

Effect of the Chinese Herbal Medicine, Chia-Wei-Hsiao-Yao-San, on Chronic Hepatitis

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Objectives: This study compared the effects of Chinese herbs formulas on the chronic hepatitis in the hospital patients. Previous studies showed that the spleen meridian seems especially important in liver diseases, so we selected "Chia-Wei-Hsiao-Yao-San" (Formula A) in order to add tonic to the spleen meridian and improve the liver meridian while "Xiao-Chai-Hu-Tang" (Formula B) adds tonic to the lung and the liver meridian. **Methods:** Eighty patients of chronic viral hepatitis (SGOT, SGPT above normal but below 400 IU/L) were included in this study randomly and divided into A and B group. In Group A, 33 patients were treated for three months with Chinese herbs (Formula A). For the same period of time, 29 patients in Group B were treated with Chinese herbs (Formula B). The effects of the treatment were evaluated by blood tests of liver function. **Results:** The Group A had decreased value of SGOT from before treatment reading of 47.5 ± 31.3 IU/L to after three-month treatment reading of 39.8 ± 26.7 IU/L and also decreased values of SGPT from before treatment reading of 72.0 ± 52.7 IU/L to after three-month treatment reading of 57.8 ± 42.5 IU/L. Both readings were statistically significant being $p < 0.01$. On the contrary, the Group B had increased values of SGOT and SGPT after three-month treatment. After three-month treatment, the SGOT and SGPT of the Group A were all significantly lower than those of the Group B. **Conclusion:** Chinese herbs formula "Chia-Wei-Hsiao-Yao-San" was more effective in lowering liver inflammation than "Xiao-Chai-Hu-Tang" that is widely used by Japanese as an effective treatment for liver diseases. This result is consistent with our hypothesis, and also matches pulse studies as well as Chinese Medicine's emphasis on maintaining the strength of the spleen in liver disease because these two systems are very closely related.

Key words: chronic viral hepatitis, spleen meridian, liver meridian, Chia-Wei-Hsiao-Yao-San

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Introduction

Before any treatment a doctor of Chinese medicine will comprehensively analyze the pulse of a patient and various other subtle symptoms. Pulse diagnosis is therefore one of the most fundamental and

distinguishing tools of this tradition. Recently hemodynamic equations were derived for the meridians that correlate the meridian with the pulse shape.^[1-5] The pressure energy distributed to each organ and its related meridian according to its resonant frequency is directly related to the blood supply toward

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this organ and meridian, while each organ is related to its meridians by the same resonance frequency. Meridian related drugs were considered as modulating the blood supply toward this specific meridian.^[9, 4,6,7,8]

Our recent concurrent studies on pulse have shown that liver diseases were closely related to the liver, lung, gallbladder and spleen meridians and especially the spleen meridian in serious liver problems.^[9-11] The Chinese herb formula Chia-Wei-Hsiao-Yao-San was commonly used in treatment of chronic hepatitis in Taiwan. The other famous formula Xiao-Chai-Hu-Tang known in Japanese as Sho-Saiko-To, which was generally used in treatment of chronic hepatitis.^[12-16] In order to compare the effect of treatment in chronic hepatitis between these two Chinese herb formulas and confirm which formula was really beneficial to the patients of chronic hepatitis in Taiwan, we considered above formulas to treat the patients of chronic hepatitis in this study.

Liver function tests are a group of blood tests that measure substances in the blood that reflect whether the liver has been injured and the extent of the injuries. In clinic, the blood tests SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) were the most common liver function tests except the ultra-sound scanning.^[17, 18] The effects of treatment were evaluated by the blood tests especial the SGOT (serum glutamic oxaloacetic transaminase) and the SGPT (serum glutamic pyruvic transaminase) in this study.

