

Kampo Medicine - Current Research

Situation on Use of Goreisan in Dialysis Patients

— From the *Goreisan Symposium 2010* —

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It was in the Korean War's casualties with acute renal failure that the effectiveness of dialysis was first recognized. Since then, dialysis has been applied widely from acute renal failure to chronic renal failure. At present nearly 300,000 people receive dialysis in Japan¹⁾ and Japan has the world-top level of dialysis technology. The advanced technology of dialysis membranes has significantly increased the effectiveness ratio of dialysis and thanks to the synthesis of erythropoietin by the genetic engineering, nephrogenic anemia occurring in the dialysis patients needs for mostly no blood transfusions in the regular life. However, there are symptoms that cannot be sufficiently handled or prevented by Western medicine such as headache, cramps in the lower limbs, hypotension occurring during a dialysis session – these symptoms cause to lower the QOL of the patients in combination with the dialysis three times a week.

Naturally there are no descriptions in classic books of Chinese medicine about clinical conditions of patients having the dialysis treatment of modern medicine, but Kampo preparations are widely used in everyday dialysis treatment. A renal failure that has fallen into the condition that needs dialysis because of Kampo treatment cannot be improved by Kampo medicines. However, various implications or unpleasant symptoms that arise during a dialysis can be relieved by Kampo medicines.

Treatment of various symptoms in dialyzed patients will be reported below from the viewpoint of the method of using *goreisan*, together with the introduction of published literatures.

Historical background of Kampo treatment in a dialysis patient

The first case report about Kampo treatment of a dialyzed patient was made in 1977 by Okada. The patient was a physician with diabetic nephropathy who was under treatment with dialysis. The author came to know from a document that the physician suddenly died²⁾ right after the conversation was carried out that as his conditions became improved with the combination use of Kampo medicines including *bunshoto* and *hochuekkito*, the frequency of routine dialysis might be reduced. The document did not mention the cause of the death, so details are not known. However, a cardiac disease or a cerebrovascular disorder might be the cause. In around '76, the cost of dialysis was covered by the government fund and presumably there were no financial burdens to the patients for paying the medical cost. Furthermore, as the patient was a physician, I do not like to think that he received less frequent dialysis. In these days, practitioners or physicians in general did not have sufficient understanding of Kampo medicines and information of Kampo was scarcely available. After that, Kampo medicines in the form of extract became popular and Kampo preparations began to be used in the everyday settings of dialysis from 90s onward.

Use status of *goreisan* in the sites of dialysis

Up until today, the use of *goreisan* for dialysis patient has been confined for the following:

1. Prevention of dialysis hypotension
2. Imbalance symptoms such as headache, nausea, cramps in the lower limbs
3. Effect on hyperpotassemia

1. Prevention of dialysis hypotension

From my experience, hypotension, which may possibly be associated with the volume of the removed water, often occurs in the patients during the latter half of a dialysis session. Especially in the patients who badly control their body weight, a large amount of water is removed and hypotension often occurs in the latter half of a dialysis even if they have taken vasopressors beforehand. In the case, to maintain the patient's blood pressure the solution of normal saline is often infused. Thus, the amount of the water removed with great pains becomes balanced out by the amount of the infused solution. Kawashima reported in 2000 about a case of diabetic nephropathy. This female patient of 64 year-old repeatedly developed hypotension during the latter half of a dialysis and an adequate amount of fluid could not be removed. Kawashima gave her an oral administration of the Extract 2.5g of *goreisan* at the start of a dialysis. With the administration, her blood pressure was controlled and the volume of the normal saline infusion decreased enabling the planned water volume to be removed. In this publication, it was further reported that changes in the circulating blood volume (Δ BV) were determined by the vascular refilling monitor of the hematocrit monitor measuring cells (Crit Lin^R of JMS Co.) for the extracorporeal circulation and that it was confirmed that the amount of the circulating blood plasma that had not been seen before the administration of the Kampo medicine was maintained during the latter half of a dialysis³⁾. The results were further tested and the report about this additional testing was presented at the 2008 Japanese Society for Dialysis Therapy.

An oral dose of the Extract 2.5g of *goreisan* was given to 10 patients on non-diabetic maintenance dialysis at the start of a dialysis to measure Δ BVs and plasma refilling rates (PRR) before and after the administration. Although the result showed

no significant differences between the values before and after the intake of the Kampo medicine, four patients showed an improvement in blood pressure fluctuations during a dialysis session and there existed a significant negative correlation between Δ BV and PRR⁴⁾. This means that there should possibly be the patients who had the water moving, due to the oral administration of *goreisan*, from the outside of the blood vessels into the inside of the blood vessels.

It may be said that *goreisan* is a prescription worth trying for the prevention of hypotension during a dialysis treatment.

