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CLINICAL STUDY

Effect of Astragali and Angelica particle on proteinuria in Chinese patients with primary glomerulonephritis

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Abstract

OBJECTIVE: To investigate the effect of the traditional Chinese herbs Astragali and Angelicae Sinensis (A & As) particle [contains Huangqi (*Radix Astragali Mongolica*), Danggui (*Radix Angelicae Sinensis*), Huzhanggeng (*Rhizoma Polygoni Cuspidati*) and Danshen (*Radix Salviae Miltiorrhizae*)] on proteinuria in glomerulonephritis patients with stage 2 chronic kidney disease.

METHODS: A prospective, multi-center, and randomized controlled clinical trial was performed for 24 weeks. From March 2011 to April 2012, 158 patients from nine hospitals in China participated. They were randomized into the A&As group (79 cases, A&As particle 15.2 g/day) and losartan group (79 cases, losartan 50 mg/day). At each follow-up visit, clinical data including blood pressure, urinalysis, 24-h-urinary protein excretion, serum albumin and serum creatinine were collected.

RESULTS: All 158 patients completed the follow-up. Proteinuria in the losartan group exhibited a biphasic time-dependent decline with a significant steady reduction from baseline to week 12 ($P = 0.0014$), and a platform level during the remaining 12-week follow-up ($P > 0.05$). In contrast, there was a continual significant decrease of proteinuria in the A & As group ($P < 0.001$). When compared with the losartan results, proteinuria in the A & As group from week 16 to week 24 was significantly reduced ($P < 0.001$). Stable eGFRs and blood pressure were also observed in both groups. Medication side effects were minimal and non-fatal.

CONCLUSION: For Chinese glomerulonephritis patients with stage 2 chronic kidney disease, therapy with A & As particles may provide effective anti-proteinuria treatment.

Key words: Angelica sinensis; Renal insufficiency, chronic; Glomerulonephritis; Proteinuria; Medicine, Chinese Traditional

INTRODUCTION

Globally, chronic kidney disease (CKD) has been increasing. In China, the prevalence of CKD in adults is

more than 10%,[1,2] and unlike in developed countries, primary glomerulonephritis (GN) rather than hypertensive nephropathy and diabetic nephropathy is the leading cause of end-stage renal disease.[3,4] For CKD, it is critical to slow down the progression of stage 2, because renal disorder could accelerate beyond this stage.[5,6] Therefore, a major challenge for Chinese nephrologist is to delay the progression of GN with stage 2 CKD.

Proteinuria is recognized as an independent risk factor for progression of GN.[7] Corticosteroid and other immunosuppresants are cornerstone therapies for proteinuria. Nevertheless, these drugs are not indicative for many GN patients with stage 2 CKD. Instead, angiotensin Ⅱ type 1 receptor blockers (ARBs) and/or angiotensin converting enzyme (ACE) inhibitors play important roles in the treatment of proteinuria.[8] However, the therapeutic effect of renin-angiotensin system blockade is not always satisfactory for Chinese GN patients with stage 2 CKD. Many of these patients, who are normotensive, cannot tolerate even moderate dosages of ARBs and/or ACE inhibitors because of systemic hypotension.[9] This condition is particularly common in Chinese patients, especially in the early stages of CKD. In addition, a higher dosage of ARBs and/or ACE inhibitors does not exert an incremental nephroprotective response.[9-11] Therefore, it is essential to explore other alternative therapeutic approaches.

In Asian countries including China, Traditional Chinese Medicines (TCM) have long been used to treat proteinuria.[12,13] Based on the personal experiences of experts from different regions in China, patients with GN have been treated with different herb formulations. Although the therapeutic effect of these on proteinuria has been demonstrated in animal studies, only a few small single-center retrospective studies have been published. The formulation of Astragali and Angelicae Sinensis (A & As) particle [contains Huangqi (*Radix Astragali Mongolica*), Danggui (*Radix Angelicae Sinensis*), Huzhanggeng (*Rhizoma Polygoni Cuspidati*) and Danshen (*Radix Salviae Miltiorrhizae*)] was developed for the treatment of GN in the 1990s at Shuguang hospital which is affiliated to Shanghai University of TCM. There are four herbs selected in the A & As particle, which are based on the theory of TCM and on extensive experience from senior physicians over several decades who have used traditional Chinese medicine to treat patients with GN. Of note, the A&As particle contains Astragali and Angelicae Sinensis, which are known to reduce proteinuria.[14,15] Several small clinical studies showed that the A & As particle and its components could improve proteinuria in patients with GN.[16,17] However, none of these individual herbs have been tested in a large clinical trial.

To investigate the effect of A & As particles on proteinuria in Chinese GN patients with stage 2 CKD, we performed a prospective, multi-center and randomized controlled clinical study using identical qualitative and quantitative preparation. Our secondary objectives were to observe A & As particle safety and tolerability.

MATERIALS AND METHODS

Selection and description of participants

The study recruited 158 patients from nine hospitals in China (Shuguang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Heilongjiang Academy of Traditional Chinese Medicine, Chinese Medicine Hospital of Hubei Province, Putuo Hospital affiliated to Shanghai University of Traditional Chinese Medicine, Zhongshan Hospital affiliated to Fu-Dan University, Yueyang Hospital affiliated to Shanghai University of Traditional Chinese Medicine, the Fifth Hospital Affiliated to Zunyi Medical College, Yangpu Hospital of Traditional Chinese Medicine, and Yinhang Community Health Center). All patients were clinically diagnosed with primary chronic glomerulonephritis.

Inclusion criteria for all recruits included the following: (a) underwent renal biopsy, (b) diagnosed with stage 2 CKD having a mild decrease of estimated glomerular filtration rate (eGFR) from 60 to 89 mL/min per 1.73 m^2 according to The National Kidney Foundation Kidney Disease Outcomes Quality Initiative definition, (c) persistent stable non-nephrotic proteinuria (0.5 to 2.5 g/day), (d) not taking ACE inhibitors and/or ARBs, or having taken these drugs but after a washout period, (e) normal blood pressure (an office blood pressure of ≤ 130/80 mm Hg in the sitting position), and (f) age between 18 and 70 years.

Exclusion criteria included: (a) secondary etiology including lupus, diabetes, and hypertension, (b) women in pregnancy or lactation, (c) serious complications including hematologic diseases, malignancy and infection, (d) acute kidney failure or renal allografts, (e) known allergy to the study drugs, (f) psychosis or uncooperative, (g) enrolled in other clinical trials in the previous 3 months, and 8) treatment with steroids and/or other immunosuppresants.

The study followed evidence-based principles and used a prospective, multi-center and randomized controlled design. Ethical guidelines were strictly conducted in accordance with the Declaration of Helsinki and with local regulations. The protocol was approved by the research ethics committee of Shuguang Hospital.

Two assessors monitored the study and were blinded to the treatment groups. All participants were clearly informed and provided written informed consent for participation. The study sponsors provided the first available allocation number, which were assigned in consecutive order, to the enrolled patients from the nine hospitals. The numbers of patients from each hospital were 18 each from Shuguang Hospital, Heilongjiang Academy of Traditional Chinese Medicine, Chinese Medicine Hospital of Hubei Province, Putuo Hospital, and Zhongshan Hospital, and 17 each from Yueyang Hospital, Fifth Hospital Affiliated to Zunyi Medical College, Yangpu Hospital of Traditional Chinese Medicine, and Yinhang Community Health Center.