

Clinical Report 2 (Japan)

Two Cases for which Boiogito (Fang-Yi-Huang-Qi-Tang, 防已黄耆湯) was effective for Rheumatoid Arthritis

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Boiogito is the first selective prescription for degenerative rheumatoid arthritis. In this case study we report on two cases of advanced rheumatoid arthritis that, as we have experienced, were responsive to “*boiogito* plus moderate amounts of other Kampo elements”.

Case Report

Age 73, Female

Chief Complaint: Polyarticular pain

History, Family history: No particular mention

History of Pharmaceutical Adverse Reaction: Felt sick by Salazopyrin. Shiozol drug eruption, renal disorder due to Rimatil, hematuria due to Methotrexate.

Present Illness: Rheumatoid arthritis occurred in 1974. Pains in nearly all joints since 1994. Antiphlogistic analgetic and immune suppressant unable to manage pain. For two years had difficulty walking and visited this department. PSL now in use for these four years.

Findings by Wakan Medicine: Face and four limbs swollen. Pain in all the joints, especially knee joint pain with the accumulation of joint fluids. Five hours of morning stiffness. Fatigable and cold limbs. Lips and gum dark red. Pigmentation in orbicularis oculus region.

Steinbrocker's staging classification: Class 4

Pulse condition: Intermediate between floating and deep, slightly weak, and slightly irregular.

Tongue condition: Purple and slightly swollen. Covered with moderate furs with puncta.

Abdominal condition: Strength - slightly flaccid, stuck feeling in pit of stomach, excessive strain of abdominal muscles, and pain at side of navel on palpation.

Course: Treated with *boiogito* plus Non-prepared *Aconiti Radix* 4g. After one year, treatment effects were assessed with the results of improvement in hours of morning stiffness from 5 to 1.5 hours. Lansbury's index score from 168 to 15., and sedimentation value to 21mm/h from 40mm/h. Edemas were alleviated with a weight reduction by 4kg. Steinbrocker's functional classition was improved to Class 3 from Class 4. At the time of this report, the patient who has a 13 year history of hospital visits, continues to visit using a cane.

Case Report

Age 62, Female

Chief Complaint: Polyarticular pain

Past History: Tonsillectomy (1965), removal of thyroid gland (1967), pregnant toxicosis (1967), artificial joint replacement (right knee joint 1995, left knee joint 1997).

Family History: Father - SLE

History of Pharmaceutical Adverse Reaction: Drug eruption due to Rimatil.

Present Illness: Rheumatoid arthritis occurred in 1962. Pain in nearly all joints since 1994. Gold drug and PSL were started. Immunosuppressant being administered since 1997. The first visit to this department of the hospital was May 28, 1997.

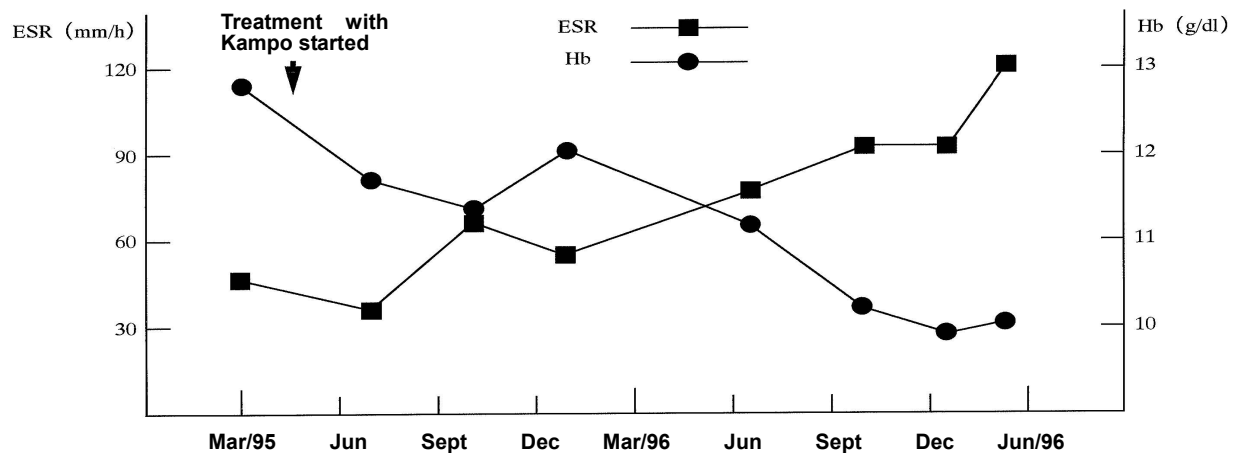
Findings by Wakan Medicine: Feels somatic fatigue, fatigable. Sensitive to cold. The body feels heavy and hands are stiff in the morning.

