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CLINICAL STUDY

Use of Xinfeng capsule to treat abarticular pathologic changes in patients with rheumatoid arthritis

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Abstract

OBJECTIVE: To observe the influence of Xinfeng-capsule (XFC) on abarticular pathologic changes (APCs) and other indices of patients with rheumatoid arthritis (RA) and explore the mechanism of action of XFC in improving such changes.

METHODS: Three-hundred RA patients were divided randomly into a treatment group (n=150) and control group (n=150). A normal control (NC) group (n=90) was also created. Changes in cardiac function, pulmonary function, anemia indices and platelet parameters of RA patients were measured. Curative effects of the two groups were compared, and comparison carried out with the NC group.

RESULTS: In 300 RA patients, late diastolic peak flow velocity (A peak) was much higher (P<0.01) and early diastolic peak flow velocity (E peak), E/A, and left ventricular fraction shortening much lower (P<0.01) than those in the NC group. Vital capacity (VC), forced vital capacity in one second, forced vital capacity (FVC), maximal voluntary ventilation (MVV), maximal expiratory flow in 50% of VC (FEF50) and FEF75 were lowered remarkably (P< 0.05 or P<0.01). Platelet count (PLT), plateletcrit (PCT) and mean platelet volume (MPV) increased markedly (P<0.05 or P<0.01), and hemoglobin (Hb) level decreased significantly (P<0.05). After XFC treatment, the A peak and PLT and PCT were much lower (P<0.05), and E/A and the number of red blood cells as well as Hb level were much higher (P< 0.05), as were FVC, MVV and FEF50 (P<0.05 or P< 0.01), in the treatment group than those in the NC group. Total score of pain and swelling in joints, uric-acid level and high-sensitivity C-reactive protein level were much lower, and superoxide dismutase level as well as the number of CD4 + CD25+ regulation T cells (Treg) and CD4+CD25+ CD127- Treg were much higher (P<0.05 or P<0.01) in the treatment group than those in the NC group.

CONCLUSION: RA patients with pathologic changes in joints also suffer from lower cardiac and pulmonary functions and from parameters of anemia and platelet factors. XFC can improve the symptoms of RA patients, ameliorate their cardiac and pulmonary functions and reduce the parameters of anemia and platelet factors. XFC lowers the immune inflammatory reaction to improve APCs in RA patients.

Key words: Arthritis, rheumatoid; Pathologic processes; Xinfeng capsule

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease which can cause disability and morbidity. One study has shown that the risk of RA patients dying of cardiovascular disease is 2-5-times higher than that of healthy individuals.[1] RA often affects the lungs and pleura to cause pulmonary interstitial fibrosis, bronchiectasis and pulmonary hypertension.[2] About 11% of RA patients will suffer from secondary pulmonary interstitial pathologic change.[3] Anemia, one of the commonest abarticular pathologic changes, is related to the activity, extent and prognosis of RA.[4] Studies have confirmed that anemia within RA is characterized mainly by anemia of chronic disease (ACD).[5,6] One study discovered that, during active RA, platelet number is enhanced, alleviated and then reduced to those seen in healthy individuals.[7]
In the present study, we observed changes in cardiac function, pulmonary function, hematology and laboratory indices of 300 RA patients. We explored the mechanism of abarticular pathologic changes within RA and studied the influence of Xinfeng capsule (XFC), a Chinese drug for strengthening the spleen, removing dampness and clearing collaterals, in subjects with RA.

MATERIALS AND METHODS

Ethical approval of the study protocol

The study protocol was approved by the ethics committee of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine (Anhui Hefei, China; 2012AH-020-01). All experiments were completed at the test center of our hospital. The center has ISO 15189 recognition (serial number of certificate, CNAS MT0111).

