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### **Foreword**

Acupuncturist Training – Present Situation and Initiatives  
**Noboru Mitsuhashi**

### **Japanese Acupuncture - Current Research**

Effects of Electroacupuncture Analgesia on Postoperative Pain after Abdominal Surgery and the Presence of Endogenous Analgesic Substances  
**Keisou Ishimaru**

### **Kampo Medicine - Current Research**

Effect of *Poria Powder with Five Herbs* on Chronic Subdural Hematoma  
**Mitsusuke Miyagami**

### **Clinical Report 1 (Japan)**

A Case Report on Acupuncture Treatment for “Complex Regional Pain Syndrome (CRPS)”  
**Shigeru Nakajima**

### **Clinical Report 2 (Japan)**

One Case that had Effect of *Dwarf Lilyturf Decoction* on Post-Herpetic Neuralgia caused by Yin Deficiency  
**Mihoh Koga**

### **Clinical Report 3 (Japan)**

One Case that had Effect of *Major Divaricate Saposhnikovia Decoction* on RA with High Level of Metacarpal Deformation  
**Hiromichi Yasui**

### **Topics – Kampo Medicine**

Water-Metabolism Regulatory Action of Chinese Herbal Medicine  
**Yoichiro Isohama**

### **Prescription (1)**

*“B” Character Decoction* (Sokeitei-Ijishogen)  
**Hiromichi Yasui**

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## Foreword

### *Acupuncturist Training – Present Situation and Initiatives*

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The environment for acupuncture and moxibustion training in Japan changed significantly ten years ago this year. Until 2000, only 26 nationwide universities and vocational schools provided such training, and every year, around 2,200 applicants from a total of 2,700 passed the national exam required to practice acupuncture and moxibustion. Following a relaxation of regulations, thereafter, universities and vocational schools for acupuncturist training increased to 100 schools on a nationwide scale as of April 2010, and as many as 4,000 applicants from a total of 5,300 passed the national exam held in February 2010. This means that the increase in the number of educational institutions that train acupuncturists brought an almost two-fold increase in the number of qualified acupuncturists compared to ten years ago.

However, the change in the environment for acupuncture and moxibustion training generated a number of issues. One is the issue of employment after graduation, and the other is the decline in the technical level of practitioners.

Acupuncturists have the choice of going into private practice, but few people actually do so immediately upon graduation. Instead, most choose to receive practical training at an established clinic to first accumulate experience in treating patients. Under current circumstances, however, there are not enough clinics in Japan to provide employment to 4,000 acupuncturists per year. At the same time, many of these new acupuncturists need to acquire practical skills at a clinic and build up confidence to treat patients, because schools that have newly begun to offer acupuncture training tend to place emphasis on providing knowledge over technical skills in preparing students for the national exam, which does not include technical evaluation.

In response to this situation, the acupuncture and moxibustion industry in Japan established the Acupuncture and Moxibustion Medical Promotion Society in 2006 to take on various initiatives related to awareness raising of acupuncture and moxibustion, the study of acupuncture and moxibustion, and training of acupuncturists.

Under the theme of “awareness raising,” the society engages in diverse activities to promote understanding of acupuncture and moxibustion in Japan, and under the “study” theme, it collects information about the treatments. For “training,” the society endeavors to establish a training system for new acupuncturists who have acquired a license but whose skills level is still low. These activities are not expected to produce immediate results, but are gradually helping to transform the acupuncture and moxibustion industry in Japan.

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## Japanese Acupuncture - Current Research

### *Effects of Electroacupuncture Analgesia on Postoperative Pain after Abdominal Surgery and the Presence of Endogenous Analgesic Substances*

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#### Introduction

We investigated the effects of electroacupuncture through a systematic review of randomized controlled trials (RCTs) in postoperative pain. 1)

The results are based on fifteen RCTs comparing electroacupuncture with sham control in the management of acute postoperative pain.

The results included one Japanese study (RCTs) by Ishimaru et al (1999). 2-3)

We have previously reported that electroacupuncture decreased the postoperative pain after abdominal surgery and significantly reduced the use of analgesic drugs, however, the mechanism of electroacupuncture analgesia has not been completely explained. In this study, The effects of surgical invasion and electroacupuncture analgesia on serum beta-endorphin, an endogenous opioid peptide that is involved in analgesic action, and adrenocorticotrophic hormone (ACTH) levels were evaluated.

#### Methods

Continuous frequency 3Hz electroacupuncture treatment was performed at acupuncture point LI4 (Hegu) and S36 (Zusanli) for 3 hours from 3 hours after the operation in 11 patients (electroacupuncture group). Another eleven patients not treated by non-electroacupuncture served as controls. Peripheral blood (5 ml) was collected before, during, immediately after operation and at 3 hour intervals thereafter until 12 hours after the operation, and serum beta-endorphin and ACTH levels were measured by radioimmunoassay (RIA).

#### Results

Surgical procedure and anesthesia time and changes in serum beta-endorphin and ACTH from

before operation until 12 hours after operation in the electroacupuncture group and non-electroacupuncture control group.

During the operations, both beta-endorphin and ACTH levels increased significantly. After the operations, these levels tended to gradually decrease to preoperative values, but the levels of serum beta-endorphin increased significantly again during the electroacupuncture treatment in the electroacupuncture group (Table 1.2.).

The degree of the postoperative pain in the electroacupuncture and non-electroacupuncture group and the consumption of the analgesic drugs (Table 3.4.).

Analgesic drugs for postoperative pain were used in 10 of the 11 cases in the control non-electroacupuncture group (Table 4.), but were used only in 1 of the 11 cases in the electroacupuncture group (Table 3).

These results suggest that the beta-endorphin levels induced by electroacupuncture reduced the postoperative pain. The results also suggest that, even under general anesthesia, the surgical invasions appear to induce the central nervous to activate stress-induced analgesia.

#### Discussion

In these results, we found that electroacupuncture is effective for postoperative pain management, as demonstrated by a significant reduction of postoperative pain scores and endogenous opioids including beta-endorphins. From other studies, likewise electroacupuncture may reduce analgesic drugs usage in the early postoperative period. 4-9)

Some studies suggested that electroacupuncture mechanisms include activation of the endogenous pain inhibitory system, release of endogenous opioids including beta-endorphins, enkephalins, and dynorphins, and non-opioid substances such as serotonin, norepinephrine, adenosine A1 receptor.10)

Future studies (RCTs) should investigate electroacupuncture mechanisms given before or after surgery.

patients No.	age	sex	surgical procedure	duration of anesthesia (minutes)	Serum beta-endorphin pg/ml							
					before ope	during ope	after ope	3 hours EA	6 hours	9 hours	12 hours	
1	67	F	choledochojejunostomy	220	3 55	41 370	47 150	10 90	8 70	10 50	10 50	
2	71	M	colectomy	170	3 19	38 90	53 90	7 71	6 52	3 30	3 13	
3	71	M	total gastrectomy	395	5 49	47 170	25 140	8 98	4 80	4 71	5 70	
4	57	F	cholecystectomy	160	2 60	22 260	26 370	8 99	22 60	26 70	8 49	
5	67	M	cholecystectomy	75	4 15	30 180	12 89	11 89	15 60	6 13	6 13	
6	41	M	subtotal gastrectomy	175	7 28	44 350	32 380	11 40	28 30	18 27	7 28	
7	57	M	subtotal gastrectomy	210	3 8	37 420	4 60	20 210	16 10	3 16	3 8	
8	65	F	high anterior resection	166	5 45	66 790	24 270	9 19	15 9	16 8	4 10	
8	88	M	miles operation and descending colostomy	225	2 90	62 580	46 540	22 190	33 60	46 40	14 60	
10	82	F	subtotal gastrectomy	200	6 82	44 160	45 130	40 92	45 95	23 80	10 30	
11	53	F	subtotal gastrectomy	166	4 20	64 320	46 540	22 90	33 60	40 40	14 60	
65.3±13.2 years					196.4±77.5	4.0±1.6 42.8±27.4	45.0±14.0 335.4±205.7	32.7±15.9 250.8±180.0	15.2±10.0 98.9±56.1	20.4±13.0 53.2±27.0	17.7±14.8 40.4±24.8	7.6±3.9 32.0±21.7

Table 1. Surgical procedure and anesthesia time and changes in serum beta-endorphin and ACTH from before operation until 12 hours after operation in the electroacupuncture group. Normal value : Serum beta-endorphin 1-10 pg/ml, Serum ACTH 5.5-50 pg/ml. EA : Electroacupuncture stimulation.

patients No.	age	sex	surgical procedure	duration of anesthesia (minutes)	Serum beta-endorphin pg/ml							
					before ope	during ope	after ope	3 hours	6 hours	9 hours	12 hours	
1	63	M	subtotal gastrectomy	150	3 52	25 350	4 140	3 60	3 50	3 40	3 -	
2	68	M	high anterior resection	225	3 37	35 190	9 90	8 90	3 63	3 55	3 38	
3	70	M	sigmoidectomy	150	7 27	6 180	9 98	8 82	7 80	5 59	7 52	
4	81	M	cholecystectomy	120	5 16	14 83	13 64	3 5	13 6	5 5	6 5	
5	74	M	subtotal gastrectomy	215	6 35	16 110	20 160	8 19	8 14	8 12	9 17	
6	71	M	low anterior resction	210	4 33	33 160	23 82	28 120	23 30	19 18	20 30	
7	74	M	total gastrectomy	225	5 24	44 210	48 320	16 54	15 66	- -	- -	
8	31	M	subtotal gastrectomy	180	5 19	34 640	33 450	6 18	7 24	6 28	5 19	
8	80	F	cholecystectomy	50	3 31	4 45	8 75	3 18	3 10	3 16	3 31	
10	69	M	subtotal gastrectomy and cholecystectomy	290	5 60	36 460	30 130	23 60	10 30	7 60	6 53	
11	70	F	total gastrectomy	205	9 80	29 180	22 149	21 93	18 80	14 80	10 60	
68.2±13.4 years					183.6±64.0	5.0±1.8 37.6±19.2	25.0±13.2 237.1±178.0	19.9±13.2 159.8±119.3	11.5±8.9 56.2±37.6	10.0±6.6 41.1±27.7	7.3±5.2 37.3±25.2	7.2±5.1 33.8±18.5

Table 2. Surgical procedure and anesthesia time and changes in serum beta-endorphin and ACTH from before operation until 12 hours after operation in the non-electroacupuncture group. Normal value : Serum beta-endorphin 1-10 pg/ml, Serum ACTH 5.5-50 pg/ml.

patients No.	Postoperative pain and the relations of the use pain-killer				
	after ope	3 hours EA	6 hours	9 hours	12 hours
1	2	2	1	0	0
2	2	2	1	1	0
3	2	2	0	0	0
4	2	2	0	0	0
5	1	1	1	0	0
6	2	2	1	1	0
7	2	2	3 Voltaren50mg	1	0
8	1	1	1	0	0
9	2	2	1	0	0
10	2	2	0	0	0
11	2	2	1	1	0

Table 3. The degree of the postoperative pain in the electroacupuncture group and the consumption of the analgesic drugs.

EA: Electroacupuncture stimulation.