Materials and Methods

Subjects

Patients with chronic viral hepatitis (with SGOT and SGPT above normal but below 400 IU/L) came to the hospital for the medications were randomly and equally divided into two groups (from August 1995 to July 1996). The procedure of the study fin-

ished within the three-month and completed by way of single blind. The patients of inclusion in the study were chronic viral hepatitis B (HbsAg(+)) or chronic viral hepatitis C (Anti-HCV(+)). They were all chronic inflammatory reaction in the liver, continuing without improvement for at least six month. The patients were excluded from the study if they possessed some diseases such as liver cirrhosis, jaundice, hypertension, diabetes mellitus and renal disease. The Institute Review Board of Taipei municipal Ho-Ping Hospital has approved this study. The procedure was fully explained to the subject and informed written consent was obtained from the subject before study. Medical and activity histories were obtained by questionnaire

Blood Tests and Ultra-sound Scanning

Tests were done in municipal Ho-Ping Hospital before the administration of Chinese herbal remedies and then after the three-month treatment. Blood tests included SGOT (serum glutamic oxaloacetic transaminase), SGPT (serum glutamic pyruvic transaminase), D-BIL (direct bilirubin), T-BIL (total bilirubin), ALP (alkaline phosphate), γ -GT (γ -glutamyl transpeptidase), ZTT (zinc sulfate turbidity), CHOL (cholesterol) and ALB (albumin)^[17-18]. Special attention was paid to SGOT and SGPT with SGPT greater than 35 IU/L and SGOT greater than 30 IU/L considered abnormal. In the patients with chronic hepatitis, before treatment and after 3 months' treatment, the assay of blood biochemistry and ultra-sound scanning were performed using the same methodology on each subject.

Chinese Herbal Remedy

Group A was treated with the formula Chia-Wei-Hsiao-Yao-San that consists of the following herbs: Angelicae Sinensis Radix-2.0 grams, Paeoniae Radix Alba-2.0 grams, Atractylodis Ovatae Rhizoma-2.0 grams, Poria-2.0 grams, Bupleuri Radix-2.0 grams,

Table 1. Comparisons of blood tests between group A (before treatment and after treatment) and group B (before treatment and after treatment).

Measures	Group A	Group A	Group B	Group B
	(Before treatment) (N = 33)	(After treatment) (N = 33)	(Before treatment) (N = 29)	(After treatment) (N = 29)
SGOT (IU/L)	47.5 ± 31.3	39.8 ± 26.7 [‡]	52.4 ± 54.4	63.9 ± 71.6 [†]
SGPT (IU/L)	72.0 ± 52.7	57.8 ± 42.5 [‡]	90.0 ± 120.8	98.6 ± 127.4 [†]
T-Bil (mg/dL)	0.8 ± 0.3	0.7 ± 0.2	0.8 ± 0.3	0.8 ± 0.1
D-Bil (mg/dL)	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1
ALP (IU/L)	185.3 ± 20.1	180.7 ± 16.1	190.3 ± 21.1	187.3 ± 18.4
γ -GT (IU/L)	32.2 ± 6.1	30.8 ± 5.8	33.0 ± 5.9	34.7 ± 4.6
ZTT (K&o-u)	7.2 ± 1.4	7.1 ± 1.2	7.1 ± 1.5	6.8 ± 1.9
CHOL (mg/dL)	189.6 ± 9.4	186.0 ± 9.2	176.4 ± 8.9	180.8 ± 9.2
ALB (g/dL)	3.2 ± 0.7	3.5 ± 0.4	3.2 ± 0.5	3.5 ± 0.4

[‡]p<0.01 vs. before treatment (Paired t-test); [†]p<0.05 vs. Group A (t-test). Data presented are mean ± SD.

