Open Add-on Study on Primary Hypertension Treated by Wuling Powder and Modified Tianma Gouteng Decoction

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Abstract  Objective: To evaluate the efficacy and safety of wuling powder and modified tianma gouteng decoction as an add-on therapy for treating essential hypertension (EH).

Methods: 116 cases of EH patients took wuling powder and modified tianma gouteng decoction for 2 weeks to treat EH without changing their former medication. New York Heart Association (NYHA) heart function classification, heart rate, blood pressure and 6-minute walking test were evaluated before and after treatment.

Results: Wuling powder and modified tianma gouteng decoction decreased the EH patients’ heart rate, systolic pressure, diastolic pressure and increased the 6-minute walking distance very significantly (P<0.01). The total effective rate on blood pressure was 92.2%, and the total effective rate on NYHA heart function improvement was 95.1%. No serious side effect appeared.

Conclusion: From this study, treating EH with wuling powder and modified tianma gouteng decoction as an add-on therapy seems to be effective and safe.

Keywords  Wuling Powder; Tianma Gouteng Decoction; Primary Hypertension; Essential Hypertension; Chronic Heart Failure

1. Introduction

Blood pressure above 140/90 mmHg is defined as hypertension. Primary Hypertension, also known as essential hypertension, consists of 90-95% of hypertension patients. Genetic and environmental factors may interact to raise blood pressure[1].

Hypertension has been affecting more and more people in the world and is the primary risk factor for mortality and morbidity since it may cause atherosclerosis, coronary heart disease, cerebrovascular diseases, as well as cardiac and renal failure etc.

Despite the antihypertensive medications such as thiazide-type diuretics, calcium channel blockers, beta blockers, direct renin inhibitors, angiotensin-converting enzyme inhibitors, and angiotensin II receptor blockers, about two thirds of patients receiving treatment still do not reach the modest goal of <140mmHg/90mmHg. EH is a chronic, lifetime disease needing to search for alternative and complementary treatment[2].

Chinese herbal medicine has been used to treat hypertension-related symptoms for over 2000 years. Tianma gouteng decoction is widely used to treat EH. One study concludes that it can lower blood pressure, reduce total cholesterol, improve clinical symptoms and quality of life, and prevent the occurrence of stroke in hypertensive patients[3]. One experimental study in rats shows: Wuling powder also can lower blood pressure, induce diuresis, excrete liquids and eliminate edema, especially good for treating essential hypertension with chronic heart failure[4].

In western medicine, it is common practice for patients who have already administered antihypertensive medications to increase numbers of antihypertensive drugs to control still elevated blood pressure. The add-on effect of the added drug is still considered to be effective if blood pressure finally attains normal range, no matter how many /what kinds of western medications have already been used before. And it is unethical to give placebo or no treatment to hypertensive patients, especially to those with elevated blood pressure and chronic heart failure. So we hypothesize that it is beneficial and convenient to use both wuling powder and tianma gouteng decoction as an open add-on therapy for treating EH and it can still demonstrate whether it is effective or not even without setting up control group.

To evaluate the efficacy and safety of wuling powder and tianma gouteng decoction as an open add-on therapy for treating EH, we collected 116 cases of EH patients to have taken wuling powder and modified tianma gouteng decoction for 2 weeks to treat EH without changing their former medication. Here is our report.

2. Material and Methods
2.1. Subject of Study

The patients were outpatients who came to consult Chinese medicine practitioner for better control. They had already administered antihypertensive drugs and were willing to administer Chinese Medicine as an add-on therapy. So no one withdrew. 116 cases of EH patients with heart function ranging from NYHA classification I to IV were included. With 60 male and 56 female cases, the average age was 63.2±13.3 years. 15 cases belonged to NYHA heart function classification I; 34, II; 36, III and 31, IV.

2.2. Inclusion Criteria

The patient according with all of the following list should be included: ① In accord with the diagnostic criteria for essential hypertension[1-3] ② Age≥35 years ③ Have been administering antihypertensive medications for at least 3 months without changing ④ Systolic pressure (SP) ≥ 140 mmHg or / and diastolic pressure (DP) ≥ 90 mmHg ⑤ Willing to administer Chinese Medicine as an add-on therapy.