Patients

The study cohort was 300 RA inpatients selected randomly in the Department of Rheumatology of the First Affiliated Hospital of Anhui University of Traditional Chinese Medicine from March 2011 to April 2013. There were 220 females and 80 males (2.75∶1) aged 23-70 [mean, (41 ± 15) years]. The course of illness was 0.3-35 [mean, (8 ± 4) years]. All cases conformed to diagnosis of RA set by the American College of Rheumatology (revised in 1987).[8]
The normal (healthy volunteer) group comprised 90 patients [64 females and 26 males; 2.46∶1; mean age, (41 ± 13) years]. None of these individuals had obvious organic disease as assessed by somatoscopy and immunologic testing. There was no significant difference in baseline data between the two groups (P>0.05, Table 1).

Table 1 Comparison of baseline data between the two groups

Item	RA (300 cases)	Normal control (90 cases)	P value
Male/female	80/220	26/64	>0.05
Age (years)	40±15	41±13	>0.05

Therapy

Patients in the treatment group took three XFC capsules at a time (*t.d.s.*, p.o.; batch number, 20100116; three-month course treatment; Drug-making Center, First Affiliated Hospital of Anhui University of Traditional Chinese Medicine). XFC consists of Huangqi (*Radix Astragali Mongolici*), Leigongteng (*Radix et Rhizoma Tripterygii*), Yiyiren (*Semen Coicis*) and Wugong (*Scolopendra*). Each capsule contained 0.5 g of crude drugs.
Patients in the control group took four 2.5 mg methotrexate (MTX) tablets (i.e., 10 mg at a time; three-month course treatment) once a week via the oral route (batch number, H20100175; Shanghai Xinyi Pharmaceutical Company Limited, Shanghai, China).
During the three-month treatment course in both groups, patients with intolerable joint pain were also administered non-steroid anti-inflammatory drugs. Patients with infections were given antibiotics.

Indices and methods for observations

Cardiac function: cardiac function before and after treatment in the two groups was determined using a VIVID®7 Ultrasound instrument (GE Healthcare, Piscataway, NJ, USA) according to the method described by Zhou *et al.*[9]
Pulmonary function: pulmonary function was determined with an Easy One Lung Function Analyzer (Beisida, Chengdu, China) according to the method described by Jian *et al.*[10]
Laboratory indices: various laboratory indices were determined before and after treatment. Blood components were determined using a XE-2100 Automatic Blood Analyzer (Sysmex, Tokyo, Japan). Erythrocyte sedimentation rate (ESR) was determined according to the method of Wei *et al.*[11] Levels of uric acid (UA), alpha-1-acid glycoprotein (α1-AGP) and high-sensitivity-C-reactive protein (hs-CRP) were determined using a 7600 Automatic Biochemical Analyzer (Hitachi, Tokyo, Japan). The UA kit and its reagents were purchased from Wako Pure Chemical Industries (Osaka, Japan). The hs-CRP kit was purchased from Fuxin Changzhen Medical Science (Shanghai, China). The α 1-AGP kit was purchased from Roche Diagnostics (Mannheim, Germany).
Regulation of T-cells: regulation of T-cells was determined in reference to the method described by Ruilian *et al.*[12] All reagents were purchased from Beckman Coulter (Fullerton, CA, USA). An Epics® XL Flow Cytometer (Beckman Coulter) was used.
Disease activity score (DAS)-28: the DAS-28[13] is an in-

dex used to measure disease activity. It is calculated according to the PREVOO method using the formula:

DAS-28=0.56 × (extracting the square root for the number of joint tenderness) + 0.28 × (extracting the square root of the number of joint swelling)+0.7×In (ESR)×1.08+0.16

DAS-28 refers to the score of 28 joints: shoulders; elbows; wrists; finger joints of both palms; near-end interphalangeal joints of both hands; and knee joints. DAS-28>5.1 suggests disease activity. DAS-28<3.2 denotes low disease activity. DAS-28<2.6 suggests disease alleviation.

