

Clinical Report 2 (Kampo Medicine)

A Case of Acute Exacerbation of Congestive Heart Failure with Chronic Renal Failure Successfully Treated with Goreisan

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Abstract

An 85-year-old man suffered from chronic renal failure and congestive heart failure since about 2 years ago. On May 12th in 2015, he admitted to this hospital due to acute exacerbation of congestive heart failure presenting exertional dyspnea and thirst. Together with resting on bed and oxygen inhalation, a new diuretics, tolvaptan, was taken in addition to his conventional diuretic drugs. However, about 2 weeks later, tolvaptan was stopped because of worsening renal function. Then, targeting to thirst and oliguria, *goreisan* was given for relieving clinical symptoms since June 3rd. Subsequently dyspnea and poor appetite diminished at the end of June and better general condition continued more than one month around the end of July.

We report a case of congestive heart failure combined with chronic renal failure, successfully treated with *goreisan*. In this case, *goreisan* improved both acute exacerbation of the congestive heart failure and the renal dysfunction with regulating water imbalance in body. Furthermore, it is very important that his prognosis was prolonged with highly quality of life.

Keywords: congestive heart failure, chronic renal failure, *goreisan*, water balance regulation

Introduction

The pathologic condition of chronic renal failure represents "water intoxication". Regardless of whether before or after dialysis, based on clinical symptoms like edema, dry mouth, vertigo, lassitude and gastrointestinal symptoms etc. as well as abdominal diagnosis, *goreisan* is the drug of first choice¹⁾. Here the formula is expected to help not only

to regulate water metabolism in the body, e.g., improve the condition of water intoxication, but also blood pressure and delay the onset of dialysis²⁾.

Congestive heart failure too, is also considered to represent "water intoxication". In addition to rest and restriction of salt intake western diuretics or cardiotonic drugs are used for the treatment. To rectify blood pressure or edema western diuretics (mainly loop diuretics like Furosemide or Spironolactone) are the standard therapy for congestive heart failure^{3,4,5)}. However, an inattentive increase in the dosage of loop diuretics may easily lead to a deterioration of kidney function and thus adversely affect the endogenous water balance. Recently a new vasopressin receptor antagonists (a diuretic called Tolvaptan) has been added to the western diuretics, allowing to comparatively easily achieve improvements of edema and congestion⁶⁾.

On this occasion an elderly patient treated with loop diuretics was hospitalized because of a sudden exacerbation of chronic renal failure complicated by congestive heart failure. The patient was first treated with Tolvaptan, which was expected to improve the edema and congestion, but the drug was not sufficiently effective. After switching to *goreisan*, however, the effects were even better than expected. The here presented valuable case report indicates, that the diuretic action of *goreisan* could be considered due to it correcting the endogenous water balance and thereby improving various symptoms including renal function.

Case: age 85, man

Chief complaint: exertional dyspnea, dry mouth

Past history: in 2002: fracture of left tibia and right ankle

Clinical course 1 (until admission):

Treatment for chronic renal failure complicated by congestive heart failure on an outpatient basis was initiated approximately 2 years earlier. On May 12, 2015 exertional dyspnea developed. On May 15 he visited our hospital and was admitted for treatment because of an acute exacerbation of the chronic renal failure complicated by congestive heart failure.

Western medical findings:

Alert, height: 153 cm, weight: 56.5 kg, facial edema, body temperature: 36.4°C, SpO₂: 91%, BP: 137/71, HR: 101/min, regular, cardiopulmonary: systolic murmur, pulmonary rales, abdomen: flat, soft; edema of the legs;

Oriental medical findings:

Subjective symptoms: exertional dyspnea, dry mouth; Objective signs: inspection: poor complexion, earthen colored; edema of face and lower extremities; pulse diagnosis: deep, thin, weak; tongue diagnosis: thin white coat with dental impressions and engorged sublingual veins; abdominal diagnosis showed lack of strength and softness of the lower abdomen. Hyochondrial fullness and tenderness as well as epigastric clapotage.

Examination results:

