Kampo Medicine - Current Research

Can Kampo Formulations become First-Line Drugs for Rheumatoid Arthritis?

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Introduction

There are 600,000 to 700,000 patients with rheumatoid arthritis (RA) in Japan (0.4–0.5% of the population, 1% of people aged over 30) with three times as many women as men afflicted by RA. Onset is most frequent between the ages of 30 and 50. The initial symptoms of the disease are symmetrical manifestation of pain in finger and toe joints and swelling of the joints (in some patients these symptoms start from the knee joints or other joints). Subsequently, about 20% of patients achieve remission within one to two years. On the other hand, about 5 to 10% of patients exhibit rapid joint degeneration as well as a strong inflammatory condition in a short period of time. The other 70% of patients experience alternate improvement and exacerbation in symptoms, progressing to gradual joint degeneration.

Pharmacological therapy by Western medicine aims to inhibit inflammation or joint destruction and non-steroid anti-inflammatory drugs (NSAIDs) or steroid drugs are used to manage joint swelling and pain caused by inflammation. In recent years, disease-modifying anti-rheumatic drugs (DMARDS) have come to be used early in the course of the disease, and if these are ineffective, TNF blockers are combined with DMARDS.

Is Kampo medicine able to open a new chapter in the treatment of RA? Although treatment of RA with Kampo formulations is common in Japan, I will introduce research that indicates Kampo formulations used in the early stages could inhibit disease progression.

Ebe's trial

Kampo medicine has long been engaged in RA treatment. "Jinkui Yaolue," written in ancient times, contains a description of RA. Practitioners today use prescriptions from this classical textbook to some effect. After the concept of the disease was clarified in recent years, RA has been treated with Kampo medicine under stricter diagnostic guidelines. Most of the treatments, however, are performed on the basis of short-term follow-ups and there are very few long-term records of the treatments available. This is because a follow-up system for the long-term prognosis of the disease was not established, such as whether joint destruction can be prevented or not.

Koji EBE focused attention on the time within three to four years after onset when it becomes clear whether the disease goes into remission, rapidly worsens, or gradually degenerates. He hypothesised that intervention with Kampo formulations at a very early stage would increase cases of early remission and observed the course of treatment in 10 cases of primary RA onset. He then provided further insights into the results.

Subjects and prescriptions

The subjects are ten individuals that satisfied the "Rheumatoid Arthritis Criteria" (Table 1) of the American College of Rheumatology (ACR) with a duration of one year or less from the start of symptoms. For all subjects, formulae were designed according to "sho" and decoctions were administered (Table 2).

Table 1: Rheumatoid Arthritis Criteria (American College of Rheumatology: ACR)

1	Morning stiffness lasts for an hour or more
2	Swelling of three or more joint areas
3	Swelling of the hand joints (wrist joints, metacarpophalangeal [MCP] joints, proximal interphalangeal [PIP] joints)
4	Symmetrical joint swelling
5	Abnormal hand radiographs
6	Subcutaneous nodules
7	Blood test shows positive for rheumatism RA is diagnosed if 4 items out of the 7 above are satisfied (however, items 1 to 4 must last for 6 weeks or more).