Glycyrrhizae Radix-2.0grams, Moutan Radicis Cortex-1.0 gram, Gardeniae Fructus-1.0 gram, Zingiberis Rhizoma-0.5 gram, Menthae Herba-0.5 gram. The crude herbs were extracted and concentrated into 3.0 grams of fluid extract (the ratio of the crude herbs to fluid extract being 5:1). Starch was added as a forming-agent to make 6.0 grams of powder. The daily dose was 16.0 grams. Group B was treated with the formula Xiao-Chai-Hu-Tang that consists of the following Chinese herbs: Bupleuri Radix-4.0 grams, Scutellariae Radix-1.5 grams, Ginseng Radix-1.5 grams, Pinelliae Rhizoma-1.0 gram, Glycyrrhizae Radix-1.5 grams, Zingiberis Recens Rhizoma-1.5 grams, Zizphi Sativae Fructus-1.0 gram. The crude herbs were extracted and concentrated into 3.0 grams of fluid extract (the ratio of crude drugs to fluid extract being 4:1). Starch was added as a forming agent to make 6.0 grams of powder. Daily dose was 16.0 grams. Every subject was given 16.0 grams per day for three months without knowing which formula they were taking. Subjects came into the hospital every two weeks for a check up. The extraction procedure follows the guidelines of

the National Goods Manufacturing Process. Both formulas are now being manufactured in Taiwan because all herbal remedies have standardized quality and quantities of ingredients.

Statistic Analysis

The Paired-t test was employed to compare the blood tests in both group A and group B between before treatment and after three-month treatment. The t-test was utilized to compare the blood tests between before treatment of group A and before treatment of group B. As the same, the t-test was utilized to compare the blood tests between after three-month treatment of group A and after three-month treatment of group B.^[19-20] A $p<0.05$ was considered statistically significant. All data are presented as mean ± SD.

Results

Eighty patients of chronic viral hepatitis were included in this study randomly and equally divided into group A and group B. Sixty-two patients com-

pleted the course of three-month treatment. Group A consisted of 24 males and 9 females between the ages of 21 to 65 with a mean age of 42.6 ± 18.0 . Group B consisted of 22 males and 7 females between 18 and 60 with the mean age of 42.6 ± 13.1 . Table 1 compared the blood tests of the liver function between group A and group B. The first two columns of Table 1 compared the blood tests between before treatment and after treatment of group A. The last two columns of Table 1 showed the blood tests between before treatment and after treatment of group B. There was no significant difference in the T-Bil, D-Bil, ALP, γ -GT, ZTT, CHOL and ALB except the SGOT and SGPT. However, the SGOT and SGPT of the group A after treatment were all significantly lower than those of the group A before treatment. After three-month treatment, the SGOT and SGPT of the group A were all significantly lower than those of the group B, whereas the SGOT and SGPT of the before treatment of group A were not significantly different from those of the before treatment of group B.

Discussion

Results indicate that Group A improved significantly while Group B had no improvement. Chinese herb formula Chia-Wei-Hsiao-Yao-San was more effective in lowering liver inflammation than Xiao-Chai-Hu-Tang which in Japan is presently the most commonly administered herbal remedy to outpatients with chronic liver disease, especially those with chronic hepatitis,^[12-16] liver cirrhosis^[21] and antifibrosis of liver in rats.^[22] The standard deviation of SGOT and SGPT were large partly due to the small number of subjects that completed the three-month treatment. Subjects in this study included mild hepatitis (SGPT <100 IU/L) and moderate hepatitis (100 IU/L < SGPT <400 IU/L) excluding severe hepatitis (SGPT >400 IU/L)^[17-18] for the reason of safety and medical eth-

ics and morals.

In our recent reports of pulse analysis which were done concurrently with this study but with different subjects,^[9-11] we have shown that the liver meridian (C₁), lung meridian (C₄), gall-bladder meridian (C₆) and spleen meridian (C₃) were closely related to the liver problems with the spleen meridian especially important in severe liver problems. Patients with severe liver problems all possessed C₃ = -2 in intensity and C₃ = -2 in phase of the pulse spectrum diagnosis and only 6 of the patients possessed C₄ = -2 in intensity.^[11] This finding suggests that the spleen, and the spleen meridian that is one of the blood forming organs is affected in severe liver problems. Formula A, used in this study is composed mainly of Hsiao-Yao-San which was formulated according to the medical text "Ho-Chi-Chu-Fung" (Sung dynasty 907-1211 A.D.). This was used as a treatment for blood deficiency-over-exertion. In the text of "The Golden Guide for Doctors" (17th century) it suggested that Hsiao-Yao-San formula functioned to "clear away liver and regulate spleen", treat women's diseases especially consumptive disease. In the new formula that was named Chia-Wei-Hsiao-Yao-San the Chinese herbs Moutan Radicis Cortex and Gardeniae Fructus were added to enhance the function of "clearing away heat" in patients with liver disease. The references are in the medical texts "Hsieh-Shih-I-An" (Hsieh Shih Medical Cases).