Quantification of the total score of main symptoms and signs

Quantification of the total score of the main symptoms and signs was done in reference to Guiding Principles for Clinical Research on New Drugs of Traditional Chinese Medicine issued by the Chinese Health Ministry.[14]

Criteria for efficacy evaluation

The standard for evaluating curative effects was calculated in reference to Guiding Principles for Clinical Research on New Drugs of Traditional Chinese Medicine issued by the Chinese Health Ministry[14] using the formula:

Total effectiveness=(cases of clinical cure + cases of obvious effects+cases of effectiveness)/total cases×100%

Statistical analyses

Statistical analyses were carried out using SPSS v17.0 (IBM, New York, NY, USA). Measurement data are the mean ± standard deviation ($\bar{x} \pm s$). The Student's *t*-test was used to compare measurement data between groups. The χ^2 test was used for enumeration data. Spearman analyses were carried out for relevant data. $P<0.05$ was considered significant.

RESULTS

Changes in parameters of cardiac and pulmonary function, anemia and platelets in 300 RA patients

Table 2 shows a comparison of changes in parameters of cardiac and pulmonary function, anemia and platelet number between 300 RA patients and 90 cases in the normal group.

Analyses of parameters of cardiac and pulmonary function, anemia indices, DAS-28, total score of symptoms and signs, and laboratory indices of 300 RA patients

Table 3 shows analyses of parameters of cardiac and pulmonary function, anemia indices, DAS-28, total score of symptoms and signs, and laboratory indices of 300 RA patients.

Table 2 Changes in parameters of cardiac and pulmonary function, anemia, and platelets in 300 RA patients ($\bar{x} \pm s$)

Parameter		Control group (*n*=90)	Treatment group (*n*=300)
Cardiac function	E peak (m/s)	1.29±0.41	1.01±0.28[a]
	A peak (m/s)	0.79±0.21	0.99±0.24[a]
	E/A	1.63±0.34	1.02±0.32[a]
	EF (%)	68.40±6.01	65.56±5.32
	FS (%)	41.45±5.36	37.38±4.46[a]
Pulmonary function	VC	92.60±15.14	84.74±16.93[a]
	FEV_1	97.22±11.11	89.02±13.10[b]
	FVC	96.17±8.46	82.63±12.62[b]
	MVV	86.70±17.91	70.67±21.58[a]
	FEF25	75.95±21.84	73.33±21.36
	FEF50	82.72±14.75	74.69±15.42[a]
	FEF75	83.77±15.3	72.12±22.25[b]
	PEF	84.13±24.41	76.35±24.68
Anemia and platelets	Hb (g/L)	116.71±13.25	102.54±18.73[a]
	PLT ($\times 10^9$/L)	169.65±90.11	234.54±62.66[b]
	PCT (%)	0.22±0.06	0.29±0.04[b]
	MPV (fL)	10.88±1.23	11.98±1.18[a]

Notes: patients in the treatment group took three XFC capsules at a time three times a day; patients in the control group took MTX, 10 mg at a time, once a week, three-month course treatment. A peak: late diastolic peak flow velocity; E peak: early diastolic peak flow velocity; EF: ejection fraction; FS: fractional shortening; VC: vital capacity; FEV_1: forced vital capacity in one second; FVC: forced vital capacity; MVV: maximal voluntary ventilation; FEF25, FEF50, FEF75: maximal expiratory flow in 25%, 50%, 75% of VC; PEF: peak expiratory flow; Hb: hemoglobin; PLT: platelet count; PCT: plateletcrit; MPV: mean platelet volume. Compared with the datum in the Normal control group, [a]$P<0.05$, [b]$P<0.01$.

Comparison of curative effects between the two groups

Table 4 shows a comparison of the curative effects between the two groups. Total effectiveness in the treatment group was higher than that in the control group (χ^2=6.166, *P*=0.013).

Curative effect of XFC on parameters of cardiac and pulmonary function, anemia indices, parameters of iron metabolism and parameters of platelet function in RA patients

Table 5 shows the Curative effect of XFC on parameters of cardiac and pulmonary function, anemia indices, parameters of iron metabolism and parameters of platelet function in RA patients.

Influence of XFC on laboratory indices in RA patients

Table 6 shows the influence of XFC on the total score of symptoms and signs of joints, regulation of T cells, and laboratory indices in RA patients.

