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Use of traditional Chinese medicine (*Ren Shen Yang Rong Tang*) against microinflammation in hemodialysis patients: An open-label trial

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Traditional Chinese medicine;
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Summary
Background: Complementary and alternative medicine such as traditional Chinese medicine (TCM) is now frequently used combined with Western medicine for treatment in chronic kidney disease (CKD).
Objective: We designed an open-label trial to investigate the safety and potential therapeutic effects of Ren Shen Yang Rong Tang (R-S-Y-R-T) in hemodialysis (HD) patients.
Methods: The experimental group was treated with additional R-S-Y-R-T combined with routine western medicine, while the control group was treated only with routine western medicine. The duration of study was 6 months. Primary outcomes were to evaluate the changes in serum hematocrit and albumin levels. Secondary outcomes including blood inflammatory markers (c-reactive protein [CRP], interleukin-6 [IL-6], and tumor necrosis factor-α [TNF-α]) were checked. Finally we also followed up the change of quality of life (QOL) in our subjects.
Results: Sixty nine respondents were enrolled in this trial. Finally a total of 59 patients (27 R-S-Y-R-T group, 32 control group) completed the 6-month follow-up. Primary outcomes showed no significant statistical change of hematocrit in either 2 group ($P > 0.05$). But the R-S-Y-R-T group had a statistical increase in serum albumin ($P < 0.05$). Secondary outcomes were that

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both TNF-α ($P = 0.003$) and IL-6 ($P = 0.001$) showed evident decrease in the R-S-Y-R-T group. CRP was identified without statistical difference in both groups ($P = 0.226$). The R-S-Y-R-T group also had a significant improvement in QOL ($P < 0.05$).
Conclusions: Our study suggests that R-S-Y-R-T could decrease chronic inflammation and increase the life quality in HD patients. Further larger clinical trial of long-term treatment with R-S-Y-R-T is necessary for evaluating treatment use.

Introduction

Traditional Chinese medicine (TCM) is widely used for the treatment of many kinds of acute and chronic diseases among Chinese populations globally. Chronic kidney disease (CKD) has also been treated with TCM for thousands of years. Ren Shen Yang Rong Tang (R-S-Y-R-T) (or Ninjin'yoeito, NYT) is a common prescription which contains 14 different herbs and active components including Radix Astragali, Radix Glycyrrhizae (Gancao), and Rhizoma Atractylodis Macrocephalae (Baizhu).[1–4] Previous experimental animal model studies revealed that the active components of Radix Astragali, Radix Glycyrrhizae (Gancao) and Rhizoma Atractylodis Macrocephalae (Baizhu) are effective in CKD therapy, such as for the inhibition of mesangial cell proliferation, and decreasing chronic inflammation and proteinuria.[5–11] Recent human studies have confirmed that Radix Astragali, and Rhizoma Atractylodis Macrocephalae (Baizhu) have obvious therapeutic effects in chronic fatigue patients, as well as in CKD patients.[12–16]

In autoimmune animal models, R-S-Y-R-T could restore the function of CD_4^+ T cells and play an important role in the abrogation of autoimmune-prone T-cell differentiation.[17–19] The anti-inflammatory effect is associated with the suppression of interleukin-6 [IL-6], and tumor necrosis factor-α [TNF-α].[19–21] Therefore, R-S-Y-R-T could be considered as an immune-modulator.[22–24]

It is well established that in end-stage renal disease (ESRD), a dysfunction of immune system and chronic inflammation results in a series of comorbidities.[25–28] Therefore, the augmentation of host immunity, especially suppression of the inflammatory response in these patients, is very important. Complementary and alternative medicine such as TCM is now frequently used combined with western medicine for treatment in CKD.[29–33] The aim of our study is to assess the issue.

Methods

Participants and study design

Ethical approval for this study was obtained from the Human Ethics Committee of Tri-service General Hospital (TSGH), National Defense Medical Center, Taipei, Taiwan. Institutional Review Board (IRB) approval number is TSGHIRB 2-101-05-017. Clinical Trials.gov Identifier number is NCT02053740. A single-center open-label trial was conducted from January 2013 to June 2013. Uremic patients on maintenance hemodialysis (HD) who informed us of their interest in our study were recruited and gave informed written consent and indicated willingness to comply with study requirements. Enrolled subjects were 18 years or older, with at least 3 months maintenance HD. The exclusion criteria were malignancy, acute infection, gastrointestinal bleeding, pregnancy, lack of mental competence and inability to comply with the requirements of study.

Eligible 123 patients were allocated to study, and the basic characteristics of demographic variables, including gender and different six attending physicians were stratified randomization matched. Finally, there were 63 patients in the experimental group and 60 patients control group. After exclusion criteria, the experimental group had 32 respondents and the control group had 37 respondents. The duration of use of R-S-Y-R-T was 6 months. Within 6 months, 10 patients withdrew. By the end of the study, there were 27 patients in the experimental group and 32 patients in the control group (Fig. 1). Blood investigation, including biochemical profiles and inflammatory markers were checked at intervals of 0, 2, 4 and 6 months during routine H.D. The questionnaire for the assessment of quality of life (QOL) was evaluated at intervals of 0, and 6 months. Criteria for discontinuation of R-S-Y-R-T treatment included subjective symptoms such as anorexia, general malaise, or any discomfort on the part of the patient.

Study medication and dosage

For this study, we used herbal granules prepared according to the formula of R-S-Y-R-T. We purchased the study products from a manufacturer with a Good Manufacturing Practice (Si Wu Tang) certification in Taiwan. This was a concentrated decoction made by water extraction in 1:13 ratio from single batched roots of the 14 plants in proportions: Radix Astragali (Huangqi) (30 g), Rhizoma Atractylodis Macrocephalae (Baizhu) (30 g), Radix Glycyrrhizae (Gancao) (30 g), Radix Angelicae sinensis (Dang Guay) (30 g), Radix Paeoniae alba (Bai Sau) (90 g), Pericarpium Citri Reticulatae (Chenpi) (30 g), Cortex Cinnamomi (Rougui) (30 g), Radix Ginseng (Renshen) (30 g), Radix Rehmanniae praeparata (Soe Dee Huang) (20 g), Fructus Schisandrae (Wuweizi) (20 g), Poria cocos (Fuling) (20 g), Cortex et Radix Polygalae (Yuanzhi) (15 g), Zingiber officinale Roscoe (Jiang) (30 g), and Fructus Jujubae (Dazao) (10 g) as prepared according to the original pharmacopeia. The plant origins in China were known to the buyer of the pharmaceutical company and the final product was free of *Escherichia coli*, Salmonella and pesticide residues. The levels of heavy metals were 1.238 ppm for lead, 0.228 ppm for arsenic, 0.10 ppm for cadmium, and <0.0022 ppm for mercury, all within regulated limits (5, 5,