The evaluation of the pain. 0:no pain, 1: movement pain, 2:rest pain, 3: use of the analgesic drugs.

patients No.	Postoperative pain and the relations of the use pain-killer				
	after ope	3 hours	6 hours	9 hours	12 hours
1	2	2	3 pentazocin 1A	1	0
2	1	1	1	1	1
3	2	2	3 voltaren 50mg	1	0
4	2	2	3 pentazocin 1A	1	0
5	2	2	2	3 voltaren 25mg	1
6	2	1	2	3 voltaren 25mg	1
7	1	3 pentazocin 1A	3 voltaren 25mg	2	2
8	2	2	3 voltaren 25mg	0	0
9	2	2	3 voltaren 25mg	0	0
10	1	2	3 voltaren 25mg	1	0
11	2	2	3 voltaren 50mg	2	2

Table 4. The degree of the postoperative pain in the non-electroacupuncture group and the consumption of the analgesic drugs.

The evaluation of the pain. 0:no pain, 1: movement pain, 2:rest pain, 3: use of the analgesic drugs.

## Conclusion

Electroacupuncture treatment may be a useful complementary and alternative medicine for acute postoperative pain management.

## Acknowledgements

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## Kampo Medicine - Current Research

### *Effect of Poria Powder with Five Herbs on Chronic Subdural Hematoma*

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#### Introduction

Chronic subdural hematoma (hereafter CSDH) is a gradual accumulation of blood below the dura mater over more than three weeks, generally after a very minor head injury. The hematoma is encapsulated, in which old liquefied blood is found. In recent years, increases in the number of the elderly and image analyzing examinations such as CT/MR images have contributed to an improved detection of CSDHs, for which surgery is a recognized and established method of treatment. However, even if CSDH shows up on CT images, some patients do not exhibit the signs and symptoms indicative of CSDH or merely show very mild symptoms. There are also patients who do not desire an operation. Moreover, the recurrence of CSDH after surgery occurs in 10 to 20%<sup>12,19,23</sup> of patients. Patients who are prone to bleeding or have complications are hesitant to undergo surgery. On the other hand, it must be kept in mind that CSDHs may heal spontaneously,<sup>3,16</sup> which is said to occur in 2.8 to 21% of patients with mild mass effect who do not show signs and symptoms or have very mild symptoms.<sup>4,15,17</sup> For this reason, non-operative treatment may be selected depending on the patient. In terms of non-operative procedures for CSDHs, hyperosmolar therapy<sup>8,22</sup> with mannitol and steroid hormone therapy<sup>1,2,18</sup> have been reported. Recently, practitioners in the field of cranial nerve surgery have had another look at Kampo treatment and treatment of CSDH with Kampo medicines<sup>9,10,14,21,15</sup> for CSDHs has occasionally been seen. However, only a few case reports have been published and Kampo treatment has not been established for CSDH.

Since January 2006, we have used *Poria Powder with Five Herbs* for some patients with CSDH and studied its efficacy.<sup>11</sup> This study reports the efficacy of the medicine for CSDH obtained through conducting CTs with long-term follow-up.

#### CT Subjects and Methodology

As stated above, surgery is an accepted treatment for CSDH. However, we used *Poria Powder with Five Herbs* for CSDH in the following types of patients (with their consent and that of their family members): (1) those who did not desire surgery, (2) those who did not exhibit signs or symptoms, or very mild symptoms, and (3) those who were prone to bleeding or presented with systemically bad health conditions. The subjects enrolled in the trial were 22 patients with CSDH (the number of hematomas was 27). Their ages ranged from 50 to 98, with 18 subjects 70 years old or above. Nine subjects had right-sided hematomas, 8 had left-sided, and 5 had bilateral. Fourteen subjects had experienced trauma. Two subjects developed recurrent CSDH after surgery as the first treatment. At the start of treatment after CSDH developed, 8 patients presented without any symptoms, 7 had headaches or dizziness, and 5 had mild motility disorder. In terms of complications, 5 patients had dementia. Each subject had one of the following complications: diabetes mellitus, dialysis, cerebral infarction, encephalorrhagia, terminal colon cancer, or jaundice.

The CT findings were examined for the maximum width of the hematomas and their CT density. Twenty hematomas, the largest number, had a maximum width of 10 to 19 mm just before treatment, 4 hematomas had 20 to 25 mm, and 3 had 9 mm or less. The CT density at the start of treatment with *Poria Powder with Five Herbs* was evaluated as iso, high, or mixed in 14 hematomas and low in 13 hematomas. The period of follow-up by CT was 4–29 weeks (Table 1).

case	age/sex	location	hematoma density	maximum thickness of hematoma before (administration of Gorei-san)	maximum thickness of hematoma after	follow (weeks)	
1.	TT	87/F	L	mixed	18	0	13
2.	KH	79/F	L	mixed	20	0	14
			R	mixed	10	0	7
3.	KY	95/M	L	mixed	25	12	29
4.	KT	82/M	R	mixed	15	0	6
5.	RB	50/M	L	mixed	18	12	4
6.	SY	81/F	L	mixed	10	0	8
7.	SK	93/M	L	mixed	12	5	8
			R	iso	10	0	8
8.	IM	89/F	L	iso	15	0	11
9.	KS	74/F	R	iso	13	8	7
10.	AY	59/M	L	high	20	10	7
			R	high	8	2	7
11.	TM	66/M	R	high	15	0	20
12.	TK	74/M	R	low	20	12	24
13.	NT	78/M	L	low	15	10	3
14.	HF	85/F	R	low	7	0	4
15.	KK	83/F	L	low	8	0	8
16.	AS	92/M	L	low	15	8	17
			R	low	10	0	17
17.	ME	82/M	R	low	10	0	10
18.	HT	72/M	R	low	12	7	19
19.	HY	78/M	R	low	10	3	8
20.	AT	80/F	L	low	15	15	24
			R	low	12	12	24
21.	IT	75/M	L	low	13	12	4
22.	YI	98/M	R	low	15	15	6

Table 1. Summary of cases with chronic subdural hematomas treated with Gorei-san.

TSUMURA Goreisan Extract Granules (Extract of *Poria Powder with Five Herbs*, 7.5 g divided into 3 doses, basically before meals) was orally administered to all patients with CSDH regardless of the patients' pathological conditions from the Kampo perspective. The patients who were able to take the medicine for four weeks or more were assigned to the study. With the disposition of the primary doctor, hemostatic agents (tranexamic acid and carbazochrome sodium sulfonate) were used in combination for 7 non-selected subjects. The effectiveness of *Poria Powder with Five Herbs* was assessed based on whether the hematoma had resolved or decreased in size as determined by a CT. Results (Figure 1, 2)

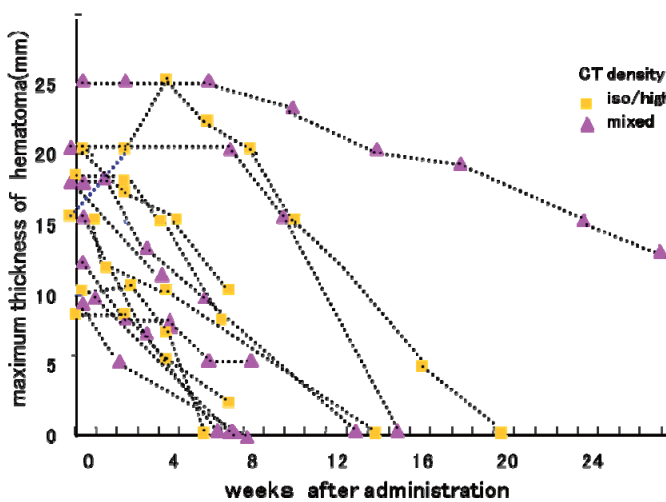


Figure 1. Change in maximum thickness of hematomas with iso/high (■) or mixed (▲) density on a CT after administration of *Poria Powder with Five Herbs*.

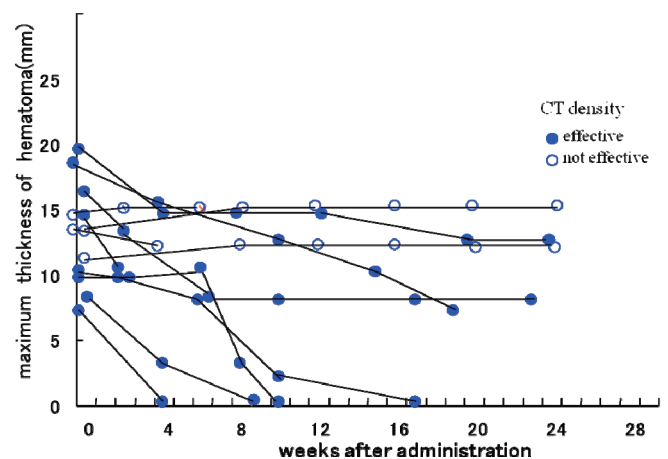


Figure 2. Change in maximum thickness of hematomas with low density on a CT after administration of *Poria Powder with Five Herbs*. ●effective cases ○ineffective cases



The treatment with *Poria Powder with Five Herbs* resulted in a high level of improvement in 23 (85%) of 27 CSDHs, including hematomas that had disappeared or shrunk, whereas treatment was ineffective for 4 CSDHs (15%) since they remained unchanged after administration of the medicine. In the 23 CSDHs responsive to *Poria Powder with Five Herbs*, 12 hematomas disappeared and 11 shrank (Table 1). In 17 CSDHs (74%) out of the 23 CSDHs that showed improvement, the hematomas began to shrink within four weeks after administration and then they gradually shrank further or disappeared. Of the 12 CSDHs that disappeared, 10 took less than 14 weeks to disappear. None of the hematomas grew after administration of *Poria Powder with Five Herbs* for four weeks or more, so there were also no CSDH cases that needed surgery. In the meantime, there were no adverse effects associated with the medication in any of the cases.

We studied the time-dependent changes in the density level of hematomas after administration of *Poria Powder with Five Herbs*. The medicine was effective in all 14 CSDHs with density levels of mixed or high/iso on a CT before treatment. That is, 14 CSDHs all improved with 8 resolved hematomas and the other 6 shrank (Figure 1). Of the 13 CSDHs with lower density on a CT, 9 showed an improvement with the hematoma disappearing or shrinking, while 4 CSDHs remained unchanged and non-responsive to the administration of *Poria Powder with Five Herbs* (Figure 2). The results of the study show that CSDHs with hematoma density levels of iso/high or mixed were more responsive to *Poria Powder with Five Herbs*. We consider that further research with many more patients will be needed.

#### A representative case

Case: K. H. (Figure 3)

79 years old, female: Bilateral chronic subdural hematoma (CSDH) (L>R).