Formula B used formula Xiao-Chai-Hu-Tang that originated from Shang-Han-Lun^[23] and was used for treating diseases of Lesser-Yang which included internal and external symptoms such as chest discomfort and alternating chills and fever. The main difference in composition of these two formulas is that Xiao-Chai-Hu-Tang has Ginseng Radix which attributive-channel (歸經) of lung meridian and invigorates-Qi (補氣) [Pen-Tsao-Kang-Mu(A.D. 1596)]. On the other hand, Chia-Wei-Hsiao-Yao-San

includes Paeoniad, Radix Alba and Atractylodis Ovatae Rhizoma which attributive-channel (歸經) of spleen meridian [Pen-Tsao-Kang-Mu]. Poria enhances the Atractylodis Ovatae Rhizoma as a tonic to the spleen meridian, while Angelica Sinesis Radix invigorates-blood (補血) that also enhances the spleen meridian.

In this study we found that the group treated with Chia-Wei-Hsiao-Yao-San for three months had improved values of SGOT and SGPT while the other group treated with Xiao-Chia-Hu-Tang did not. We could thus conclude that Xiao-Chai-Hu-Tang formula is suitable for liver problems with abnormality in the lung meridian while Chia-Wei-Hsiao-Yao-San formula is suitable for liver problems with abnormality in the spleen meridian. This is consistent with the teaching of Zhung-Jing Chang who stated in "Gin Kuei Yao Lueh"^[24] that liver disease eventually damages transmits to the spleen, therefore the physician needs to maintain the strength of the spleen. Besides, from the pulse spectrum analysis along with meridian related drug theory, this study again suggests that each meridian has its own physiological function and pathological importance (Yellow Emperor's Medic Sinica).^[25]

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方劑加味道遙散對慢性肝炎之療效

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目的：比較不同的方劑對醫院慢性肝炎病患的治療效果。先前的研究顯示脾經對於肝病具有特別重要的意義，因此選擇假設能夠增強脾經以及肝經的方劑加味道遙散（A方劑）和假設能夠增強肺經及肝經的方劑小柴胡湯（B方劑）作臨床治療效果的探討。**方法：**80位慢性病毒性肝炎病患（肝功能指數SGOT、SGPT超過正常值的範圍但在400 IU/L以下）參與本研究，經由隨機方式分為A、B兩組，A組共有33位病患使用A方劑治療三個月，B組則有29位病患使用B方劑同樣治療三個月，以肝功能有關的各項血液生化指標作為臨床療效評估的依據。**結果：**A組病患血中的SGOT值，治療前為 47.5 ± 31.3 IU/L 經過三個月的給藥治療下降為 39.8 ± 26.7

IU/L，另外病患血中的SGPT值，也由治療前的 72.0 ± 52.7 IU/L下降為 57.8 ± 42.5 IU/L，兩組皆具有統計學上的顯著差異，p值小於0.01，相反的B組病患經過三個月的給藥治療之後，血中的肝功能指數SGOT值以及SGPT值，不降反升。經過三個月的給藥治療之後，A組病患血中的肝功能指數SGOT、SGPT皆比B組病患要來得低且具有統計學上的差異。**結論：**這個結果顯示加味道遙散降低肝臟發炎的效果要比小柴胡湯的效果為佳，雖然日本宣稱小柴胡湯具有治療各類肝臟疾病的效果。本研究的臨床結果不僅印證了我們對於這二種中藥方劑的假設，並且也與脈學研究指出肝病要實脾以及肝臟與脾臟相互影響的生理意義相吻合。

關鍵詞：慢性病毒性肝炎，脾經，肝經，加味道遙散

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