Steinbrocker's staging classification: Class 4

Pulse condition: Slightly deep, weak and irregular.

Tongue condition: Pale white with tooth scars.

Abdominal condition: Strength - moderate. Stuck feeling in pit of stomach and pain at side of navel on palpation.



Course: Fig 1 shows the course of ESR and Hb after the treatment with *boiogito* plus Non-prepared *Aconiti Radix* 2g. After one year, the morning stiffness disappeared and joint scores was reduced to 13 from 40 with an improvement in Lanbury's index to 19% from 86%. Loxoprofen and Diclofenac suppository were no longer required. Steinbrocker's functional classification was Class 3 without any difference between before and after the treatment.

Following is the record the patient wrote in her rheumatism note.

Since the start of Kampo medication, the body feels light. Able to go to a supermarket for shopping with the support of a baggage cart. Facial swelling slightly reduced. Have become able to wash the face as previously.

This case may be a successful example of Kampo medication. However, her husband called to tell of her death in 1999. (The death was not related to rheumatoid arthritis.)

I have experienced many cases of rheumatoid arthritis for which *boiogito* was effective. *Boiogito* are considered the first-line medication for rheumatoid arthritis with the main symptom of joints pain in the lower extremities.

If the course is prolonged, the practitioner can increase the amounts of *Sinomeni Caulis et Rhizoma*, *Astragali Radix*, and *Atractylodis Lanceae Rhizoma* and to add moderate amounts of *Aconiti Radix Processa* and non-prepared *Aconiti Radix*.

Case Series

Kampo Treatment for Rheumatoid Arthritis

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Introduction

Rheumatoid arthritis is a systemic inflammatory disease characterized by chronic destructive processes with non-suppurative arthritis as its leading symptom. Even today, there is no established therapy available for this condition. Here I would like to discuss the application of Kampo for the treatment of rheumatoid arthritis.

Materials and Methods

Over the 12 years from April 1994 until April 2006, 46 patients (7 men and 39 women) of the total 73 patients who consulted the Center for Oriental Medicine of the Suwa Chuo Hospital were the subject of this study. The morbidity duration was on the average 11.6 years and the Steinbrocker function as well as the average value of the disease stage classification were Class 2.2 and Stage 2.4 respectively. Prior to consultation, 36 patients had been treated with western medications.

For the evaluation of the effects of Kampo treatment I used the Lansbury index. Generally, duration of the morning stiffness, articular scores, grip power and the erythrocyte sedimentation rate are used for the calculation of the Lansbury index. Since I did not measure the grip power in this study, this parameter was excluded and therefore calculated as a modified Lansbury index. A marked effectiveness was defined as a drop in this modified Lansbury index to below 25% of the pretreatment value after one year of treatment with Kampo medications. Below 50% was designated as effective, below 75% as slightly

effective and other results assessed as ineffective. The results before and after the Kampo treatment were compared using the paired t-test.

Results

Marked effectiveness was observed in 43.5%, effectiveness in 15.2%, slight effectiveness in 17.4% and no effect in 23.9%. Among the 36 patients receiving western medications, 24 patients could either discontinue that medication or reduce the dosage. The modified Lansbury index dropped from 41.7% to 19.1% ($p < 0.0001$, Figure 1), the average Class staging fell from 2.2 to 1.8 ($p < 0.0001$) and thus indicated a significant improvement. Other improvements of the CRP and γ -globulin values were also observed (Table 1).