On November 19, X year, the patient fell down and banged her head. On January 10 of the

following year, she visited our facility, complaining of a mild gait disorder. CT examination revealed a bilateral CSDH (right: 8 mm, left: 5 mm) with iso density and the administration of hemostatic agents (carbazochrome sodium sulfonate 3 tablets and tranexamic acid 3 tablets) was commenced. A CT scan during a follow-up visit on February 7 indicated enlarged hematomas, having a maximum width of 10 mm on the right and 20 mm on the left, with mixed density on both sides. For this reason, *Poria Powder with Five Herbs* 7.5 g (divided into 3 doses) was commenced with the hemostatic agents. The hematomas began to decrease in size after seven weeks: the right hematoma disappeared and the left one remained unchanged with a maximum width of 20 mm. However, the extent of the hematoma tended to decrease. On April 20, the density decreased to low and shrinkage was obvious. In the 14<sup>th</sup> week, the CSDH dissolved completely (Figure 3). The gait disorder also disappeared and she recovered her normal gait.

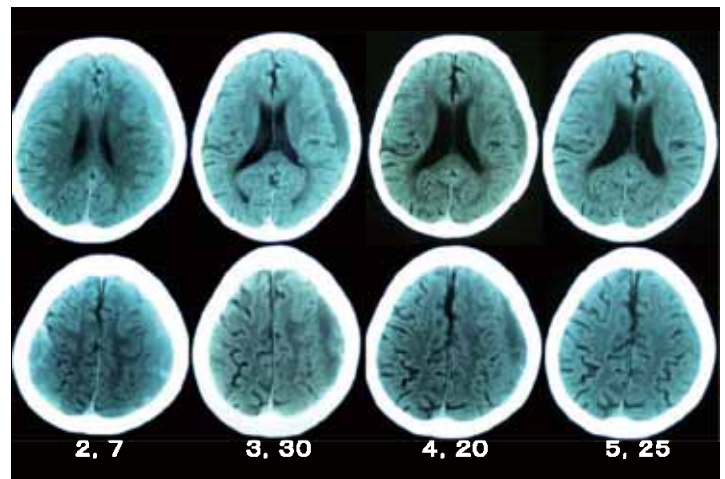


Figure 3. CT scan of case 2 (K.H.) before and after administration of *Poria Powder with Five Herbs*. 06,2,7; before administration, 06,3,30; 06,4,20; and 06,5,25; 7, 10 and 14 weeks after administration of *Poria Powder with Five Herbs*, respectively.

#### Discussion

A widely-accepted theory<sup>13</sup> of the etiology and growth mechanism of CSDH is that hematoma

enlargement occurs through blood leakage and constant or intermittent bleeding from neovascular vessels in a false membrane into the capsule and the cavity of a hematoma in order to enhance local fibrinolytic activity inside the hematoma and its outer membrane. On the other hand, the old theory of osmosis pressure is still prevalent, but the cause is not known in detail. As nonsurgical management of CSDHs, the use of diuretics or steroids has been claimed to be effective. More specifically, effectiveness has been reported for mannitol 20% osmotherapy by Suzuki, et al.<sup>22</sup> and Kinjyo, et al.;<sup>8</sup> the combination therapy with steroid hormone and 50% glucose by Ambrosetto, et al.;<sup>1</sup> and the steroid-alone hormone therapy by Glover, et al.<sup>2</sup> and Rudiger, et al.<sup>18</sup>

In recent years, CSDH has occasionally been treated using the aquaretic Kampo medicines of “*Poria Powder with Five Herbs*” and “*Minor Bupleurum Decoction, Poria Powder with Five Herbs*.” Seki, et al.<sup>21</sup> used *Poria Powder with Five Herbs* in 8 cases of CSDH and obtained improvement in 4 cases. Konuki<sup>10</sup> and Ueno, et al.<sup>25</sup> reported that hematomas had resolved in all cases with the combination treatment of *Poria Powder with Five Herbs* and prednisolone. Muramatsu, et al.<sup>14</sup> reported the effectiveness of *Poria Powder with Five Herbs*; they used the Kampo medicine alone in 11 cases and in 10 of the cases, the hematomas disappeared or shrank. Kitahara<sup>9</sup> had favorable results using *Minor Bupleurum Decoction, Poria Powder with Five Herbs*, which is made up of two formulae: “*Poria Powder with Five Herbs*” and “*Minor Bupleurum Decoction*”. Kitahara reported that improvement could be obtained even if administration of antithrombogenic agents continued.

Since 2008, a number of reports on the treatment of initial and recurrent CSDHs with *Poria Powder with Herbs* have been published and all of these reports suggest its usefulness.

We treated 22 cases of CSDHs (27 hematomas): *Poria Powder with Five Herbs* alone was administered in 15 cases, and *Poria Powder* and hemostatic agents were administered in combination in 7 cases, resulting in effectiveness in 23 hematomas — 12 hematomas were resolved and the other 11 shrank. We believe this improvement was due to the effectiveness of *Poria Powder with Five Herbs* rather than spontaneous healing. This is based on the following: (1) cases that had a tendency for the hematomas to grow before the administration of *Poria Powder with Five Herbs*, and many cases that did not have a tendency for the hematomas to shrink were included; (2) there were cases that showed a tendency for the hematomas to shrink from an early stage after the administration of *Poria Powder with Five Herbs*; and (3) higher rates of effectiveness of the treatment were shown compared to the frequency of spontaneous resolution of CSDHs in the past. In general, the hematomas started to shrink three to four weeks after the start of administration of *Poria Powder with Five Herbs*, and they disappeared within 14 weeks after administration in most cases. There were only a few cases in which shrinkage started within 2 weeks. To assess the effect of CSDH treatment with this Kampo medicine, a continued administration for at least three to four weeks or more is required.

*Poria Powder with Five Herbs*, which consists of the five crude drugs of arisaema rhizoma, tuckahoe, polyporus sclerotium, atractylodes lancea rhizoma, and cassia twig, is a typical diuretic Kampo medicine. This diuretic medicine clinically has anti-edema action<sup>6,20</sup> and is generally prescribed for pathological conditions such as headache, cerebral edema, ascites, gastroenteritis, ophthalmic disorders, hangover, and pain. Although the mechanism of the effect of the medicine on CSDHs is unclear, the diuretic actions may be the main contributing factor as the usefulness of mannitol osmotic diuretic agents has been reported.<sup>8,22</sup>

Unlike the diuretic agents used in Western medicine such as mannitol, this Kampo diuretic medicine is characterized by the role of antidiuretic actions in a hydrated state and the role of regulating the actions of water metabolism in a hyperhydrated state.<sup>24</sup> It is said that the diuretic mechanism is involved in the inhibition of water channel aquaporins (AQPs), which increase water permeability in cell membranes, whereas *Poria Powder with Five Herbs* inhibits the action of the aquaporins.<sup>5,20</sup> According to Isohama,<sup>5</sup> the constituent crude drugs of *Poria Powder with Five Herbs*, especially *Atractylodes lancea rhizoma*, *Polyporus sclerotium*, and *Tuckahoe (poria sclerotium)*, inhibit cell membrane water permeability. In particular, AQP4, which is most abundant in the brain but also distributed in large numbers in astroglia cells adhered to endocapillary cells, is said to be involved in water permeability.<sup>6</sup> *Atractylodes lancea rhizoma*, the crude drug of the *Atractylodes* family contained in *Poria Powder with Five Herbs* used for CSDH treatment, has been used in many medicines as well as the ones used in our experiment. Ueno, et al.<sup>25</sup> have also reported that *Poria Powder with Five Herbs* containing *Atractylodes ovatae rhizoma* was effective for CSDHs.

Our experiment suggests that *Poria Powder with Five Herbs* is more effective if the hematoma density on a CT is iso, high, or mixed, compared to low density. The reasons, however, are not known in detail. Meanwhile, in the cases of relatively new hematomas with iso density or high density, hematoma capsules often show the sinusoidal channel layer, which is filled with capillaries. On the other hand, in the hematomas with low density, old bleeding to a certain extent can possibly be found with relatively fewer vessels. This means that CSDHs with low density have a comparatively long course and the vessels in the hematoma capsule may be relatively scarce. So, it is possible that AQP4 surrounding the vessels are also relatively reduced, causing the reduced

inhibition of water permeability.

*Poria Powder with Five Herbs* is orally administered for treatment, unlike mannitol or steroid drugs, and it did not cause any adverse effects in the cases in our study<sup>11</sup> and in other reported cases.<sup>10,14,21,24,25</sup> We consider *Poria Powder with Five Herbs* to be an easy-to-use medicine and useful for the future nonsurgical management of CSDHs.

#### Conclusion

1. *Poria Powder with Five Herbs* was administered in 22 cases of CSDH with 27 hematomas for four weeks or more and the results showed it was effective in 23 hematomas (85%) with the hematomas disappearing or shrinking.
2. *Poria Powder with Five Herbs* did not cause any obvious adverse effects in the cases in our own study and in reported cases to date. It is a safe and useful drug for nonsurgical therapy of chronic subdural hematomas.

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## Clinical Report 1 (Japan)

### *A Case Report on Acupuncture Treatment for „Complex Regional Pain Syndrome (CRPS)“*

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### Introduction

Chronic pain, edema, skin temperature anomalies, sweating and other symptoms are associated with the refractory and chronic pain of complex regional pain syndrome (CRPS) that may be triggered with surgeries or injuries. CRPS was once called reflex sympathetic dystrophy (RSD) or causalgia. Its morbidity is approximately 5 in 100,000 people and is therefore a disease of comparatively low incidence. We report a case of acupuncture treatment for a patient who had been diagnosed of RSD.

### [Case Report]

Patient: Age 52 years, female.

First visit: March 10, 2008

Chief complaints:

#1 dull pain of the left hand

#2 edema of the left hand, stiffness

#3 irregular symptoms of feeling of sensations of heat in the left hand, cold and sweating

#4 feeling of weakness of the left upper extremity

### ■ Present illness:

The patient underwent surgery for left thumb tendosynovitis in June 2007. Following the surgery a tingling sensation of the surgical scar and a feeling of traction gradually developed. Moreover, symptoms of dull pain, a sensation of heat in the left hand, edema, stiffness, a sensation of cold, irregular sweating and a sense of weakness of the left upper extremity developed. Based on the results of a detailed examination performed in a different clinic the physician diagnosed as RSD. From July 2007 to February 2008 left stellate ganglion blocks (SGBs) were performed and resulted in a mild improvement of

the symptoms, but now the injection site on the left side of the neck became painful. Concerns about continuous nerve block treatment finally brought the patient to our clinic.

### Past history:

In 2004 temporomandibular arthrosis (treated with acupuncture in this acupuncture clinic)

### Life style:

Alcohol: moderate amount of beer; tobacco: does not smoke

**Family history:** nothing particularly noteworthy.

**General symptoms:** appetite: normal, bowel movements: once a day; sleep: normal; stiffness of the back of the neck; shoulder stiffness, weariness of the muscles around the left temporomandibular joint.

**General physical findings:** Height: 155 cm; weight: 51 kg; blood pressure: 128/80 mmHg; pulse rate: 56 bpm (regular pulse)

**Local physical findings:** Jackson and Spurling test (-), TOS tests (-); deep tendon reflexes (+: no left-right differences), pathologic reflexes (-)

Left hand: edema (+), feeling of heat (+), redness (+), muscle atrophy (-), sensation (normal: no left-right differences), nociception (little finger, digital pad: slightly hypersensitive), tenderness (-).

Right hand: Nothing particularly noteworthy.

