Kampo Medicine - Current Research

Treatment of Chronic Renal Failure with Kampo Medicine

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This used to be a disease unknown in our field, but is now encountered due to the advances in modern medicine in daily practice. Hypertension, chronic liver failure, hyperlipidemia and similar conditions are recognized as some of many currently problematic pathologic conditions. Among these, often only the terminal stages are recognized as diseases and thus subject to treatment. Examples are the collection of ascites due to liver cirrhosis or the development of uremia caused by chronic renal failure.

Famous physicians of the past have diagnosed such diseases during stages where they "are not yet manifest" and seemed to have contrived a variety of therapeutical means for curing them before reaching the terminal stage. Or else these physicians tried to extend the time required to reach the terminal stage as much as possible. Again, occasionally they may have initiated treatment in some cases after certain aspects of the terminal stage became manifest.

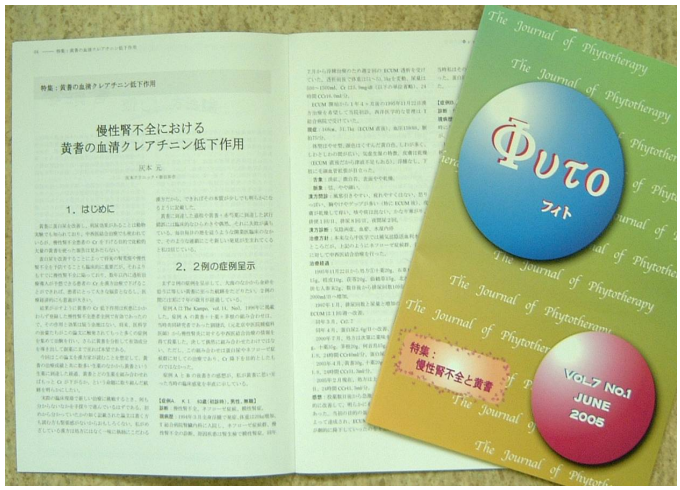
Today, due to advances in modern medicine, we are able to infer the prognosis and course of almost any disease. Yet, even though that may be possible, it still does not allow us to stop the progression of the disease. This often leaves us without any therapeutical means for its treatment.

Chronic renal failure is a classical example of such a disease. Modern medicine is making efforts to achieve its cure and new procedures like dialysis, substituting for the lost renal function, have been developed and currently benefit many people. Yet, for both therapists and patients, dialysis compares to being chained and leaves both parties wishing for more freedom. However, even though the gradually declining renal function and simultaneously gradually increasing BUN and creatinine concentrations can be controlled to some degree by rigorous diet and the application of Kremezin (spherical carbonaceous absorbent), the disease relentlessly destroys these therapeutic efforts and pushes the patient towards dialysis.

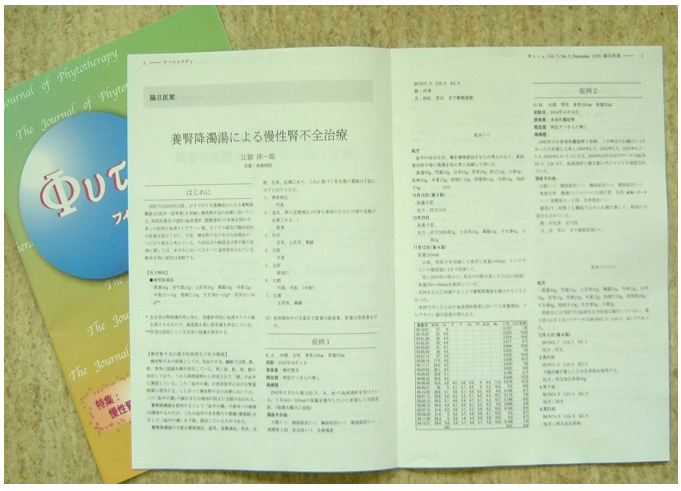
Modern Kampo medicine has become able to treat several renal diseases that will lead to chronic renal failure from the stage "where they are not yet manifest". The question now is, whether there are also therapeutic tools and techniques applicable to the terminal stage of chronic renal failure.

The answer to this question has recently been provided by two Kampo specialists who have published two outstanding reports:[1,2)]

Picture 1: Hajime Haimoto, Serum Creatinine Level Lowering Effects of *Astragali* Radix in Patients with Chronic Renal Failure Φυτο Vol. 7, No. 1, p4-9, 2005



Picture 2: Yoichiro Ebe, Clinical Experiences Using the *yojinkodakuto(Nourishing the Kidney and Depressant Turbid Dampness Decoction* in Patients with Chronic Renal Failure Φυτο Vol. 7, No. 2, p4-11, 2005



1. Dr. Haimoto's work

Haimoto, at the beginning of his work, describes clinical examples he experienced himself. Based on two specific cases, he is now convinced that *Astragali* Radix is capable of lowering the creatinine concentration.

