

Observation on the Therapeutic Effect of Heat-clearing and Dampness-eliminating Dredging Collaterals Combined with Papaya Antirheumatic Pills on Treatment of Damp-heat Obstructive Ankylosing Spondylitis

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Abstract: *Objective:* Therapeutic effect of heat-clearing and dampness-eliminating dredging collaterals combined with papaya antirheumatic pills on treatment of damp-heat obstructive ankylosing spondylitis. *Methods:* A total of 200 patients with ankylosing spondylitis who were treated in our hospital from January 2018 to October 2019 were selected as the research objects and randomly divided into 2 groups, each with 100 patients. The control group was treated with leflunomide + papaya antirheumatic pills, and the observation group was treated with self-drafted recipe of heat-clearing and dampness-eliminating, the curative effect, visual analogue score (VAS), barthel AS function index (BASFI) score, biochemical indicators and adverse reactions between the two groups were compared. *Results:* After 12 weeks of treatment, the efficacy of the observation group was higher than that of the control group. The pain score, BASFI score, and biochemical index were lower than those of the control group, and the differences were statistically significant ($P < 0.05$); There was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$). *Conclusion:* Heat-clearing and dampness-eliminating dredging collaterals combined with papaya antirheumatic pills is effective in the treatment of damp-heat obstructive ankylosing spondylitis, which is beneficial to reduce the degree of pain and inflammation of the affected area, helps patients remain active, and improves activities of daily living.

Keywords: Damp-heat obstructive ankylosing

spondylitis; Heat-clearing and dampness-eliminating dredging collaterals; Papaya antirheumatic pills; Degree of pain; The biochemical index

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Ankylosing spondylitis (AS) is a progressive chronic spinal disease. It is mainly characterized by chronic inflammatory manifestations of tendon ligaments and central axis joint attachment points. The main symptoms are peripheral arthritis, inflammatory low back pain, extra-articular manifestations and tendonitis. As the condition continues to develop, joint ankylosis and spinal deformity will occur, which will greatly affect the work and life of patients. Western medicine is used for symptomatic treatment clinically, but long-term medication has many side effects, and the condition is often not effectively controlled or even recurrent. Traditional Chinese medicine can be treated according to the patient's symptoms, and has the advantages of multi-level treatment and good targeting. In recent years, the treatment of ankylosing spondylitis through Chinese medicine has gradually become a hot spot in clinical research. The purpose of this research was to investigate the efficacy of heat-clearing and dampness-eliminating dredging collaterals combined with papaya antirheumatic pills in treating damp-heat obstructive ankylosing spondylitis, which is shown as follows.

1 Information and methods

1.1 General information

With the approval of the Medical Ethics Committee of our hospital, 200 patients with ankylosing spondylitis who were treated in our hospital from January 2018 to October 2019 were selected as the research objects and randomly divided into 2 groups, each with 100 patients. The control group included 56 males and 44 females. Age: 15-62 years old, with an average of (33.35 ± 4.63) years old; The course of the disease was 1-6 years, with an average of (2.67 ± 0.89) years. The observation group included 54 males and 46 females. Age: 17-61 years with an average of (32.16 ± 5.03) years old; The course of the disease was 1-6 years, with an average of (2.88 ± 0.75) years. With the comparative analysis of the data of two groups, the difference was not statistically significant ($P > 0.05$) and comparable.

1.2 Inclusion criteria

(1) Inclusion criteria: Western medicine meets the diagnostic criteria for ankylosing spondylitis, the time of lower back pain is ≥ 3 months^[1]; the extent of chest expansion is significantly lower than that of peers; The lumbar spine has limited movement in lateral flexion and anterior and posterior directions; Traditional Chinese medicine conforms to the diagnostic criteria for damp-heat obstructive ankylosing spondylitis mentioned in *Clinical Guidelines for New Chinese Medicines*^[2]. The main symptoms are: restricted lumbar spine motion, unbearable spinal pain, lumbosacral pain; Accompanying symptoms: limbs drowsiness, dryness of the mouth or thirst, swelling and pain in limbs and joints, yellow urine and dry stool; tongue veins: red tongue, yellow greasy fur, slippery pulses; The patients were classified into grades 1-3 by X-ray examination; Both patients and their families voluntarily signed informed consent. (2) Exclusion criteria: Those who have used glucocorticoids or immunosuppressive drugs within 1 month; Those who have used biological agents within 3 months; Patients with advanced ankylosing spondylitis whose joints have been disabled or obvious deformities that needs surgery. Those with severe multiple organ dysfunction; Pregnant or lactating women; People with severe primary disease, blood disease or mental disorder; Those who are allergic or intolerant to the drugs used in this research.