**Subjective symptoms during the night:** no nocturnal pain of the left hand. However, there is a sensation of edema.

**Subjective symptoms in the morning:** stiffness of the left hand.

### Comprehension of the pathologic condition:

(1) Following surgery for left thumb tendovaginitis gradual development of dull pain, edema, stiffness, a sensation of heat and cold, irregular sweating and a sense of weakness of the left upper extremity. (2) Findings during the first examination. Based on the above described (1) and (2) the clinical characteristics were considered to match those of a CRPS.

**Patient impression obtained during the medical interview:** speaks impatiently. Appeared slightly tired.

**Informed consent:** CRPS is a refractory condition. The therapist had performed acupuncture and moxibustion treatment only once about 4 years ago for a patient with CRPS, but this patient dropped out when the symptoms had improved to about 1/2 of their original intensity. The above described situation was explained to the patient and the acupuncture and moxibustion treatment started after obtaining the patient's consent.

**Acupuncture and moxibustion treatment plan:** Initially the approach was to gradually apply local stimulation while observing the course. Moreover, we applied acupuncture and moxibustion treatment also for the stiffness from the back of the neck to the shoulders and around the left temporomandibular joint.

**Observation plan (evaluation):**

Prior to the performance of the SGB treatment the severity of the symptoms of the CRPS was rated on a 10-step Numerical Rating Scale (below called NRS).

➤ The NRS10 for the symptoms (1) - (7) prior to the performance of the SGB treatment:

- (1) Edema: the edema is so severe that the patient cannot wear M size rubber gloves
- (2) Pain: dull pain (heaviness + pain)
- (3) Redness: the entire hand is red
- (4) Irregular symptoms of sensations of heat in the left hand, cold and sweating: Depending on the time the patient experienced hot and cold sensations and sweating on an irregular basis.
- (5) Stiffness of the left hand. Hand and fingers could not be flexed.
- (6) Sense of weakness of the upper extremity: This sensation covered an area from the upper arm to the tip of the fingers.
- (7) Numbness: pulling sensation at the site of the surgical incision + numbness

➤ NRS for the acupuncture and moxibustion treatment after the first examination

- (1) Edema: NRS 6
- (2) Pain: NRS 6
- (3) Redness: NRS 6
- (4) Irregular symptoms of sensations of heat, cold and sweating: NRS 5
- (5) Stiffness of the hand: NRS 7
- (6) Sense of weakness of the upper extremity: NRS 7
- (7) Numbness: NRS 0

**Acupuncture and moxibustion treatment and course** (disposable needles, 40 mm, No.1 were used)

➤ **First treatment (March 10, 2008):**

Supine position: GV20 (Hyakue, Baihui), left ST6 (Kyosha, Jiache), left ST7 (Gekan, Xiaguan), left GB3 (Jokan, Shangguan), bilateral LI11 (Kyokuchi, Quchi), bilateral GB34 (Yoryosen, Yanglingquan) - retaining the needles for 10 minutes.

Single insertion at interdigital points (distal). Single needling of interdigital points (proximal) - indirect moxibustion, 5 cones.

Prone position: bilateral GB20 (Fuchi, Fengchi), bilateral GB21 (Kensei, Jianjing), bilateral BL43 (Koko, Gaohuang), bilateral SI10 (Jue, Naoshu) - retaining the needles for 10 minutes. At the same time warming moxibustion on the shoulders (box moxibustion)

➤ **Second treatment (March 21, 2008):**

On the morning following the treatment the stiffness of the left hand and fingers had decreased. Alleviation of the sense of weakness of the left upper extremity. In addition to the first treatment pressure applied to the left auricle resulted in some alleviation of the ipsilateral arm, so that the posterior part of the auricular was needled. GV20 (Hyakue, Baihui), bilateral LR3 (Taisho, Taichong) retaining the needles for 10 minutes. Left carpal tunnel, Tinel sign (-)



➤ Third treatment (March 31, 2008):

Alleviation of the sense of weakness of the left upper extremity. However, mild pain had developed around the temporomandibular joint. Development of stiffness of the MPs of the left first and fifth fingers. Additional treatment of right ST6 (Kyosha, Jiache), right ST7 (Gekan, Xiaguan), right GB3 (Jokan, Shangguan), retaining the needles for 10 minutes.

➤ Fourth treatment (April 4, 2008):

Following the treatment of pain and stiffness of the MP of the left first and fifth fingers the alleviation of the symptoms continued for 1 week, but after that returned to the original state. Sensation of heat and swelling in the left thenar and hypothenar. Single insertion without retaining the needle into in the left thenar and hypothenar (40 mm, #01). The NRS scores were: (1) edema 6, (2) pain 6, (3) redness 2, (4) irregular symptoms of a sensation of heat, cold and sweating 4, (5) stiffness of hands and fingers 7, (6) weakness of the upper extremity 7, (7) numbness 0.

➤ Sixth treatment (April 25, 2008):

Development of pain near the left sternoclavicular joint, right blepharospasms.

➤ Seventh treatment (May 2, 2008):

No change of the pain near the left sternoclavicular joint. Disappearance of the right blepharospasms.

➤ Ninth treatment (May 16, 2008):

Sneezing has become impossible because of the pain near the left sternoclavicular joint; development of left blepharospasms. Needle retaining at bilateral KI26 (Ikuchu, Yuzhong), CV14 (Koketsu, Juque). Later indirect moxibustion (use of moxibustion paper); 5 cones of half rice grain size.

➤ Tenth treatment (May 26, 2008):

Disappearance of the left blepharospasms. Relief

of the pain near the left sternoclavicular joint. Appearance of sneezing and hiccups.

➤ Twelfth treatment (June 11, 2008):

Irritation by weakness of the left upper extremity and stiffness of hands and fingers.

The NRS scores were: (1) edema 5, (2) pain 5, (3) redness 1, (4) irregular symptoms of a sensation of heat, cold and sweating 2, (5) stiffness of hands and fingers 4, (6) weakness of the upper extremity 5, (7) numbness 0.

➤ Fourteenth treatment (June 27, 2008):

Relief of left chest pain and stiffness.

➤ Fifteenth treatment (July 11, 2008):

General relief of the symptoms.

The NRS scores were: (1) edema 2, (2) pain 2, (3) redness 0, (4) irregular symptoms of a sensation of heat, cold and sweating 1, (5) stiffness of hands and fingers 2, (6) weakness of the upper extremity 5, (7) numbness 0.

➤ Seventeenth treatment (August 8, 2008):

Due to the general relief of the symptoms I planned to extend the treatment intervals to 1 month. For the stiffness of the hands and fingers carpal tunnel needling (single insertion) was added.

The NRS scores were: (1) edema 0, (2) pain 0, (3) redness 0, (4) irregular symptoms of a sensation of heat, cold and sweating 0, (5) stiffness of hands and fingers 1, (6) weakness of the upper extremity 2, (7) numbness 0.

➤ Eighteenth treatment (September 5, 2008):

The previously applied needling of the carpal tunnel seemed to have been effective, since there is almost no stiffness of hands and fingers. The NRS scores were: (1) edema 0, (2) pain 0, (3) redness 0, (4) irregular symptoms of a sensation of heat, cold and sweating 0, (5) stiffness of hands and fingers 0, (6) weakness of the upper extremity 2, (7) numbness 0.

➤ Twentieth treatment (October 31, 2008):

General improvement of all symptoms.

The NRS scores were: (1) edema 0, (2) pain 0, (3) redness 0, (4) irregular symptoms of a sensation of heat, cold and sweating 0, (5) stiffness of hands and fingers 0, (6) weakness of the upper extremity 2, (7) numbness 0.

period of approximately 7 months led to the following improvement of the NRS scores: edema 6→0, pain 6→0, redness 6→0, irregular symptoms of a sensation of heat, cold and sweating 5→0, stiffness of hands and fingers 7→0, weakness of the upper extremity 7→2.

The improvement was maintained by subsequent regular treatments.

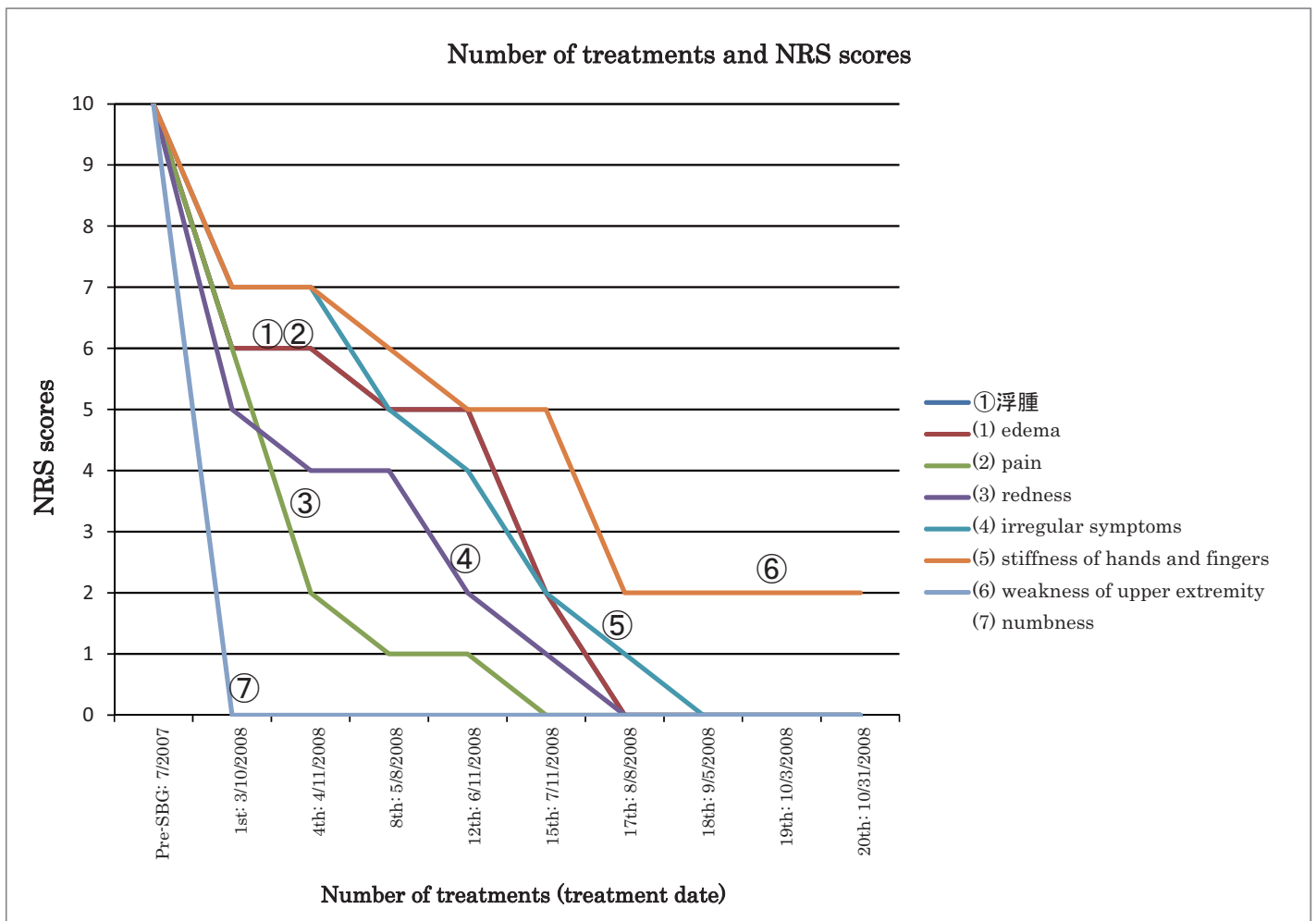


Figure 1: Number of treatments and NRS scores

**Number of treatments and NRS scores** (Figure 1: Number of treatments and NRS scores)

Shows the improvement of the NRS scores with increasing number of treatments.

