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CLINICAL STUDY

^{1}H nuclear magnetic resonance-based metabolomic study on efficacy of Qingrehuatan decoction against abundant phlegm-heat syndrome in young adults with essential hypertension

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Abstract

OBJECTIVE: To observe the influence of Qingrehuatan decoction (QRHT) on serum metabolic profile in young essential hypertension (YEH) patients with abundant phlegm-heat syndrome and provide a basis for treatment with the decoction.

METHODS: Twelve male YEH patients were randomly selected and serum samples were collected for examination before and after 4 weeks of the treatment with QRHT. Twelve healthy males were randomly selected and their serum samples were collected as a control. All serum samples were detected using metabolomic technology with ^{1}H nuclear magnetic resonance. Differences in metabolites were studied by principal component analysis and partial least squares-discriminate analysis, which produced scores and loadings plots.

RESULTS: After 4 weeks of treatment, serum substances could be distinguished between the YEH patients with abundant phlegm-heat syndrome and the control patients. The specific serum endogenous metabolites tended to improve after the treatment. QRHT can appropriately increase the levels of glucose, lactic acid, citric acid, high-density lipoprotein, phosphatidylcholine, glycerophosphate choline, hydroxybutyrate, alanine, and glutamate. QRHT could also decrease the levels of low-density lipoprotein/very low-density lipoprotein, lipids, N-acetyl glycoprotein, and O-acetyl glycoprotein.

CONCLUSION: QRHT can effectively ameliorate metabolic disorders in YEH Patients with abundant phlegm- heat syndrome. ^{1}H NMR-based metabolomic technology can provide an objective basis for the treatment of YEH patients with abundant phlegm-heat syndrome using QRHT.

Key words: Magnetic resonance spectroscopy; Metabolomics; Hypertension, essential; Clearing heat resolving phlegm; Phlegm-heat obstructing lung

INTRODUCTION

Hypertension is a widely recognized disease that may cause many common serious diseases, such as coronary disease and strokes. Approximately 7 million annual deaths are attributed to hypertension worldwide.[1] When classified as an average BP measurement of > 140 mm Hg systolic or > 90 mm Hg diastolic, hypertension occurs in approximately 26% of adults worldwide. And this is expected to increase to 1.56 billion people (29%) by 2025.[2]

Many people in China have turned to Traditional Chinese Medicine (TCM) for antihypertensive treatment.[3] Moreover, the efficacy and safety of TCM in the treatment of hypertension has been confirmed by several clinical studies.[4-7]

Previous studies have shown that hypertension is a metabolic disease.[8] Metabolomics is a key technology for systems biology which uses a holistic approach to biological and biomedical research, while TCM emphasizes holism and individual treatment and works with the principle of metabolomics. Therefore, many TCM studies have used metabolomics to explain mechanisms of syndrome differentiations and conversion.[9-11] Based on clinical observation, it was found that Qingrehuatan decoction (QRHT, the empirical prescription for clearing heat and dissipating phlegm) has therapeutic efficacy in treating hypertension. ^{1}H nuclear magnetic resonance (NMR) metabolomics was used to study the function and mechanism of QHRT.

MATERIALS AND METHODS

Subjects

Twelve male young essential hypertension (YEH) patients aged 32 to 40 [average: (36 ± 4) years] were selected in the department of Cardiology of Guang'anmen Hospital from May 2010 to January 2012 and served as the treatment-naive group before taking QRHT. They also served as the treatment-experienced group after taking QRHT for 4 weeks. Twelve healthy males aged from 30 to 40 [average: (36 ± 4) years] were included as a control group. All patients gave informed consent and the trial was approved by the Ethics Committee of Guang'anmen Hospital.

Diagnostic criteria

The diagnosis of hypertension followed A Draft of Chinese Guidelines for Hypertension Prevention and Treatment (revised edition in 2010).[12] Three measurements on separate days (usually at 2-week intervals) of the blood pressure ≥ 140 and/or ≥ 90 mm Hg, were sufficient for a diagnosis of hypertension. Grade 1: hypertension was defined as systolic pressure 140-159 mm Hg and/or diastolic pressure 90-99 mm Hg. Grade 2: hypertension was defined as systolic pressure 160-179 mm Hg and/or diastolic pressure 100-109 mm Hg. Grade 3: hypertension was defined as systolic pressure ≥ 180 and/or diastolic pressure ≥ 110 mm Hg. Secondary hypertension was excluded. According to the latest standards of World Health Organization, candidates aged 44 or under were included.[13,14]

Symptoms of abundant phlegm-heat syndrome in TCM

The diagnosis of abundant phlegm-heat syndrome followed the definition in PRC National Standard for Clinic Terminology of Traditional Chinese Medical Diagnosis and Treatment — Syndromes.[15] The main clinical manifestation of abundant phlegm-heat syndrome includes disturbed mind and *Qi* movement, cough and dyspnea, yellow thick sputum, fever and thirst, irritability and restlessness, insomnia and dreamful sleep, red tongue with yellow and greasy fur, rapid or slippery pulse.

Inclusion criteria

Inclusion criteria were as follows: diagnosis of grade 1 or 2 essential hypertension in accordance with the guidelines described previously. The diagnosis was conducted by two associate chief TCM physicians. Patients were included if they were initially diagnosed with hypertension, had hypertension without regular administration for years, or had no antihypertensive administration in the last 2 weeks. Patients were aged from 18 to 45 and were informed and consented to participate in the study.

Exclusion criteria

Exclusion criteria were as follows: patients aged under 18 or over 45 years old; patients with secondary hypertension; patients who regularly use drugs or have used antihypertensive drugs in the last 2 weeks; patients with Grade 3 hypertension; patients with blood sugar or fat abnormalities, hepatic dysfunction, Aminotransferase (ALT/AST) ≥ 1.5-fold normal value, renal dysfunction, males with creatinine (Cr) > 106 μmol/L, females with Cr > 97 μmol/L, blood urea nitrogen > 7.1 mmol/L, thyroid function abnormality, hematopoietic function abnormality, or mental diseases; patients with allergic physique and/or allergies to many drugs; patients participating in other clinical trials in the last month; patients unwilling to participate in this clinical trial; patients failing to take medication regularly or with incomplete data.

Reagents and instruments

Chemicals used included: 99.8% deuterium oxide (D_2O), batch number: 20111112 (Cambridge Isotope Laboratories Inc. Corporation, Andover, MA, USA); and 3-(trimethylsilyl) propionic-2,2,3,3-D_4 acid sodium salt (TSP-deuterated), batch number: 1668-E (Merck Corporation, Montreal, Canada). Instruments included: refrigerated centrifuge (Beckman, Pasadena, CA, USA); standard pipettes 100-1000 μL (GILSON