1.3 Method

Control group: Oral Leflunomide (Jiangsu Yabang Epsom Pharmaceutical Co., Ltd., National Medicine Standard H20080420, Specification: 10mg) 10mg / time, twice / day; Oral papaya antirheumatic pills (Hubei Rongentang Pharmaceutical Co., Ltd., production batch number: 20150105). Dosage and administration: 5g / time, 3 times / day.

Observation group: On the premise of the above, combined with heat-clearing and dampness-eliminating prescription, the composition of the prescription is: Atractylodes 10g, coix seed 30g, cortex phellodendri 10g, cassia twig 12g, glabrous greenbrier rhizome 15g, Honeysuckle stem 15g, caulis spatholobi 30g, szechuan lovage rhizome 10g, lumbricus 15g, white mustard seed 10g, hizoma sinomeni causet 10g. Take 600ml of water and fry to 300ml for each dose. Both groups were evaluated after 12 weeks of continuous administration.

1.4 Evaluation Index

(1) With reference to the ASAS20 efficacy standard, the clinical efficacy was evaluated from 4 aspects: overall evaluation, spinal pain score, spinal inflammation score, and barthel AS function index after 12 weeks of administration. Achievement: At least 3 items have improved by more than 20%, and the absolute score has improved by ≥ 1 point. One item that has not improved by 20% has at least no deterioration compared with before treatment. Failure: The above criteria have not been met. (2) The pain degree was evaluated by visual analogue scale (VAS) before and after 12 weeks of treatment. The total score was 10 points. The higher the score, the more severe the pain. (3) Barthel functional index (BASFI): Before and after treatment, the BASFI scale was used to evaluate the functional recovery of patients from functional activities (8 questions) and daily living ability (2 questions). With a total of 10 points, the higher scores indicate higher overall fatigue. (4) After 12 weeks of treatment, 2 mL of venous blood was taken from two groups of patients to measure the C-reactive protein (CRP) level by enzyme-linked immunosorbent assay; the red blood cell sedimentation rate (ESR) level was measured by Weiss method. (5) After 12 weeks of treatment, adverse reactions such as diarrhea, nausea, vomiting, and rash were recorded and compared between the two groups.

1.5 Statistical methods

SPSS 18.0 software was used for data processing. Count data were expressed as percentages, χ^2 test was used and $\bar{x} \pm s$ was used to represent measurement data. *T* test was used and $P < 0.05$ was considered statistically significant.

2 Result

2.1 Efficacy

After 12 weeks of treatment, 92 patients in the observation group met the standards and 8 patients

failed; 79 patients in the control group met the standards and 21 patients failed. The compliance rate in the observation group was 92.00% higher than the control group at 79.00%, and the difference was statistically significant ($\chi^2 = 6.816$, $P = 0.009$).

2.2 Degree of pain

There was no significant difference in VAS score between the two groups before treatment ($P > 0.05$); the VAS score of the observation group was significantly lower than that of the control group after 12 weeks of treatment, and the difference was statistically significant ($P < 0.05$). See Table 1.

Table 1. Comparison of postoperative VAS scores between the two groups ($\bar{x} \pm s$, points)

groups	before treatment	after treatment	<i>t</i>	<i>P</i>
control group(n=100)	7.16±0.89	5.38±1.05	12.932	0.000
observation group(n=100)	7.23±0.68	3.43±0.96	32.301	0.000
<i>t</i>	0.625	13.706		
<i>P</i>	0.533	0.000		

2.3 BASFI score

The BASFI score (4.86 ± 1.03) of the observation group before treatment was compared with the control group (4.58 ± 0.87), and there was no significant difference ($t = 2.077$, $P = 0.039$); After 12 weeks of treatment, the BASFI score of the observation group (2.71 ± 0.94) was significantly lower than that of the control group (3.39 ± 1.02), and the difference was statistically significant ($t = 4.902$, $P = 0.000$).

2.4 Biochemical index

The CRP level (6.76 ± 1.89) mg/L and ESR level (18.87 ± 10.24) mm/h in the observation group were significantly lower than those in the control group (11.01 ± 3.68) mg/L and (25.31 ± 8.13) mm/h after 12 weeks, and the difference was statistically significant ($t = 10.273$, 4.925 , $P = 0.000$).

2.5 Adverse reactions

After 12 weeks treatment, there were 4 cases of leukopenia, 3 cases of transaminase elevation, 6 cases of gastrointestinal reactions in the control group, and the total incidence of adverse reactions was 13.00%; Observation group showed 2 cases of leukopenia, 1 case of transaminase elevation, 7 cases of gastrointestinal reactions, and the total incidence of adverse reactions was 10.00%; There was no significant difference between the groups ($\chi^2 = 0.442$, $P = 0.506$).