A total of 20 treatments administered over a

**Discussion**

Yoshiki Hamada wrote in his summary of the CRPS seminar held in February 2007 titled "Early Diagnosis of CRPS and Points to Consider":

"The Lankford classification is clinically of extreme importance and an early initiation of treatment of the minor type of the condition may often lead to favorably functional recovery without the development of refractory symptoms".

Table 1 shows the Lankford classification. This shows that it classifies the condition into a major and a minor type.

➤ Moreover, in Yoshiki Hamada's summary "Early Diagnosis of CRPS and Points to Consider" it also says:

"Twenty out of 25 patients (80%) for whom the treatment was initiated within 6 months of the onset recovered functions so far, that they were able to return to ordinary daily life within one year, but in 70% of these cases the condition had been classified as minor type."

➤ The Lankford classification includes the items "palpation impossible" for the major type and "palpation possible" for the minor type. The question whether palpation is possible or not is considered to be closely related to the possibility of administering acupuncture treatment.

➤ In this patient the condition was palpable and it is therefore reasonable to think, that a state of hyperaesthesia was present in the area treatable by acupuncture.

## Lankford Classification

Clinical form	Symptoms and Sign
<b>Minor traumatic dystrophy</b>	Minor clinical symptoms like pain and swelling. Functional disorders were extremely mild and there was mild allodynia (palpation possible)
<b>Major traumatic dystrophy</b>	There was severe pain, swelling, functional disorder and allodynia (palpation possible)
<b>Minor causalgia</b>	Mild pain, swelling, functional disorder and allodynia (palpation possible)
<b>Major causalgia</b>	Motor- and sensory nerve injury (Michell Causalgia)
<b>Shoulder-Hand syndrome</b>	Shoulder and wrist joint pain secondary to myocardial infarction, swelling etc. CRPS symptoms

**The Lankford classification does not describe the degree of allodynia**

## Conclusion

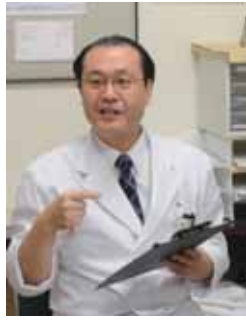
- (I) In this case the clinical condition of the CRPS based on NRS evaluations showed already signs of improvement when the patient first visited this acupuncture clinic. The characteristics of the clinical symptoms of CRPS may vary significantly depending on the disease progression in individual patients. In this case the acupuncture treatment for the various symptoms of this patient with CRPS appeared to have been effective.
- (II) CRPS is associated with severe physical and mental stress. Acupuncture treatment seems also to be helpful for secondary symptoms caused by irritation and concerns.
- (III) Although this was only one case, this one case gave me the impression, that the concepts pertaining to indications and contraindications of acupuncture treatment for CRPS should be reconsidered.

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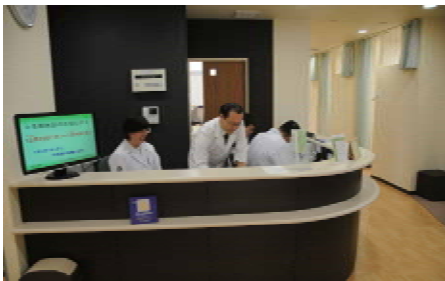
**Midori no Kaze Acupuncture Clinic affiliated with the Morinomiya College of Medical Arts and Science / Midori no Kaze Acupuncture Clinic**

The clinic affiliated with the Morinomiya College of Medical Arts and Science and the affiliated acupuncture and moxibustion clinic established in 1982 were reopened in January 2010 after moving to the third floor of a new building under the name "Midori no Kaze Acupuncture Clinic / Midori no Kaze Clinic".

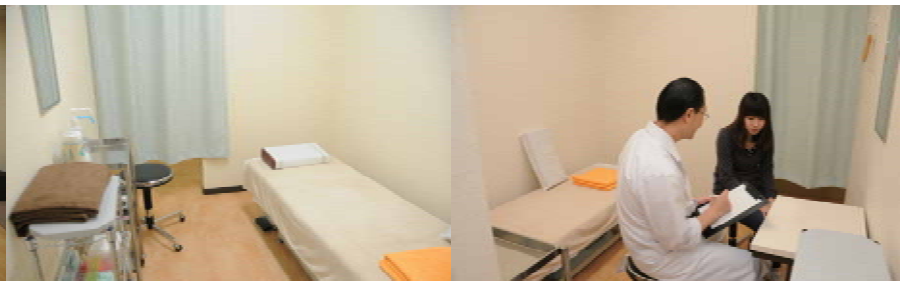


The clinic section has the following departments: orthopedics, rehabilitation, internal medicine, Kampo medicine and acupuncture and moxibustion. This facility also focuses on the training of the next generation of medical personnel and has the function of providing opportunities for clinical practice for the students of the Morinomiya College of Medical Arts and Science.

< Midori no Kaze Acupuncture Clinic (3<sup>rd</sup> Floor) >



Clinic reception



Acupuncture and moxibustion treatment room





Clinic staff



Clinical practice in the department of acupuncture and moxibustion

**< Midori no Kaze Clinic (1st Floor) >  
Orthopedics**

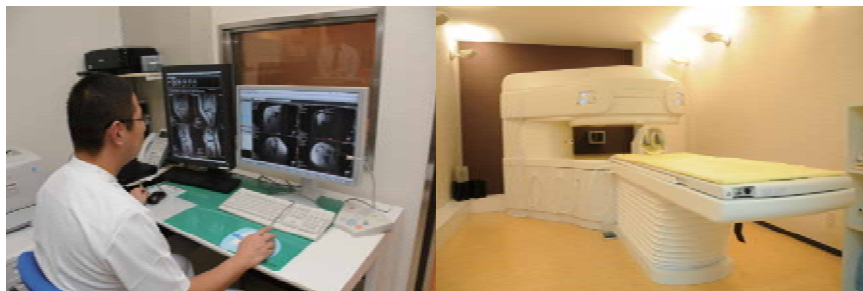


Physician: Yoshio Miyazaki; physician:  
Takahiro Shintani  
Director of the Midori no Kaze Clinic

**Internal medicine, Kampo medicine**



Professor of the department of health  
services of the Morinomiya College of  
Medical Arts and Science



MRI

**< Midori no Kaze Clinic (2nd Floor) > Rehabilitation**





## Clinical Report 2 (Japan)

*One Case that had Effect of Dwarf Lilyturf Decoction on Post-Herpetic Neuralgia caused by Yin Deficiency*

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Different types of individual therapies have been attempted to treat post-herpetic neuralgia, which is one of the conditions for which Kampo medicines are very frequently used. As we recently had a successful case that had benefits of *Dwarf Lilyturf Decoction*, we will hereunder report it with our observations and a bit of our views.

### [Case]

Male of 85 years old. Small build and thin, aged person with fair complexion.

### [Chief complaint]

1. His speech began to slur 2 to 3 years ago.
2. 10 years suffering of postherpetic neuralgia (left lumbar area L3/Level 4).
3. Habitual constipation.

### [Origin and course]

About 10 years ago, herpes zoster developed in the left lumbar area L3/Level 4 and then PHS was induced. The pain was severe and even the rubbing of clothing against the skin caused pain. The patient had been receiving treatment by the pain clinic of a certain university hospital with the prescription of *Cassia Twig Decoction plus Atractylodes and Aconite* for 2.5 months. He said that the administration of this medicine brought a pain relief for a while. Lying down on the bed for a clinical examination produced pain.

He had had the feeling of being unable to

speak articulately and properly for 2-3 years. At the Department of Neurology and Internal Medicine of a certain university hospital, he had received MRIs due to walking with unsteady steps and it was found that there were small cerebellar infarctions x 3 places. He had been told by the physician that the symptoms would not be associated with the infarctions and Parkinsonism was suspected, for which Madopar had been administered “experimentally to see his reactions to the medication.” When he visited us, it did not seem that words did not come out easily although he had the dry tongue that prevented his smooth speaking. While talking, he incessantly drank water from a plastic bottle.

### [Drugs currently being taken]

(Trade name)

Blopress / Rythmodan / Arotinolol / Magnesium Oxide / Biofermin / Neurotropin / Cerekinon / Tryptanol / Madopar / *Cassia Twig Decoction plus Atractylodes and Aconite* / Mendon → Myslee / Lendormin / Depas

### [Living environment]

He had been living in a care facility for about a year.

### [Findings]

Food intake, frequency, and time were well regulated so that he had a weight loss to 44 kg from 50 kg. Now he prepared by himself in-between snacks and eat them. Although he was sensitive to cold by nature, he claimed that the feet felt warm and burning in this winter. There was no itchy sensation in the skin but the tongue was dry and red colored. The abdominal strength was reduced with the soft abdominal wall and stools were palpated.

**[Diagnosis]**

The dryness of the body was intense and his pattern/syndrome was diagnosed as being caused by yin deficiency.

**[Treatment]**

Neurotropin, Triptanol, and GASTAR causing the side effect of dry mouth were discontinued. Likewise, Biofermin and Madopar were discontinued because of the uncertainty of these drugs' effectiveness. *Cassia Twig Decoction plus Atractylodes and Aconite* was also discontinued as it contributes to dryness. The pain-relief action of Aconti tuber, one of the ingredients of this Kampo medicine may help kill pain temporarily, but its continued use has a high potential of exacerbating 2 above.

The administration of 3 packs each of TSUMURA Bakumondoto (*Dwarf Lilyturf Decoction*) and TSUMURA Mashiningan (*Hemp Seed Pill*) was started in equal doses three times a day.

**[Treatment and course]**

The amount of saliva increased within 2 weeks and the patient became aware that he was able to speak smoothly. However the pain remained as ever.

After 5 weeks, he did not complain of the pain in the lumbar region in abdominal examinations.

After 8 weeks, when he was asked about the pain, his reply was "have forgotten about it!"

His complexion was good with healthy glow. He was aware of skin moist. Sleep improved and bowel movements became regular.

Same medication was continued.

In this patient, the symptoms might have improved only by excluding excessive drugs and an inappropriate Kampo medicine.

This was a case that provoked the author to think about iatrogenic diseases.

The author considered that the root cause of the patient's symptoms was yin deficiency lacking "the amount of fluids" to enrich yin and that the pain was caused by the "stagnation of nourishment." As the mouth was severely dry and the large intestine of the stomach-intestines was also dry, leading to constipation, firstly stomach-yin deficiency was approached. *Dwarf Lilyturf Decoction* which works on the lung, was effective because the inextricable relationship exists between the large intestine and the lung.

