CASE REPORT

Chinese Prescription Kangen-karyu against Metabolic Syndrome: Successful Treatment of Three Patients

Tsutomu Kitazawa1 Kazuyuki Hiratani1 Chan Hum Park2 Takako Yokozawa3*

1. Shinseikai Toyama Hospital, Toyama, 939-0243, Japan
2. Institute of New Frontier Research Team, Hallym Clinical and Translational Science Institute, Hallym University, Chuncheon, 24252, Republic of Korea
3. Graduate School of Science and Engineering for Research, University of Toyama, Toyama, 930-8555, Japan

ARTICLE INFO

Article history
Received: 12 May 2021
Accepted: 18 May 2021
Published Online: 18 June 2021

Keywords:
Metabolic syndrome
Traditional Chinese medicine
Kangen-karyu
Case report

ABSTRACT

Metabolic syndrome is the cluster of diseases, which is manifested by central obesity, impaired glucose tolerance, lipodystrophy, and high blood pressure. These metabolic syndrome-related traits significantly increase the risk of type 2 diabetes, adverse cardiac events, stroke, and hepatic steatosis. In the past decade, several organizations have proposed different diagnostic criteria. The use of traditional Chinese medicine to treat metabolic syndrome has received increasing attention due to its wide availability. In this paper, we report a case of three patients with metabolic syndrome with improved administration of 7.5 g of Kangen-karyu extract per day for 6 months. We present and discuss evidence supporting the possibility of using Kangen-karyu for metabolic syndrome.

1. Introduction

Metabolic syndrome, a major public health problem worldwide today, is a cluster of clinical, metabolic, and biochemical abnormalities, such as central obesity, high blood pressure, impaired glucose tolerance, and dyslipidemia. These metabolic syndrome-related traits significantly elevate the risk of type 2 diabetes mellitus, adverse cardiovascular events, stroke, and hepatic steatosis. The pathogenesis of metabolic syndrome is multifactorial, with the interplay of environmental, nutritional, and genetic factors [1-3]. Thus, metabolic syndrome has become one of the major burdens of the health care system.

The concept of metabolic syndrome was first presented by Kylin in 1923, who described a syndrome involving hypertension, hyperglycemia, and gout [4]. However, this concept did not attract much attention until Dr. Reaven mentioned syndrome X, clustering of metabolic risk factors, in 1988, which is similar to metabolic syndrome [5]. The WHO (World Health Organization) and EGIR (European Group for the Study of Insulin Resistance) released their diagnostic criteria for metabolic syndrome [6,7]. The definition of metabolic syndrome in Japan, which is characterized by the accumulation of visceral fat with the co-occurrence of several risk factors, was established in 2005 [8]. Epidemiological studies demonstrated that a condition clustering several risk factors like metabolic syndrome
will lead to a greater risk of cardiovascular diseases than a single risk factor \cite{9-11}. The accumulation of visceral fat is essential for the diagnosis of metabolic syndrome and is considered to be located upstream of the cascade clustering several risk factors and subsequent cardiovascular diseases. Therefore, the main purpose of the treatment of metabolic syndrome is the effective reduction of multiple risk factors and the following cardiovascular diseases through the reduction of visceral fat. In the treatment of metabolic syndrome, oriental medicine is an outstanding example of alternative and complementary medicine with a long history, a unique theoretical system, and a variety of herbal remedies. Many traditional Chinese medicine (TCM) has been tested for the treatment of metabolic syndrome. We have conducted pre-clinical animal experiments to investigate the effectiveness of multi-target treatment of TCM for various human diseases. In our previous studies, Kangen-karyu (a crude drug consisting of Salviae Miltiorrhizae Radix, Cnidii Rhizoma, Carthami Flos, Paeoniae Radix, Aucklandiae Radix, and Cyperi Rhizoma, as shown in Table 1; Guan-Yuan-Ke-Li in Chinese), a TCM modified from Kan-shin No. 2 (Guan-xin No. 2 in Chinese) \cite{12}, may play a protective role against metabolic syndrome \cite{13-15}. Kangen-karyu has been used clinically as a treatment for cardiovascular disease, including angina pectoris and cerebrovascular diseases \cite{16,17}. The results of our previous study provide important evidence that this prescription ameliorates metabolic syndrome.

Based on these results, Kangen-karyu was administered to three patients with metabolic syndrome, and report its therapeutic usefulness.