2. Effect of *goreisan* on headaches, nausea, and cramping lower limbs

Headaches and nausea in the introduction stage of dialysis are called disequilibrium syndrome and these symptoms increase pain and suffering of the patient who do not get used to dialysis. Their cause is described as cerebral swelling secondarily developed by changes in the osmotic pressure of the blood due to the removal of urea nitrogen and other elements from the blood. Headaches are often-observed complaints even in maintenance dialysis patients. And other than migraines, there is a different type of headache associated with changes in the body fluid, similarly in the introduction stage of dialysis. Some patients have the type of headache which may be caused by medication overuse and coping with this type of headache is a difficult task. Cramping lower limbs is also a symptom that often occurs in dialysis patients. They suffer the cramping during a dialysis and sometimes during the night time. *Shakuyakukanzoto* often has marked effects on cramps as in healthy people, but it cannot be effective at all times⁵⁾⁶⁾.

The author had once conducted a questionnaire survey with 180 maintenance dialysis outpatients at Tsuchiura Kyodo Hospital, in which they were

asked about the presence of headache, nausea, and lower legs cramps and confirmed their willingness of taking a Kampo medicine; and 20 of them were administered *goreisan* to verify its effectiveness. The subjects were aged 41 to 76 with the dialysis history of 7 to 223 months. Primary diseases were diabetes in 6 patients, chronic glomerulonephritis in 9, and connective tissue disease in 2, and polycystic kidney disease / pregnancy kidney / renal sclerosis in 1 individually. Headache in 16, nausea in 2 (nausea and headache overlapping in 1), and cramps in lower limbs in 5 (cramps and headache overlapping in 2), to all of which *goreisan* was orally administered twice / morning and night (for partial cramps in the lower legs, the administration was once in the morning of the dialysis day). Improvements in subjective symptoms after 8 weeks were compared against score 10 of before-the-administration to see how the scores declined. The results showed headache disappeared completely in 4 patients, 70%-90% improvement in 7, 30%-40% improvement in 4, and no change at all in 1. As for nausea, 90% improvement in 2, and for lower limbs cramps, disappeared in 1, 70% improvement in 1, 50% improvement in 1, and 20%-30% improvement in 2. Physical conditions changed by the administration were constipation in 5, and soft stools / increased blood pressure / feeling legs light / joint pain relief / relief of cramps in 1 individually. In one patient with nausea, the symptom disappeared but constipation developed, so that the oral administration was discontinued voluntarily but the symptom did not recur⁷⁾. It has been verified from these results that *goreisan* is effective for improving complaints of dialyzed patients.

There is another document reporting that *goreisan* was used for maintenance dialysis patients who developed cerebrovascular disorders during a dialysis with worsening disordered consciousness during the session⁸⁾.

3. Effect of *goreisan* on hyperpotassemia / hyperkalemia

As kidney failure progresses, the levels of blood potassium (K) become elevated with high frequency. The author has often experienced cases where plasma K did not decline sufficiently sometimes even if the K concentration of the dialysis solution was controlled. This is the result from the weak ability to remove K in hemodialysis compared to peritoneal dialysis. Therefore, instructions are given to the patients to avoid taking K from articles of food as much as possible. However, only a few patients can continue to strictly adhere to the diet. On the other hand, some patients die suddenly due to the blood K levels elevated by overeating of K-rich foods, especially fruit. The patients with high levels of plasma K at ordinary times take the oral administration of potassium absorbing agents, which are hard to drink and have the risk of solidification in the intestinal tract, leading to an intestinal obstruction.

Tajima et al. reported that a patient with high levels of blood K showed an improvement in the levels of plasma K after the administration of *goreisan*. According to the report, the female patient of 50s whose plasma K had once increased to 7mEq/ml complained of pain in the shoulder joints and received the administration of this Kampo medicine; the levels of K that had not fallen below 6mEq/ml declined to around 5mEq/ml. Later *goreisan* was replaced with *shosaikoto*, but the K levels were maintained⁹⁾. Then, Muramatsu made a report with Tajima with an addition of one more patient¹⁰⁾.

And Naito also reported that the level of plasma K decreased after the administration of *goreisan* in patients with chronic renal failure in the maintenance period. In the report, a comparison was made between the group of high levels of K (an average of Cr 4.5mg/dl,

$K \geq 6\text{mEq/ml}$) and the group of relatively high levels of K (an average of Cr 1.9mg/dl, $5 \leq K < 6\text{mEq/ml}$). The results showed that in the group of high levels, an average of 6.6mEq/ml declined to an average of 5.6mEq/ml due to the administration of *goreisan*, whereas in the group of relatively high level of K, no changes were observed in effect from an average of 5.2mEq/ml to 5.3mEq/ml. Moreover, no changes were observed in the amount of potassium in urine during the administration of this Kampo medicine. Thus, it may be possible that although *goreisan* does not affect the levels of plasma K in blood K of high levels but not high enough to the life-threatening extent, the Kampo acts to correct the high levels of blood K that exceeds 6mEq/ml¹¹⁾. However, the mechanisms are not known.

The above is the report on the reality of various applications of *goreisan*, together with reports by great physicians. I hope that the application of this Kampo medicine will further expand in the sites of maintenance dialysis.

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