## Clinical Report 3 (Japan)

*One Case that had Effect of Major Divaricate Saposhnikovia  
Decoction on RA with High Level of Manipularian Deformation*  
Hiromichi Yasui  
Japan Institute of TCM Research

### [Case]

Female of 79 years old

Initial visit: November 4, 2009

Chief complaint: With deformed finger joints on both hands, unable to open them.

Current medical history:

Since the diagnosis of rheumatoid arthritis of about 20 years ago, the patient had received treatment. The daily dose of 5mg of prednisolone was started six years ago. The deformation of both hands began to progress about 5 years ago. About a year ago, the fingers of both hands drifted into the ulnar-deviated positions, in which they (fingers) pointed toward little fingers. All fingers became bent with pains, and gradually advanced to the inability of their extension. The deformation of toes was prominent. From a week ago, hand fingers were being unable to open at all, causing her great difficulty in carrying out normal activities of daily living, such as using chopsticks at mealtimes and using the toilet. Due to pains in both shoulders, upper limbs could not be raised. Toes on both feet were also deformed. Loxoprofen relieved morning pains, so that it was routinely used.

Appetite: Ordinary

The patient always had dry mouth. She frequently drank water.

Sleep: She had difficult in falling asleep, but it was not a special problem.

Defecation: Once/day

Urination: 10-12 times/day

Present condition: 134cm (as her back was hunched, the height was inaccurate.) and 42kg.

Because of the deformed lumbar spines, her back was greatly hunched over.

Pulse: Sunken and thin

Tongue: Pale red with no furs. Smooth without lingual papillae.

Diagnosis: Deficiency of qi and blood and weak constitution / liver-kidney deficiency / wind-cold dampness causing accumulation and stagnation of excess fluids.

Method of treatment: To tonify qi and blood/to dispel wind and disperse swelling

Prescription: *Major Divaricate Saposhnikovia Decoction* with adjustment

bJapanese angelica root 4gm

Peony root 4gm

Prepared rehmannia root 4gm

Astragalus root 4gm

Divaricate saposhnikovia root 4gm

Eucommia bark 4 gm

Atractylodes Lancea Rhizoma 4gm

Dried ginger rhizome 1gm

Cnidium Rhizome 3gm

Ginseng 2gm

Rhizoma and Root Forbes Notopterygium 2gm

Twotooth Achyranthes Root 2gm

Licorice Root 2gm

Chinese Date 2gm

Prepared Aconiti Daughter Tuber 2gm

Course: The pain in the fingers on the hands improved within 2 weeks and they could be opened slightly. After 4 weeks, they could be further opened with the pain in the right shoulder resolved, allowing the right arm to be elevated. However the pain in the left shoulder still remained. At this point, non-prepared Aconiti tuber 0.5g was added. The patient showed CRP0.3 and KL-6 188 on December 17. On January 13 of year X-1, the fingers on both hands could be opened further wider and the pain in the left shoulder disappeared and no problems were left with both upper limbs. On March 18, the level of CRP was 0.00 whilst that of RF was 201. In May, the patient resumed his farm work. In the visit to the hospital of August 18, she showed further recovery and was more cheerful.

**[Discussion]**

The patient with the history of RA for 20 years could not open fingers of both hands, causing the difficulty in carrying out her daily living. Furthermore, she had the back hunched and pains in the joints of both shoulders, so that even motions gave her excruciating pains and she was at a complete loss. Thus she visited our clinic. Unlike in the initial stage of RA development, disabilities and limits to motions due to the deformation as well as continuing pains as ever threatened her daily living.

The patient had the long time stagnation of wind-dampness which obstructed the flows of qi and blood, resulting in deficiency at the same time. Because of this, strong medicines for disorders in the acute stage cannot appropriately be used. Wind-dampness must be eliminated while qi and blood are being tonified and replenished to allow for their flows to be recovered. The patient disease was long-standing, leading to the deficiency of the liver-kidney, which further caused the inability of producing nutrients for muscles and bones. Therefore, the liver and kidney needed to be replenished.

How could such conditions of the chronic phase be improved in a short period of time, and even if possible, improvements would be limited. Notwithstanding, only a little improvement could improve the quality of the patient's life. Especially whether or not she could open and close the hand fingers did matter a lot to her.

*Major Divaricate Saposhuikovia Decoction* has the action of replenishing deficient qi and blood and eliminating wind-dampness being stagnant in muscles and bones. Two weeks after the start of administration, the hand fingers became able to open and close, and then general pains became gradually improved, making the patient's daily living less difficult. Some functional recovery in other patients with RA that has progressed to develop deformity over an extended period of time can be expected to a certain degree, if not complete, and the quality of life will be enhanced by means of identifying the etiology to provide appropriate procedures. *Major Divaricate Saposhuikovia Decoction* is a recommendable medication for such cases.

## Topics – Kampo Medicine

### *Water-Metabolism Regulatory Action of Chinese Herbal Medicine*

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#### 1. Introduction

“Water retention” in oriental medicine is an abnormality of water metabolism in vivo and appears with symptoms such as stagnation of water which circulates in the body, namely edema and urological impairment, or exocrine impairment which is an abnormality in the extracorporeal excretion of water. An action that alleviates these symptoms and then normalizes the water metabolism in vivo is called “water excreting action”. Representative water excreting agents are those which have a strong urinary-volume increasing action such as Wu-ling-san and Zhu-ling-tang. In addition, a moistening action that alleviates dry mouth or airway accompanying inflammation, such as that provided by Mai-men-dong-tang, is a water excreting action in a broad sense. However, it is difficult to say if the basic pharmacological mechanism of such water excreting actions in these Chinese herbal medicines has been elucidated sufficiently. For instance, Wu-ling-san, which increases the urinary volume without changing serum electrolyte concentrations,<sup>1)</sup> shows the urinary-volume

increasing action only when an edema tendency is present, and doesn't affect the urinary volume in a state of dehydration.<sup>2)</sup> It is presumed unlikely that the mechanism is based on the inhibition of re-absorption of electrolytes, as is the case with diuretics in

Western medicine, or on the increase in glomerular filtration volume. On the other hand, if the action in which Mai-men-dong-tang stimulates salivary secretion and then improves dry mouth in patients with Sjogren's syndrome<sup>3)</sup> is based on a simple agonist action of muscarine receptors, the mechanism is contradictory in that this Chinese medicine exerts a certain improving effect on symptoms of bronchial asthma.

In recent years, the water channel called aquaporin (AQP), which regulates the water permeability of cell membranes, was discovered and 13 types of isoforms have been identified to date (Table 1). Defective mice for each AQP have been made and analyses of the phenotypes have progressed. As a result, deficiencies of AQP1, AQP2, and AQP3, which exist in the kidneys and cause a notable increase in urinary volume,<sup>4-6)</sup> and deficiency of AQP4 in the cerebral astroglia causing inhibition of the formation of cerebral edema,<sup>7)</sup> have been clarified. That is, the efficiency of water metabolism in vivo, which has been explained only by physicochemical potentials such as osmotic and hydrostatic pressures, is influenced greatly by the permeability of cell membranes which are regulated by AQP.

AQP	Water permeability	In vivo distribution	Phenotypes in defective mice
AQP0	Low	Lens (eyeball)	Cataract
AQP1	High	Red blood cells, lungs, kidneys, brain, eyeballs, vascular endothelium	Excessive urination
AQP2	High	Kidneys	Excessive urination, dry skin
AQP3	High	Skin, kidneys, lungs, eyeballs, digestive tract	Alleviated cerebral edema symptoms
AQP4	High	Kidneys, brain, lungs, digestive tract	Reduced external secretion
AQP5	High	Salivary glands, sweat glands, lungs	-
AQP6	Low	Kidneys	-
AQP7	High	Fat tissue, kidneys, testicles	Visceral obesity Testicular hypertrophy
AQP8	High	Kidneys, liver, pancreas, digestive tract, testicles	-
AQP9	Low	Liver, white blood cells, brain, testicles	-
AQP10	Low	Digestive tract	-
AQP11	?	Brain, liver, kidneys	Polycystic disease kidney
AQP12	?	?	-

Table 1. In vivo distribution of AQP isoforms and phenotypes in defective mice



Based on the hypothesis that the unique water-metabolism regulatory action of Chinese herbal medicines may result from the functional regulation of AQPs, we conducted basic pharmacological studies. In this paper, we present part of the actions of Chinese herbal medicines of Kampo formulae on AQPs that have been elucidated.

## 2. AQP-inhibitory action of Wu-ling-san and constituent crude drugs

The action of drugs on AQP activity can be evaluated by investigating the water permeability of cell membranes expressing AQPs. A cell suspension is rapidly mixed with a high or low osmotic-pressure solution in a stopped-flow spectrophotometer. Then, changes in the cellular volume are measured over time and the permeability is calculated from the initial velocity of variable velocity.<sup>8)</sup> First, using MLE-12 cells of a mouse pulmonary epithelial cell strain, which express AQP5, we investigated the action of Wu-ling-san on the water permeability of cell membranes. It was found that Wu-ling-san inhibits the water permeability of the cell membranes in a manner dependent on the processing concentration (0.03–3 mg/ml) and the inhibitory action of a concentration of 1 mg/ml or higher was equivalent to that of HgCl<sub>2</sub> (500 μM), a representative AQP inhibitor (Fig. 1A).

Among crude drug extracts composing Wu-ling-san, the inhibitory action on the water permeability of cell membranes is found in Atractilodes and Poriporus (Fig. 1B). Thus, we presumed that these crude drugs might be the main components involved. In addition, Wu-ling-san and Atractilodes didn't affect the cell membrane potential and moreover, they inhibited the water permeability of proteoliposome containing AQP5 proteins prepared in vitro. It is assumed that the inhibitory action of Wu-ling-san and Atractilodes on the water permeability of cell membranes is based on the inhibition of AQP's

water channel function, but does not influence the aqueous spontaneous diffusion through the migration of electrolytes and lipid membranes.

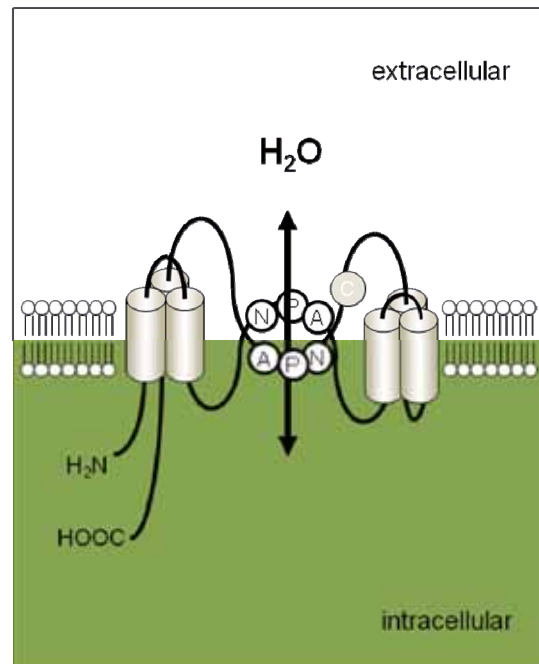


Figure 1. Basic structure of Aquaporin

The active components contained in Wu-ling-san and Atractilodes were also investigated. The AQP-inhibitory action of Atractilodes and Poriporus disappeared in the presence of EDTA, which indicates that the components containing a bivalent metal are important for suppression of AQP by crude drug extracts. When the metal components were investigated by ICP-MS analyses, it was found that manganese, chromium, and copper were present in abundance. Then, we conducted experiments using the inorganic salts of these metals and observed a notable AQP-inhibitory action of MnCl<sub>2</sub>, similar to Wu-ling-san. Thus, we presumed that the action might depend on the components in these crude drugs that contain manganese.

