Clinical Investigation

Report on Four Cases of Chronic Renal Failure Effectively Treated with Astragali Radix

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黄耆が奏功した慢性腎不全の4症例

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Abstract

Chinese herbal medicine has historically been used for the treatment of renal disease. There are some medicines such as rhubarb and Ompito that delay the need for dialysis. However, they only attenuate the 1/Cr-time slope but cannot reduce the Cr level. In this study, four chronic renal failure (CRF) patients who had not responded to any Western medicine were treated effectively with Astragali Radix, a traditional herbal medicine. Serum creatinine (Cr) was clearly improved, and necessity for dialysis was delayed. In two patients, Cr was controlled stably over four years. There were no adverse effects, and no noteworthy changes in the levels of serum phosphorus, potassium and uric acid between before and after treatment were observed. This study suggests that Astragali Radix is a useful agent in the treatment of CRF.

Key words: chronic renal failure, Chinese herbal medicine, Astragali Radix

要旨

漢方薬はこれまでも腎疾患に応用されてきた。漢方薬の大黃や温脾湯には、透析導入までの期間を延ばす働きがあることが知られている。しかし、その効果は1/Crの傾きを改善するにとどまり、Cr自体を改善するわけではない。今回、西洋薬が無効であった慢性腎不全患者に漢方薬の黄耆が奏功した4症例を報告する。4例ともCr値は明らかに改善し、透析導入までの期間が延長された。このうち2例は4年以上にわたり安定的に推移している。4例とも副作用は認めず、また治療前後で血清リン、カリウム、尿酸値に変化はなかった。黄耆は慢性腎不全の有力な治療薬となりうる。

キーワード：慢性腎不全，漢方薬，黄耆

Introduction

In Asian countries numerous kinds of plants have been used as food, sources for food additives, spices and traditional herbal medicines. Some examples of drugs developed from traditional herbal medicines are ephedrine from *Ephedra sinica*, morphine from *Papaver somniferum*, quinine from *Cinchona*, and cocaine from *Erythroxylon coca*, among others.

Chinese herbal medicine has been used over the centuries for the treatment of renal disease. However, experimental studies of Kampo medicine for chronic renal failure (CRF) have just started in these past twenty years. Rhubarb and rhubarb containing Ompito (Wen-Pi-Tang in Chinese) can delay the progression of CRF¹⁾²⁾, but can not reduce the level of Cr. Western medicines such as carbon absorbant

(AST-120)³⁾ or angiotensin-converting enzyme inhibitors (ACEIs)⁴⁾ improve the 1/Cr-time slope, but they also can not decrease the Cr level. In the present circumstances, there is still no complete cure for CRF.

In this study Astragali Radix was shown to improve the serum Cr level without any major side effects. There is very possibility that Chinese medicine can become the treatment of choice for CRF.

Decoction of Astragali Radix

Fifteen grams of dried Astragali Radix was mixed in 600 ml of water and boiled down to 300 ml. The aqueous extract was filtered with a sieve and the resulting decoction was administered 3 times a day before meals.

Figure. 1 Clinical course of case 1

(a) 1/Cr-time slope up to before and after Kampo treatment is shown. Arrow indicates the start of Kampo treatment. After Kampo treatment 1/Cr-time slope was improved.

(b) Changes of serum Cr, e-GFR and BUN are shown as squares, triangles and circles, respectively. Arrow indicates the start of Kampo treatment. Serum Cr and BUN were improved with Astragali Radix.

Case reports

We report four CRF patients treated for at least one year with Astragali Radix.

Case 1 was a 15-year-old female with focal glomerulonephritis. At the age of 10, she was diagnosed with albuminuria in a school medical examination. Because of being mentally challenged, with epilepsy and renal insufficiency, she had been hospitalized since fifth grade and treated with enalapril maleate, allopurinol, benzbromarone, sodium bicarbonate, carbamazepine and alfacalcidol. Despite treatment, her Cr was deteriorating and she was sentenced from attending physician with **Fig.1 a** that it is necessary for dialysis within a few years. When she visited our hospital her weight was 44 kg and height was 148 cm. Her heart rate was 62 beats per min and her blood pressure was 98/62 mmHg. There were no abnormalities in her physical examination except for facial edema. Cr, blood urea nitrogen (BUN) and 24-hour creatinine clearance (Ccr) were 3.0 mg/dl, 51 mg/dl and 22.4 l/day, respectively. Urinalysis showed $\pm$ for protein and none for blood on dipstick examination. After administration of Astragali Radix, her Cr level improved from 3.0 to 1.49 mg/dl (**Fig.1 b**) and Ccr simultaneously showed an increase from 22.4 to 47.1 l/day. Presently, Cr is controlled in a range of 1.49 to 1.60 mg/dl.

