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Effects of sulfasalazine combined with moxibustion methods on patients with cold-dampness obstruction type ankylosing spondylitis

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Abstract: Twenty-four patients with cold, dampness, obstructive ankylosing spondylitis were treated with sulfasalazine and sulfasalazine in combination with moxibustion for 3 weeks. The results showed that the combined treatment of traditional Chinese and western medicine was significantly higher than those of western medicine treatment, meanwhile, the scoreofsymptoms quantification, C-reactive protein and erythrocyte sedimentation rate of the integrated Chinese and western medicine treatment were significantly lower than those of western medicine treatment, and the level of physical signs was significantly higher than that of western medicine treatment, and there were no significant differences in adverse reactions. Moxibustion combined with sulfasalazine in the treatment of cold and damp obstructive ankylosing spondylitis can effectively improve the characteristics of the body, relieve pain symptoms and improve the prognosis.

Keywords: Ankylosing spondylitis, cold and dampness resistance, moxibustion, sulfasalazine, efficacy, prognosis, laboratory indicators.

INTRODUCTION

Ankylosing spondylitis (AS) is a systemic disease characterized by inflammation in the ankle joint and attachment points to the spine. It is a kind of rheumatism with unclear pathogenesis. It often causes cumulative damage to the ankle, resulting in spinal rigidity and fibrosis as well as lesions of varying degrees in muscle, bone, lung, and eye, etc. and it seriously affects quality of life of patients (Sieper *et al*., 2017). Treatment of ankylosing spondylitis predominantly focused on controlling inflammation, improving clinical symptoms, and preventing malformation, etc. Sulfasalazine has anti-inflammatory, immunosuppressive effects and often used in the treatment of AS (Heijde *et al*., 2017). In recent years, the combination of traditional Chinese medicine and Western medicine has also been widely used to treat this disease. Traditional Chinese medicine holds that AS results from Yang deficiency and exogenous cold dampness evil invasion, and belongs to the cold-dampness obstruction type disease (Molnar *et al*., 2018). Moxibustion is a traditional Chinese medicine therapy which consists of burning dried mugwort on particular points on the body with the intention of stimulating circulation to regulate the dysfunctions (Pray *et al*., 2017). Therefore, this study aimed to explore effects of moxibustion+sulfasalazine on patients with cold-dampness obstruction type AS.

MATERIALS AND METHODS

Baseline data

Eighty-four patients with cold-dampness obstruction type AS admitted from June 2015 to June 2018 were selected as study subjects. The research has been approved by the ethics committee of our hospital. Inclusion criteria was defined according to Western medical guideline (Cai, 2004), namely a: limited lumbar motion; b: low back pain, morning stiffness occurred over 3 months, with no relief after rest but relief after activity; the chest circumference change measured under deep inhalation and exhalation is lower than healthy people of the same gender and age. Imaging findings of ankle arthritis showed bilateral > II or unilateral > III or IV. Patients who meets one of above clinical manifestations and imaging findings of ankle arthritis can be diagnosed as AS.

The cold-dampness obstruction type was confirmed with reference to Chinese medicine guideline (Zhen, 2002), namely a: lumbosacral, back pain, morning stiffness as main symptoms, which increased in coldness and reduced in heat condition. b: joint pain which is sensitive to cold, severe coolness of the extremity, and heavy limbs. C: white and greasy tongue coating with thready and slippery pulse. The patient can be diagnosed as cold-dampness obstruction type with above manifestations. Exclusion criteria was patients who has recently been treated; or not take medicines according to doctor's advice; or patients with cardiovascular and cerebrovascular diseases; were allergic to moxibustion or combined with dysfunctions in heart, kidney, liver and other important organs. The observation group (N=42) and the control group (N=42) were randomly assigned. The baseline data of the two groups was comparable (P>0.05, table 1).This study complies with the Helsinki Declaration of the World Medical Association.

Methods

The control group was given sulfasalazine (0.25g, Shanghai ZhongxiSunve Pharmaceutical Co., Ltd.,

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H31020450), with oral administration of 0.25, 0.5 and 0.75 g for the first, second and third week, respectively, 3 times a day. On the basis of this treatment, the observation group additionally received moxibustion therapy.

The main points of moxibustion were placed on the neck, back, waist, sacral Du Meridian, Bladder Meridian of Foot-Taiyang, Jiaji points, and Ashi points. The supine position was set to ensure the patient's comfort and fully expose the moxibustion points. Moxa was ignited in wooden boxes which would be placed on the neck, back, waist and ankle, so that moxibustion points were fully covered. The top of the moxibustion box was covered with a piece of hot cloth to prevent heat loss. The temperature is controlled at about 40°C to make patient's skin flush. After the moxa was burned out, moxibustion boxes were taken off. Moxibustion is usually practiced for 20–30 min, 3 times/week. Both groups had been treated continuously for 12 weeks.

