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Effect of Buyang Huanwu Decoction on Platelet Related Biological Indexes in Pulmonary Fibrosis Model Rats

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Abstract

Objective: Taking Bu Yang Huan Wu Decoction as the research object, a rat model of pulmonary fibrosis was replicated to study the changes in platelets during the development of pulmonary fibrosis, providing a certain research basis for the clinical application of Bu Yang Huan Wu Decoction to alleviate the pathological state of pulmonary fibrosis. Research Method: The animals selected by this experiment are SD rats, which are randomly divided into blank groups, model groups, and complement (14.0g/kg) and low-low groups (3.5g/kg). The pelvic fibrosis rats were obtained in the bronchus injection of bolithycin solution (7mg/kg). After the continuous molding 21 d, the rats were continuously administered for 14 d. After the last time it was administered for 1 H, the abdominal aortic blood was taken to take blood, and the relevant testing indicators were continued. Research **Results:** Compared with the blank group, the blood viscosity of the rats in this group is significantly higher under the variable variable transmission in the full blood viscosity, and the viscosity of low -cut blood is significantly increased, and the viscosity of the plasma also increased significantly; the content of platelet indicators VWF,FN, β-TG, and PF4 all increased significantly. Related parameters have significantly elevated PLT, MPV,PCT,PDW, PLCR are significantly increased; the PT content of coagulation parameters is significantly reduced, and the increase in FIB content is significant; The content of inflammation factor parameters TNF-α, IL-1β, and IL-17 increased significantly, and the IL-10 content was significantly reduced. Compared with the model group, the high-dose group significantly reduces the full blood viscosity of low, medium and high-cut, and plasma viscosity is significantly reduced; platelet indicators FN, β-TG,VWF and PF4 are decreased significantly; related parameters PLT, MPV, PCT, PDW, PLCR are all significantly reduced; significantly increased coagulation parameter PT content, significantly reduced the FIB content ; IL-1β, IL-17, TNF-α have decreased significantly, significantly increased IL-10 content; The whole blood viscosity under the variable rate has significantly reduced effect, and the plasma viscosity is significantly reduced. A significant reduction of platelet indicators VWF, FN, β-TG, PF4 content, the t-PA content is significantly increased; MPV and PLCR have decreased significantly, which is significantly reduced by significant reduction PLT, PDW, PCT; significantly increased PT content of coagulation parameters, significantly reduced the FIB content ; Reduce , the IL-10 content increases significantly. Conclusion: 1) Bleomycin replicated pulmonary fibrosis model can cause abnormal changes in hemorheology; Abnormal changes of platelet parameters; 2) Buyang Huanwu Decoction improved the blood stasis level of pulmonary fibrosis, reduced blood viscosity and platelet parameters, inhibited the release of inflammatory factors, and alleviated the pathological state of lung tissue in pulmonary fibrosis.

Keywords: Buyang Huawu Decoction, Pulmonary Fibrosis, Platelets, Inflammatory Factors

1. Introduction

According to the syndrome differentiation of pulmonary fibrosis, "lung asthenia" and "lung obstruction" belong to the category of lung diseases in the theory of traditional Chinese medicine. The pathogenesis of pulmonary fibrosis is the invasion of external pathogens, internal arrest of phlegm turbidity, blood stasis, and accumulation of heat and poison, which lead to pathological changes such as lung and kidney deficiency, qi deficiency and blood stasis, phlegm-heat interaction, and obstruction of lung collaterals. Long illness leads to lung deficiency, phlegm and

turbidity retention in the body, and then transforms water to drink blood stasis, resulting in lung loss of ventilation and lung gas fullness, which is often induced or aggravated by experiencing external pathogens again. [1]In the process of clinical treatment of pulmonary fibrosis, the way to effectively improve the blood stasis state and clinical symptoms of patients with pulmonary fibrosis requires correct dialectics first, and then treatment, through the rational use of traditional Chinese medicine to treat, to achieve good therapeutic effect. The "Yilin Qiaocuo" of the Qing Dynasty physician Wang Qingren first recorded the Buyang Huanwu Decoction. In this prescription, Astragali is used as the essential drug for invigorating qi, and it is combined with the radix sinensis, Chuangxiong, and Carthagim, which play the role of invigorating qi, activating blood and channeling collaterals. It has a good improvement on qi deficiency and blood stasis, which is the fundamental cause and pathogenesis of pulmonary fibrosis.