3 Discussion

Ankylosing spondylitis belongs to the category of “arthralgia” and “serum negative osteoarthritis” in traditional Chinese medicine. The theory of traditional Chinese medicine believes that arthralgia is caused by the governor vessel disorder due to insufficient kidney Qi, which causes wetness, coldness, wind, and hotness to invade the human body. With the addition of stasis and phlegm blockage, various intricate symptoms leads to the prolonged disease. In the early and middle stages of the disease, the main type is humid heat. The main symptoms are pain in the lower back, pain and swelling in the joints of the lower limbs, accompanied by local burning, and the whole body is heavy, fatigued, with yellow urine, sticky stool, red tongue, yellow greasy and slippery pulse. According to the theory of syndrome differentiation in traditional Chinese medicine, damp-heat and obstructive ankylosing spondylitis is caused by the heat transformed from the attack of exogenous pathogens and hurt the joints. Therefore, the main treatment should be clearing away heat and dampness, and promoting blood circulation. Leflunomide is a commonly used drug for rheumatoid arthritis and autoimmune diseases in western medicine. It can exert anti-inflammatory effects through immunosuppressive effects, but has long-term side effects. In order to improve the therapeutic effect, it was combined with papaya antirheumatic pills in this research^[3].

The results of this research showed that the efficacy of the observation group was higher than that of the control group after 12 weeks of treatment, and the VAS score, BASFI score, and biochemical indicators were lower than those of the control group. There was no significant difference in adverse reactions between the two groups, indicating that heat-clearing and dampness-eliminating dredging collaterals combined with papaya antirheumatic pills is effective in treating damp-heat obstructive ankylosing spondylitis, which is conducive to alleviating the pain and inflammation, and improving the patient's activity function and daily life ability. Papaya antirheumatic pill is mainly composed of phellodendron amurense, salvia miltiorrhiza, gypsum, mulberry, honeysuckle stem, comfrey and rhizoma dioscoreae tokoro etc., which has the functions of dispelling wind to eliminate dampness, warming meridians and unblocking collaterals, relieving pain of the joints, and strengthening bones. Salvia miltiorrhizae can promote blood circulation, remove blood stasis, relieve pain and prevent thrombosis; Gypsum can clear heat and relieve muscle penetration; Mulberry has the effects of wind-expelling and pain-alleviating, removing dampness and paralysis; Comfrey can cool blood and promote blood circulation, detoxify and dispel rashes; Rhizoma dioscoreae tokoro has the function of dispelling wind to eliminate dampness and relieving swelling and pain. The above medicines can dispel wind and relieve pain, eliminate dampness, remove blood stasis, promote blood circulation and detoxicate.

In order to improve the treatment effect, this study is based on the theory of pathology and syndrome differentiation. After consulting a large number of classics, symptomatic treatment is performed for the purpose of clearing heat and dampness. Among which phellodendron amurense clears heat and dampness, purging fire and detoxifying; Coix seed is good for spleen and dampness, detoxification and disintegration; Atractylodes can dry the spleen, dispel wind and cold; Caulis spatholobi has the effects of lowering blood pressure, replenishing blood, and anti-cancer; Glabrous greenbrier rhizome has the effects of clearing away heat and dampness, diuretic and detoxifying; Honeysuckle vine clears heat and detoxifies, dispels

wind and removes obstruction in the meridians; Cassia twig can warm the meridians, harmonize yingfen and weifen, relieve pain and inflammation, nourish tendons, clear heat and detoxify; Lumbricus can expel wind and clear heat, diuretic and clear the collaterals; White mustard seeds have the effect of dredging collaterals and relieving pain, replenishing Qi and removing stasis; Rhizoma sinomeni cauliset can warm and disperse cold, dehumidify and debilitate, clear heat and diuretic. The above medicines have the effect of clearing heat and dehumidifying, dredging collaterals and relieving pain. Modern pharmacological research shows that honeysuckle stem contained in honeysuckle can inhibit the growth of staphylococcus and subtilis at a specific concentration, and has a strong antiviral effect after entering the human body, which can effectively inhibit inflammation; phellodendron amurense can effectively inhibit the activity of hemagglutinin PHA, stimulate T cells to promote cell proliferation, and at the same time inhibit the RNA expression of inflammatory factors such as IL-2, INF- γ , and has good anti-inflammatory effects; The water extract of Glabrous greenbrier rhizome has a good inhibitory effect on the inflammatory response caused by xylene. By selectively inhibiting the release of lymphokines, the cellular immune response can be effectively suppressed.

In summary, heat-clearing and dampness-eliminating dredging collaterals combined with papaya antirheumatic pills is effective in the treatment of damp-heat obstructive ankylosing spondylitis, which is beneficial to alleviate the pain and inflammation of the affected area, and improve the patient's activity function and daily life ability.

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