

arch and right lower pulmonary vein as the boundary. The imaging features of each lung area were calculated. According to the percentage of lesion area in the total area of the selected slice, 0: no abnormal change; 1: cumulative range < 5%; 2 points: 6%-25%; 3 points: 26%-50%; 4 points: 51%-75%; 5 points: 76%-100%. According to the routine, the upper edge of aortic arch, tracheal carina and 1cm level above right diaphragm were selected as the representative levels for evaluation. The pulmonary fibrosis score was the sum of the scores of all the pathological changes in all the pre-selected levels of the six lung regions; (4) Adverse reactions: the occurrence, severity and treatment measures of adverse reactions were recorded.

2.4 Statistical Methods

SPSS 23.0 statistical software package was used to analyze the data \pm Standard deviation ($\bar{x} \pm s$) F test was used to compare the three groups, t test was used to compare the two groups and the same group before and after treatment; The counting data were compared between groups χ^2 inspection. $P < 0.05$ was statistically significant.

III. RESULTS

3.1 Comparison of Clinical Efficacy

There was significant difference among the three groups ($P < 0.05$). The effective rate of group C was higher than that of group A ($t = 36.781$, $P < 0.05$); The effective rate of group A was also higher than that of group B ($t = 34.652$, $P < 0.05$). There was significant difference among the three groups ($P < 0.05$). There was no significant difference between group C and group A ($t = 0.982$, $P > 0.05$). But group C and group A were higher than group B ($t^1 = 29.462$, $P < 0.05$); $t^2 = 21.212$, $P < 0.05$). See Table 2 for details.

TABLE II. Comparison of clinical efficacy of three groups of patients

		Effectiveness	Invalidity	Efficiency (%)
Mild to moderate group	A group (15)	10	5	66.67
	B group (14)	6	8	42.86
	C group (16)	14	2	87.50
	χ^2 value			6.452
	P value			0.022
Severe group	A group (17)	11	6	64.71
	B group (18)	8	10	44.44

C group (16)	10	6	62.5
χ^2 value			34.322
P value			0.001

3.2 Comparison of Lung Function

FEV1, FVC and DLCO were significantly different in the light and moderate group ($P < 0.05$). FEV1, FVC and DLCO in group C were higher than those in group A, and the difference was statistically significant ($t_1=14.232, P<0.05; t_2=21.462, P<0.05; t_3=20.651, P<0.05$); FEV1, FVC and DLCO in group A were also higher than those in group B, and the difference was statistically significant ($t_1=18.022, P < 0.05; t_2=24.098, P<0.05; t_3=33.871, P<0.05$). FEV1, FVC and DLCO were significantly different in the three groups ($P<0.05$). There was no significant difference between group C and group A ($t_1=2.312, P>0.05; t_2=0.834, P>0.05; t_3=2.983, P>0.05$). But FEV1, FVC and DLCO in group C were higher than those in group B, and the difference was statistically significant ($t_1=18.762, P<0.05; t_2=19.351, P<0.05; t_3=22.381, P<0.05$). Group B: $t_1=17.791, P<0.05; t_2=21.623, P<0.05; t_3=29.087, P<0.05$). See Table 3 for details.

TABLE III. Comparison of FEV1, FVC and DLCO between the three groups

	FEV1 (L)		FVC (L)		DLCO (%)	
	Before	After	Before	After	Before	After
	treatment	treatment	treatment	treatment	treatment	treatment
A						
group (15)	1.68±0.32	2.11±0.35	1.91±0.41	2.69±0.34	60.59±3.35	75.24±6.33
B						
Mild to moderate group (14)	1.65±0.35	1.73±0.22	1.92±0.38	2.44±0.36	60.61±3.32	68.83±6.31
group C (16)	1.69±0.37	2.74±0.36	1.89±0.39	2.92±0.43	2.58±0.37	77.46±0.46
F value	3.509	18.346	2.509	9.346	0.598	19.324
P value	0.546	0.018	0.902	0.013	0.478	0.009

Severe group	A group (17)	1.28±0.36	1.86±0.42	1.72±0.46	2.35±0.42	60.34±3.37	76.13±6.29
	B group (18)	1.21±0.41	1.68±0.26	1.71±0.46	2.12±0.46	60.31±3.35	67.78±5.42
	C group (16)	1.29±0.47	1.84±0.39	1.68±0.47	2.32±0.41	60.28±3.32	76.04±5.38
	F value	4.201	21.432	2.091	12.362	1.201	31.235
	P value	0.408	0.009	0.306	0.011	0.362	0.002

3.3 Comparison of HRCT Scores

There was significant difference in HRCT scores among the three groups ($P < 0.05$). The HRCT score of group C was higher than that of group A ($t = 17.251$, $P < 0.05$); The HRCT score of group A was also higher than that of group B ($t = 12.761$, $P < 0.05$).

