treatment	4.14±0.35^{abd}	0.75±0.19	4.20±1.13	0.43±0.03
	7d after treatment	3.21±0.29^{acd}	0.73±0.22	4.19±1.23	0.45±0.01

Table 5: Comparison of hemorheological indicators between the two groups at 3, 5, and 7 days after treatment (2).
Note: Compared with the same group before treatment, $^{a}P<0.05$; compared with the same group at 3 d after treatment, $^{b}P<0.05$; compared with the same group at 5 d after treatment, $^{c}P<0.05$; compared with the control group in the same period, $^{d}P<0.05$

Side Effects of XBJ Injection

One bleeding event occurred in the control group, and there was no bleeding event in the observation group. No significant difference is observed in the incidence of bleeding events between the two groups (P>0.05).

Discussion

Seen from the results of efficacy indicators, improvement of oxygenation index, pulmonary arterial systolic pressure and APACHE-II was more significant in the observation group than in the control group (P<0.05), indicating that XBJ combined with thrombolysis has more advantages and can improve clinical indicators more quickly, which will have a positive effect on the disease prognosis. Meanwhile, there is no significant difference in bleeding events between the two groups (P>0.05), and all cases in the two groups are free of adverse reactions such as allergies and impaired organ function. It can be seen that the preparation extraction technique is mature with reliable safety. At the same time, we attempt to elaborate the reasons for this result from apelin-13, inflammatory factors and hemorheology, and investigate the possible mechanisms of action.

Apelin is an endogenous ligand of angiotensin receptor-like protein J receptor (APJ receptor), which was first discovered in 1998[10]. Apelin precursors can be decomposed into a variety of Apelin active peptides. Apelin-13 is one of them and has the strongest potential efficacy[11,12].

Studies have shown that apelin-13 can reduce pulmonary vascular resistance and increase cardiac output, thereby improving pulmonary hemodynamics in the short term[13]. Meanwhile, studies have shown that apelin-13 levels in PE patients are significantly increased[14]. This study revealed variation trend of apelin-13 level in PTE thrombolysis, and apelin-13 had greater decrease in XBJ combined with thrombolysis than in conventional thrombolysis. It is speculated that effectiveness of the treatment improves pulmonary hemodynamics, thereby leading to changes in apelin-13 secretion in related tissue cells, but the mechanism of mutual regulation between apelin-13 and pulmonary hemodynamics remains unclear. Apelin-13 is expected to become an important indicator for early diagnosis and prognostic assessment of pulmonary embolism after continuing research.

Under PTE, pulmonary endothelial cells are damaged due to ischemia and hypoxia, thereby activating inflammatory cells to synthesize and release inflammatory factors under the intervention of various humoral factors[4], while inflammatory factors can aggravate pulmonary hypertension[15]. Multiple studies have shown that inflammatory response increases permeability of pulmonary vessels and increases exudation, resulting in alveolar and media

edema, which impairs diffuse function of the lungs and affects normal oxygenation. Animal experiments have shown that XBJ injection can achieve lung protection by inhibiting the levels of inflammatory factors[16-19]. This study indicate that both groups have decreased inflammatory factors TNF-α, IL-1, IL-6, IL-8 and HMGB-1 after treatment, but the observation group has faster decrease than the control group. The observation group had a lower decline than the control group under the time window. Under the same time window, the observation group had more significant improvement than the control group in oxygenation index, pulmonary arterial systolic pressure and APACHE-II score ($P<0.05$), suggesting that XBJ can faster and more significantly reduce the level of inflammatory factors, reduce permeability of pulmonary capillaries and reduce exudation, thereby promoting improvement of lung function[20,21].

This study attempts to illustrate the advantages of XBJ in treating PTE from the perspective of hemorheology. No similar research has been previously reported. The results showed that XBJ had no significant effect on hematokrit, RBC deformation index, erythrocyte rigidity index and plasma viscosity. Decrease in low shear blood viscosity and RBC aggregation index was more significant in the observation group than in the control group. Low shear blood viscosity is mainly affected by red blood cell aggregation. Therefore, it suggests that XBJ can reduce whole blood viscosity and increase blood flow by inhibiting red blood cell aggregation, thus reducing the incidence of thrombus. Platelet aggregation constitutes an important link in thrombosis. The results show that XBJ can inhibit platelet aggregation, thereby promoting thrombus inhibition. These effects of inhibiting the occurrence of thrombus are in line with XBJ's function of promoting blood circulation and removing blood stasis in TCM theoretical prescription, which play a positive role in the treatment of pulmonary embolism. The mechanism of XBJ in inhibiting the aggregation of red blood cells and platelets can be further studied, so that XBJ treatment scope can be extended to other diseases[16-30].

Conclusions

To conclude, this study shows that XBJ combined with thrombolysis can better improve clinical indicators of high-risk PTE by regulating apelin-13, inhibiting inflammatory factors and adjusting hemorheology as a safe and reliable choice.

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