Experimental evaluation of traditional herb prescriptions given to patients with chronic renal failure in China, using rats with subtotal nephrectomy

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Abstract

Three traditional herbal prescriptions reported to be effective for treating chronic renal failure in China were studied using nephrectomized rats. Each prescription was given orally to rats for 80 days after excision of five-sixths of their kidney volume. Increased duration of 91 Shen-Shuai-Chong-Ji (91 腎衰衝剤) administration was associated with a progressive decrement of blood urea nitrogen (BUN), compared with the corresponding control values. A significant decrease of BUN was also observed in rats given Da-Huang-Lin-Pi-Chong-Ji (大黄霊脾衝剤) or Bu-Shen-Sheng-Xue-Chong-Ji (補腎生血衝剤), and these effects became more marked as the administration period was extended. Not only were total serum protein and albumin increased in rats given the three prescriptions, but also the serum levels of creatinine, methylguanidine and guanidinosuccinic acid were reduced significantly and urinary protein excretion was suppressed in the Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji groups. Histologically mesangial proliferation, extracapillary lesions, glomerular sclerosis index and tubulo-interstitial lesions, which were conspicuous in rats not given the prescriptions after nephrectomy, were improved considerably in the above two groups.

Key words Chronic renal failure, 91 Shen-Shuai-Chong-Ji (91 腎衰衝剤), Da-Huang-Lin-Pi-Chong-Ji (大黄霊脾衝剤), Bu-Shen-Sheng-Xue-Chong-Ji (補腎生血衝剤), prescription, nephrectomy, rat.

Introduction

The prognosis of patients with chronic renal failure has markedly improved along with the establishment of hemodialysis therapy and advances in medical care technology. However, continuation of maintenance dialysis is a great burden on the patients from both a mental and physical aspect, and social problems including financial issues have arisen due to the increase in the number of dialysis patients. Under these circumstances, various conservative therapies are available for chronic renal failure, such as a low-protein, high-caloric diet, essential amino acid therapy, and administration of activated charcoal or lactulose.[1-3] Although these treatment methods show some clinical effects, methods other than dialysis and renal transplantation are still urgently needed for treatment of chronic renal failure. Traditional Chinese medicine shows some promise in this field, producing clinically effectively results and giving rise to some optimism in the treatment of chronic renal failure.[4,5]

Our research group has developed three prescriptions suitable for patients with any stage of chronic renal failure, especially the early and middle stages,

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without producing side effects. These prescriptions not only relieve the clinical symptoms, but also reduce the levels of blood urea nitrogen (BUN) and creatinine (Cr), improve calcium phosphate metabolism and lipid conditions, and increase the serum erythropoietin level to improve the patient's anemia.[6-8] In order to confirm the effectiveness of the three prescriptions, we examined various biochemical indices and renal histology in an animal model of chronic renal failure.

Materials and Methods

Animals: Male Wistar rats were obtained from Shizuoka Agricultural Cooperative Association for Laboratory Animals (Hamamatsu, Japan).

Prescriptions: The following prescriptions were used (figures indicate proportions of each ingredient, expressed in parts per whole): 91 Shen-Shuai-Chong-Ji (91 腎衰衝剤) (Rhei Rhizoma 15, Salviae Miltiorrhizae Radix 30, Codonopsitis Radix 30, Aconiti Tuber 10, Epimedii Herba 30, Cordiceps 5), Da-Huang-Lin-Pi-Chong-Ji (大黄䗪脾衝剤) (Rhei Rhizoma 25, Salviae Miltiorrhizae Radix 30, Codonopsitis 30, Aconiti Tuber 10, Epimedii Herba 30, Fossilia Ossis Mastodi 30, Ostreae Testa 30, Curculiginis Rhizoma 15, Phellodendri Cortex 10, Anemarrhenae Rhizoma 10, Morindae Radix 15) and Bu-Shen-Sheng-Xue-Chong-Ji (補腎生血衝剤) (Rhei Rhizoma 10, Salviae Miltiorrhizae Radix 15, Codonopsitis 15, Aconiti Tuber 10, Epimedii Herba 15, Curculiginis Rhizoma 15, Morindae Radix 15, Astragali Radix 15, Angelicae Radix 15, Lycii Fructus 15, Polygoni Multiflori Radix 15, Mucunae Caulis 15). All of the crude drugs were products of China. The extract was obtained by boiling the above crude drugs gently in 1,000 ml of water for 60 min, and about 500 ml of decoction was obtained. The extract was then concentrated under reduced pressure to leave a brown residue. The yields of 91 Shen-Shuai-Chong-Ji, Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji were about 25-30 %.

