

## Clinical Evaluation of Integrative Chinese and Western Medicine in Treating SARS\*

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**ABSTRACT** **Objective:** To evaluate the effective treatment with integrative Chinese and western medicine (ICWM) of severe acute respiratory syndrome (SARS). **Methods:** The 65 cases of SARS patients were treated with ICWM and 37 cases with western medicine (WM) alone as the control in our hospital from March 11 to April 30, 2003. The results were analyzed, with T subset profile tested for all the 102 patients. **Results:** Sixty-five cases of SARS patients treated with ICWM included 52 mild cases of whom 51 cases were cured (98.1%) and no patient died. As to the 13 severe cases in this group, 9 were cured (69.2%) and 2 died (15.4%). Of the 37 cases treated with WM alone, 16 out of the 18 common cases were cured (88.9%) and 10 out of the 19 severe cases were cured (52.6%), with the other 9 died (47.4%). Comparison between the two groups ( $P=0.061$ ) showed the difference was close to the value for statistical significance. But considering that the number of samples was small, more cases are needed for further study. The immune function examination: in cases of the common type, after ICWM treatment,  $CD_4^+$  T lymphocytes were increased from  $360 \pm 247$  cell/mm<sup>3</sup> to  $563 \pm 479$  cell/mm<sup>3</sup> ( $P < 0.05$ ). In the group treated with WM alone,  $CD_4^+$  T lymphocytes were increased from  $331 \pm 193$  cell/mm<sup>3</sup> to  $772 \pm 354$  cell/mm<sup>3</sup> ( $P < 0.05$ ). As to the severe cases after ICWM treatment,  $CD_4^+$  T lymphocytes increased from  $352 \pm 279$  cell/mm<sup>3</sup> to  $525 \pm 490$  cell/mm<sup>3</sup> ( $P > 0.05$ ). In the group of severe cases treated with WM alone,  $CD_4^+$  T lymphocytes reduced from  $229 \pm 69$  cell/mm<sup>3</sup> to  $205 \pm 108$  cell/mm<sup>3</sup> ( $P > 0.05$ ). While after ICWM treatment,  $CD_4^+$  T lymphocytes were significantly higher than that of the group treated with WM alone ( $P < 0.05$ ). **Conclusion:** Compared with the group treated with WM alone, ICWM can significantly improve the prognosis, reduce the mortality as well as improve the immune function of SARS patients.

**KEY WORDS** integrative Chinese and western medicine, severe acute respiratory syndrome, therapy, T lymphocyte subsets

Severe acute respiratory syndrome (SARS), a new infectious disease discovered recently, has been widespread in many regions of China, which severely threatens human health. In order to explore the effective treatment of SARS, we carried out integrative Chinese and western medicine (ICWM) treatment to increase the cure rate and reduce mortality.

### METHODS

#### The SARS Patients

The 102 cases of SARS patients, ages 13-70 years old, admitted to our hospital from March 11, 2003 to April 30, 2003, were all diagnosed by Beijing Center for Disease Control and Prevention. Their diagnosis conformed to the Clinical Diagnosis Guideline (trial) issued by Ministry of Health (MOH) of People's Republic of China. All patients were fever at the beginning, accompanied by shivering cold, dry cough, fatigue, shortness of breath and headache.

X-ray chest film and computerized tomography (CT) showed that there was high density shadow and solid shadow in unilateral or bilateral sides of lung.

Exclusion criteria for SARS patients: Patients with cancer, immune systematic disease and suspected SARS patients were excluded.

#### General Data

The 102 patients were divided into two groups: ICWM group and WM group. There were 65 patients in the ICWM group,

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male 23, female 42 cases; mean age  $37.0 \pm 12.0$  years old; mean illness course  $4.5 \pm 3.6$  days. Severity degree of disease of the 65 cases: common type 52, and severe type 13. There were 37 patients in the group treated with WM alone, male 12, female 25 cases; mean age  $40.9 \pm 17.3$  years old; illness course  $4.4 \pm 3.6$  days. Severity degree of disease of all the 37 cases: common type 18, and severe type 19. In the general data of the two groups there exists no significant difference ( $P > 0.05$ ).