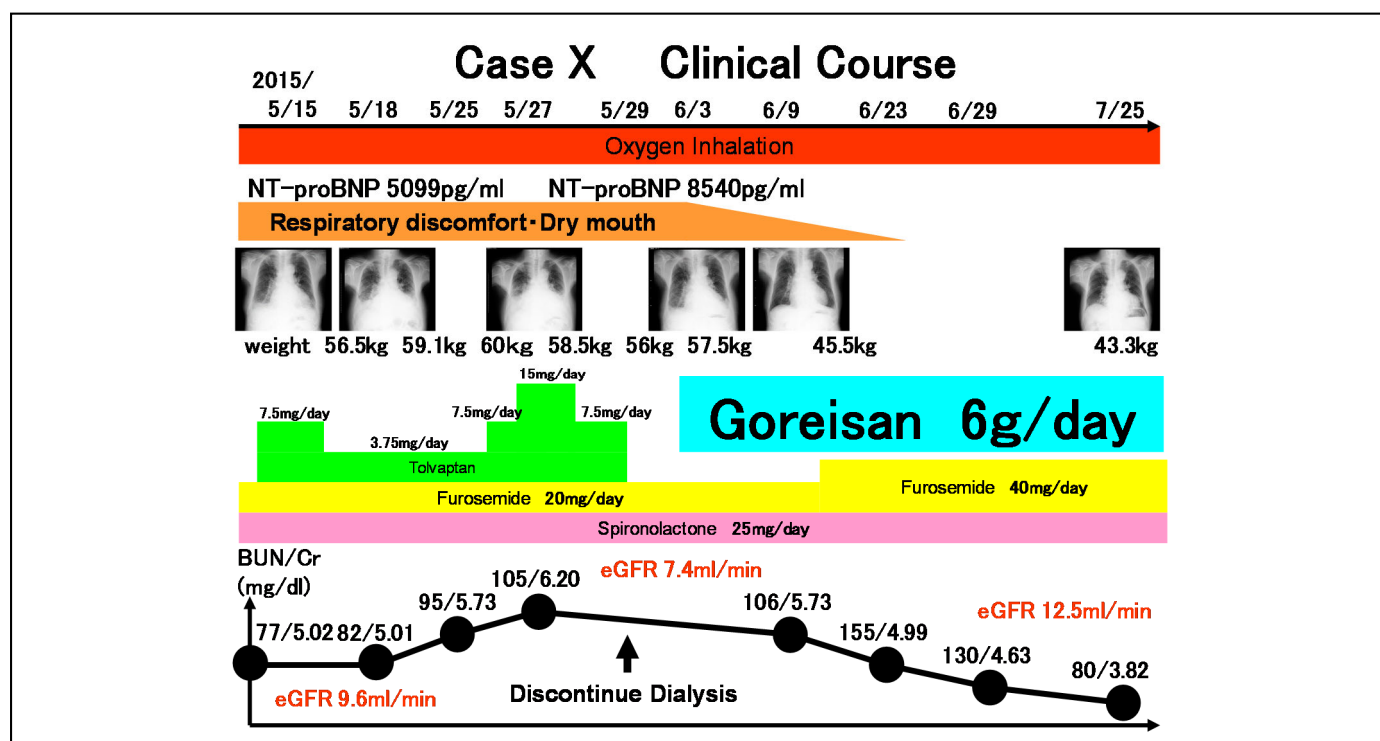
Blood examination:

white count: 3,500, hemoglobin: 7.4 g/dl, CRP: 0.61 mg/dl, urea nitrogen: 77 mg/dl, creatine: 5.02 mg/dl, eGFR: 9.3 ml/min/1.73m², NT-proBNP 1,383 pg/ml, albumin: 3.3 g/dl;

chest x-ray: enlarged cardiac shadow, bilateral pleural effusion, pulmonary congestion

Clinical course 2 (after admission): Figure 1

After admission the medication, including the western loop diuretics (Furosemide and Spironolactone) prescribed during the treatment as an outpatient were continued. In conjunction with rest and initiation of oxygen inhalation the diuretic Tolvaptan was added to the regimen on May 16, the day following admission. Yet, the dyspnea continued and renal function deteriorated further. On May 29 administration of Tolvaptan was discontinued. After consultation with the patient and his family it was decided not to initiate dialysis and instead conservative treatment, including palliative care, chosen. From June 3 *goreisan* (Kotaro Pharmaceutical Co., Ltd., 6 g/day) was added to the otherwise unchanged regimen in order to improve the subjective symptoms of dyspnea, dry mouth and lack of appetite, targeting the dry mouth and decreased urine volume. Later, body weight gradually decreased and the pleural effusion decreased too. By the end of June the dyspnea, dry mouth and lack of appetite had improved. After a while, over a period of about 1 month until the end of July, the general condition stabilized. By the end of August the patient's general condition deteriorated because of an infection and he died of multiple organ failure.



Discussion

Goreisan is comprised of the five crude drugs Alisma rhizome, Polyporus umbellatus, Poria cocos, Atractylodes lancea rhizome and cassia bark. It is widely used as a diuretic for intermediate conditions between deficiency and excess with water intoxication as its indication. In the classic Shan Han Lun the pathologic condition is specified as the lesser yang disease state and the formula widely used for dry mouth, diabetes, acute or chronic nephritis, nephrosis, edema, uremia etc.^{1,2)}.

On the other hand, western diuretics are used to reduce the preload, but even increase urine volume when there is edema in the presence of dehydration. In case of elderly people dehydration, electrolyte anomalies, hypotension and similar conditions can easily complicate the situation, so that the administered dose must be carefully considered³⁾.