HRCT scores of the three groups in the severe group were statistically significant ($P < 0.05$). There was no significant difference between the HRCT scores of group C and group A ($t = 1.291$, $P > 0.05$). But HRCT scores of group C and group A were higher than those in group B, and the difference was statistically significant ($t^1 = 9.028$, $P < 0.05$); $t^2 = 11.292$, $P < 0.05$). See Table 4 for details.

TABLE IV. Comparison of HRCT scores of three groups

		Before treatment	After treatment
Mild to moderate group	A group (15)	26.14±13.57	19.81±12.47
	B group (14)	25.98±13.28	21.46±11.99
	C group (16)	25.48±12.67	18.04±11.17
	F value	0.405	6.453

	P value	0.876	0.043
	A group (17)	42.24±17.88	24.43±15.54
	B group (18)	43.58±18.32	29.35±16.34
Severe group	C group (16)	43.24±17, 43	25.07±14.56
	F value	0.309	17.467
	P value	0.784	0.006

3.4 Comparison of Adverse Reactions

There was no significant difference in the number of adverse reactions among the three groups ($P>0.05$). The number of adverse reactions in group C was higher than that in group A and group B ($t_1=12.021$, $P<0.05$; $t_2=18.291$, $P<0.05$).

In patients with gastrointestinal reactions, by changing the medication time to intrameal or using anti acid drugs, the symptoms were significantly improved or disappeared; Photosensitive reaction, it is recommended that patients do a good job in the sun protection work; Patients with elevated liver enzymes should be treated with liver protective drugs. All patients with adverse reactions through symptomatic treatment can be tolerated, no patients quit. See Table 5 for details.

TABLE V. Comparison of adverse reactions among the three groups

		Gastroin			Total	χ^2 value	P value
		testinal	Photoa	Elevated			
		reaction	llergy	liver			
			and	enzymes			
			rash				
Mild to moderate group	A group (15)	5	2	1	8	0.908	0.203
	B group (14)	4	2	2	8		
	C group (16)	4	3	1	8		
Severe group	A group (17)	8	3	3	14	21.892	0.008
	B group (18)	9	3	3	15		
	C group (16)	11	2	5	18		

IV DISCUSSIONS

Pifenicone is the first drug that has been proved to have certain effect on idiopathic pulmonary fibrosis through clinical trials. Relevant study [6] shows that pifenicone can effectively improve FEV1 and FVC in patients with idiopathic pulmonary fibrosis. Similar conclusions can be drawn in this study. It is found that FEV1, FVC and DLCO have been improved to different degrees after treatment with pifenidone, the mechanism is that PFP can down regulate fibroblast growth factor, tumor necrosis factor, platelet derived growth factor and transforming growth factor β . The production and expression of one of them can reduce the proliferation of fibroblasts and extracellular matrix deposition, thus achieving the aim of anti fibrosis [7].

The degree of lung function damage of idiopathic pulmonary fibrosis is related to HRCT signs. The bronchointerstitial, interlobular septum, the thickening of the interlobular stroma and the inflammatory exudation of the surrounding tissues were diffuse and distributed in HRCT. When the pulmonary fibrosis was reversed, the area and degree of the frosted glass shadow and the mesh shadow were gradually reduced on HRCT. The results showed that HRCT score could be decreased and there were statistical differences between the two groups. Acetylcysteine is also an antioxidant, by blocking NF- κ B signal transduction pathway, free radical scavenging and leukocyte aggregation were inhibited to inhibit inflammatory response and alleviate the damage of inflammatory response to lung tissue [8]. However, the effect of levycysteine alone is not good, so it is not recommended to treat IPF alone, especially for severe IPF.

In this study, it was found that the combination of pifenicone or pifenicone alone and acetylcysteine was superior to that of the patients in the single acetylcysteine group in clinical efficacy, lung function index (FEV1, FVC and DLCO) and HRCT score improvement index. Among them, in the light and moderate groups, the use of PFP and acetylcysteine was better than that of the patients in the single group in clinical efficacy, lung function index (FEV1, FVC and DLCO) and HRCT score improvement index, but in the severe group, there was no significant difference in these three aspects. There are many reports on the treatment of idiopathic pulmonary fibrosis with pifenicone and acetylcysteine, but the results are different. Some studies have suggested that [9], for patients with idiopathic pulmonary fibrosis in the middle and late stage, the treatment of pifenicone and acetylcysteine is more obvious than that of single use. Some studies also believe that [10-11], the combination of pifenicone and acetylcysteine can not improve the tolerance of patients with idiopathic pulmonary fibrosis to pifenicone, and it is not even as good as the treatment with pifenone alone in clinical efficacy. The results are similar to this.