In the first patient, in whom the chronic renal failure was due to membranous nephropathy, administration of *Astragali* Radix resulted in a drastic increase in urine volume that led to a decrease in creatinine. The second patient suffered from uremia caused by chronic nephritis. When treatment with Kampo medicine did not produce any improvements at all, addition of *Astragali* Radix to the prescription also resulted in an abrupt decrease in the creatinine concentration (within one month from 8.8 mg/dl to 7.4 mg/dl.)

Based on these results, Haimoto thought that the use of *Astragali* Radix alone might be able to induce a decrease in creatinine concentration and thus started the following research.

Serum creatinine level lowering effects of *Astragali* Radix in patients with early chronic renal failure.

Ten patients (one of these dropped out of the study because of the development of efflorescences) with early chronic renal failure who consulted his clinic between February 2002 and February 2005, were treated with a combination of 3-4 crude drugs centering on *Astragali* Radix. Observations of the patients showed that underlying diseases of the patients varied widely.

This treatment resulted in a decrease in creatinine concentration by 0.3-0.9 mg/dl and the effect continued over a prolonged time. The effects of *Astragali* Radix appeared after a rather short period (within 2 months) and a gradual decrease of the initially high creatinine levels continued even over an observation period of more than 2 years. In patients with initially low values, the concentration fell to the upper limit of the normal range, but subsequently did not improve any further. Changes in serum potassium levels were not observed.

Among the nine patients observed, one presented a particularly interesting case. The patient was a 62-year old man with an initial creatinine level of 1.3 mg/dl. From the age of 56, the value started to increase gradually and reached 1.7 mg/dl by the age of 61. At that stage, treatment with *Astragali* Radix and several other crude drugs, did not produce any improvement; but when *Paeoniae* Radix Rubra was added to the prescription, the concentration decreased after one month to 1.21.
Based on this experience this researcher concluded that a combination of *Astragali* Radix + *Paeoniae* Radix Rubra would be even more effective.

Summarizing the above described results shows that Haimoto proposed the following protocol for the treatment of patients with early chronic renal failure: "In patients with chronic renal failure first administer *Astragali* Radix (15-30 g) (where even the administration of *Astragali* Radix alone is effective, as Haimoto's case report presented in the previous issue clearly shows[3]). However, when the administration of *Astragali* Radix alone does not induce a decrease in the creatinine level, *Paeoniae* Radix Rubra (10-15 g) is added. If the creatinine concentration still does not fall, *Rhei* Rhizoma is added."

Table 1 shows the variations in serum creatinine and potassium(K) observed in 9 patients who were treated with Kampo medications by Haimoto. The underlying diseases in these patients included a variety of diseases like chronic nephritis, IgA nephropathy, diabetic nephropathy and unknown causes (suspected drug induced nephritis). The prescriptions used for these patients all contained 15-30 g of *Astragali* Radix. For patients for whom an improvement in proteinuria is imperative, 10-15 g of *Imperatae* Rhizoma and 15-35 g of *Houttuyniae* Herba were added. In patient No. 4, *Astragali* Radix alone did not produce any improvement, but after addition of *Paeoniae* Radix Rubra a successful reduction of the creatinine concentration was

achieved.

Table 1 Variations in serum creatinine and potassium(K) in 9 patients receiving Kampo treatment

No.	Sex	Age	Cr/K before medication	After 2 months	After 6 months	After 9 months	After 12 months	After 24 months
1	F	65	1.9／5.7	2.0／5.6	—	1.6／4.2	1.6／4.3	
2	M	76	2.8／4.9	2.2／4.7	2.1／	—	2.1／4.6	1.9／5.0
3	M	61	1.9／6.7	1.7／5.6	1.7／5.2	1.5／6.8**	1.3／4.8	1.5／5.6
4	M	61	1.7／4.7	1.9／4.5	1.8／4.8	1.5／5.2	1.4／	
5	M	56	1.6／4.7	1.1／	1.1／	1.2／4.5	1.2／4.5	
6	F	59	2.3／4.1	2.1／4.3	1.9／4.4	1.8／4.9	1.7／4.5	
7	M	72	1.7／4.8	1.3／4.8	1.3／4.1			
8	M	39	1.6／4.8	1.4／4.3	1.4／4.4	1.3／4.4	1.2／4.9	1.9*／4.8
9	M	61	2.9／5.3	2.6／5.6				

* Patient discontinued Kampo medication on his own initiative

** Start of rigorous low potassium diet

New applications of old methodology

In the dawn of the Kampo medical age, prescriptions did not exist right from the beginning, but the effects of each individual crude drug were doubtlessly confirmed separately. Records of such activities of ancient people may still be found in the "Shen Nong (Shinno) Legend", describing a legendary forefather of pharmacotherapy who allegedly tested 100 plant species per day on himself to confirm their effects. Kampo preparations are composed of individual crude drugs whose effects are well known. Haimoto also discovered that *Astragali* Radix lowers creatinine concentration through confirmation of the effects of each individual crude drug.

The process of this discovery was a dramatic one and reading through that work is very rewarding. This discovery not only represents a great blessing for patients with chronic renal failure, but will also make a major contribution to the research in this field. In a field where diseases are considered to be incurable by modern medicine, this finding may represent the appearance of a new therapeutic drug. This circumstance can only be described as the emergence of a new research field.