Experimental design: Rats weighing about 200 g underwent resection of two-thirds of the left kidney and total excision of the right kidney at 10- to 14-day intervals.[9,10] Their BUN level was determined after recovery from the operation, and they were divided into four groups, avoiding any intergroup difference in the BUN level. The first group (control) was given water, while the other three groups were given 91 Shen-Shuai-Chong-Ji, Da-Huang-Lin-Pi-Chong-Ji or Bu-Shen-Sheng-Xue-Chong-Ji at 150 mg/kg body weight/day orally for 80 consecutive days. BUN was determined every 10 or 20 days during the administration period, and serum Cr, methylguanidine (MG), guanidinosuccinic acid (GSA), total protein, albumin and urinary protein excretion were determined at the end of the administration period. Urea nitrogen, total protein and albumin were determined using commercial reagents (BUN Kainos obtained from Kainos Laboratories, Inc., Tokyo, Japan; A/G B-Test Wako obtained from Wako Pure Chemical Industries, Ltd., Osaka). Cr, MG and GSA were measured using a Japan Spectroscopic liquid chromatograph with a step-gradient system by the method of Higashidate *et al.*[11] A fluorescence spectrometer, model FP-210 (excitation 365 nm, emission 495 nm; Japan Spectroscopic Co., Tokyo, Japan) was used for the detection of Cr, MG and GSA on the column. The animals were sacrificed after 80 days, and the renal tissues obtained were fixed in Bouin's solution, embedded in paraffin, and cut into thin sections. The sections were stained with hematoxylin-eosin, periodic acid-Schiff or periodic acid-methenamine silver stain, and examined by light microscopy. Mesangial proliferation was rated as normal, slight, moderate or severe, and the percentage of glomeruli having extracapillary lesions relative to total glomeruli was calculated as the incidence of extracapillary lesions. All glomeruli were observed for glomerular sclerosis, and sclerotic lesions in each glomerulus were rated in terms of their proportion as grade 0-4, using the method of Raij *et al.*,[12] where grade 1 represents involvement of up to 25 % of the glomerulus, while grade 4 represents sclerosis of 75-100 % of the glomerulus. The glomerular sclerosis index was obtained by averaging the scores for all glomeruli. The degree of tubulo-interstitial lesions was assessed according to three grades, *i.e.*, normal, mild and severe. Rats with 50 or less glomeruli were excluded from the analysis. Eight rats were used for each experimental group. Values are expressed as means±S.E.

Statistics : Statistical analysis of the data was performed by Dunnett's method.

Results

Histological findings

Eight rats were subjected to analysis in each group. As shown in Table I, no rats in the 91 Shen-Shuai-Chong-Ji group showed normal proliferation of the mesangium, the proliferation being rated as slight in 2 and moderate in 6. In each of the groups given Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji, there were 4 rats with slight or moderate proliferation, respectively, while no rats showed

Table I Histopathological evaluation of the kidney on day 80 in the groups treated with the various prescriptions.