Table 1 Variations in laboratory values before and after treatment

	Before treatment	After treatment
Leukocytes (/mm ³)	8002±3469	6055±1762*
Eosinophils (/mm ³)	5194±2784	3786±1467*
Lymphocytes (/mm ³)	1830±641	1629±557*
Hemoglobin (g/dl)	12.6±1.5	12.7±1.6
Platelets (/mm ³)	31.4±10.7	28.1±8.6
Total protein (mg/dl)	7.5±0.6	7.0±1.3*
γ -globulin (mg/dl)	1.37±0.53	1.17±0.32*
CRP (mg/dl)	3.2±3.0	1.7±2.6*
ESR (mm/hr)	50.6±33.5	34.2±26.5*
CH ₅₀ (mg/dl)	42.3±3.7	40.2±5.3

* $p < 0.05$ mean±SD CH₅₀ had been measured in 12 patients

Side effects of non-prepared *Aconiti Radix* were observed in 13 patients but alleviated in all patients with a decrease in dosage (Table 2)¹⁾. During the evaluation one year later it was found that 5 patients received roasted aconite, 10 patients received salt *Aconiti Radix* (aconite

soaked in salt water, sprinkled with lime stone and dried) and 23 patients received non-prepared *Aconiti Radix*, so that a total of 38 patients had been treated with aconite and the maintenance dose was on the average 3.2g/day.

Side effects of *Astragali Radix* were observed in 2 patients who received 20 g/day, which corresponds to 5-6 times the usual dosage. Yet, when treatment was switched to *Hedysari Radix* the treatment could be continued²⁾.

Table 2 Side effects of aconite

Age	Sex	Aconite	Toxic amount (g)	Measures	Outcome	Prescriptions	Initial symptoms
65	Female	raw aconite	5.5	brewing instructions	improvement	<i>tokikenchuto</i>	Numbness around lips
28	Female	raw aconite	5.0	aconite dosage reduction	improvement	<i>keishikaryojutsubuto+α</i>	Numbness around lips
54	Female	raw aconite	4.0	aconite dosage reduction	improvement	<i>boiogito</i>	Sensation of physical instability
62	Male	raw aconite	1.5	aconite dosage reduction	improvement	<i>keishikaryojutsubuto+α</i>	Sensation of physical instability
54	Male	raw aconite	3.5	aconite dosage reduction	improvement	<i>boiogito</i>	Nausea
63	Female	raw aconite	5.0	switching to salt aconite	improvement	<i>boiogito plus aconite</i>	Numbness around lips
50	Female	raw aconite	2.0	aconite dosage reduction	improvement	<i>keishakuchimoto</i>	Epigastric discomfort
53	Female	raw aconite	5.0	aconite dosage reduction	improvement	<i>bushito+α</i>	Tingling sensation of cheeks, insomnia
78	Female	roasted aconite	4.5	aconite dosage reduction	improvement	<i>bushito</i>	Numbness in lips, Blackouts
56	Female	roasted aconite	1.0	discontinuing aconite	improvement	<i>hochuekkito plus aconite</i>	Stuffed nose, headache
49	Female	roasted aconite	0.7	aconite dosage reduction	improvement	<i>bukuryoshigyakuto</i>	Rising blood pressure
50	Male	roasted aconite	1.0	discontinuing aconite	improvement	<i>boiogito</i>	Epigastric discomfort
65	Female	processed aconite powder	0.5	Discontinuing	improvement	<i>daibofuto</i>	Nausea

Table 3 shows the variations in the Lansbury index obtained with prescriptions that led to slight improvements or better results. *Boiogito+a* followed by *keishikaryojutsubuto+a*, *bushito*, *keishinieppiichito+a* were most frequently effective. When in the *boiogito* a higher than usual dosage of both *boiogito* was used. The preparations were found to be effective quite frequently. Moreover, when the use of *keishikaryojutsubuto+a* by itself did not produce sufficient results, combination with *boiogito* often allowed to increase its effectiveness³⁾. In the present study a combination was used for 4 out of the 7 patients treated with *keishikaryojutsubuto+a*.

<i>boiogito</i>	13 cases
<i>keishikaryojutsubuto+a</i>	8 cases
<i>uzuto</i>	3 cases
<i>keishinieppiichito +a</i>	3 cases
<i>daibofuto</i>	2 cases
<i>bukuryoshigyakuto</i>	2 cases
<i>Others</i>	4 cases

Discussion

In the classic of Kampo therapy, "Shang Han Lun (Discussion of Cold-induced Disorders)" and "Jin Gui Yao Lue (Essentials from the Golden Cabinet), various passages such as "painful suffering of bones and joints, painful suffering of the body, relate to athralgia⁴⁾, slightly tensed limbs, pain of bones and joints, pain affecting the entire body, pain in the joints of the limbs, people having difficulties in bending and extending their joints, pain causing by light touch, pain in the various joints and inability to bend or extend them, inability of rolling over etc." According to

these descriptions rheumatoid arthritis seems to have existed 2,000 years ago and treated with Kampo medicine.