The common adverse reactions of pifenicone and acetylcysteine include gastrointestinal adverse reactions, skin photoallergy and liver enzyme rise, but the degree is usually light, the patients can tolerate it, and the adverse reactions can be eliminated after treatment. In light and moderate patients, the adverse reactions of the two groups were similar to those of the combination of pifenicone and acetylcysteine, so the combination of the two did not increase the adverse reactions. However, in the severe patients, the adverse reactions of pifenicone combined with acetylcysteine are much higher than that of the single use of

pifenone. Therefore, in the case of close curative effect, there are more adverse reactions in combination. It is suggested to use pifenone alone.

In conclusion, it is suggested that the patients with idiopathic pulmonary fibrosis should be classified first. For light and moderate patients, it is suggested to use pifenone and acetylcysteine to improve the pulmonary function index and symptoms of pulmonary fibrosis; For severe patients, only pifenone was used; Pifenone has curative effect on IPF in light, moderate and severe patients.

ACKNOWLEDGEMENTS

This research was supported by the study on the correlation between neutrophils, eosinophils and their cytokines and COPD, asthma and ACOs .Project of Liaoning Provincial Department of Science and Technology (Grant No. 20170540400).

REFERENCES

- [1] Chen XR, Bao YX (2019) The latest diagnosis and treatment progress of acute exacerbation of idiopathic pulmonary fibrosis. *Clinical pulmonary miscellaneous* 24:733-737
- [2] The interstitial pulmonary disease group of respiratory science branch of Chinese Medical Association (2016) Chinese expert consensus on diagnosis and treatment of idiopathic pulmonary fibrosis. *Chinese Journal of tuberculosis and respiration* 39:427-432
- [3] Liu H, Li JX, Tian JL, Wang C, Wang YX, Wan YF, Weng Q, Xu MY (2018) Selective effects of fenitrothion on murine splenic T-lymphocyte populations and cytokine/granzyme production. *Journal of Environmental Science and Health Part B* 53:319-326
- [4] Yang ZG, Ma XT, Wang SQ, Tang XY (2008) Determination of plasminogen related protein in patients with idiopathic pulmonary fibrosis. *Journal of Zhengzhou University (Medical Edition)*43:774-776
- [5] Wang ZJ, Zhang YT, Gu XF, Yu XL, Meng LH, Liu YB, Zhang XM (2018) The changes of CT scores and the influence of quality of life in 36 patients with idiopathic pulmonary fibrosis treated by Fei Fei Fang. *Chinese Journal of traditional Chinese medicine (formerly Chinese Medical Journal)* 33:3682-3685
- [6] Raghu G, Noth I, Martinez F (2017) N-acetylcysteine for idiopathic Pulmonary fibrosis: the door is still open. *Lancet Respir Med* 5:1-2
- [7] Peng K, Liu H (2017) The effects of pifenone on NOX4 and TGF in elderly patients with chronic obstructive pulmonary disease complicated with pulmonary fibrosis- β L expression impact. *Journal of clinical and experimental medicine* 16:1294-1296
- [8] Guo HJ, Wang J (2019) Application of pifenone combined with acetylcysteine in the treatment of idiopathic pulmonary interstitial fibrosis. *Heilongjiang medical science* 42:229-230
- [9] Sakamoto S, Muramatsu Y, Satoh K, Ishida F, Kikuchi N, Sano G, Sugino K, Isobe K, Takai Y, Homma S (2015) Effectiveness of combined therapy with pirfenidone and inhaled N-acetylcysteine for advanced idiopathic pulmonary fibrosis:a case-control study. *Respirology* 20:445-452
- [10] Behr J, Bendstrup E, Crestani B, Guenther A, Olschewski H, Skoeld CM, Wells A, Wuyts W, Koschel D, Kreuter M (2016) Safety and tolerability of acetylcysteine andpirfenidone combination therapy in idiopathic pulmonary fibrosis:arandomized, double-blind, placebo-controlled, phase 2 trial. *The Lancet Respiratory Medicine* 4:445-453

[11] Lederer DJ, Martinez FJ (2018) Idiopathic pulmonary fibrosis. *N Engl J Med* 378:1811-1823

Aided project: 2017054040, the study on the correlation between neutrophils, eosinophils and their cytokines and COPD, asthma and ACOs