### Treatment Protocol

The patients in both groups were treated with Thymopetidium of 80 mg/d and Levofloxacin of 400 mg/d, i. e. the common type treated with methylprednisolone of 40–80 mg/d and the severe type with methylprednisolone of 80–180 mg/d. Dosage of methylprednisolone could be reduced, when body temperature was reduced, symptoms improved and result of chest X-ray examination showed that density shadow and solid shadow of lung began to be absorbed, and 2/3 of the first dosage could be reduced at the beginning.

Following the guideline of SARS prevention and treatment with TCM issued by State Administration of TCM, the course of SARS was divided into 4 stages: Early stage, middle stage, critical stage and recovery stage.

In the group of ICWM, for common type SARS patients in the early stage and middle stage, Xingnao Injection (醒脑注射液, Musk, Tumeric root, Giant-hyssop, Grass-leaved Sweetflag rhizome, Borneol, Menthol, and produced by Shijiazhuang Changcheng Pharmaceutical Group Co., Ltd) 40 ml/d and Shenmai Injection (参脉注射液, composed of Red Ginseng, Lilyturf root, and produced by Shijiazhuang Shengwei Pharmaceutical Group Co., Ltd.) 40 ml/d should be used; Shengmai Injection (生脉注射液, composed of Red Ginseng, Lilyturf root, Magnolia vine fruit, produced by Jian-

gsu Suzhong Pharmaceutical Group Co., Ltd) 60 ml/d should be used in the recovery stage. And in the critical stage Shenfu Injection (参附注射液, composed of Red Ginseng, Aconite root, and produced by Ya'an Sanjiu Pharmaceutical Group Co., Ltd.) 20–80 ml/d should be used. For severe type SARS patients, Chinese herbal preparation should be used. The basic formula includes fresh Gypsum, bitter Apricot seed, Chinese Ephedra, fresh Licorice, Anemarrhena rhizome, Honysuckle flower, and American Ginseng. Added according to syndrome differentiation were the following: Poria, Patriniae herb, Glabrous greenbrier rhizome, Peppergrass, Red Sage root for damp-heat-toxic syndrome; Straight Ladybell root, Lilyturf root, and Dogwood fruit were added for patients of deficiency of both qi and yin. The patients should take the above formula one dose a day, to be divided into two portions, orally taken, and the treatment lasts for 2–3 weeks.

### Laboratory Findings

Data of T lymphocyte subset and chest X-ray examination taken before and after treatment were collected.

Routine examination: When admitted to hospital, WBC were  $(1.5 - 11.1) \times 10^9/L$ , mean  $(4.54 \pm 2.01) \times 10^9/L$ , platelets were  $(40 - 295) \times 10^9/L$ , mean  $(145.03 \pm 49.45) \times 10^9/L$ . Chest X-ray or CT results suggested that there was high density shadow or solid change in one side of the lung or in both.

T lymphocyte subset examination:  $CD_3^+ T$ ,  $CD_4^+ T$ ,  $CD_8^+ T$  subset in blood were determined with Countert Eplics-XL, flow cytometer of USA. Fluorescence labeling monoclonal antibody was purchased from Immunotech Company, France.

### Statistical Analysis

Chi-square test, *t*-test, Fisher's Exact test were used for statistical analysis.

## RESULTS

### Criteria for Efficacy Evaluation

Full recovery: When patients discharged from hospital, 3 levels should be classified according to the Guideline for SARS patients of MOH. (1) Cured; normal body temperature for over 7 days without using any antipyretics, and respiratory symptom was obviously improved. Chest X-ray image showed significant absorption. (2) Improved; Fluctuating in body temperature, significant improvement of symptoms in respiratory system, some absorption in image of lungs. (3) Death.

### Effect Shown in the Two Groups

After treatment, the total effectiveness of common type SARS patients in both groups was similar. As to the severe type, compared with WM group, mortality in ICWM group was reduced,  $P = 0.061$ . The value is close to the significant margin. Due to small sample in this study, we need to collect more cases for further study. The detailed result is given in Table 1.

**Table 1. Comparison of Effectiveness in Two Groups [case (%)]**

Groups	Type	n	Cured	Improving	Death
ICWM	Common	52	51(98.1)	1(1.9)	0(0.0)
	Severe	13	9(69.2)	2(15.4)	2(15.4)*
WM	Common	18	16(88.9)	2(11.1)	0(0.0)
	Severe	19	10(52.6)	0(0.0)	9(47.4)

Note: \*  $P=0.061$ , compared with WM group

### Results of T Lymphocyte Subset Determined before and after Treatment

The results indicated that in common type SARS patients after treatment the  $CD_4^+$  level was increased suggesting the prognosis would be improved. The difference between pre- and post-treatment was statistically significant ( $P < 0.01$ ). However, the difference between ICWM and WM after treatment was insignificant ( $P > 0.05$ ). In severe type SARS patients, ICWM treatment can significantly increase  $CD_4^+$  level. Compared with WM group, the difference was significant ( $P < 0.05$ ). See Table 2.