Parameter		Control	91 Shen Shuai Chong Ji	Da Huang Lin Pi Chong Ji	Bu Shen Sheng Xue Chong Ji
Degree of mesangial proliferation	normal	0	0	0	0
	slight	1	2	4	4
	moderate	5	6	4	4
	severe	2	0	0	0
Incidence of extracapillary lesions(%)		35.0±6.9	24.0±2.9[b]	17.1±3.4[c]	17.8±3.0[c]
Glomerular sclerosing index		1.76±0.29	1.37±0.12[a]	0.97±0.11[c]	0.98±0.14[c]
Severity of tubulo interstitial lesion	normal	2	4	6	5
	mild	3	4	2	3
	severe	3	0	0	0

Significantly different from the nephrectomized control value : [a]$p<0.05$, [b]$p<0.01$, [c]$p<0.001$.

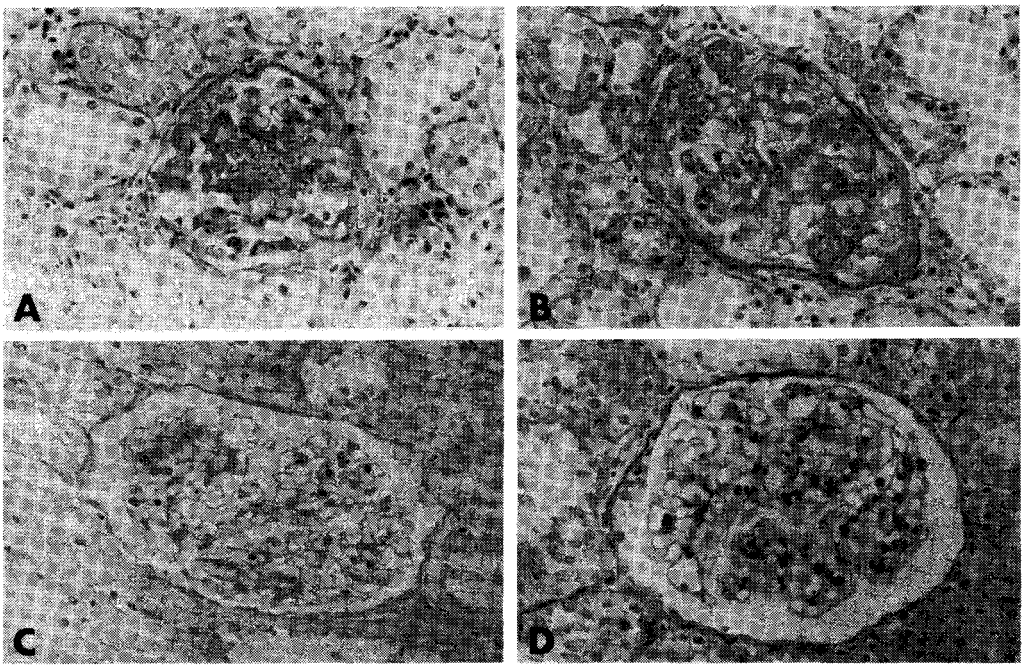

Fig. 1 Photomicrographs of glomeruli obtained from rats in the control (A), 91 Shen-Shuai-Chong Ji treated (B), Da-Huang-Lin Pi-Chong Ji treated (C) and Bu Shen Sheng Xue Chong Ji treated (D) groups. ×50.

normal or severe proliferation. Table I shows the percentages of extracapillary lesions. In comparison with the value of 35.0±6.9 % for the control group, the percentage was significantly decreased to 24.0±2.9 % in the 91 Shen Shuai-Chong-Ji group, 17.1±3.4 % in the Da-Huang-Lin-Pi-Chong-Ji group and 17.8±3.0 % in the Bu-Shen-Sheng-Xue-Chong-Ji group. The glomerular sclerosis index was 1.76±0.29 in the control group, and this was reduced to 1.37±0.12 in the 91 Shen-Shuai-Chong-Ji group, a reduction of 22 %. However, it was markedly decreased to 0.97±0.11 in the Da-Huang-Lin-Pi-Chong-Ji group and to 0.98±0.14 in the Bu-Shen-Sheng-Xue-Chong-Ji group. The degree of severity of tubulo-interstitial lesions was normal in 2 rats, mild in another 3 and severe in the remaining 3 in the control group, as shown in Table I. In the 91 Shen-Shuai-Chong-Ji group, it was normal in 4 rats and mild in 4. In the Da-Huang-Lin-Pi-Chong-Ji or Bu-Shen-Sheng-Xue-Chong-Ji group, it was normal in 6 or 5 rats, and mild in 2 or 3, respectively. There were no rats with severe lesions in the three groups. The typical glomerular morphology seen in the examined kidneys is illustrated in Fig. 1.