Table 2

	Date of First Consultation	Sex･Age	Disease Duration before First Consultation	Stage	TCM (Traditional Chinese Medicine) Diagnosis	Treatment	Prescriptions	Combined Drug
1	Feb. 9, 1991	Male 81	1.5 months	1	Dampness-heat impediment	Clear heat to transform into dampness	*senpito with adjustment*	Analgesic
2	Jul. 9, 1985	Male 70	5 months	1	Dampness-heat impediment	Clear heat to transform into dampness. Then, reinforce kidney	*senpito with adjustment*	Analgesic
3	Apr. 30, 1999	Female 51	6 months	1	Wind-damp impediment	Dissipate cold to transform into dampness	*Kedishikajutsubuto* with addition of *Ephedrae* Herba, *Asiasari* Radix and *Coicis* Semen	Analgesic
4	May 22, 1955	Male 50	3 months	1	Damp impediment	Transformed dampness to modify statis	*Stephaniae Tetrandrae* Radix *Coicis* Semen, *Atractylodis Lanceae* Rhizoma, *Atractylodes* Rhizoma, *Phaseoli* Semen, *Paeoniae* Radix Rubra, *Clematidis* Radix and others	Analgesic
5	Mar. 27, 1995	Female 58	11 months	2	Wind-damp impediment	Dissipate cold to transform into dampness	*keishikajutsubuto with adjustment*	None
6	Mar. 11, 1987	Female 43	3 months	1	Damp-wind impediemnt	Dissipate cold to transform into dampness	*keishikaryoujutsubuto with adjustment*	None
7	Jan. 12, 1990	Male 70	3 months	1	Wind-damp impediment	Dissipate cold to transform into dampness. Convert damp heat-impediment in mid-course	*keishikajutsubuto with adjustment. Later senpito with adjustment*	Analgesic
8	Apr. 17, 1992	Female 58	12 months	2	Damp-wind impediment	Transformed dampness to dissipate cold	*Stephania tetrandra* Radix, *Armeniacae Semen*, *Coicis* Semen、*Clematidis* Radix、*Aconiti* Radix Processa, *Cinnamomi* Cortex, *and others*	None
9	Apr. 18, 1997	Female 45	7 months	1	Wind-damp impediment	Dissipate cold to transform into dampness	*Keishikajutsubuto with adjustment*	None
10	Jul. 10, 1994	Female 41	3 months	1	Dampness-heat impediment	Clear heat to transform into dampness	*senpito with adjustment later keishikajutsubuto with adjustment*	Analgesic

Assessment (Evaluation Criteria)

Remission criteria developed by Pinals et al. was used for the assessment (Arthritis Rheum 1981).

It is essential that 5 or more of the following be satisfied for at least two months.

1. Morning stiffness does not last for 15 minutes or more
2. No fatigue
3. No joint pain
4. No joint tenderness or no pain on motion
5. No soft tissue swelling in joints and tendon sheaths
6. Erythrocyte sedimentation rate is less than 30 mm/h for males and less than 20 mm/h for females

Results

1. Complete remission was attained in 9 cases out of 10.
2. Case 10 ended in complete remission with 2.5 years of treatment. However, 2 years later in January 1999, the disease recurred. Four months of Kampo treatment starting in April led to another remission.
3. Case 9 ended in incomplete remission after one year of Kampo treatment. The case sometimes satisfied 5 of the 6 remission criteria and sometimes satisfied 3 to 4 criteria. However, 7 months after the start of Kampo treatment, the patient was able to run. About a year later (March 1998), the patient commenced hard work that required steady walking of 10,000 to 20,000 paces a day. As of March 2000, the patient was continuing work of a similar nature.
4. Case 7 ended in complete RA remission after three years of Kampo treatment. Six years later in March 1998, however, connective tissue disease accompanied by vascular inflammation developed. The disease was controlled by Kampo medicines and Predonin (6–20 mg). In March, the disease worsened and the patient was admitted to a university hospital where arthritis nodosa was diagnosed. Chronic renal failure occurred concurrently and dialysis started in June. The patient died in October.

As described above, Ebe reports that remission was attained in 9 cases out of 10 primary RA cases with incomplete remission in one case. Excellent treatment effects are shown.

However, due to the low number of cases available for the research, it is too early to conclude whether these results were produced under biased evaluations or were fortuitous, and that Kampo medicines are extremely effective for cases of primary RA onset. If a number of future primary RA cases yield good results, Kampo medicines could become first-line drugs in the treatment of RA.

Conclusion

This research by Ebe contributes to extending the possibility of Kampo therapy, resulting in increased treatment options available for patients with RA. In assessing the effectiveness of Kampo therapy, DB-RCTs (double blind-randomized controlled trial) are difficult to conduct. Thus, to satisfy a similar level of EBM requirements, Ebe has suggested that investigations use a definite number of subjects who have received Kampo treatment from an initial period (six months to one year from onset). He also suggests that if 10-year follow-up reveals a lower rate of shifting to polyarticular destruction type and mutilans type compared to Western medicine research groups, it could be said that Kampo treatment is efficacious. Later in 2008, he presented an additional report on the research at the 23rd Kyoto Kampo Academic Symposium, which contained more cases that referred to the ACR's "Rheumatoid Arthritis Criteria" and "Early Diagnosis of Rheumatoid Arthritis" prepared by the then Ministry of Health and Welfare of Japan. I will report on this at a later date.

Reference

1) Ebe K.: Φυτο Vol.1 No.4, 4-12,1999