Outcome Measurement

The changes of the following indicators were evaluated before treatment and at 12 weeks post treatment. The cold-dampness obstruction type symptoms were scored on basis of "Guidelines for Clinical Research of TCM New Drugs" (Zhen, 2002). The three main and secondary symptoms of cold dampness and obstruction are divided into 24 points, according to the scoring criteria such as severe (6 points), moderate (4 points), light (2 points), none (0 points). The two groups were scored with the nimodipine method before and after treatment. Symptom quantification score = [(pre-treatment symptom score—post-treatment symptom scorfe)/symptom score before treatment] ×100%; Physical indicators (Bradbury *et al*., 2018): Occiput-wall distance (OWD) is the measurement of distance between bony prominence of the 7th cervical vertebra or occiput and the wall in a standing position, which was recorded before and after treatment. Schober test was performed as follows. A measure of lumbar spine motion in which parallel horizontal lines are drawn 10 cm above and 5 cm below the lumbosacral junction in the erect subject; with maximum forward flexion, the distance between the lines was recorded before and after treatment. Visual Analogue Scale (VAS) with a range of 0~10 points indicated the sense of pain. The higher the score, the stronger the pain. 5ml of venous blood was collected from patient's elbow, centrifugated for 10 min at a radius of 5cm, 3000r/min. Serum was extracted and C-reactive protein (CRP) level was measured with enzyme-linked immunosorbent assay (ELISA) (Shenzhen Jingmei Bioengineering Co., Ltd.) Erythrocyte sedimentation rate (ESR) was determined by Westergren method. All adverse reactions were observed.

Response evaluation criteria

The efficacy was evaluated after 12 weeks of treatment. The specific evaluation is based on the changes in the quantitative scoring of symptoms and physical indicators in the Guiding Principles for Clinical Research of New Chinese Medicines (Zhen, 2002). Relief: Patient's OWD and Schober test results were significantly improved, and his/her quantification score was reduced by more than 95%; Excellence: symptoms were partially improved, SQS decreased by more than 75%; Improvement: symptoms were partially improved, SQS decreased by more than 30%; Failure: symptoms were not improved, SQS decreased by less than 30%. Total response rate = (Relief + Excellence + Improvement) / total number of cases × 100%.

STATISTICAL ANALYSIS

The data was analyzed with SPSS18.0, the normal distribution measurement data is represented by ($\overline{X}\pm s$). The comparison is performed by independent sample t test. Comparisons within each group is examined with paired sample t test, the count data is expressed by the ratio and calculated with $\chi 2$ test, $P<0.05$ indicates significant difference.

RESULTS

Response rate comparison

The response rate of the observation group was higher than that of the control group ($P<0.05$, table 2).

Comparison of indicators between the two groups

The two groups showed lower symptom scores and OWD, higher Schober results after treatment.

The observation group showed lower symptom scores and OWD as well as higher Schober results than the control group ($P<0.05$, table 3).

Comparison of VAS scores between the two groups

After treatment, the VAS scores of both groups were reduced, and the observation group showed significantly lower VAS than the control group ($P<0.05$, table 4).

Comp***arison of CRP and ESR between the two groups***

After treatment, the CRP and ESR levels in both groups were lower than those before treatment. The levels of CRP and ESR in the observation group were significantly lower than those in the control group ($P<0.05$, table 5).

Adverse reactions

In the course of treatment, 2 cases and 4 cases of nausea and vomiting were observed separately inthe observation group and the control group. The incidence of adverse reactions were 4.76% and 9.52%, respectively, and the difference was not statistically significant ($\chi 2=0.718$, $P=0.397$).

DISCUSSION

The incidence of ankylosing spondylitis in China is about

Table 1: Comparison of general data between the two groups

Group	n	Gender		Age (year old)	Disease course (year)
		Male	Female		
Observation group	42	20(47.62)	22(52.38)	35.09±2.21	4.05±1.32
Control group	42	24(57.14)	18(42.86)	35.14±2.18	4.13±1.28
χ^2/t		0.764		0.104	0.282
P		0.382		0.917	0.779

Table 2: Comparison of clinical effects between the two groups [*n*(%)]

Group	n	Mitigation	Marked	Effective	Ineffective	Total effective
Observation group	42	22 (52.38)	11 (26.19)	5 (11.90)	4 (9.52)	38 (90.48)
Control group	42	17 (40.48)	8 (19.05)	6 (14.29)	11 (26.19)	31 (73.81)
χ^2						4.696
P						0.046

Table 3: Comparison of indicators between the two groups（$\bar{x}$±s）

Group	n	Symptom score (fraction)		Pillow wall distance (cm)		Schobertest (cm)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	42	19.26±0.74	12.60±0.57*	1.62±0.19	0.24±0.03*	2.10±0.13	5.24±0.16*
Control group	42	19.14±0.52	15.09±0.41*	1.58±0.23	0.75±0.09*	2.08±0.17	4.10±0.14*
t		0.860	22.983	0.869	34.840	0.606	34.750
P		0.392	0.000	0.387	0.000	0.546	0.000

Note: Compared with before treatment, *$P<0.05$

0.3% to 0.5% (Ozkaramanli *et al*., 2018). It tends to first develop in teenagers and young adults with no obvious abnormalities at the initial stage. Patients may only experience some mild symptoms, such as weight loss, fatigue, etc. However, the symptoms grow over time. Joint lesions will occur, such as ankle arthritis, lumbar disease, thoracic lesions, cervical lesions, peripheral joint disease, etc., which seriously affects the life quality (Kuperus *et al*., 2018).