Biochemical findings

The changes in BUN following administration of the three prescriptions are summarized in Table II. The BUN in control rats increased gradually to 73.9 mg/dl at 20 days, 78.7 mg/dl at 40 days and 86.4 mg/dl at 80 days, reflecting chronic progressive uremia, as shown in Table II. In contrast, the BUN level was significantly lowered in rats given 91 Shen-Shuai-Chong-Ji, Da-Huang-Lin Pi-Chong-Ji and Bu-Shen Sheng-Xue-Chong-Ji; in particular, rats given Da-Huang Lin-Pi-Chong-Ji showed levels of 57.1 mg/dl at 30 days, 55.6 mg/dl at 40 days and 58.3 mg/dl at 60 days, indicating suppression of the increase in BUN. The effects of Bu-Shen-Sheng-Xue Chong-Ji were similar to those of Da-Huang-Lin-Pi-Chong-Ji. As shown in Table III, the Cr level was lowered significantly in rats given these two prescriptions. The MG value was also decreased markedly and significantly. These decreasing actions were particularly potent in rats after administration of Bu-Shen-Sheng-Xue-Chong-Ji, the MG level being decreased significantly to 1.54 μg/dl. The GSA level after administration of Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji showed significant change, being 42 % and 48 % lower than the control level, respectively. In contrast, the Cr value in rats given 91 Shen-Shuai-Chong-Ji showed a significant increase. The level of serum total protein was 5.89 g/dl in rats that had not undergone nephrectomy ; in nephrectomized control rats, it decreased significantly with the progression of renal failure, reaching 4.90 g/dl on day 80. The albumin level also behaved in a way similar to total

Table II Effect of three prescriptions on blood urea nitrogen.

Day	Group	BUN (mg/dl)
0	Nephrectomized rats	64.8±2.2
10	Nephrectomized rats	
	Control	64.6±2.3
	91 Shen Shuai Chong Ji	54.5±2.2[c]
	Da Huang Lin Pi Chong Ji	57.5±2.5[c]
	Bu Shen Sheng Xue Chong Ji	60.3±2.7[a]
20	Nephrectomized rats	
	Control	73.9±3.9
	91 Shen Shuai Chong Ji	57.8±3.1[c]
	Da Huang Lin Pi Chong Ji	62.4±2.5[c]
	Bu Shen Sheng Xue Chong Ji	69.9±4.0
30	Nephrectomized rats	
	Control	77.5±3.7
	91 Shen Shuai Chong Ji	66.5±3.1[c]
	Da Huang Lin Pi Chong Ji	57.1±2.3[c]
	Bu Shen Sheng Xue Chong Ji	62.2±4.0[c]
40	Nephrectomized rats	
	Control	78.7±5.3
	91 Shen Shuai Chong Ji	63.6±4.7[c]
	Da Huang Lin Pi Chong Ji	55.6±2.8[c]
	Bu Shen Sheng Xue Chong Ji	57.6±4.2[c]
60	Nephrectomized rats	
	Control	84.7±8.3
	91 Shen Shuai Chong Ji	67.6±7.3[b]
	Da Huang Lin Pi Chong Ji	58.3±5.3[c]
	Bu Shen Sheng Xue Chong Ji	60.2±6.0[c]
80	Nephrectomized rats	
	Control	86.4±9.7
	91 Shen Shuai Chong Ji	67.3±5.9[c]
	Da Huang Lin Pi Chong Ji	57.6±3.9[c]
	Bu Shen Sheng Xue Chong Ji	57.4±3.8[c]
	Normal rats	16.8±0.3

Significantly different from each nephrectomized control value : [a]$p<0.05$, [b]$p<0.01$, [c]$p<0.001$.