### Table 1. Composition of Kangen-karyu.

<table>
<thead>
<tr>
<th>Common name</th>
<th>Botanical name</th>
<th>Family name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salviae Miltiorrhizae Radix</td>
<td><em>Salvia miltiorrhiza</em> Bunge</td>
<td>Labiatae</td>
</tr>
<tr>
<td>Cnidii Rhizoma</td>
<td><em>Cnidium officinale</em> Makino</td>
<td>Umbelliferae</td>
</tr>
<tr>
<td>Paeoniae Radix</td>
<td><em>Paeonia lactiflora</em> Pallas</td>
<td>Paeoniaceae</td>
</tr>
<tr>
<td>Carthami Flos</td>
<td><em>Carthamus tinctorius</em> L.</td>
<td>Compositae</td>
</tr>
<tr>
<td>Aucklandiae Radix</td>
<td><em>Aucklandia lappa</em> Dene.</td>
<td>Compositae</td>
</tr>
<tr>
<td>Cyperi Rhizoma</td>
<td><em>Cyperus rotundus</em> L.</td>
<td>Cyperaceae</td>
</tr>
</tbody>
</table>

#### 2. Case Presentation

##### 2.1 Case 1

A 68-year-old male with hypertension, hypercholesterolemia, borderline diabetes, and obesity reports an improvement in metabolic syndrome when administered Kangen-karyu extract. This patient subsequently changed his lifestyle and continued to receive conventional treatments: antihypertensive drugs (amlodin: 5 mg/day, azilva: 20 mg/day) and an antilipidemic agent (lipitor: 5 mg/day). However, he came to our hospital, seeking to recover his functional level with medicine including herbal medicine. Kangen-karyu prescription (7.5 g/day) was administered three times a day. Before Kangen-karyu prescription administration, his initial anthropometric measurements included a BMI of 30.3 kg/m$^2$: body weight 82.6 kg (182.1 lb), height 165 cm (5.41 ft), and an abdominal circumference of 105.8 cm (3.47 ft), which classified him as obese. In the blood pressure test, his systolic blood pressure (SBP)/diastolic blood pressure (DBP) was 133/85 mmHg. Serum hemoglobin A1c (HbA1c) or glycated hemoglobin was 7.3%, displaying poorly regulated blood glucose. Serum lipids levels were as follows: total cholesterol: 230 mg/dL, low-density lipoprotein (LDL)-cholesterol: 142 mg/dL, LDL-cholesterol/high-density lipoprotein (HDL)-cholesterol: 2.3, and triglycerides: 353 mg/dL, indicating dyslipidemia. When Kangen-karyu extract was administered for 6 months, BMI and abdominal circumference were slightly reduced. The levels of triglycerides, total cholesterol, LDL-cholesterol, LDL-cholesterol/HDL-cholesterol, and HbA1c were reduced. Meanwhile, other parameters such as liver and kidney function parameters [aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea nitrogen and creatinine (Cr)] were not affected by Kangen-karyu extract administration. However, physical and subjective symptoms such as headache, feeling of heaviness in the head, and mottled skin have improved. In addition, the tongue coating was slightly improved when Kangen-karyu was administered. Herein, we present evidence supporting the use of Kangen-karyu prescription for metabolic syndrome.

##### 2.2 Case 2

Kangen-karyu extract was effective for a 64-year-old woman with hypertension and hypercholesterolemia. This patient also changed her lifestyle and continues to receive existing treatments: antihypertensive drugs (amlodin: 5 mg/day, micardis: 20 mg/day), but has not received hypolipidemia drugs. She presented to our hospital, seeking to recover her functional level with herbal medicine, and
was administered 7.5 g of Kangen-karyu extract per day. Before Kangen-karyu prescription administration, her initial anthropometric measurements included a BMI of 25.2 kg/m²: body weight 58.0 kg (127.8 lb), height 152 cm (4.99 ft), and an abdominal circumference of 90.5 cm (2.97 ft), which classified her as obese. In the blood pressure test, her SBP/DBP was 133/88 mmHg. Serum HbA1c was 5.7%, displaying regulated blood glucose. Serum lipids levels were as follows: total cholesterol: 246 mg/dL, LDL-cholesterol: 179 mg/dL, HDL-cholesterol: 54 mg/dL; LDL-cholesterol/HDL-cholesterol: 3.3, and triglycerides: 183 mg/dL, indicating dyslipidemia. After 6 months, administration of Kangen-karyu prescription showed a slight decrease in BMI and abdominal circumference. Her SBP/DBP was reduced from 133/80 to 115/77 mmHg. The level of total cholesterol was reduced from 246 to 235 mg/dL. The elevated level of LDL-cholesterol was slightly decreased, and HDL-cholesterol was slightly elevated on treatment with Kangen-karyu prescription during the follow-up period. At that time, oral administration of Kangen-karyu prescription significantly decreased the elevated serum triglyceride level. Hepatic functional parameters (AST and ALT) also decreased at the 6-month follow-up. However, there was no change in HbA1c for Kangen-karyu treatment. Regarding the score using the questionnaire, it showed amelioration to 75% of the level on non-administration. The physical and subjective symptoms involving headache, stiff shoulders, feeling heavy in the head, and mottled skin had improved. According to the tongue diagnosis, there was a notable improvement in vessels below the tongue following the treatment of Kangen-karyu prescription for 6 months, although the tongue color, fur color, and thickness ameliorated only slightly. The results reported herein identified the therapeutic usefulness of Kangen-karyu to treat blood stasis.