Case 2 was a 59-year-old male. At the age of 41, he could not get insurance because of albuminuria and at the age of 51 he was diagnosed with diabetes. When he visited our hospital his weight was 110 kg and height was 181 cm. His heart rate was 94 beats

per min and his blood pressure was 129/79 mmHg. Laboratory studies demonstrated normal complete blood count (CBC) and normal serum electrolytes except for potassium (K); (K, 5.3 mEq/l; Cr, 2.36 mg/dl; BUN, 34 mg/dl; glucose, 150 mg/dl; HbA1c, 6.9%). Urinalysis showed 40-896 mg/dl of protein. Urinary glucose was not detected. Microscopic evaluation demonstrated 1-4 red blood cells per high-power field (HPF) and hyaline casts, granulated casts and waxy casts were seen. It was thought that the renal insufficiency depended on glomerulonephritis rather than on the diabetes, as his control of the diabetes was comparatively good and albuminuria was detected before his diabetes diagnosis. He had B hepatitis and underwent cholecystostomy at 35 years old and 42 years old, respectively. He had been treated with candesartan cilexetil, amlodipine besilate, glimepiride, pioglitazone hydrochloride, atorvastatin calcium hydrate, allopurinol, aspirin and furosemide but neither renal function (**Fig. 2 a**) nor urinary protein improved. His Cr level has ameliorated from 2.36 to 1.55 mg/dl with Astragali Radix (**Fig. 2 b**). This past one year, his Cr has been controlled in a range of 1.55 to 1.82 mg/dl.

Case 3 was a 31-year-old male who, at the age of 13, presented with proteinuria at a school medical check-up. Renal function gradually worsened from 3-4 years ago in spite of treatment with candesartan cilexetil, amlodipine besilate, atenolol, pravastatin sodium, dipyridamole, allopurinol, imidapril hydrochloride, omeprazole, and carbon absorbent (**Fig. 3 a**). Forty-five gram of low protein diet a day has been practiced for three years. Physical examination

Figure. 2 Clinical course of case 2

(a) 1/Cr-time slope up to before and after Kampo treatment is shown. Arrow indicates the start of Kampo treatment. After Kampo treatment 1/Cr-time slope was improved.

(b) Changes of serum Cr, e-GFR and BUN are shown as squares, triangles and circles, respectively. Arrow indicates the start of Kampo treatment. Serum Cr and BUN were improved with Astragali Radix.

Figure. 3 Clinical course of case 3

(a) 1/Cr-time slope up to before and after Kampo treatment is shown. Arrow indicates the start of Kampo treatment. After Kampo treatment 1/Cr-time slope was improved.

(b) Changes of serum Cr and BUN are shown as squares and circles, respectively. Arrow indicates the start of Kampo treatment. Serum Cr and BUN were improved with Astragali Radix for first 4 months, but then slowly turned worse. BUN was not improved consistently.

of the patient was unremarkable. When he visited our hospital his weight was 67 kg and height was 170 cm. His heart rate was 60 beats per min and his blood pressure was 139/89 mmHg. His father had type 2 diabetes. At 4 months of treatment with Astragali Radix, serum Cr concentration had improved from 5.32 to 3.34 mg/dl, but it then turned worse slowly again (Fig. 3b). BUN worsened approximately throughout and Hb was not improved in spite of using of epoetin alfa.

Case 4 was a 68-year-old male who suffered from acute glomerulonephritis 35 years ago, with persis-

tent occult urinary blood and albuminuria thereafter. Since his diagnosis, he underwent annual medical examinations, and his serum Cr remained below 1.0 mg/dl for about 30 years. Because of deterioration of Cr and BUN, treatment with amlodipine besilate, olmesartan medoxomil, and allopurinol was started 4 years ago, but his Cr and BUN continued to worsen (Fig. 4a). At his first visit to our hospital, his weight was 74.7 kg and height was 165.8 cm. His heart rate was 82 beats per min and his blood pressure was 115/72 mmHg. Urinalysis showed albuminuria and hematuria with the urinary sediment

Figure. 4 Clinical course of case 4

(a) 1/Cr-time slope up to before and after Kampo treatment is shown. Arrow indicates the start of Kampo treatment. After Kampo treatment 1/Cr-time slope was improved.