2. Materials

2.1 Experimental Animals

Animal rats, category SD, clean grade, 40rats, weighing 200-220g, half female and half male, were provided by Liaoning Changsheng Biotechnology Co., LTD. SYXK(black)2017-004(animal license No.). Animals were kept in an indoor environment at a temperature of 20 to 22 °C, given solid feed, and drinking water freely.

2.2 Experimental Drugs

Buyang Huanwu Decolorization: 120 grams of Astragali, 6 grams of angelica tail, 5 grams of red peony, 3 grams of Chuangxiong, 3 grams of safflower, 3 grams of peach kernel, and 3 grams of earth dragon. The traditional Chinese medicinal materials used were purchased from the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine in strict accordance with the family, genus and species specified in the Pharmacopeia of the People's Republic of China 2020 Edition.

Bleomycin hydrochloride for injection: (national approved name H20055883, produced by Hanhui Pharmaceutical Co., LTD., specification 15,000 bleomycin units, batch number 20026111).

2.3 Experimental Reagents

See Table 1 for experimental reagents.

Table 1. Experimental Reagents

Reagent names	Manufacturer	Lot number
IL - 1 beta	Nanjing Jiancheng Bioengineering Institute	20201210
IL-10	Nanjing Jiancheng Bioengineering Institute	20201210
IL-17	Nanjing Jiancheng Bioengineering Institute	20201210
vWF	Nanjing Jiancheng Bioengineering Institute	20201210
Fn	Nanjing Jiancheng Bioengineering Institute	20201210
PF4	Nanjing Jiancheng Bioengineering Institute	20201210
Beta TG	Nanjing Jiancheng Bioengineering Institute	20201210
TNF alpha	Nanjing Jiancheng Bioengineering Institute	20201210
PT	Shanghai Changdao Biotechnology Co. LTD	1812126
TT	Shanghai Changdao Biotechnology Co. LTD	1801007
APTT	Shanghai Changdao Biotechnology Co., LTD	1812009
FIB	Shanghai Changdao Biotechnology Co., LTD	1804041
Saline solution	Harbin Sanlian Pharmaceutical Co. LTD	1910201203

2.4 Experimental Apparatus

The experimental apparatus is shown in Table II.

Table 2. Experimental Apparatus

Instrument Name	Manufacturer
Bio-rad imark microplate reader	Bole Inc
LBY-N7500B automatic hemorheology meter	Beijing Plisen Instruments
TGL-16G high speed table top centrifuge	Suzhou Jiemei Electronics Co
X500i automatic blood cell analyzer	Hisen Meikang Co., Japan

C2000-A automatic coagulation instrument	Beijing Plisen Instruments
DZKW-D-1 water bath	Shanghai Medical Analytical Instrument Factory
Proline micropipette	BIOHIT
NW10LVF Ultrapure Water system	Heal Force
H-2050R ultra-fast refrigerated centrifuge	Hunan Xiangyi
ELX-800 microplate reader	BIOTEK

3. Methods

3.1 Experimental Modeling

Forty SD rats were weighed and randomly divided into 4 groups (blank group, model group, supplemented high-dose group, supplemented low-dose group, 10 rats in each group). Rats were fed with normal diet and free water for 7 days. By means of endotracheal intubation, the model group, the high-dose group and the low-dose group were injected twice with bleomycin saline solution (7 mg/kg) through the trachea, 0.2 ml of the weight of 100 g rats were given, and the blank group was injected with the same volume of saline solution through the trachea. The blank group was injected with the same volume of normal saline solution. The rats were put back into the cage and given normal diet and water freely.

3.2 Grouping and Drug Administration

After 21 days of animal model establishment, normal saline solution (1 ml/100g) was given to the model group and blank group, and Buyang Huanwu decoction solution (1 ml/100g) was given to the high-dose and low-dose groups for 14 consecutive days. During this process, the rats were fed with normal diet and drank water freely. The rats were weighed every week.