Observation of adverse reactions

During treatment, no obvious adverse reactions were noted in the treatment group. During treatment in the MTX group, four patients with transaminase levels exceeding two-times the upper limit of normal and two patients with obvious gastrointestinal discomfort withdrew from clinical research. No cases dropped out from the two groups. Therefore, eventually, there were

Table 3 Analyses of parameters of cardiac and pulmonary function, anemia indices, DAS-28, total score of symptoms and signs, and laboratory indices of 300 RA patients

Parameter		Cardiac function			Pulmonary function			Anemia	
		E peak	EF (%)	FS (%)	MVV	FEF50	PEF	Hb content	Serum iron
Joint symptoms	DAS-28	- 0.447[b]	0.103	0.203	0.397	- 0.29	- 0.294	0.029	0.022
	Joint pain	0.082	0.083	0.042	0.396	0.365	0.328	0.040	0.028
	Joint swelling	- 0.235	0.086	- 0.225	- 0.328	- 0.429	- 0.376	- 0.049	- 0.091
	Joint tenderness	- 0.108	- 0.074	- 0.017	- 0.409	- 0.426	0.420	- 0.278	- 0.171
TCM symptoms	Reduced appetite	0.389[a]	0.399[a]	0.112	0.315	0.410	0.310	0.056	0.045
	lassitude	0.445[b]	0.447[b]	0.155	- 0.294	- 0.359	0.396	0.047	0.139
	Loose stool	0.145	0.078	0.147	- 0.386	- 0.360	- 0.305	- 0.103	- 0.178
	Joint heaviness	- 0.076	0.142	0.152	- 0.389	- 0.420	0.289	- 0.172	- 0.138
	Local fever	0.131	0.385[a]	0.192	0.312	0.375	0.387	- 0.278	- 0.347[a]
Laboratory indic indexes	IgG	0.445[b]	0.131	0.303	- 0.264	- 0.397	- 0.299	- 0.342	- 0.042
	IgA	0.137	0.013	0.131	- 0.398	- 0.317	- 0.386	- 0.013	- 0.084
	IgM	0.149	0.152	0.019	- 0.357	- 0.403	- 0.358	- 0.191	- 0.172
	RF	0.025	- 0.471[a]	- 0.169	- 0.387	- 0.387	- 0.386	- 0.453[a]	0.207
	SOD	0.317[a]	0.243	0.118	0.163	0.348[a]	0.053	0.142	0.417[a]
	α1-AGP	- 0.439[b]	- 0.031	- 0.246	- 0.398	- 0.420	0.289	- 0.245	- 0.037
	ESR	- 0.113	0.109	0.152	- 0.298	- 0.411	- 0.302	0.183	0.082
	hs-CRP	- 0.362[a]	- 0.173	- 0.242	- 0.295	- 0.325	- 0.322	0.018	0.063

Notes: E peak: early diastolic peak flow velocity; EF: ejection fraction; FS: fractional shortening; MVV: maximal voluntary ventilation; PEF: peak expiratory flow; Hb: hemoglobin; IgG, A, M: immunoglobulin G, A, M; RF: rheumatoid factor; SOD: superoxide dismutase; α 1-AGP: alpha-1-acid glycoprotein; ESR: erythrocyte sedimentation rate; hs-CRP: high-sensitivity C-reactive protein; DAS: disease activity score; TCM: Traditional Chinese Medicine; FEF50: maximal expiratory flow in 50% of VC. [a]*P*<0.05, [b]*P*<0.01.

Table 4 Comparison of curative effects between the two groups [*n* (%)]

Group	*n*	Cure	Obvious effect	effectiveness	Non-effectiveness	Total effect
Treatment	150	5 (3.33)	42 (28.00)	88 (58.67)	15 (10.00)	135 (90.00)[a]
Control	144	5 (3.47)	29 (20.14)	80 (55.56)	30 (20.83)	114 (81.43)

Notes: patients in the treatment group took three XFC capsules at a time three times a day; patients in the control group took MTX, 10 mg at a time, once a week. [a]*P*<0.05, as compared with the datum in the control group. XFC: xinfeng capsule; MTX: methotrexate.