Table III Serum guanidino compounds on day 80 in the groups treated with the various prescriptions.

Group	Cr (mg/dl)	MG (μg/dl)	GSA (μg/dl)
Nephrectomized rats			
Control	1.45±0.12	3.48±0.34	36.04±4.45
91 Shen-Shuai-Chong Ji	1.75±0.27[a]	3.56±0.45	36.71±5.32
Da Huang-Lin Pi-Chong-Ji	1.04±0.05[b]	1.96±0.22[c]	20.95±2.04[c]
Bu Shen Sheng Xue-Chong-Ji	0.96±0.07[c]	1.54±0.17[c]	18.88±3.46[c]
Normal rats	0.68±0.05	N.D.	N.D.

N.D., not detectable. Significantly different from the nephrectomized control value : [a]$p<0.05$, [b]$p<0.01$, [c]$p<0.001$.

Table IV Serum total protein and albumin on day 80 in the groups treated with the various prescriptions.

Group	Total protein (g/dl)	Albumin (g/dl)
Nephrectomized rats		
Control	4.90±0.09	3.51±0.06
91 Shen Shuai-Chong Ji	5.31±0.10[a]	3.80±0.07[a]
Da Huang Lin Pi-Chong-Ji	5.69±0.05[a]	4.09±0.03[a]
Bu Shen Sheng Xue Chong-Ji	5.76±0.07[a]	4.12±0.06[a]
Normal rats	5.89±0.05	4.01±0.02

Significantly different from the nephrectomized control value : [a]$p<0.001$.

Table V Urinary protein excretion on day 80 in the groups treated with the various prescriptions.

Group	Protein (mg/kg B.W./24 h)
Nephrectomized rats	
Control	247.3±16.6
91 Shen-Shuai Chong-Ji	222.0±17.5[a]
Da Huang Lin Pi Chong Ji	169.6±9.8[b]
Bu Shen Sheng Xue Chong Ji	174.0±12.1[b]
Normal rats	43.1±1.2

Significantly different from the nephrectomized control value : [a]$p<0.05$, [b]$p<0.001$.

protein. However, in rats given the 91 Shen-Shuai-Chong-Ji, Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji for 80 days, the data indicated a significant increase in total protein and albumin levels, the levels being 8 % and 8 %, 16 % and 17 %, and 18 % and 17 % higher, respectively, than the corresponding level in the rats that had undergone nephrectomy (Table IV). As shown in Table V, urinary protein excretion in nephrectomized control rats reached about 250 mg/kg body weight/24 h by day 80, compared with a level of about 43 mg/24 h in normal rats. When the effect of oral administration of the three prescriptions was examined, urinary protein excretion was decreased significantly from 247.3 mg/24 h to 169.6 mg/24 h in the Da-Huang-Lin-Pi-Chong-Ji group and from 247.3 mg/24 h to 174.0 mg/24 h in the Bu-Shen-Sheng-Xue-Chong-Ji group. Oral administration of 91 Shen-Shuai-Chong-Ji also caused a significant decrease in urinary excretion, although to a lower extent.

Discussion

According to traditional Chinese medicine theory, chronic renal failure is generally considered to be Qi-Yang deficiency, *i.e.* energy exhaustion, accompanied by Xie-Oi repletion. The clinical treatment principle is to replenish Qi-Yang and drain off Xie-Qi.[13] The three prescriptions used in this experiment included both Chinese medicinal principles : complementary herbs and eradicating herbs. Rhei Rhizoma is considered to be one of the most effective drugs for draining off Xie. Codonopsitis Radix, Aconiti Tuber and Epimedii Herba supply Qi, and warm Yang. Salviae Miltiorrhizae Radix has also had wide clinical use in China as a drug for treatment of vascular system disturbance ; its pharmacological effects are reported to include vasodilation, reduction of blood pressure and inhibition of platelet aggregation.[14-17] The above