## 3. Isoform selectability of AQP inhibition by Atractilodes and various metals

Figure 2 shows the results of an investigation of the isoform selectability of manganese found as



an AQP-inhibitor of Wu-ling-san, using the oocytes of *Xenopus laevis* (African clawed frog), which express AQP1–AQP5. Isoform selectability of AQPs was observed in the AQP-inhibitory action of manganese, in which AQP3, AQP4, and AQP5 were suppressed and AQP1 and AQP2 were not markedly affected. Wu-ling-san showed a similar action to manganese in the experimental system. On the other hand, HgCl<sub>2</sub>, which has been conventionally known as an AQP-inhibitor, suppressed all isoforms except for AQP4 and the AQP-inhibitory profile of manganese was thus apparently different from that of mercury. Among AQPs that were markedly suppressed by manganese, it is known that AQP3 is distributed in the renal epithelium and skin in large amounts and animals with the deficiency have excessive urination. Thus, it can be assumed that the suppression of AQP3 may be a part of the mechanism for the urinary-volume increasing action of Wu-ling-san. In addition, AQP4 is a main isoform in the brain and is present in large quantities in the cell membranes of astrocytes in contact with the vascular endothelium. As shown in this experiment, it is noteworthy that AQP4 was not affected by mercury and Wu-ling-san and manganese suppressed AQP4.

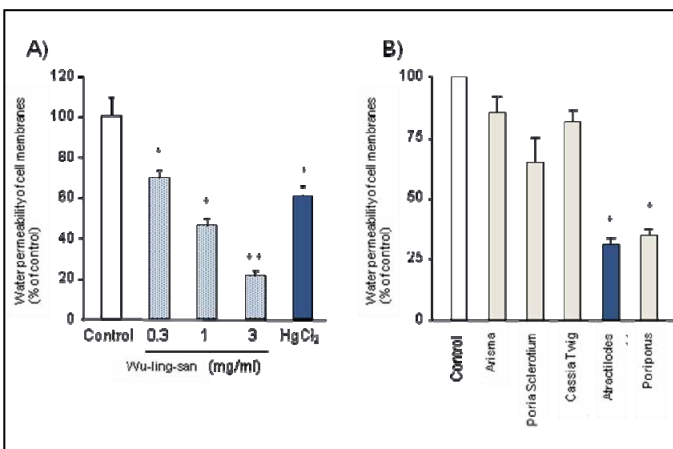


Figure 2. Actions of Wu-ling-san and its crude drugs on water permeability of cell membranes of pulmonary epithelial cells

#### 4. In vivo effect of the inhibitory action of Wu-ling-san on water permeability

In mice with an AQP4 deficiency, it is reported that cerebral edemas induced by various pathologic stimuli were notably alleviated.<sup>7)</sup> That is, AQP4 inhibitor can be expected to exert an inhibitory action on cerebral edema. Accordingly, to evaluate the effectiveness of the AQP-inhibitory action of Wu-ling-san in vivo, we investigated the inhibitory action on cerebral edema, using a mouse water-toxicosis model. Cerebral edemas in mice were induced through intraperitoneal administration of 20% distilled water of the body weight and antidiuretic hormone. In this experiment, all the control mice in which Wu-ling-san was not administered had spasms within two hours after the intraperitoneal administration of the distilled water and then died. However, in the mice in which Wu-ling-san (1 g/kg) was administered orally 30 minutes before the intraperitoneal administration of the distilled water, only one of the five animals died within 24 hours and the remaining four animals didn't show any notable excited symptoms of the central nerves (Figure 3).

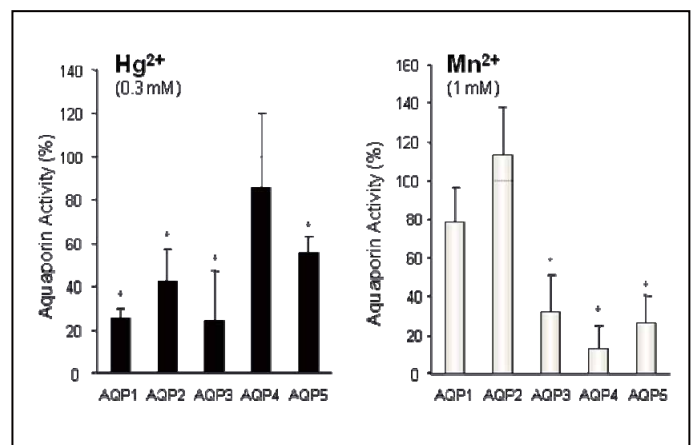


Figure 3. Comparison of AQP-inhibitory actions between mercury and manganese

In order to relate the results directly to the AQP inhibition by manganese contained in Wu-ling-san, further studies, such as on the action of Wu-ling-san without manganese, will be necessary. However, we consider it noteworthy that these results reveal the effectiveness of Wu-ling-san as an anti-cerebral edema agent.

#### 5. AQP5 inhibition of nitrogen monoxide and action of Chinese herbal medicine

The water-utilization actions of Chinese herbal medicines include not only the urinary-volume increasing and anti-edema actions previously discussed, but also a moisturizing action for dry symptoms. It can be understood that the moisturizing action enables recovery from decreased external secretions, such as saliva, sweat, and airway fluids when a disease is present, and moisturizes the skin and various mucosal tissues. AQP5 exists in the epithelial cells of secretory glands and become conduits when water is released passively in accordance with the secretion of ions such as  $\text{Cl}^-$ .<sup>9)</sup> However, whether or not the activity of AQP5 changes in pathologic conditions, such as inflammation, is not sufficiently known. We investigated the action of nitrogen monoxide (NO) that is produced in quantity when inflammation occurs during AQP5 activity and found that NO inhibits the passage of water molecules through AQP5 by means of S-nitrosylation of cysteine residue (Figure 4) adjacent to the pore structure of AQP5 (Figure 5). It was found that although Mai-men-dong-tang, which is known to have a moisturizing action and is effective for symptoms of Sjogren's syndrome, didn't affect the function of AQP5 itself, the S-nitrosylation and functional inhibition of AQP5 by NO were markedly suppressed. Thus, it is assumed that the recovery action of the AQP5 function decreased with inflammation, namely the external secretions, and may be involved, at least partially, in the moisturizing action of this medicine.

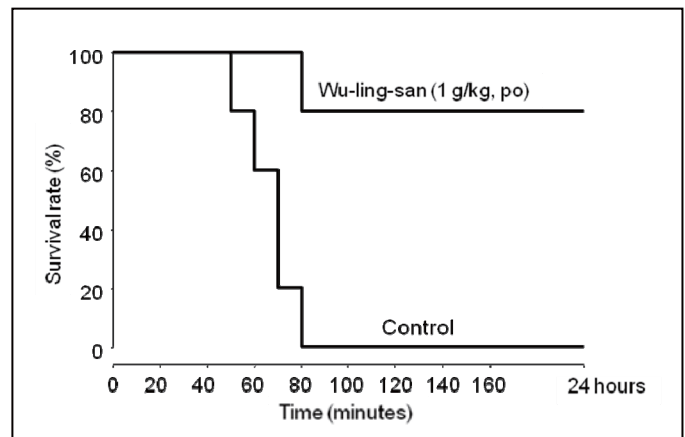


Figure 4. Action of Wu-ling-san on survival rate in mice with acute water toxicosis

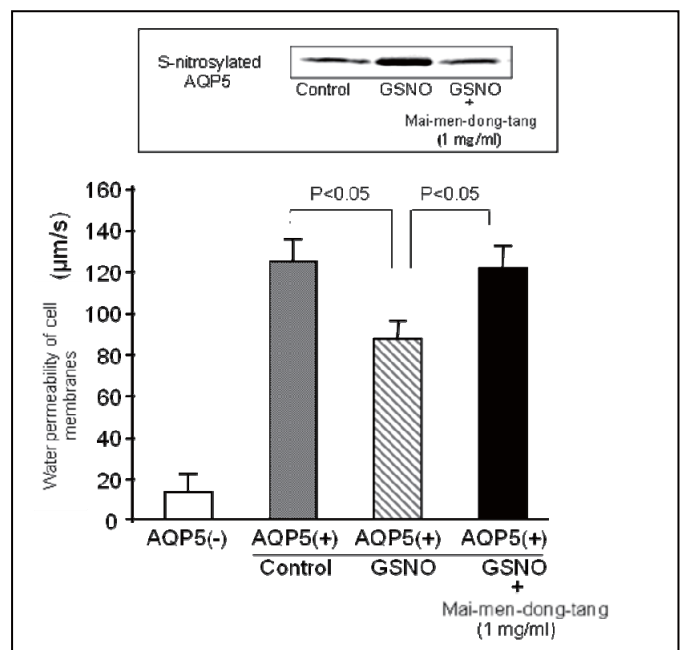


Figure 5. Action of Mai-men-dong-tang on S-nitrosylation and functional inhibition of AQP5 caused by nitrogen monoxide

#### 6. Conclusion

Chinese herbal medicines of Kampo formulae are drugs with multiple components and its actions result from the complex pharmacological actions of the multiple active substances it contains, which are synergistic, additive, and antagonistic. Because these medicines are, in general, administered orally, it is necessary to be aware of the presence of active metabolites as well as the components contained in the crude

drug itself. Thus, in order to evaluate the efficacy of Chinese herbal medicine and clarify its features, in vivo studies using human or animal models with specific diseases will be important. On the other hand, when functions of specific proteins are focused on to investigate the actions of Chinese herbal medicine, a new action may be elucidated, as was done in this study. As stated previously, AQPs have recently gained attention as new target molecules for the development of new water-metabolism regulatory drugs. In 2003, Doctor P. Agre was awarded the Nobel Prize in Chemistry for the discovery of aquaporin water channels. It comes as a surprise and a fresh reminder of the ancient wisdom that Chinese herbal medicines described in “Shang han lun”, a book written 1800 years ago, have regulatory actions on up-to-date target molecules.

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## Prescription (1)

*“B” Character Decoction (Sokeitei-Ijishogen)*

Hikomichi Yasui

Japan Institute of TCM Research

*“B” Character Decoction* was a formula invented about 200 years ago in Japan by Nan-yo Hara (1752-1820). He created several new formulae and four of them have names starting with Ko, Otsu, Hei, or Cho. *“B” Character Decoction* is the most well known formula of them all. After this, Sohaku Asada (1815-1894) modified the *“B” Character Decoction* and the modified formula is now called *“B” Character Decoction*.