2.3 Case 3

A 65-year-old man with high blood pressure, dyslipidemia, type 2 diabetes, chronic kidney disease, and hyperuricemia was previously diagnosed with metabolic syndrome. Subsequently, the patient continued to receive existing treatments: an antilipidemic agent (livaro: 1 mg/day) and antihypertensive agent (micardis: 20 mg/day). In addition, Kangen-karyu prescription (7.5 g/day) was treated three times a day for 6 months. Before Kangen-karyu prescription administration, his initial anthropometric measurements included a BMI of 27.4 kg/m²: body weight 81.6 kg (179.7 lb), height 173 cm (5.68 ft), and an abdominal circumference of 98.4 cm (3.23 ft), which classified him as obese. His SBP/DBP was 130/86 mmHg. Serum HbA1c was 6.1%, displaying poorly controlled blood glucose. Serum lipids levels were as follows: total cholesterol: 216 mg/dL, LDL-cholesterol: 118 mg/dL, HDL-cholesterol: 46 mg/dL, and triglycerides: 306 mg/dL, indicating hyperlipidemia. In addition, his serum Cr level of 1.69 mg/dL had moderately impaired renal function (eGFR 33.0 ml/min/1.73 m²) according to the Modification of Diet in Renal Disease equation [19]. The level of serum uric acid was 8.6 mg/dL, representing hyperuricemia derived from kidney disease. This patient was also an alcoholic, and alcohol consumption was assessed by questioning. He was categorized as a heavy consumer (≥ 30 g alcohol/day) according to the average daily alcohol consumption proposed by Agarwal [19]. Therefore, enzymes related to the hepatobiliary system and myocardial infarction were determined to assess their effects on the relationship between metabolic syndrome and alcohol consumption. ALT, gamma-glutamyl transpeptidase (γ-GTP), and creatine phosphokinase (CPK) were found to be poorly controlled. There were no significant changes in the activities of AST, alkaline phosphatase, or lactate dehydrogenase. During the administration of Kangen-karyu extract, BMI and the abdominal circumference showed no changes, but the systolic/diastolic blood pressure decreased from 130/86 to 126/70 mmHg. The level of total cholesterol had reduced from 216 to 197 mg/dL at the 6-month follow-up. The increased levels of LDL-cholesterol and LDL-cholesterol/HDL-cholesterol were slightly reduced on treatment with Kangen-karyu prescription. Oral treatment of Kangen-karyu prescription significantly decreased the elevated triglyceride level. Other parameters such as eGFR, Cr, uric acid, AST, ALT, γ-GTP, and CPK were improved by the Kangen-karyu treatment. At that time, the physical and subjective symptoms such as cold limbs, fatigue, and insomnia had partially disappeared. There was a slight improvement in the tongue coating. Kangen-karyu extract exhibits good efficacy in the administration of lifestyle-induced metabolic syndrome.

3. Discussion

Therapy for metabolic syndrome is multifaceted, as is the syndrome itself. Effective preventive approaches include lifestyle modification, mainly weight loss, exercise and diet, and the treatment comprises the appropriate use of pharmacological drugs to decrease the particular risk factors [20]. TCM has received much attention as potential sources of novel therapeutic drugs due to their multiple beneficial effects and absence of side effects toxic and/or toxicity [21]. Up to now, many TCM have been tested for the treatment of metabolic syndrome. We chose Kangen-karyu, TCM modified from herbal formular
of Kan-shin No. 2 [12]. It has been clinically used as an administration for cardiovascular disorders, involving cerebrovascular disorder and angina pectoris [16,17]. Kangen-karyu is being proposed as a new therapeutic material based on preclinical studies related to various human diseases [13,14,22-27]. To add to these findings, we reported evidence supporting its preventive and/or therapeutic potential against metabolic syndrome in a rat model [14]. Treatment of Kangen-karyu significantly improved high-fructose-induced metabolic syndrome such as hypertension, hyperlipidemia, and hyperglycemia, through the reductions of triglyceride and cholesterol contents with the modulation of sterol regulatory element-binding protein-1 (SREBP-1) and the nuclear factor-kappa B signaling pathway in the liver. We also reported the lipid-regulatory activity of Kangen-karyu on type 2 diabetes-induced dyslipidemia [15]. The results of our pre-clinical experiment provide scientific evidence that the use of this prescription for the treatment of metabolic syndrome is becoming increasingly popular due to its wide availability. We administered Kangen-karyu extract to metabolic syndrome patients, and evaluated its treatment-based usefulness.