five drugs are considered to be basic prescriptions. In addition, Cordiceps, Curculiginis Rhizoma, Morindae Radix and Astragali Radix also can replenish patients' energy and warm their Yang. Angelicae Radix, Lycii Fructus, Polygoni Multiflori Radix and Mucunae Caulis have a replenishment effect on Yin and blood exhaustion. Phellodendri Cortex and Anemarrhenae Rhizoma can overcome Re-Du retention in patients with chronic renal failure. Hence, to the fundamental prescriptions, we added these herbs to match the various symptoms shown by patients with chronic renal failure. For example, if the patients suffered fatigue and dizziness, their energy was replenished using Cordiceps, Astragali Radix and Angelicae Radix. If the patients suffered chills, the warming medicines Curculiginis Rhizoma and Morindae Radix were supplied. Patients with chronic renal failure have accompanying gastrointestinal symptoms, such as anorexia, nausea and vomiting, usually induced by uremic toxin retention, which impairs gastrointestinal function. For this condition, we added the exhausting heat Chinese medicines Phellodendri Cortex and Anemarrhenae Rhizoma to drain off excessive toxins.

Patients with chronic renal failure treated clinically with the three prescriptions showed very good effects. Not only were the symptoms relieved but blood chemical indices also improved.[6-8] According to our clinical experience in treating patients with chronic renal failure, 91 Shen-Shuai-Chong-Ji produces its effect faster than Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji and is more effective. Generally, the BUN and Cr levels of patients were decreased in a week or so after oral administration of the decoction. Therefore, we treated patients with high levels of BUN and Cr, such as 70 mg/dl and 7.0 mg/dl respectively, with 91 Shen-Shuai-Chong-Ji. During the one-month treatment course, 91 Shen-Shuai-Chong-Ji showed marked effects on patients with chronic renal failure. Although Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji took longer to show their effects, the benefit was more long lasting. It was necessary to take the prescriptions for one month or so for their clinical actions to become apparent. On the other hand, patients with chronic renal failure usually have accompanying disturbance of lipids and electrolytes, and anemia. Lipidemia of the patients was improved after taking 91 Shen-Shuai-Chong-Ji. Da-Huang-Lin-Pi-Chong-Ji reduced considerably the level of serum phosphorus in patients with chronic renal failure. A hemoglobin-increasing action was particularly evident after administration of Bu-Shen-Sheng-Xue-Chong-Ji.

Although we obtained good clinical effects with the three prescriptions, their mechanism of action must be elucidated further to increase their clinical effectiveness and for extracting the effective substances present in the herbs. Therefore, the three prescriptions were examined using nephrectomized rats, a widely used animal model for investigating the progression of glomerular disorders. Since Brenner's group demonstrated by the micropuncture method that the glomerular disorder in nephrectomized model animals is closely related to glomerular hemodynamics,[18] this model has been considered important for investigating the onset and progression of glomerular disorder, since it can be used for testing hypotheses related to a key issue in nephrology, the onset and progression of glomerular disease.

In the present study, to analyse the effects of the three prescriptions on renal tissue lesions, we focused on four parameters, which revealed that mesangial proliferation was advanced in rats that had undergone excision of five-sixths of their kidney volume. In these rats, extracapillary lesions such as crescents or adhesion, the glomerular sclerosis index and tubular interstitial lesions, were also evidently advanced. In contrast, nephrectomized rats given Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji orally exhibited milder lesions. These two prescriptions restrain the process of glomerular sclerosis, which follows glomerular hypertrophy, together with mesangial proliferation, perhaps by suppressing the high intra-glomerular blood flow and elevated intraglomerular pressure produced by nephrectomy. As the above two prescriptions also reversed the increase of BUN, Cr, MG and GSA in rats with chronic renal failure, it is possible that they improve the systemic milieu and eliminate the vicious circle, thereby exerting beneficial effects. Therefore, it seems that the removal of certain toxins causing damage to renal function is responsible for the favorable maintenance

of cellular function. However, these effects of 91 Shen-Shuai-Chong-Ji were less marked than those of Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji.