Table 5 Curative effect of XFC on parameters of cardiac and pulmonary functions, anemia indices, parameters of iron metabolism and parameters of platelet in RA patients ($\bar{x} \pm s$)

Parameter		Control (n=144)		Treatment (n=150)	
		Before treatment	After treatment	Before treatment	After treatment
Cardiac function	E peak (m/s)	0.97±0.27	1.03±0.22	0.89±0.27	1.08±0.21[a]
	A peak (m/s)	0.96±0.28	0.78±0.24[a]	0.99±0.29	0.64±0.22[bc]
	E /A	1.06±0.62	1.32±0.50[a]	0.90±0.39	1.69±0.05[bc]
	EF (%)	67.23±5.97	70.00±2.78	65.89±5.74	70.89±4.01[a]
	FS (%)	40.33±12.75	41.21±9.43	39.92±4.72	41.32±8.69
Pulmonary function	VC	85.14±14.82	89.13±13.42	84.92±11.83	91.83±14.22[a]
	FEV_1	86.81±12.52	94.58±13.83[a]	84.50±14.62	96.98±13.40[b]
	FVC	83.24±11.46	86.33±13.14	84.21±13.34	96.23±10.30[bd]
	MVV	72.43±18.72	77.16±19.24	75.38±18.71	85.64±19.56[ac]
	FEF25	81.11±18.90	83.73±16.48	80.16±20.19	84.29±22.51
	FEF50	74.84±16.38	76.01±14.93	73.33±16.52	83.62±13.96[ad]
	FEF75	71.44±21.23	83.41±18.70[a]	72.31±21.17	83.83±16.65[b]
	PEF	81.13±18.49	83.62±17.13	77.43±21.26	83.31±19.86
Anemia and iron metabolism	RBC ($\times 10^{12}$/L)	3.82±0.27	3.71±0.43	3.56±0.42	3.91±0.53[ac]
	Hb (g/L)	99.62±11.10	114.10±18.90	88.62±13.10	112.10±14.90[ac]
	SF (ng/L)	144.77±83.89	152.21±113.89	118.95±82.16	152.73±134.51[a]
	Tf (g/L)	1.66±0.74	1.82±0.51	1.65±0.62	1.97±0.62[a]
Platelets	PLT ($\times 10^9$/L)	242.05±62.95	223.65±83.17	241.58±58.89	199.93±23.86[ac]
	PCT (%)	0.28±0.48	0.31±0.15	0.39±0.14	0.25±0.07[ac]
	MPV (fL)	13.86±1.30	11.70±1.38	11.83±0.99	12.29±5.77

Notes: patients in the treatment group took three XFC capsules at a time three times a day; patients in the control group took MTX, 10 mg at a time, once a week, three-month course treatment. A peak: late diastolic peak flow velocity; E peak: early diastolic peak flow velocity; EF: ejection fraction; FS: fractional shortening; VC: vital capacity; FEV_1: forced vital capacity in one second; FVC: forced vital capacity; MVV: maximal voluntary ventilation; FEF25: maximal expiratory flow in 50% of VC; PEF: peak expiratory flow; Hb: hemoglobin; RBC: red blood cell; SF: serum ferritin; Tf: transferrin; PLT: platelet count; PCT: plateletcrit; MPV: mean platelet volume. [a]P<0.05, [b]P<0.01, as compared with the datum before treatment in the same group; [c]P<0.05, [d]P<0.01, as compared with the datum after treatment in the control group.

150 cases in the treatment group and 144 cases in the control group.

DISCUSSION

We investigated the curative effect of XFC on RA. We noted no obvious adverse reactions in the treatment group. During treatment in the MTX group, four patients with transaminase levels exceeding two-times the upper limit of normal and two patients with obvious gastrointestinal discomfort withdrew from clinical research. No cases dropped out from the two groups. The prevalence of total effectiveness in the treatment group was 90%, much higher than that in the control group (79%) (P<0.05), suggesting that XFC has a curative effect and safe as RA treatment.