The dosage was as follows: high dose group: 14.0 g/kg(clinical equivalent dose) crude drug; Low dose group: 3.5 g/kg(1/4 of the clinical equivalent dose).

3.3 Sample preparation

Rats were required to fast for 12 hours and drink freely before harvesting. After a maximum of 1 hour of intragastric administration, the samples were collected by abdominal aorta blood sampling. The anticoagulant tubes were EDTA anticoagulant tube, sodium citrate anticoagulant tube and heparin sodium anticoagulant tube, and the total volume of blood collected was about 10 ml. Platelet-related parameters, whole blood, plasma viscosity indexes, four coagulation parameters and inflammatory factors were measured.

At the same time, part of the lung tissue from the same part was collected and processed for pathological histomorphology observation.

3.4 Histopathological Detection Methods of Lung Tissue

Lung tissue was stained according to the operation method of HE staining kit, and then observed under light microscope.

3.5 Index Detection

3.5.1 Whole blood viscosity and plasma viscosity measurement methods

(1) Whole blood viscosity

The three shear parameters were set to 10, 60, and 200, respectively, by automatic hemorheology meter, and then anticoagulant blood was taken to determine whole blood viscosity.

(2) Plasma viscosity

The anticoagulant blood was centrifuged for 10 min at 3000 r in a centrifuge, the upper plasma solution was taken, and the plasma viscosity was determined using the same instrument as 2.5.1.

3.5.2 Determination method of platelet parameters PLT, PDW, MPV, PCT and PLCR

2 ml of EDTA-K2 anticoagulant blood was used for determination of related parameters using a complete blood cell analyzer.

3.5.3 Methods of APTT, PT, TT and FIB determination of coagulation

The contents of APTT, PT, TT and FIB were determined, and the corresponding reagents of the kit were added. After that, the indexes were detected by automatic coagulation meter.

3.5.4 Determination Method of Platelet Factor vWF, Fn, PF4 and β-TG

vWF, Fn, PF4, β-TG, t-PA and PAI-1 were detected according to the instructions of ELISA kit.

3.5.5 Determination of inflammatory factors IL-1β, IL-10, IL-17 and TNF-α

IL-1β, IL-10, IL-17 and TNF-α were detected according to the instructions of ELISA kit.

3.6 Statistical Analysis

SPSS16.0 software was used for statistical analysis by one-way ANOVA. Data $\bar{x} \pm s$ indicated that P<0.05 had significant difference.

4. Results

4.1 Whole Blood Viscosity and Plasma Viscosity

The regulatory effects on whole blood viscosity and plasma viscosity are shown in Table 3.

Table 3. Regulation effect of Buyang Huanwu Decoction on whole blood viscosity and plasma viscosity in pulmonary fibrosis model ($\bar{x} \pm s$)

Groups	Number of animals (n)	Dose(g/kg)	Whole blood viscosity (mPa·s)			Plasma viscosity (mPa·s)
			Low cut 10-1	Medium cut 60-1	Cut 200-1 for high	
Blank	9	—	7.19±0.53*	4.30±0.16**	3.57±0.29*	1.18±0.05*
Model	9	—	7.91±0.63	4.68±0.25	3.93±0.21	1.24±0.03
Tonic Yang High	9	14.0	7.27±0.37*	4.44±0.22*	3.61±0.41*	1.20±0.03*
Nourishing Yang low	9	3.5	7.21±0.55*	4.37±0.27*	3.66±0.37*	1.19±0.04*

Note: Compared with model group: *P<0.05,**P<0.01.

Table 3 showed that, compared with the blank group, the whole blood viscosity at medium shear rate was significantly increased in the model group (P<0.01), and the whole blood viscosity and plasma viscosity at low and high shear rates were significantly increased (P<0.05). Compared with the model group, the whole blood viscosity and plasma viscosity at low, medium, and high shear rates in the high-dose supplement group were significantly decreased (P<0.05). The whole blood viscosity at low, medium, and high shear rates in the low-dose supplement group also showed a significant downward trend (P<0.05), and the plasma viscosity value also decreased significantly (P<0.05).

3.2 Platelet Related Parameters

The regulatory effects on platelet related parameters are shown in Table 4.

