Effect of Chinese Herbal Medicine for Calming Gan (肝) and Suppressing Hyperactive Yang on Arterial Elasticity Function and Circadian Rhythm of Blood Pressure in Patients with Essential Hypertension

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ABSTRACT  Objective: To observe the effect of Chinese herbal medicine for calming Gan (肝) and suppressing hyperactive yang (平肝潜阳, CGSHY) on arterial elasticity function and the circadian rhythm of blood pressure in patients with essential hypertension (EH). Methods: Adopting a parallel, randomized design, sixty-four patients with EH of stages I and II were randomly divided into two groups according to a random number table, with 32 in each group. The patients in the treatment group were treated with CGSHY and those in the control group were treated with Enalapril. All patients were given 24-h ambulatory blood pressure monitoring (ABPM) before and after a 12-week treatment. Trough/peak (T/P) ratios of systolic and diastolic blood pressure (SBP & DBP) of each group were calculated. The circadian rhythm of their blood pressure was observed at the same time. The changes in elasticity of the carotid artery in the patients, including stiffness parameter ($\beta$), pressure-strain elastic modulus (Ep), arterial compliance (AC), augmentation index (AI), and pulse wave velocity (PVW $\beta$) were determined by the echo-tracking technique before and after a 12-week treatment. In the meantime, their levels of nitric oxide (NO) and endothelin-1 (ET-1) were measured respectively. Results: After treatment, all parameters in the ABPM and the elasticity of the carotid artery ($\beta$, Ep, AC and PVW $\beta$) were markedly improved, the level of NO was increased, and ET-1 was decreased in both groups as compared with values before treatment ($P<0.05$ or $P<0.01$). Further, the improvements in the ratio of T/P of SBP & DBP and the levels of NO and ET-1 in the treatment group were more significant than those in the control group ($P<0.05$). There were no significant differences in all parameters in the ABPM monitoring and the elasticity of the carotid artery, the recovery of blood pressure circadian rhythm, and the therapeutic effect of antihypertension in EH patients between the two groups ($P>0.05$). Conclusions: Chinese herbal medicine for CGSHY may lower the blood pressure smoothly and recover the circadian rhythm of blood pressure in EH patients. They may also improve the carotid elasticity of EH patients similar to that of Enalapril. The mechanism of action of Chinese herbs on EH might be related to the regulation of vascular endothelium function.

KEYWORDS  essential hypertension, circadian rhythm of blood pressure, Chinese herbal medicine for calming Gan and suppressing hyperactive yang, artery elasticity function

Essential hypertension (EH) is one of the most important risk factors for cardiovascular diseases. It is considered to be a complex trait to which genetic, environmental, and demographic factors contribute interactively. It is the major cause of morbidity and mortality and is also the third highest risk factor for lifetime burden worldwide. With the research on the progression of hypertension for several decades, more attention has been paid to the blood vessel as a target organ. The arterial elasticity function has been evaluated and considered as the important marker of organ damage in the ESC/ESH hypertension guideline (2007). It has been observed that day-night patterns in blood pressure (BP) are closely tied to...
to the 24-h sleep-wake cycle and are influenced by several endogenous circadian rhythms as well as cyclic exogenous factors. The ideal anti-hypertension medications are the ones that steadily control the blood pressure for 24 h\(^2\).

The authors treated patients with EH by using Chinese herbal medicine for calming Gan (肝) and suppressing hyperactive yang (平肝潜阳, CGSHY) and gained good therapeutic effect, while the patients’ clinical symptoms such as headache and dizziness were improved\(^3,4\). This study observed the effect of CGSHY on the arterial elasticity function and circadian rhythm of blood pressure in patients with EH.

**METHODS**

**General Materials**

The patients were recruited from those attending the Department of Cardiopathy of Xiangya Hospital, Central South University, from January 2006 to December 2008, at the Department of Cardiology, Central South University. Patients were aged \(\geq 18\) years and had a diagnosis of stage I or II EH (European Society of Hypertension-European Society of Cardiology Guidelines\(^1\)) as determined by conventional BP measurements [systolic BP (SBP) 140-179 mm Hg or diastolic BP (DBP) 90-109 mm Hg] and confirmed by 24-h ambulatory blood pressure monitoring (ABPM) at the time of recruitment. The diagnosis of hypertension based on 24-h ABPM required an awake mean BP of \(>135/85\) mm Hg or an asleep mean BP of \(>120/70\) mm Hg.

Pregnant women, shift workers, heavy drinkers (alcohol intake \(>80\) g/d), heavy smokers (\(>20\) cigarettes/d), and heavy exercisers were excluded, as were individuals with severe arterial hypertension (stage III, BP \(>180/110\) mm Hg), type 1 diabetes, secondary arterial hypertension and concomitant cardiovascular disorders (including unstable angina pectoris, heart failure, stroke, life-threatening arrhythmia, nephropathy, and retinopathy), or myocardial infarction or coronary revascularization within the past year.

A total of 169 EH patients were included using the standard of pressure average value \(>130/80\) mm Hg in 24-h ABPM detection after stopping antihypertensive agents for two weeks, and 64 (37.9%) patients with a disturbance in the circadian rhythm of their blood pressure were diagnosed by the standard of descent percentage in night BP \(<10\%\) by a 24-h ABPM examination were enrolled in the study.

The 64 patients were randomly assigned to two groups according to a random number table. The 32 patients in the treatment group were 19 males and 13 females; their mean ages were 57.8 \(\pm 7.1\) years, with a history of hypertension for 4.6 \(\pm 2.4\) years. At the time of enrollment, the hypertension stage was classified as stage I in 11 patients and stage II in 21 patients, among which 16 had left ventricular hypertrophy and 5 patients had slight proteinuria. The 32 patients in the control group were 18 males and 14 females; their mean ages were 58.5 \(\pm 6.3\) years, with a history of hypertension for 4.8 \(\pm 2.7\) years. At the time of enrollment, the hypertension stage was classified as stage I in 10 patients and stage II in 22 patients, among which 15 patients had left ventricular hypertrophy and seven patients had slight proteinuria. The differences in the two groups in terms of gender, age, hypertension history, hypertension grade, and related complication were statistically insignificant (\(P>0.05\)).

**Study Design**

This study was a parallel and randomized trial, the study protocol was approved by the State Ethics Committee of Clinical Research in Central South University, and all patients signed written informed consent forms.

**Treatment**

The patients in the control group were assigned to receive a 12-week of monotherapy with Enalapril (Produced by the Yangtze River Pharmaceutical Group, Jiangshu Province, China) 10 mg per day, once a day, taken on waking in the morning. If the DBP was over 90 mm Hg after two weeks of treatment, the dosage of Enalapril could increase to 20 mg per day, once a day, taken on waking in the morning. If the DBP was also over 90 mm Hg after treatment, the other mechanism of antihypertension drugs could be added until the end of the 12-week study.

Meanwhile, Chinese herbs were applied to the treatment group. The decoction of CGSHY was composed of *Rhizoma Gastrodiae* 10 g, *Ramulus Uncariae cum uncis* 20 g, *Concha Haliotidia* 30 g,