In terms of parameters of cardiac function, RA patients had much lower early diastolic peak flow velocity (E)/late diastolic peak flow velocity (A) and left ventricular fractional shortening (FS) values (P<0.01), much higher A peaks (P<0.01) and much lower E peaks (P<0.01) than the 90 cases in the normal control group. These results are similar to those of other studies.[15] We found that the early stage of pathologic change in the cardiac function of RA patients was manifested in reduced diastolic function and no obvious symptoms. After treatment, the A peak decreased obviously (P<0.05 or P< 0.01) and E/A increased noticeably (P<0.05 or P< 0.01) in both groups. Ejection fraction (EF) was increased remarkably in the treatment group (P<0.05). The A peak was much lower (P<0.05) and E/A much higher (P<0.05) in the treatment group than those in the control group, suggesting that XFC can improve the parameters of cardiac function in RA patients markedly. Spearman analyses showed that, in RA patients, the E peak was obviously in a positive relationship with levels of superoxide dismutase (SOD) and immu-

Table 6 Influence of XFC on laboratory indices of RA patients ($\bar{x}$ ±s)

Parameter	Control (*n*=144)		Treatment (*n*=150)	
	Before treatment	After treatment	Before treatment	After treatment
Total score of joint pain	5.8±2.3	2.9±0.6[a]	5.5±2.1	2.1±0.6[ac]
Total score of joint swelling	4.6±3.2	3.0±1.1[b]	4.5±2.8	2.1±1.1[ac]
Total score of joint tenderness	5.1±2.2	2.7±1.8[a]	4.9±2.0	2.2±1.6[a]
Total score of joint rigidity in the morning	2.7±2.9	1.1±1.2[b]	2.4±3.0	1.2±1.1[a]
IgG (g/L)	17.8±5.6	15.1±4.5[b]	18.0±6.4	13.2±5.6[a]
IgA (g/L)	3.0±1.7	2.6±1.7	2.9±1.3	2.7±1.4
RF (U/mL)	153.4±36.5	146.0±33.2	165.1±42.0	147.3±38.4
ESR (mm/h)	47.2±24.6	25.2±20.5[a]	51.6±21.4	24.1±18.9[a]
hs-CRP (mg/L)	42.1±13.2	25.2±13.4[b]	48.7±15.7	17.2±11.7[ac]
UA (μmol/L)	254.4±56.7	243.0±43.2[b]	305.0±84.0	212.5±39.5[ac]
SOD (U/mL)	112.5±38.5	144.4±44.9[b]	108.5±31.1	148.7±33.0[a]
CD4+CD25+ (%)	4.96±2.67	5.6±2.5	4.3±2.2	5.7±2.9[a]
CD4+CD25+CD127- (%)	4.23±1.34	4.8±1.3[b]	4.1±1.0	5.3±1.3[a]

Notes: patients in the treatment group took three XFC capsules at a time three times a day; patients in the control group took MTX, 10 mg at a time, once a week, three-month course treatment. [a]P<0.01, [b]P<0.05, as compared with the datum before treatment in the same group; [c]P<0.05, as compared with the datum after treatment in the control group. IgG, A: immunoglobulin G, A; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate; hs-CRP: high-sensitivity C-reactive protein; SOD: superoxide dismutase; UA: uric acid.

noglobulin (Ig)G (P<0.01) and in negative relationship with DAS-28 as well as levels of α1-AGP and hs-CRP (P<0.05 or P<0.01). DAS-28 is related to cardiac damage in RA patients and is a comprehensive index for evaluating RA.[16] We found that the E peaks of RA patients were obviously in a negative relationship with DAS-28 (P<0.01), suggesting that cardiac damage in RA patients is closely related to disease activity.

Determination of the pulmonary function of 300 RA patients revealed the most severe pathologic changes to take place in forced expiratory flow at 50% of forced vital capacity (FEF50), followed by FEF25 and FEF75, and then followed by vital capacity (VC), expiratory reserve volume (ERV), peak expiratory flow (PEF) and maximum voluntary ventilation (MVV). After XFC treatment, inspiratory capacity (IC), MVV, forced vital capacity (FVC), forced expired volume in one second (FEV_1), FEV_1/FVC, FEF25, FEF50, FEF75 and PEF of RA patients were improved. The reduction in pulmonary function was manifested in decline of ventilation and diffusion. Improvement of FVC, MVV and FEF50 in the treatment group was much greater than that in the control group (P<0.05 or P<0.01). FEF50 of RA patients was obviously in a positive relationship with SOD level (P<0.05), suggesting that the pulmonary function of RA patients was closely related to pulmonary blood vessels and oxidation in pulmonary alveoli.