Taking the side effects of western diuretics like Furosemide into account, in particular in case of long-term administration, the dehydration may possibly lead to renal dysfunction or cerebrovascular disorders. Short-term combination with *goreisan* while carefully observing the pathologic condition, or else switching to *goreisan* to increase the diuretic effect, is also considered to be effective. When taking the side effect dehydration into account, it is possible to optimally utilize the advantage of *goreisan* to promote diuresis only in the presence of edema, possibly decreasing the side effects of western diuretics.

Moreover, if a dose increase of the western diuretics is in certain cases difficult due to the general condition, combination with diuretic Kampo formulas like *goreisan* can be effective. However, recently the western diuretic Tolvaptan has made its debut on the clinical scene. Edema and congestion can now comparatively easily be alleviated, the drug causes only minor blood pressure fluctuations and is said to be safer than western loop diuretics⁶⁾. Some reports have described the ease of water control during the initial stage of dialysis⁷⁾.

The pathologic condition of chronic renal failure

is precisely the manifestation of water intoxication. Endogenous water balance in renal failure is marked by an imbalance between the water of the blood and the water compartment outside of blood vessels. In other words, the equilibrium between tissues and body cavities has been disrupted. Moreover, while there is excess water in the tissues and body cavities, it cannot moisten the blood. *goreisan* adjusts this condition, supplies cells and the blood with water and since it lowers osmotic pressure, during strong inhibition of the diuresis, it ameliorates the disrupted water equilibrium in the body and should therefore be understood not to be simply a diuretic. Regarding this property its effect can be expected to delay the the timing of dialysis initiation in cases of renal failure complicated by congestive heart failure. Also, in cases of organic renal diseases it is by virtue of its properties given priority over treatment with western diuretics and the guidelines pertaining chronic renal failure as a chronic renal disease have been adjusted⁸⁾.

Then again, congestive heart failure as a pathologic condition too represents a true form of water intoxication. It is marked by progressive intravascular dehydration and an excess of water in the alimentary tract.

In case of organic disease, similar to organic renal diseases, based on its properties, this formula should be given priority over western diuretics. The details have been arranged in form of the treatment guidelines divided into acute and chronic cardiac insufficiency^{6,7)}. Cardiac diseases that are indications for Kampo medicines are functional disorders associated with cardiac neurosis. Again, not so much the acute phase but rather the chronic phase is the disease stage at which treatment is administered. In case the western diuretics are insufficiently effective, Kampo formulas are often administered as required to alleviate symptoms, promote diuresis and stabilize the general condition.

Moreover, in case a right heart insufficiency is observed when considering Kampo treatment

mokuboitō (Mu Fang Yi Tang⁹⁾) may be one of the choices that can be used. To alleviate the symptoms of edema or cold pattern *Kumibinroutō*¹⁰⁾ is also said to be useful. *Goreisan* is often used in cases of heat pattern associated with a decrease in urine volume and edema. It can also be used for anasarca caused by cardiac insufficiency as well as a diuretic in cases of pleural effusion due to congestive heart failure during the still comparatively acute phase. It is considered to correct the intravascular dehydration and reduce the amount of excessive water within the alimentary tract^{11,12)}.

This patient was a case of acute deterioration of chronic renal failure complicated by congestive heart failure and not a single organ acute exacerbation like acute exacerbation of congestive heart failure or acute exacerbation of chronic renal failure alone. The heart and the kidneys maintain a close correlation called cardiorenal coupling. In spite of the presence of edema or pulmonary congestion the diuretic Tolvaptan was probably due to the decreased renal function not very effective.

Goreisan on the other hand does not only improve the edema and congestion, but also renal function. Since it promotes the inflow of unevenly distributed excess water into the blood vessels, it increases renal blood flow, which can be interpreted as helping making it easier for western diuretics to recover their effects. Thus, the diuretic effect of *goreisan* improves the responsiveness to western loop diuretics through its regulation of the water balance and was therefore considered to contribute to improvements of clinical symptoms, ADL as well as delaying the timing of initiation of dialysis. We are hoping that the comparatively early addition of *goreisan* to the regimen in this kind of acute exacerbation of chronic renal failure complicated by congestive heart failure will be a promising therapy.

Isohama is conducting research indicating that *goreisan* regulates water balance via aquaporin^{13,14,15)}. Similarly, the diuretic Tolvaptan is

also said to exert its effects via aquaporin⁶⁾. In this case Tolvaptan could not sufficiently exert its effects because of the deteriorating renal function, but *goreisan* was conceivably effective because of differences between the two agents on the molecular level. A new disease concept "aquaporin disease" has been proposed and *goreisan*, unlike western diuretics, seems to be a formula with bright prospects regarding its ability to prevent "water moving into directions generally not allowed".

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