Table 4. Regulation effect of Buyang Huanwu Decoction on platelet-related indexes in pulmonary fibrosis model ($\bar{x} \pm s$)

Groups	Number of animals(n)	Dose(g/kg)	PLT(×109/L)	PDW(fL)	MPV(fL)
Blank	9	-	988.8±35.69**	10.30±0.42*	6.15±0.16*
Model	9	-	1034.5±21.57	10.63±0.14	6.45±0.27
Tonic Yang High	9	14.0	1004.5±37.3*	10.43±0.12*	6.18±0.07*
Nourishing Yang low	9	3.5	1003.4±26.69**	10.33±0.11**	6.15±0.17*

Note: Compared with model group: *P<0.05,**P<0.01.

Table 4. Regulation Effect of Buyang Huanwu Decoction on platelet related indexes in pulmonary fibrosis model ($\bar{x} \pm s$)

Groups	Number of animals(n)	Dose(g/kg)	PCT	PLCR(%)
Blank	9	-	0.61 ±0.05*	4.18±0.26*
Model	9	-	0.67 ±0.04	4.76±0.70

Nourishing Yang high	9	14.0	0.61±0.05*	4.16±0.57*
Low tonic Yang	9	3.5	0.62±0.06*	4.15±0.59*

Note: Compared with model group: *P<0.05,**P<0.01.

Table 4 showed that compared with the blank group, the PLT value of the model group was significantly increased (P<0.01), and the PDW, MPV, PCT and PLCR values were significantly increased (P<0.05). Compared with the model group, the PLT, MPV, PCT, PDW and PLCR values in the high-dose group showed a significant downward trend (P<0.05). Fill and low dose group of MPV, PLCR, PCT values were reduced significantly (P < 0.05), and at the same time extremely significantly reduced PLT, PDW values (P < 0.01).

4.3 Coagulation Related Indexes

The results of the effects on coagulation indexes are shown in Table 5.

Table 5. Effect of Buyang Huanwu Decoction on coagulation indexes in pulmonary fibrosis model ($x \pm s$)

Groups	Number of animals(n)	Dose(g/kg)	APTT(s)	TT(s)	PT(s)	FIB(g/L)
Blank	9	—	18.03±1.69*	61.21±2.88*	15.59±0.88*	2.16±0.21*
Model	9	—	16.64±1.37	58.74±3.19	14.73±1.01	2.38±0.26
Tonic Yang High	9	14.0	17.98±1.19*	60.01±3.26	15.51±0.61*	2.19±0.14*
Nourishing Yang low	9	3.5	17.47±1.16*	59.48±4.21	15.47±0.68	2.15±0.19*

Note: Compared with model group: *P<0.05,**P<0.01

Table 5 showed that compared with the blank group, the contents of coagulation parameters APTT, TT, PT and FIB in the model group had a significant increase trend (P<0.05). Compared with the model group, the levels of APTT, PT and FIB in the high-dose supplement group were significantly decreased (P<0.05), and only the contents of APTT and FIB in the low-dose supplement group were significantly decreased (P<0.05).

4.4 Platelet Related Factors

The regulatory effects on the expression of platelet-related factors are detailed in Table 6.

Table 6. Regulation effect of Buyang Huanwu Decoction on platelet factors in pulmonary fibrosis model ($x \pm s$)

Groups	Number of animals(n)	Dose(g/kg)	vWF(U/L)	Fn(mu g/L)	Beta TG(mu g/L)	PF4(mu g/L)
Blank space	9	—	601.3±28.2*	45.09±4.39*	27.43±2.47*	3.06±0.64*
Model	9	—	693.1±99.5	55.42±7.76	37.55±5.80	4.48±0.87
Tonic Yang High	9	14.0	614.7±61.9*	48.86±7.25*	30.97±6.77*	3.52±0.51*
Nourishing Yang low	9	3.5	619.1±25.5*	47.47±8.16*	31.14±5.37*	3.67±0.36*

Note: Compared with model group: *P<0.05,**P<0.01.

Table 6 showed that the levels of platelet factors vWF, Fn, β-TG and PF4 in the model group were significantly higher than those in the blank group (P<0.05). Compared with the model group, the contents of vWF, Fn, β-TG and PF4 in the high-dose buyang group and the low-dose buyang group showed a significant downward trend (P<0.05).