(b) Changes of serum Cr and BUN are shown as squares and circles, respectively. Arrow indicates the start of Kampo treatment. Serum Cr was improved with Astragali Radix. At the 10 months, the patient participated in a festival on a hot day, and his Cr worsened from dehydration. BUN was not improved.

containing erythrocytes, hyaline casts, epithelial casts and waxy casts. Physical examination was unremarkable. The patient's social and family histories were unremarkable. His serum Cr concentrations was improved with Astragali Radix from 3.13 to 2.36 mg/dl at twenty-month treatment (**Fig. 4 b**).

All cases of serum Cr were obviously improved with one year of treatment with Astragali Radix. However, Astragali Radix did not reduce either BUN or the amount of urinary protein. We can not conclude that Astragali Radix improves renal function because Ccr of cases 2, 3 and 4 were not measured, but it is a fact that Astragali Radix delays the necessity for dialysis in patients with CRF. There were no remarkable changes in the levels of serum potassium, phosphorus, and uric acid between before and after treatment.

Discussion

In recent years, growing numbers of patients have progressed to end-stage renal disease and the medical costs of dialysis have been increasing. Preventing the aggravation of CRF has become a most important problem for nephrologists. There are some medicines such as rhubarb, Ompito and AST-120 that delay the need for dialysis. ACEIs and angiotensin receptor antagonist have been reported to retard progression in patients with early CRF and albuminuria. However, they only attenuate the 1/Cr-time slope but can not reduce the Cr level.

Kampo formulae have been used for medical purposes for centuries. Its prescription is not a single,

but a mixture of several herbs. Haimoto H⁵⁾, Ebe Y.⁶⁾ and we⁷⁾ have reported that Kampo prescriptions that include Astragali Radix significantly improved the serum Cr level regardless of the underlying disease at any time from the early stage of renal insufficiency to end-stage renal failure. Even if the patients are undergoing dialysis, their Cr levels will decrease⁶⁾. This study was designed to estimate the efficacy of Astragali Radix alone.

In Japan, documentations of the pharmacological effects of herbs started in the third decade of the 19th century. Astragali Radix is one of the representative traditional herbal medicines and has been used historically for the treatment of edema, hypertension, night sweating, viral infection, skin wounds, inflammatory diseases and proteinuria in China and Japan^{8~11)}. In recent years, although investigations of herbs have begun to flourish, they are still insufficient.

The quantity of Astragali Radix we used was equivalent to 3-5 times the usual dosage in Japan, but it is the usual dosage in China. As a result of deteriorating renal function, we administered the larger quantity comparable to the dosage used in China. In our previous study, three out of 28 patients who took 30 g of Astragali Radix a day with other traditional herbs interrupted treatment because of itching⁷⁾. While they were taking Kampo formulae, serum Cr was improved successfully. But after interruption of treatment, one case needed dialysis and the other two showed worsening Cr levels. Then, we set Astragali Radix at 15 g per day. Adverse ef-

fects were not observed and there were no remarkable changes in the levels of serum phosphorus, potassium and uric acid between before and after treatment.

In this study, we actually treated five CRF cases. Although cases 2-5 did not undergo renal biopsy, all were thought to have glomerulonephritis, based on their histories of the present illness and laboratory data. Treatment with Astragali Radix alone resulted in a Cr-lowering effect in all cases. One of the five cases stopped taking Astragali Radix for a while because of aortocoronary bypass surgery (case 5), and was excluded. But while being treated with Astragali Radix, his Cr level improved from 1.97 to 1.67.

Astragali Radix had a useful effect on the Cr level, but it could not change BUN. The diuretic action of Astragali Radix might be one of the reasons for this, but it can not explain all of it. The fact that serum Cr and Ccr were improved simultaneously in case 1 suggests that Astragali Radix probably acts directly on glomerular function. In any case, Astragali Radix avoid or at least delays the necessity for dialysis in patients with CRF, and those who interrupted Astragali Radix-containing Kampo treatment had rapid deterioration of renal function in a previous study. This strongly suggests that this Chinese medicine may become a first-choice therapeutic option for CRF.

Conclusion

Astragali Radix reduced the serum Cr level without any major side effects. But Astragali Radix did not improve BUN, proteinuria and anemia. Astragali Radix avoid or at least delays the necessity for dialysis in patients with CRF. This study suggests that Astragali Radix is a useful agent in the treatment of CRF.

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