In the present study, the pretreatment Lansbury index of 43.5% of the patients improved and fell below 25%, thereby verifying a certain usefulness of Kampo medications. Yet, since the manufacture of Kampo placebos is associated with many difficulties, the evaluation of therapeutic effects included no control group.

Although the modified Lansbury index did not show any improvements, the eleven patients in whom the treatment was assessed as ineffective, still continued to visit our clinic after one year. Asking the patients for their reasons to continue the treatment, two stated, it allowed them to discontinue immunomodulators, one stated the ability to discontinue immunosuppressive drugs, three stated reduction in arthralgia, one reported the ability to walk with a walker, one a reduction in edema and feeling of greater comfort, one cited an improvement in the tendency to feel cold, and two said they were under the impression it is better to take the Kampo medicine. These 11 patients seemed to regard the Kampo therapy as having certain positive effects.

When the use of *keishikaryojutsubuto+a* by itself did not produce sufficient results, addition of *Sinomeni* Caulis et Rhizoma and *Astragali* Radix often increased its effectiveness⁴⁾. Side effects of *Aconiti* Radix were observed in 13 patients (Table 3). This was probably due to the gradual increase in the dose of *Aconiti* Radix until sufficient therapeutic effects were obtained. The incidence of adverse reactions of Disease Modifying Antirheumatic Drugs (DMARDs) is said to be 60%⁵⁾. Thus, the incidence of adverse reactions of therapeutic drugs for rheumatoid arthritis represents a problem. Often the mode of

action of Kampo medicines varies from that of western medications, but if *Aconiti* Radix is used carefully, there should be few side effects. The indication for Kampo medicines also depends on the disease stage. A combination therapy with western medications is possible. Rheumatoid arthritis is considered to be one of the diseases for which Kampo medications may be expected to be sufficiently effective.

Significance of the use of Kampo formulations for rheumatism

(1) Improvement of symptoms other than arthralgia may be expected.

Kampo medicine does not simply eliminate pain, but also bestows a feeling of wellness and improves feelings of coldness etc.

The symptoms of rheumatoid arthritis may improve simultaneously.

(2) Many Kampo formulations affect the immune system.

Some people assert that "*hochuekkito* and *juzentaihoto* act on the immune system, but *keishikaryojutsubuto*, *boiogito*, drugs for overcoming blood stagnation simply alleviate the pain". However, this concept is mistaken. While *boiogito* and formulation for dissolving blood stagnation do alleviate pain, they also improve γ -globulin and antinuclear antibody levels. Just alleviating the pain cannot explain this improvement in γ -globulin and antinuclear antibody levels. Thus, Kampo medications may be classified as immunomodulators.

(3) In contrast to the delayed activity of immunomodulators, Kampo formulations have fast-acting properties.

Evaluation of results after one year in this study revealed that if no effects appeared between the second to fourth week, either changing the prescription or else adding *Aconiti*

Radix, *Sinomeni Caulis et Rhizoma*, *Astragali Radix* etc. might enhance the pharmacologic effects of the Kampo formulations.

Reference

- 1) Kazuhiko Nagasaka: Discussion of 33 cases presenting with aconite intoxication, *Journal of Traditional Medicines*, 16 (4), 168-174, 1999
- 2) Kazuhiko Nagasaka, others: Investigations of side effects of Ogi, Kampo and Modern Therapy, 8 (1) 35-38, 1999
- 3) Mosaburo Kainuma, others: Significance of prescriptions with added *Sinomeni Caulis et Rhizoma*, *Astragali Radix* for the treatment of chronic rheumatoid arthritis, *Journal of The Japan Society for Oriental Medicine*, 48 (6) 91, 1998(collection of abstracts)
- 4) The Japan Kampo Medicin Association, academic department: *Shokanzatsubyoron*, Toyo Gakujutsu Shuppansha, Japan, 2000
- 5) Kouichiro Ishikawa, others: Trial results of long-term "Bucillamine" application for the treatment of chronic rheumatoid arthritis, *Inflammation*, 8 (2) 169-180, 1988