4.5 Expression of Inflammatory Markers

The results of the effects on the expression of inflammatory markers are detailed in Table 7.

Table 7. Effect of Buyang Huanwu Decoction on inflammatory indexes in pulmonary fibrosis model ($\overline{x} \pm s$)

Groups	Number of animals(n)	Dose(g/kg)	IL - 1 beta (ng/L)	IL-10(ng/L)	IL-17(ng/L)	TNF alpha (ng/L),
Blank	9	—	48.07±34.3*	172.9±36.6*	348.2±26.7*	304.3±40.2*
Model	9	—	73.29±17.1	128.1±30.1	421.1±60.7	378.1±50.5
Tonic Yang High	9	14.0	50.03±11.8*	160.5±45.3*	369.2±55.4*	314.1±48.8*
Nourishing Yang low	9	3.5	51.77±27.2*	155.8±29.1*	373.7±43.6*	340.9±31.1*

Note: Compared with model group: *P<0.05,**P<0.01.

Table 7 showed that compared with the blank group, the contents of IL-1β, IL-17 and TNF-α in the model group showed a significant trend of increase (P<0.05), and the content of IL-10 showed a significant trend of decrease (P<0.05). Fill high dose group of IL - 1 beta, IL - 17, the content of TNF alpha compared with model group, have lower trend significantly (P < 0.05), the trend of IL - 10 content increased obviously (P < 0.05), low dose group of IL - 1 beta, IL - 17, the content of TNF alpha compared with model group, The content of Il-1β, IL-17, and Tnf-α in the low-dose group had a significant trend of decreasing (P<0.05), and the content of IL-10 had a significant trend of increasing (P<0.05).

4.7 Pathological Sections of Lung Tissue

HE staining results Figure 1

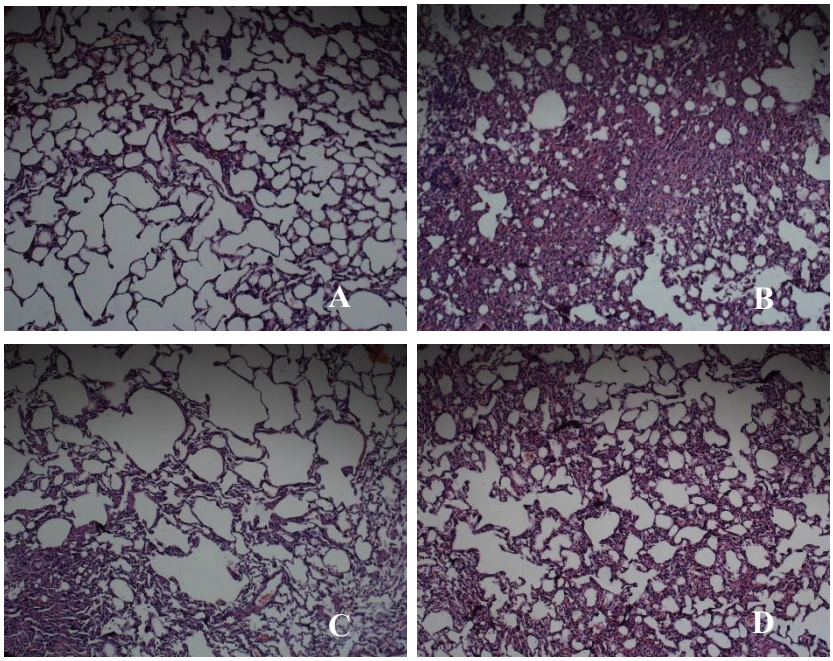

Figure 1. Effect of Buyang Huanwu Decoction on pathological morphology of lung tissue in rats with pulmonary fibrosis (x100)

Notes: A blank group; B model group; C group: D group: high group

Figure 1. The pathological observation of lung tissue in the blank group showed that there were inflammatory cells infiltration in the local lung interstitium, clear and complete alveolar structure, smooth alveolar wall, and a small amount of congestion in the alveolar. In the model group, there were large areas of parenchymal lesions in the lung tissue, changes in the shape and structure of the alveoli, obvious congestion in the alveoli, and a large number of inflammatory cells infiltration in the lung interstitium. In the high-dose Buyang Huanwu decoction group, the parenchymal lesion area of lung tissue was reduced, but more inflammatory cells infiltration in lung interstitium was still observed. In the low-dose Buyang Huanwu decoction group, the number of alveolar epithelial cells in the

lung tissue was reduced, the degree of inflammatory cell infiltration in the lung interstitium was improved, and local congestion in the alveolar was scattered. The results showed that the lung tissue of the model group had epithelial cell proliferation, alveolar structure changes, and a large number of inflammatory cell infiltration, and the inflammatory infiltration state of alveolar was significantly improved after Buyang Huanwu decoction treatment.