2. Ebe's new preparations

Yoichiro Ebe, who is also known as the developer of the classical formulation theory, has discussed chronic renal failure from a point of view of this classical formulation theory, "*yojinkodakuto (Nourishing the Kidney and Depressant Turbid Dampness Decoction)*" for the treatment of intractable diseases. Theoretically one of the active ingredients of this preparation is *Astragali* Radix. Ebe's approach differs completely from that of Haimoto, but the conclusions reached resemble each other very closely.

Ebe with his joint researchers, Hashimoto, et al., has reported improvements achieved with the use of this preparation in three patients with chronic renal failure in the Clinical Journal of Chinese Medicine Vol. 25, No. 4, (2004), later 7 other patients in Vol. 26, No. 1 (2005) and finally introduced 13 cases in the『Φυτο』Vol. 7, No. 2, (2005). The underlying diseases in these patients included such diversified conditions as chronic nephritis, gouty nephropathy, diabetic nephropathy, multicystic renal cysts etc. regardless of whether they were of renal or postrenal nature. Moreover, the course of the individual conditions in these patients closely resemble those described by Haimoto, although they included more severe cases

than the patients described by Haimoto. These reports also describe patients in which the creatinine concentration did not rise even after 3 years of treatment, but on the contrary tended to decrease and the condition did not progress for more than a year, although the patients had already been in the preparatory stage for dialysis. In patients who were already on a dialysis regimen, an increase in urine volume led to improvements in the creatinine concentration, so that it was in some cases even possible to decrease the frequency of the dialysis.

In order to comprehend this preparation it is necessary to master the classical formulation theory. Since this theory represents a very detailed system, it is difficult to represent it here in a simplified form. Here I would like to restrict myself to the presentation of my conclusions. People who do no know the entire theory will be able to obtain certain results using the below described formula.

Yojinkodakuto(Nourishing the Kidney and Depressant Turbid Dampness Decoction)

Astragali Radix	30 g
Paeoniae Radix Rubra	15～30 g
Smilacis Rhizoma	30 g
Dioscoreae Hypoglaucae Rhizoma	10 g
Salviae Miltiorrhizae Radix	12 g
Pinellia Tuber	12～15 g
Trichosanthes Semen	10 g
Glycyrrhizae Radix	6～15 g*
Poria	12～30 g**

* In addition to the renal protective activity of *Glycyrrhizae* Radix there is also a dose dependent serum potassium lowering effect, so that its dose should be determined based on the laboratory values.

** *Poria* is basically used in twice the amount of raw licorice.

Ebe lists the following precautions pertaining to the use of this preparation.

1. *Imperatae* Rhizoma (bai mao gen) may aggravate the renal failure and its effect may last in some cases up to 3 months. Since the pharmacologic actions of *Imperatae* Rhizoma are heat clearing, detoxification and draining damp, this drug is frequently used in Chinese medicine for the treatment of chronic renal failure. Yet, based on past experiences, it has become clear that this drug may aggravate chronic renal failure. Even though founded on known Chinese medical drug effects, new crude drugs should be added to this preparation very carefully.
2. Since Kremezin absorbs ingredients compornents of herbs, a combination therapy with this preparation may obscure the effects of the Kampo preparation.
3. In case of dermal efflorences caused by *Astragalus membranaceus* Bunge or Astragalus mongholicus Bunge is said to range generally between 1 and 3%. In patients with renal failure this ratio reached approximately 10% (4/38), indicating that the said incidence may increase. (Author's note: in the case of astragalus induced efflorences, it might be beneficial to switch the prescriptions to Hedysarum polybotrys Hand.-Mazz.)
4. *Yojinkodakuto* apparently does not affect renal anemia. Conversely, in patients with severe anemia marked by a hemoglobin value of less than 7.0 g/dl, it may induce nephrocyte apoptosis or necrosis and thereby further aggravate the renal failure. With the use of this drug under these circumstances, improvements in creatinine concentration or similar parameters are not observed. Accordingly, it is essential to treat anemia with erythropoietin.
5. Generally, when treating renal failure with Kampo medicines there is a fear of increasing potassium uptake. Yet, raw *Glycyrrhizae* Radix has a dose dependent serum potassium lowering effect allowing control of the potassium level based on serum potassium concentration.
6. In dialysis patients, the use of this preparation induces a decrease in creatinine concentration, an effect that is even observed in almost anuretic

patients. In some cases, it may further increase urine volume.

Above, I introduced the treatment patterns of Haimoto and Ebe for chronic renal failure. As stated at the beginning of the paper, there are no other actively pursued treatment alternatives apart from dialysis and so far nobody believed in the existence of drugs or preparations that might improve the creatinine values. However, the work of these two researchers has clearly shown that preparations centering around *Astragali* Radix are apparently capable of producing at least a certain degree of improvement, the effects of which continue for prolonged periods of time. Although these practitioners used completely different approaches, the conclusions they arrived at were remarkably similar.

These two dissertations provide good news for patients suffering from chronic renal failure.

References

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