In the present cases, there was an improvement in metabolic syndrome following the treatment of Kangen-karyu prescription for 6 months. Most notably, the levels of serum triglycerides, total cholesterol, and LDL-cholesterol decreased following the administration of Kangen-karyu prescription. The body weight, BMI, abdominal circumference, and blood pressure reduced compared with before treatment, as shown in Figure 1. At that time, the somatic and subjective symptoms had partially improved. Here, we present a therapeutic effect of Kangen-karyu based on metabolic parameters.

In TCM, tongue diagnosis plays an important role in the organ’s meridians and conditions. The characteristic of the tongue reflects the condition of organ and imbalance of Qi and blood. TCM practitioners observe the tongue appearance such as the body color and coating of tongue to determine the pathogenic factors. The color of tongue reflects the state of the Yin organs, blood, and nutritive Qi. Coating of tongue is observed from the tip to root and reflects the hot or cold aspects of the body [28,29]. The tongue provides a geographic map of organ systems; characteristics of the tongue in each of these areas provide information critical to the TCM diagnosis [28]. Therefore, tongue diagnosis was evaluated by TCM doctors who collected

![Figure 1. Clinical effects of Kangen-karyu.](https://doi.org/10.30564/jim.v10i1.3230)
the information with a digital camera. The researchers checked tongue characteristics, such as the coat color, coat weight, coat surface, tongue action, and vessels below the tongue. In case 2, there was a notable improvement in vessels below the tongue following the treatment of Kangen-karyu extract for 6 months, although the tongue color, fur color, and thickness ameliorated only slightly. Most notably, vessels below the tongue were recovered by Kangen-karyu administration to near-normal levels. These in cases 1 and 3 revealed a slight improvement in the tongue coating of the treatment group.

It has been proposed that metabolic syndrome develops as a result of the reciprocal action of several environmental factors. In particular, alcohol consumption is one of the most prevalent habits in the general population [30]. The harmful effects of heavy alcohol consumption are due to an increase in plasma triacylglycerol and increased blood pressure [31,32]. Each of these factors is a component of metabolic syndrome. In case 3, interesting findings were obtained with regard to enzymes related to the hepatobiliary system and myocardial infarction: the levels of AST, ALT, γ-GTP, and CPK decreased compared with non-administration. Although the association of metabolic syndrome with alcohol consumption is complex and controversial, as both protective and detrimental effects have been reported [30,31], we report evidence to support the use of Kangen-karyu as an adjunctive therapy for patients with lifestyle-induced metabolic syndrome. The administration for metabolic syndrome involves the management of a cluster of chronic diseases such as high blood pressure, dyslipidemia, diabetes mellitus, and obesity. However, TCM has received much attention as a source of multi-target strategies due to its multiple beneficial effects and absence of toxic and/or side effects. The present cases provide strong evidence to support the administration of Kangen-karyu extract to near-normal levels. These in the information with a digital camera. The researchers checked tongue characteristics, such as the coat color, coat weight, coat surface, tongue action, and vessels below the tongue. In case 2, there was a notable improvement in vessels below the tongue following the treatment of Kangen-karyu extract for 6 months, although the tongue color, fur color, and thickness ameliorated only slightly. Most notably, vessels below the tongue were recovered by Kangen-karyu administration to near-normal levels. These in cases 1 and 3 revealed a slight improvement in the tongue coating of the treatment group.

4. Conclusions

We report scientific evidence supporting the use of Kangen-karyu as an adjunctive therapy for patients with metabolic syndrome. Kangen-karyu shows good efficacy in the treatment of patients with metabolic syndrome.

Funding

No funding was received for this study.

Conflict of Interest Statement

The authors declare no conflict of interest.

References

[8] Evaluation Committee on Diagnostic Criteria for Metabolic Syndrome. Metabolic syndrome: defi-