The formula is now available in the extract form and often used as a specialized prescription for hemorrhoids (piles) in clinical sites. The constituents of the prescription are mostly as follows:

Japanese Angelica Root 6 gm  
 Bupleurum Root 5 gm  
 Scutellaria Root 3 gm  
 Licorice Root 3 gm  
 Cimicifuga Rhizome 1 gm  
 Rhubarb 1 gm

(In the original prescription made by Nan-yo Hara, Japanese angelica Root was not used but instead Chinese Date and Fresh Ginger were contained.)

[Efficacy] Cool and activate the blood/enhance qi

[Indications] Blood heat, blood stasis, reduced qi movement

[Drug actions] Japanese Angelica Root activates the blood and its circulation. Bupleurum Root frees qi movement in the triple energizers and Cimicifuga Rhizome enhances sunken qi. Combined use of these three kinds of drugs resolves obstructed network vessels (meridian)

caused by qi binding in the lower energizer. Scutellaria Root clears heat generated by qi stagnation and blood stasis. Rhubarb enters the qi system and the blood system, clears the heat and purge the fire and cool the blood and then expels toxins. Licorice Root has the actions of harmonizing various drugs as well as clearing heat and resolving toxins.

### Clinical application

*“B” Character Decoction* is used for various types of hemorrhoids and its use is especially suitable for the relatively acute condition in which there are constipation, pain and small amounts of bleeding. *“B” Character Decoction* is also used for prolapsed hemorrhoids in the initial stage.

#### 1. Hemorrhoids

Yoshio, et al. administered *“B” Character Decoction* 6.8 gm to 98 patients with hemorrhoids for 8 weeks to compare subjective symptoms (pain, bleeding, prolapse) and objective symptoms (bloating, size of hemorrhoid) before and after the administration. They report the results of the overall improvement rate that markedly improved accounted for 28.6%, improved 39.6%, and slightly improved 23.5%. For the rate of usefulness, extremely useful accounted for 22.4%, quite useful 41.8%, and slightly useful 21.5% with the recurrence rate of 15.2% after the discontinuation of administration. The recurrence timing was after 2.5 to 7 months after the discontinuation of administration<sup>1)</sup>.

When this prescription is clinically used for hemorrhoids, generally it is not used by itself but it is often used in combination with other prescriptions. For example, Keishibukuryogan (*Cassia Twig and Tuckahoe Pill*) is combined if blood stasis is complicated; Hochuekkito (*Middle-Reinforcing and Qi-Benefiting Decoction*) if there is distinguished qi deficiency; Yokukansan (*Liver-Inhibiting Powder*) if there is

marked liver qi depression; and Orengekuto (*Coptis Detoxifying Decoction*) if there is an excess heat toxin.

#### Case 1: Hemorrhoid

The patient was a male of 27 years old. He had been suffering hemorrhoids since his school days. Recently, an anal fissure (bleeding hemorrhoid) and internal hemorrhoids of a finger-tip size became inflamed like attacks several times a year so that the patient was somewhat neurotic. Although his doctor recommended a surgery, he could not be away from work for hospitalization for as many as a week. So he did everything he did but the condition did not improve at all. He felt like using “Kampo” and visited the clinic.

He was quite healthy except for the affected area although there was the sho of blood stasis. Therefore, the decoction of “*B*” *Character Decoction* was administered for continuous two months without effects. Since there were no reasonable conditions for changing the prescription and the patient said that it took a lot of trouble to prepare the decoction, I decided to use the Extract Tablet of Keishibukuryogan (*Cassia Twig and Tuckahoe Pill*) as a drug for dispelling blood stasis.

Three weeks later, the bleeding stopped and pain was also relieved. After continuous use for six months, an examination indicated that the internal hemorrhoids reduced to the size of a piece of soybean and the blood sho of the face and the lower abdomen disappeared. Two years passed without the medication. However, there has been no recurrence.

(Akira Ishihara, Two Cases in Clinical Trial on “*B*” *Character Decoction*, The Association of East-Asia Medicine Vol.12 3-go p61, 1965)

#### Case 2: Hemorrhoidal bleeding

Patient: Female of 34 years old

Chief complaint: Bleeding

Current medical history: When constipated, she had bleeding and the toilet bowl became bright red, which began to happen several years ago. Whenever bleeding occurred, the patient used over-the-counter suppositories. As bleeding became severe four days ago and did not stop with suppositories, she visited our clinic.

Findings at the initial visit: There were three internal hemorrhoids in the 3 o'clock, 7 o'clock, and 11 o'clock positions. From the internal hemorrhoid in the 7 o'clock position, ruptures and bleeding were observed. The internal hemorrhoid was positioned in the 1 o'clock direction.

Treatment: TSUMURA “*B*” *Character Decoction* Extract Granules (for ethical use) were used with TSUMURA Orengekuto Extract Granules (for ethical use). On the 2<sup>nd</sup> day of the administration, the bleeding disappeared. After one month of administration, a proctoscopic examination showed the bleeding stopped and the internal hemorrhoids changed in color from bright red to dark red.

(Tomonori Kawai, Jishitu ni taisuru Kampo Seizai Heiyo Ryoho, Kampo Shinryo Vol.7, 2-go, p50, 1988)

#### Case 3: Bleeding hemorrhoids and pain

Patient: Female of 59 years old

Chief complaints: Bleeding and pain

The patient had a medium physical constitution and no anemia with slightly dark complexion. Appetite and sleep were normal. Bowel movements were diarrhea-constipation. She was sensitive to cold (+) with no dry mouth, and no sweat. The abdominal sho was shown in Figure 1. There were two hemorrhoids with the size of a piece of soybean in the 7 o'clock position.



After three months of administration of “*B*” *Character Decoction* 8.0 + Hochuekkito (*Middle-Reinforcing and Qi-Benefiting Decoction*) 6.0 (3x), no bleeding was observed. After five months, the patient complained pain only sometimes. A cure was achieved within eight months.

(Shigeru Tanaka, *Jishitu to Kampo Chiryō*, *Kampo Shinryō* Vol.5, 1-go, p42, 1986)

#### 1. Prolapsed hemorrhoid

“*B*” *Character Decoction* works to recover the qi movement bound in the lower energizer. So this formula is also used for prolapsed hemorrhoids. Bupleurum Root and Cimicifuga Rhizome contained in the prescription enhance stagnant qi movement by their action of raising qi and drooped organs caused in conjunction with lowering qi. The prolapsed hemorrhoids which are the sho of deficiency are often accompanied by spleen deficiency, in which case Hochuekkito, for example, is used in combination.

#### Case 4: Prolapsed hemorrhoid and pain

Patient: Female of 45 years old

Chief complaints: Prolapsed hemorrhoid and pain

Sometimes hemorrhoid prolapsed during a bowel movement, which began to happen several years ago. Pain was added and became persistent from two months ago.

The patient face was pale but did not have anemia. The lower half of her body was cold. Appetite and sleep were normal. Bowel movements were once/day with one slightly soft stool. The dry mouth condition was (+) with sweat (-). The overall abdomen was weak and soft without resistance. The affected area: The hemorrhoid with a size of a finger tip was in the state of an everted flower and the surrounding tissues were congested and swollen. Intense pain

was felt intense in palpation. “Shiunko” was applied and then the hemorrhoid was pushed back. Shiunko was used as an external medication.

I judged that an intense sensation of cold with normal appetite was the sho of deficiency of qi and blood. On the basis of this, Prepared Aconiti Daughter Tuber 1.5 + Shikunshito (*Four Gentlemen Decoction*) 8.0 (3x) were administered for two months. Then the prolapsed hemorrhoid became able to retract somehow. Therefore, the medications were changed to “*B*” *Character Decoction* 7.0 + Hochuekkito 7.0 (3x). For constipation the patient complained of, Mashiningan (Hemp Seed Pill) 4.0 (as needed) was used after dinner. Further two months later, prolapsing was reduced to only a little during a bowel movement. Further three months later, subjective symptoms relieved. The medications were suspended again for further two months.

(Shigeru Tanaka, *Jishitu to Kampo Chiryō*, *Kampo Shinryō*, *Kampo Shinryō* Vol. 5, 1-go, P39, 1986)

#### 1. Itching around the anus

Anal itching is often caused by damp-heat in the lower energizer. This prescription has the action of recovering qi movement in the lower energizer and concurrently dispelling damp-heat, by which the itchy sensation in the anus and the anterior pubic region can be relieved.

#### Case 5: Bleeding hemorrhoids and itching around the anus

Patient: Male of 38 years old.

Initial visit: July 30, 1983

Present medical history: The patient had been complaining of bleeding from the anus and itching around the anus for about two years.

Present condition: The patient was of large build, fatigable, and unable to have sufficient

sleep with pale complexion. The patient was a heavy sweater (whole body). The anus felt no pain but there were bleeding and an itchy sensation around the anus. Bowel movements were once a day with one stool and there was a sensation of residual stool. Appetite was good. The tongue was covered with thin white furs and moist. Pulse was floating with strength. The abdomen was generally soft with a slight bloating feeling in the chest and hypochondrium on right and left sides, and there was a slight tension over the abdominal muscles in palpation.

[Treatment and course]

During the administration of Otsujitokyodaio, subjective symptoms gradually improved. By the end of the 100 day administration, they become resolved.

(Genpo Ogata, Kampo Chiryō Shorei-Senshu (1) P236, Gendai Shuppan Planning Co., Ltd. 1988)

#### 1. Hemorrhoidal disease during puerperium

Pregnancy and child birth delivery have adverse influences on the development of hemorrhoids and its worsening. There is a documentation reporting that “*B*” *Character Decoction* was successfully applied to these problems.

Honda said that 58% of puerperal women become affected with hemorrhoids, 30% of the women develop hemorrhoids after delivery although they did not have hemorrhoids during pregnancy, and 60% of the women who had hemorrhoids during pregnancy do not have relief within one month after delivery and rather tend to have exacerbated symptoms such as bleeding, prolapse, and pain during the period of one-month-after delivery. He administered “*B*” *Character Decoction* to 30 patients with hemorrhoids observed on the 1<sup>st</sup> day of the puerperium, reporting the results of significant improvements in four symptoms of “painful bowel

movements,” “bleeding,” “prolapse,” and “swelling,” slightly effective in 11 patients (36.7%), and quite effective (36.7%) with the overall effectiveness rate of 73.3%<sup>2)</sup>. Akagi, et al. also administered “*B*” *Character Decoction* for anal symptoms during pregnancy/puerperium and obtained mostly similar results<sup>3)</sup>.

- 1) Yoshio T, Yanagida K, Sumiyama Y, et al.: *Naijikaku ni taisuru Otsujito no Rinsho Koka*, Journal of New Remedies and Clinics 40:2087-2096, 1991
- 2) Honda T, et al.: *Fujin to Ji-shikkan-sono 4 – Kampo (Otsujito) no Koka – Bosei-Eisei*, Vol. 31 No. 1, 1990
- 3) Akagi K, et al.: *Ninshin/Sanjyoku no Komon Shojyo eno Otsujito no Toyo Koka*, Kampo Shinryo Vol. 15 No. 3, P41-42, 1986