**Table 2. Comparison of  $CD_4^+$  between the Two Groups of ICWM and WM in Pre- and Post-treatment (cell/mm<sup>3</sup>,  $\bar{x} \pm s$ )**

Group	Type	n	$CD_4^+$	
			Pre-treat	Post-treat
ICWM	Common	43	360±247	563±479*
	Severe	9	352±279	525±490
WM	Common	18	331±193	772±354*
	Severe	19	229±69	205±108

Note: \*  $P < 0.01$ , compared with pre-treatment of the same group

### Result for X-ray Image Dynamic Changes of the Common Type in Two Groups After Treatment

Chest X-ray film was taken every 3-5 days, and then changed to once every 7 days when the shadow was absorbed; the mean time of shadow absorption of ICWM group was 11.2 days after treatment, while that of WM in post-treatment was 12.3 days. The time of shadow absorption of ICWM group was shorter when compared with WM group, however, there was no statistically significant difference between them.

## DISCUSSION

SARS is a new kind of pneumonia with potential death<sup>(1)</sup>. SARS began in winter or spring. It has strong infectivity with the patients' condition aggravating quickly. Therefore, it belongs to the Wenbing (febrile epidemic) category in TCM theory. The main symptoms of SARS are fever, shivering cold, dry cough, shortness of breath, dyspnea, and fatigue. In the critical stage, even respiratory failure might happen.

It was found through clinical observation that the following characteristics have been seen which have also been described in TCM medical books: (1) Recognizing the rule of development: There are 4 phases: Wei (卫), Qi (气), Ying (营) and Xue (血). Mainly the disease is located in Qi and Wei phases. Later on it enters into Ying and Xue phases. The disease mainly stays in the

Upper Energizer and in some cases invades Lower Energizer according to Triple Energizer (Sanjiao) system. (2) Transmission law: The pathogenic factor invades Fei first. Then it is reversely transmitted to Xinbao, when confused mental state appeared. Then it further moves to Wei. (3) Three stages are divided for developmental process. At the initial stage, heat-toxin is the main problem. In the critical stage, damp-toxin becomes the main point. In the recovery stage, the chief problem changes to deficiency. (4) Type changes: it changes from type of heat-toxin to type of damp-toxin in Fei, and then in the recovery stage, it turns to injured type of both qi and yin.

According to the above-mentioned characteristics, the basic formula of Maxing Shigan decoction (麻杏石甘汤) is used in which Gypsum, Chinese Ephedra, bitter Apricot seed and fresh Licorice are prescribed. Anemarrhena rhizome and Honeysuckle flower could be added if heat is predominating; Poria, Patrinia herb, Peppergrass herb, Mongolian Snakegourd could be added if damp is predominating; Straight Ladybell, Lilyturf root, Dogwood fruit could be added if deficiency is predominating. The Fei is susceptible to qi-yin deficit. Therefore, in the treatment process, protecting qi-yin should be always borne in mind and paid closer attention to. That is why we have already mentioned the addition of Chinese herbs into the formula with the func-

tion of protecting qi and yin.

Many evidences indicated that immune function of SARS patients is in an abnormal state<sup>(2)</sup>, T lymphocyte function is impaired, especially CD<sub>4</sub><sup>+</sup> T cell count was decreased. If this reduction cannot be reversed quickly, the patients would die. Therefore, improving SARS patients' immune function is the key in the course of treatment. In early stage, we used American Ginseng to enhance the immune function. The clinical results indicated that in severe cases of SARS, after being treated with ICWM, CD<sub>4</sub><sup>+</sup> T cell count increased, immune function enhanced, and the mortality decreased.

ICWM holds that treatment of SARS with ICWM should begin early and be used in the whole course. Also the signs should be recognized when formulating the TCM recipe. The preliminary results suggested that application of ICWM for SARS patients can improve the symptoms, reduce the mortality as well as help the patients to restore their immune function.

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