In recent years, the hyperfiltration theory based on data from subtotally nephrectomized animals has become dominant, and the relationship between hyperfiltration and progression of renal disease, particularly glomerulosclerosis, has been pointed out by Brenner *et al.*[18,21] According to this theory, an increase in glomerular filtration leads to glomerular sclerosis, inducing a further decrease in renal function. However, some currently available data are inconsistent with this. Yoshida[22] and Ichikawa[23] have suggested that some growth factors may induce glomerular hypertrophy together with mesangial proliferation after subtotal nephrectomy, leading to glomerular sclerosis. Furthermore, Yoshioka *et al.*[24] have stated that glomerular hypertrophy induces some type of impairment in the glomerular basement membrane or epithelial cells, leading to leakage of protein. The results of our present study showed that Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji ameliorated the leakage of urinary protein, and also hypoproteinemia and hypoalbuminemia, suggesting that these two prescriptions may delay the progression of glomerular hypertrophy. As reported previously, Rhei Rhizoma, Salviae Miltiorrhizae Radix and Aconiti Tuber, which are fundamental herbs in Chinese prescriptions, improve glomerular function.[25,28] Taking these facts into consideration, it is suggested that these prescriptions inhibit the process of glomerular sclerosis which follows glomerular hypertrophy and the mesangial proliferation induced simultaneously by some growth factor after nephrectomy.

In summary, the present findings indicate that administration of Da-Huang-Lin-Pi-Chong-Ji and Bu-Shen-Sheng-Xue-Chong-Ji suppresses high levels of BUN, Cr, MG and GSA, and ameliorates both hypoproteinemia and hypoalbuminemia, with reduced urinary excretion of protein. It is further suggested that the effects of these two prescriptions on chronic renal failure are closely related to the improvement in renal histology. On the other hand, our experimental results showed that 91 Shen-Shuai-Chong-Ji did not obviously prevent the process of glomerular sclerosis, which follows glomerular hypertrophy, in parallel with mesangial proliferation. Therefore it could not effect significant reversal of the increased urinary protein produced by nephrectomized rats. However, its effects on BUN and Cr in a clinical setting might be connected with improvements in lipid metabolism. Clinical research has confirmed that total cholesterol, triglyceride and low-density lipoprotein in patients with chronic renal failure are reduced, and that high-density lipoprotein is significantly increased after taking 91 Shen-Shuai-Chong-Ji. As reported by Grond *et al.*,[29] Cappelli *et al.*[30] and Portman *et al.*,[31] lipid deposition in glomeruli may plays an important role in the pathogenesis of chronic renal failure. It seems that regulation of the lipid metabolism imbalance causing damage to glomerular structures is responsible for the favorable amelioration of renal function. This suggests that factors other than hyperfiltration are involved in the progression of renal failure. As mentioned above, 91 Shen-Shuai-Chong-Ji appears to control lipid metabolism. However, since lipid metabolism has not been investigated in animal experiments, more detailed clarification of these issues is desirable.

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和文抄録

漢方理論から方剤を組立，慢性腎不全患者においてその有効性が中国で明らかにされている3方剤を実験的に評価するため，5/6腎摘ラットを用い検討した。80日間経口投与期間中，91腎衰衝剤投与群のBUN値が低下したが，そのような作用は大黄霊脾衝剤と補腎生血衝剤投与群でも認められた。しかし後者の2方剤では投与日数の延長とともにその作用が著しく増強する結果が得られた。一方，80日間投与した総蛋白，アルブミンレベルは3方剤ともに増加したが，クレアチニン，メチルグアニジン，グアニジノコハク酸レベルの有意な低下と尿蛋白排泄量の抑制作用は大黄霊脾衝剤，補腎生血衝剤で認められ，メサンギウム増殖の程度，管外性病変の程度，糸球体硬化性病変の程度，尿細管間質病変の広がり等の組織

学的所見も大黄霊脾衝剤，補腎生血衝剤でかなり改善していた。

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