Analyses of blood and iron metabolism showed that 300 RA patients had much higher platelet count (PLT), plateletcrit (PCT) and mean platelet volume (MPV) (P<0.05 or P<0.01) and much lower hemoglobin (Hb) level (P<0.05) than 90 cases in the normal control group. After XFC treatment, anemia indices [number of red blood cells (RBCs) and Hb level] and parameters of iron metabolism serum ferritin (SF), transferrin (Tf) and mean corpuscular volume (MCV) increased obviously (P<0.05) and PLT and PCT declined noticeably (P<0.05). Hb content was negatively related to local fever and rheumatoid factor (RF) of joints, and positively related to SOD level (P<0.05). Studies have discovered that, at the active stage of RA, PLT and PCT increase obviously and are related to the active indices P-selective element, ESR and hs-CRP.[17,18] After treatment of RA patients with XFC, the supermicroscopic structure of platelets was improved, and expression of PLT and P-selective element was reduced.

We found that after XFC treatment in RA patients, pain, swelling and morning-rigidity of joints was improved. After treatment in the two groups, UA level, hs-CRP level and ESR were reduced obviously and SOD level as well as the number of CD4+CD25+Treg cells and CD4+CD25+CD127- Treg cells was noticeably enhanced (P<0.05 or P<0.01). However, the XFC group was superior to the MTX group in reducing levels of UA and hs-CRP and enhancing SOD levels as well as the number of CD4+CD25+Treg cells and CD4+CD25+CD127- Treg cells (P<0.05 or P<0.01). UA takes part in the generation and development of coronary atherosclerosis of elderly female patients, and levels of UA in patients with coronary heart disease increase.[19] We found that the UA levels of RA patients was enhanced obviously (P<0.05). Hyperuricemia, like

hyperglycemia, hyperlipemia and hypertension, is a dangerous risk factor for cardiovascular disease, and our results are similar to those in other studies.[14]

Mild RA affects only the joints and muscles of the four limbs, whereas severe RA can affect internal organs. Lingering arthralgia syndrome can affect the heart, lungs and blood vessels. In terms of traditional Chinese medicine (TCM), the pathogenesis of lingering arthralgia syndrome lies in: a feeble spleen and stomach; internal dampness and turbidity; deficient *Qi* and blood; imbalance between *Ying* and *Wei*; stagnation of phlegm and stasis in the collaterals.[20] TCM syndromes and signs are characterized by spleen deficiency, exuberant dampness and deficiency complicated with excess. XFC consists of Huangqi (*Radix Astragali Mongolici*), Leigongteng (*Radix et Rhizoma Tripterygii*), Yiyiren (*Semen Coicis*) and Wugong (*Scolopendra*) mainly for reinforcing *Qi* and strengthening the spleen. Huangqi (*Radix Astragali Mongolici*), Leigongteng (*Radix et Rhizoma Tripterygii*), Yiyiren (*Semen Coicis*) can regulate immunity, protect myocardiac cells, improve pulmonary damage, rectify anemia, reduce disease activity and prevent dysfunction of immunity caused by the immune suppression of Leigongteng (*Radix et Rhizoma Tripterygii*).

We found relevant indices for abarticular pathologic changes in RA patients to be closely related to laboratory indices and symptoms. XFC used to treat RA can obviously improve symptoms and laboratory indices, ameliorate cardiac and pulmonary functions, effectively treat anemia and improve platelet parameters, with a total curative effect superior to that of MTX. Its mechanism of action lies in reduction of UA level, hs-CRP level and ESR, enhancing SOD levels, regulating the number of T cells, and reducing the risk of repeated relapse of the immune inflammatory reaction.

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