5. Discussion

Pulmonary fibrosis is characterized by qi deficiency and blood stasis. Qi deficiency and blood stasis are the core pathogenesis of this disease. Buyang Huanwu Decoction is from the famous doctor Wang Qingren of the Qing Dynasty, "Yilin Qiaojie · Xianqu · Paralysis and Wei Lun". In this prescription, a large number of qi invigorating drugs and multi-flavor blood promoting drugs are combined, including radix astragali, Dangguiwei, red peony, Chuangxiong, peach kernel, safflower and Dilong, whose functions are to invigorate qi, promote blood circulation and channel[2-3] collaterals. In the formula, four astragalus is used as the main medicine, qi is the mother of blood, and qi is the blood, which is consistent with the fundamental[4] of qi deficiency and blood stasis in the pathogenesis of pulmonary fibrosis.

5.1 Pulmonary Fibrosis and Hemorheology

The changes of hemorheology from a macroscopic perspective are mainly reflected in the two characteristic parameters of whole blood viscosity and plasma viscosity, which are a core index to measure the degree of blood viscosity, and they are also regarded as a key indicator for the diagnosis of pulmonary fibrosis and blood stasis. The high, medium and low shear rate of whole blood viscosity show different degrees of change, and the influencing factors mainly include red blood cell related parameters and plasma viscosity. By regulating the friction resistance of blood, the above parameters make the viscosity show different dynamic behavior under different shear rate conditions. Fibrinogen is the main factor that affects plasma viscosity, and it is also an important coagulation factor. Fibrinogen can increase the expression level in acute infection, inflammation, and trauma, and also accelerate the formation of pulmonary fibrosis and blood stasis.[5-6]

The results showed that the whole blood viscosity value of the rats in the pulmonary fibrosis group was significantly higher than that in the blank group, and the plasma viscosity increased significantly, indicating that the abnormal change of blood rheology is one of the microscopic symptoms after the occurrence of pulmonary fibrosis. Buyang Huanwu decoction treatment group had a significant effect on the whole blood viscosity and plasma viscosity under different shear rates. The results indicate that the abnormal hemorheological status of rats with pulmonary fibrosis can be effectively improved by Buyang Huanwu decoction.

5.2 Pulmonary Fibrosis and Platelet Activation

The adhesion of platelets to non-platelet surfaces is mainly mediated by von Willebrand factor (vWF). vWF is A macromolecular glycoprotein synthesized in endothelial cells and was first identified in the plasma of hemophilia A patients. Its adhesion function is a key factor for platelet adhesion. When vascular injury occurs, vascular endothelial cells are stimulated to release vWF and initiate the platelet adhesion process, which can bind to glycoproteins GPIb receptor, GPI b-ix and subendothelial collagen on the platelet membrane. vWF further binds to the activated GPIIb-IIIa receptor, and platelet aggregation and blood coagulation are aggravated, which leads to the formation[7-8] of pulmonary fibrosis and blood stasis. The abnormal expression of platelet active substances indicates that the activation and release of platelets are hyperactive, which is common in various blood stasis diseases and prethrombotic states[9-10].