Non-steroidal anti-inflammatory drugs and analgesic antipyretics were often prescribed in Western medicine for the treatment of ankylosing spondylitis (Ciccia *et al*., 2017). Sulfasalazine is a commonly used drug. As a 5-aminosalicylic acid precursor, it can be converted to aminosalicylic acid after metabolism, increasing the plasma concentration in mucosal cells of the intestinal wall, and effectively plays its role of anti-inflammatory and immune regulation. It showed obvious analgesic effect in treatment of ankylosing spondylitis. However, its efficacy in relieving clinical symptoms is still far from satisfactory (Saracoglu *et al*., 2017).

In traditional Chinese medicine, ankylosing spondylitis is similar to “Dyphosis”, “Osteoarthrosis”, “Bi syndrome” and so on. According to the treatise on the communication of the force of life with heaven in Inner Canon of The Yellow Emperor, patient with AS is deficiency in origin and excess in superficiality, which is due to insufficiency of the kidney, deficiency of Governor Vessel, and blocking of the channels with the invasion of exogenous evil, leading to poor circulation of qi and blood and malnutrition of the bones, muscles and joints, resulting in the symptoms of low back pain, soreness and weakness, and most cases belong to the cold-dampness obstruction type (Krüger *et al*., 2018). Moxibustion therapy is a traditional TCM therapy, of which mugwort is neutral in nature and could regulate the twelve major meridians. Moxibustion therapy could stimulating circulation through the pointsand inducing a smoother flow of blood and qias well as mitigating against cold and dampness in the body by transferring the nature of mugwort along the meridians to the whole body (Kucuk *et al*., 2017). Traditional Chinese medicine pointed out that ankylosing spondylitis mainly involved the spinal joints, which is passed by the Du Meridian and Bladder Meridian of Foot-Taiyang. The acupuncture points should be carefully selected during the moxibustion process (Emery *et al*., 2018).

In the moxibustion therapy of this study, the Du Meridian of the neck, back, waist and ankle, the Bladder Meridian of Foot-Taiyang, and the Jiajiacupoint were selected as the main acupuncture points. The results of the study showed that patients underwent moxibustion showed significantly better clinical indicators, VAS scores, and laboratory indicators, etc. than patients received sulfasalazine alone.

Table 4: Comparison of VAS scores between the two groups（$\bar{x}$±s，fraction）

Group		VAS score	
	n	Before treatment	After treatment
Observation group	42	5.96±1.40	1.24±0.17*
Control group	42	6.04±1.22	1.85±0.23*
t		0.279	13.822
P		0.781	0.000

Note: Compared with before treatment,*$P<0.05$

Table 5: Comparison of CRP and ESR indicators between the two groups（$\bar{x}$±s）

Group	n	CRP (ng/ml)		ESR (mm/h)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	42	42.18±0.63	10.51±1.38*	22.49±0.83	7.36±0.68*
Control group	42	42.35±0.70	17.92±1.51	22.35±0.97	14.50±0.71
t		1.170	23.476	0.711	47.068
P		0.245	0.000	0.479	0.000

Note: Compared with before treatment，*$P<0.05$

The underlying mechanism may be that, from the perspective of human anatomy and science of channels and collaterals, the Du Meridian is located in the middle of the spine and manages all Yang channels. Bladder Meridian of Foot-Taiyangis below the spinous process, which link with the kidney and pertains to the urinary bladder. It can reduce deficiency of kidney essence and nourish the bones. The Jiaji points are also under the spinous process, which aid the regulation of Qi that passed through the Du and Kidney Meridian. Through long time treatment on acupuncture points, moxibustion therapy exerts the effect of dispelling coldness and relieving pain, warming and recuperating kidney yang, strengthening the collaterals, muscles and bones, strengthening the body resistance and eliminating the pathogenic factor. Combined with anti-inflammatory of sulfasalazine, the clinical symptoms and prognosis of patients will further improved.

Calik *et al*. (2018) reported that through the long-term moxibustion of the Du Meridian and the bladder Meridian, distribution and circulation of qi as well as immune function were significantly improved. The results of this study also confirm the effectiveness of TCM syndrome differentiation.

CONCLUSION

In summary, moxibustion combined with sulfasalazine can effectively improve the symptoms, relieve pain symptoms, and improve prognosis in the treatment of cold-dampness obstruction type ankylosing spondylitis, and is worthy of application. This study demonstrates the effectiveness of TCM syndrome differentiation and provides a reference for future clinical treatment of ankylosing spondylitis.

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