2.3. Exclusion Criteria

The patient according with any one of the following list should be excluded: ① Secondary hypertension ② Age < 35 years ③ Gestational hypertension ④ Have been administering antihypertensive medications for less than 3 months or have changed medication within 3 months ⑤ SP < 140 mmHg and DP < 90 mmHg ⑥ Unwilling to administer Chinese Medicine as an add-on therapy.

2.4. Treatment Methods

All EH patients took wuling powder and modified tianma gouteng decoction for 2 weeks without changing their former medication. Formula: Poria 12 grams, Polyporus 12 grams, Rhizoma Atractylodis Macrocephalae 12 grams, Rhizoma Alismatis 12 grams, Ramulus Cinnamomi 12 grams, Rhizima Atractylodis Macrocephalae 12 grams, Spica Prunellae 30 grams, Scutellariae Radix, 12 grams, Radix Astragali 15 grams, Radix Puerariae 15 grams, Radix Rehmanniae 15 grams, Spica Prunellae 15 grams, Herba Siegesbeckiae 15 grams, Radix Stephaniae Tetrandrae 15 grams.

One dose per day, simmer gently for about 35 minutes to produce 300~400ml decoction, divide into two times daily oral administration.

2.5. Indexes Measurement

NYHA heart function classification, 6-minute walking test (6MWT), heart rate (HR), SP, DP were evaluated before and after treatment according to methods provided by the book and guidelines[5-7]. NYHA heart function classification, 6MWT were evaluated during 8:00-12:00 am; HR, SP, DP were measured by electronic measuring device two times a day (8:00-9:00 am and pm), taking the mean values.

2.6. Criterion of Therapeutical Effect on Blood Pressure

The criterion is exactly based on “Guideline for clinical research on new drug of Chinese Medicine treating essential hypertension” which forms one chapter of a book called “Guidelines for clinical research on new drug of Chinese Medicine” compiled by State Food and Drug Administration of China[6]. Markedly effective: one of the followings. ① DP decreases ≥ 10 mmHg and returns to normal; ② DP decreases ≥ 20 mmHg and doesn’t return to normal. Effective: one of the followings. ① DP decreases < 10 mmHg and returns to normal; ② DP decreases ≥ 10~19 mmHg and doesn’t return to normal. ③ SP ≥ 30 mmHg. Ineffective: the above criteria had not been met. Total effective rate was the combination of markedly effective rate and effective rate.

2.7. Criterion of Therapeutical Effect on Heart Function

The criterion is exactly based on “Guideline for clinical research on new drug of Chinese Medicine treating heart failure” which forms one chapter of a book called “Guidelines for clinical research on new drug of Chinese Medicine” compiled by State Food and Drug Administration of China[6]. Markedly effective: NYHA heart function classification returned to I or was improved two classes. Effective: NYHA heart function classification was improved one class. Ineffective: NYHA heart function classification had no change or deteriorated. Total effective rate was the combination of markedly effective rate and effective rate.

2.8. Statistics

Paired sample T-test was used to analyze HR, SP, DP and 6MWT differences between pre-treatment and post treatment.

Table 1. Changes in HR, SP, DP, 6MWT (X ±S)

|              | Pre-treatment (n=116) | Post-treatment (n=116) |
|--------------|-----------------------|------------------------|
| HR (bpm)     | 78±6.5                | 69±6.7*                |
| SP (mmHg)    | 158±9.4               | 120±8.6*               |
| DP (mmHg)    | 87±6.8                | 76±7.5*                |
| 6MWT (m)     | 394±52                | 498±63*                |

*compared with pre-treatment P<0.01

3. Result

3.1. Changes in Heart Rate, Blood Pressure and 6-Minute Walking Test (Table 1)
Wuling powder and modified tianma gouteng decoction as an add-on therapy decreased the EH patients’ heart rate, systolic pressure, diastolic pressure and increased the 6-minute walking distance very significantly (P<0.01).