Through the detection of vascular endothelial injury markers, von Willephrine and fibronectin, it was found that the levels of the two indexes in the plasma of the model group were significantly increased, indicating the presence of vascular endothelial cell injury. After the intervention of Buyang Huanwu decoction, the levels of vWF and Fn in the administration group were significantly lower than those in the model group, indicating that this prescription can inhibit platelet adhesion function and improve the state of vascular endothelial injury, and it is speculated that it may play a role in preventing thrombosis through this mechanism. In addition, compared with the blank control group, the plasma levels of β-thromboglobulin and platelet factor 4 in the model group were significantly increased, suggesting that there was a large number of platelet activation in the model group accompanied by the release of particle content, and platelets were in a high aggregation state, which led to the formation of blood hypercoagulation state, increased the risk of thrombosis and may promote the progression of lesions. However, Buyang Huanwu decoction intervention could significantly reduce the levels of β-thromboglobulin and platelet factor IV released by platelets. These results indicated that Buyang Huanwu decoction could inhibit platelet release, reduce platelet activation and alleviate platelet aggregation.

At the same time, judging from the results, the values of platelet parameters in the rats with pulmonary fibrosis showed a significant trend of increasing. The reason may be that the aggregation ability and adhesion ability of platelets are significantly increased when they are activated. After drug intervention, the levels of platelet parameters showed a significant decrease trend, indicating that the pathological state of platelet aggregation and adhesion was effectively improved and blood viscosity was reduced. It is speculated that the dynamic changes of platelet parameters can be used as one of the potential theoretical basis for the differentiation of pulmonary fibrosis.

5.3 Pulmonary Fibrosis and Coagulation Function and Inflammatory Response

Among the endogenous and exogenous coagulation pathways, the inflammatory response is closely related. Firstly, the exogenous coagulation pathway is activated, and the inflammatory process can activate coagulation function, inhibit fibrinolysis and cytokine secretion, and increase the expression of adhesion molecules on endothelial cells and increase by the change of coagulation function. The above changes will stimulate inflammation and coagulation abnormalities. The coagulation-inflammation-coagulation interaction mainly involves the coagulation factor VIIa in the extrinsic pathway, and the coagulation factors IX and X, thrombin and fibr[11-12]in in the intrinsic pathway. In addition, TNF-α, IL-1β and other inflammatory factors secreted by vascular endothelial cells and inflammatory cells also enhance the coagulation response, further promoting inflammatory response and coagulation formation. The endogenous coagulation pathway refers to the coagulation pathway carried out by membrane surface phospholipids after platelet activation. Activated platelets promote the secretion of adhesion molecules (fibrinogen, vWF) to upregulate various endothelial adhesion molecules and induce the release[13-14] of IL-8. Thrombospontin stimulates the expression of TF in monocytes and inhibits the release of t-PA. In addition to activating platelets, thrombin can also promote the conversion of fibrinogen to fibrin, which leads to the formation[15-16] of blood hypercoagulable state. APTT is associated with the endogenous coagulation pathway, while PT is associated with the exogenous coagulation pathway. Fibrinolytic activity is reflected by TT and FIB, and these factors may increase blood viscosity, increase platelet aggregation, and increase the risk of blood stasis.

In this study, FIB was significantly increased in the model group. Compared with the model group, Buyang Huanwu decoction decreased FIB content, indicating that it can reduce the content of fibrinogen. Buyang Huanwu decoction can inhibit the production of solid fibrin, thereby reducing blood viscosity, improving the activity of fibrinolysis system, and improving platelet aggregation, which is also one of the mechanisms of this prescription to inhibit platelet aggregation. The results showed that the contents of pro-inflammatory cytokines IL-1β, IL-17 and TNF-α in plasma showed a significant upward trend, while the expression level of anti-inflammatory factor IL-10 showed a significant downward trend. The application of Buyang Huanwu decoction could increase the expression of anti-inflammatory factors, decrease the expression of inflammatory factors, and decrease the value of platelet parameters. Platelet activation was inhibited, and the pathological state of qi deficiency and blood stasis in pulmonary fibrosis was further improved.

6. Conclusion

In conclusion, the pulmonary fibrosis model reproduced by bleomycin in this study can cause abnormal changes in blood rheology, abnormal changes in platelet parameters and abnormal expression of inflammatory factors. Buyang Huanwu decoction not only regulates the blood viscosity, but also improves the platelet related indicators in the pulmonary fibrosis model, so as to alleviate the pathological state of blood stasis, inhibit the release of inflammatory factors, and alleviate the pathological state of lung tissue in the model rats. It provides a certain experimental basis for clinical and scientific research on the mechanism of pulmonary fibrosis and drug treatment.

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