3.2. The Efficacy of Wuling Powder and Modified Tianma Gouteng Decoction on Blood Pressure

After taking wuling powder and modified tianma gouteng decoction for 2 weeks as an add-on therapy without changing the EH patients’ former medication, markedly effective rate and effective rate on blood pressure showed 44.8% (52/116) and 47.4% (55/116) respectively. Hence, total effective rate on blood pressure was 92.2% (107/116).

3.3. The Efficacy of Wuling Powder and Modified Tianma Gouteng Decoction on Heart Function

There were 15 EH patients with NYHA heart function I at the beginning of the study, for whom it was impossible to judge NYHA heart function classification improvement. Markedly effective rate and effective rate on NYHA heart function improvement showed 52.5% (53/101) and 42.6% (43/101) respectively. Hence, total effective rate on NYHA heart function improvement was 95.1% (96/101).

3.4. The Safety of Wuling Powder and Modified Tianma Gouteng Decoction on Treating EH

5 cases of EH patients with severe leg and ankle edema reported urinary frequency and/or nocturia at the beginning of the treatment, after several days of treatment, when severe leg and ankle edema were gone, it disappeared, suggesting it result from pharmacological action of wuling powder inducing diuresis, excreting liquids and eliminating edema. There was no other severe side effects such as dry mouth, insomnia, feverish dysphoria, tidal fever, tachycardia, palpitation, dizziness, gastrointestinal discomfort, and serum electrolyte disturbance etc.

4. Discussion

The renin-angiotensin-aldosterone system (RAAS) is a main concern in blood pressure control. Angiotensin II increases blood pressure by stimulating the adrenal cortex to release aldosterone, which causes potassium excretion and sodium and water reabsorption. Angiotensin II also increases blood pressure by promoting the secretion of antidiuretic hormone, which also leads to fluid retention.

Chinese herbal medicines have been used to treat EH effectively for over 2000 years. Wuling powder, consisting of Poria, Polyoporus, Rhizima Atractylodis Macrocephalae, Rhizoma Alismatis, Ramulus Cinnamomi, is one of the important decoction in the Treatise on Exogenous Febrile Diseases and a commonly used formula, which has the function of inducing diuresis, excreting liquids and eliminating edema. Ramulus Cinnamomi can lower blood pressure, reinforce cardiac contractility, reduce blood-lipid and blood sugar etc. [8, 9]

One experimental study in rats shows wuling powder has satisfying therapeutic effects on increasing the discharge of urine, decreasing the blood pressure and keeping the balance of the serum electrolyte with renal hypertension[4].

Tianma gouteng decoction, consisting of Rhizoma Gastrodiae, Gastradia Tuber, Loranthi Ramulus, Gardeniae Fructus, Haliotidis Concha, Caulis Polygoni Multiflori, Eucommiae Cortex, Herba Leonuri, Cyathulae Radix, Scutellariae Radix, Poria, tonifies the liver and the kidney, clears away the liver-heat, suppresses the liver-yang, and stops liver-wind. It is used to treat headache, dizziness, sleeplessness and high blood pressure caused by the liver-heat, liver-yang and liver-wind. Clinical studies and animal experiments revealed that tianma gouteng decoction could decrease angiotensin II, endothelin, the superoxide dismutase, calcium gene related peptide, improve insulin resistance, and attenuate left ventricular and aortic hypertrophy[10-12].

In clinical practice, sometimes some other herbs may also be added to tianma gouteng decoction to boost up blood pressure lowering effect. Since Radix Astragali[13,14] and Radix Rehmanniae[15] can lower blood pressure and strengthens cardiac contractility, and Radix Puerariae[16], Spica Prunellae[17], Herba Siegesbeckiae[18], Radix Stephaniae Tetrandrae[19,20] have the antihypertensive characteristic, we modified tianma gouteng decoction and added these six herbs to reinforce the formula’s efficacy.

The add-on effects of wuling powder and modified tianma gouteng decoction to existing antihypertensive treatments have demonstrated that wuling powder and modified tianma gouteng decoction seems to be effective and safe to control high blood pressure and improve NYHA heart function.

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