

## Clinical Report 1 (Japan)

*Facility Introduction – Hyogo Prefectural Research  
Institute and Affiliated Clinic;*

*Effect of Acupuncture Treatment in Intractable Hiccups*  
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### Facility Introduction

#### Hyogo Prefectural Research Institute and Affiliated Clinic

Following the intentions of the former governor of Hyogo Prefecture Tokitada Sakai pertaining to the "request clarification whether oriental medicine cannot be applied to health care and welfare for the residents of Hyogo prefecture" the Hyogo Prefectural Research Institute and Affiliated Clinic was established in 1977 as the first such public facility next to the Hyogo Prefectural Amagasaki Hospital.

Later, in connection with the application of health insurance to medical treatment using Kampo medicine, we started treatment in the department of oriental medicine established next to the Hyogo Prefectural Amagasaki Hospital. In the clinic affiliated with the research institute people receive approximately 10,000 acupuncture and moxibustion treatments annually. Since its establishment to the present day In this facility we have performed research and conducted treatment here for about 31 years related to both Kampo medicine as well as acupuncture and moxibustion treatment.

The Hyogo Prefectural Amagasaki Hospital is a general hospital that employs, including internees, 140 physicians, is visited by an average of 2,000 outpatients per day and has 500 beds. The patients included in the present study were inpatients for whom initially various other possible forms of treatment other than acupuncture and moxibustion were administered, but due to the failure to achieve any effects the physician in charge referred these patients to our department.

### Introduction

"Singultus" (hiccup) is an involuntary spasm of

the respiratory muscles, mainly the diaphragm. Hiccup is triggered by disorders of the brain stem controlling the contraction movements of the diaphragm, or stimulation of the peripheral phrenic or vagus nerves. Moreover, it can also be triggered by direct stimulation of the diaphragm. Generally employed treatments include drinking cold water, drinking a decoction of persimmon calyx, applying pressure to the eyeballs, or people notice after a while, that the symptom has been relieved. The condition mostly resolves spontaneously after a period varying between several minutes and several hours. However, there are also refractory forms of hiccup that tend to persist, occasionally for periods of more than several weeks. Hiccup persisting for more than 48 hours is called "refractory hiccup". So far no treatment form has been established, but in case the "refractory hiccup" is caused by diseases of the central nervous system the administration of anticonvulsants, or if diseases of the digestive tract contribute to the etiology antiemetic drugs are frequently used. Yet, in some cases even the administration of these drugs has no effect on the hiccup and may make the treatment very difficult.

Generally, the number of patients with hiccup coming for acupuncture treatment is small. Actually, we treated in the clinic affiliated with our research institute over a 4-year period from 2005 only 10 patients with "refractory hiccup", of which 8 had also been inpatients in the nearby Amagasaki Hospital. Protracted hiccup may lead to sleep disturbances and physical exhaustion, resulting in weight loss and the development of depressive conditions. In particular if patients in severe conditions are forced to be hospitalized, the wasting of physical strength due to the hiccup can develop into a life-threatening problem. Occasionally inpatients with hiccup can be in serious trouble because of their resistance to pharmacologic treatment and are then referred to acupuncture and moxibustion therapy. In this manuscript we introduce 3 inpatients and simultaneously present an outline of the acupuncture and moxibustion

treatment administered to 10 patients with refractory hiccup.

### [ Case No. 1 ]

[ Name ] Mr. B  
 [ Age, sex ] 52 years, male  
 [ Occupation ] employee  
 [ Chief complaint ] diarrhea, loss of appetite  
 [ History ] at age 37: cerebral infarct  
 [ Allergy history ] none  
 [ Present illness ]

- Starting in November (200B-1) gradual loss of appetite, development of a tendency towards diarrhea, passing 4-5 times per day small amounts of stool.
- Occasionally the stools were mixed with red, bloody fluid. Lower abdominal pain also occurred occasionally.
- Body weight: loss of 4 kg
- An irrigoscopy performed on March 1 of 200B showed a constriction and niveau raised suspicion of colon cancer and led to the hospitalization of the patient on the same day.

[ Diagnosis ] rectal cancer (liver metastases), refractory hiccup (postsurgically)

[ Acupuncture treatment ]

PC6 (Naikan / Neiguan) and ST36 (Soku Sanri / Zusanli), depth of needle insertion: 3 mm, low frequency electrical stimulation at 2 Hz, duration of electrical stimulation: 20 min.

During the hospital stay one treatment per day, 5 per week.

[ Clinical course ]

March 1: Admission to the surgery ward

March 10: Low anterior resection of the rectal cancer to relief the ileus. Postsurgical development of refractory hiccup.

March 20: Start of acupuncture treatment for "refractory hiccup". After the acupuncture treatment the hiccup stopped for half a day.

March 21: Second acupuncture treatment. After the acupuncture treatment the hiccup stopped for half a day.

March 22: Third acupuncture treatment. After the acupuncture treatment the hiccup stopped for half a day.

March 23: Fourth acupuncture treatment. After the acupuncture treatment the hiccup stopped completely.

March 24 to 31: Fifth to tenth acupuncture treatment. Hiccup (-)

April 2: Discharge. Switch to treatment as an outpatient at the research department for oriental medicine. Hiccup (-)

April 6: Eleventh acupuncture treatment. Hiccup (-)

April 12: PET examination showed areas of high uptake in the liver and porta hepatis. Elsewhere metastases were not observed.

April 26: Twelfth acupuncture treatment. Hiccup (-)

May 2: Thirteenth acupuncture treatment. Hiccup (-). Acupuncture treatment discontinued. Initiation of arterial injection of the anticancer agent 5FU.

[ Results of the acupuncture treatment ]

In this patient the refractory hiccup developed following resection of a rectal cancer. In the presence of multiple liver metastases the application of drugs that might put a strain on the liver was avoided as far as possible. When the physician in charge was struggling to find a treatment for the persistent hiccup he learned about the possible effectiveness of acupuncture treatment and referred the patient the research department for oriental medicine. From the surgery on March 10 until the patient was introduced to acupuncture treatment the hiccup continued day and night over a period of 10 days, but after the first acupuncture treatment stopped at least for half a day. After four treatment sessions the hiccup stopped completely and did not recur later.

### [ Case No. 2 ]

[ Name ] Mr. G  
 [ Age, sex ] 73 years, male  
 [ Occupation ] guard

[ Chief complaint ]        rotatory vertigo

[ History ]                TBC at the age of 20.  
                                  Hypertension

[ Present illness ]        On December 11 200G an  
attack of rotatory vertigo led to difficulties in  
walking.

Consultation as an emergency outpatient at the  
Amagasaki Hospital at 9 am of the same day.  
Consciousness was clear. CT findings raised  
suspicions of cerebellar infarction.

Admission on the same day

[ CT findings on the day of the admission ]

Demonstration of a cerebellar infarction over a wide  
area of the right cerebellar hemisphere. Condition of  
the brain stem could not be evaluated.

[ Diagnosis ]        cerebellar infarction, refractory  
hiccup (postsurgically)

[Acupuncture treatment ]

          PC6 (Naikan / Neiguan) and ST36 (Soku Sanri /  
          Zusanli), depth of needle insertion 3 mm, low  
          frequency electrical stimulation at 2 Hz,  
          duration of electrical stimulation: 20-30 min.

During the hospital stay one treatment per day, 5  
per week.

[ Clinical course ]

December 11: Admission to the ward of the  
          neurosurgery department

The observation of a sudden arrest of respiration  
and drop in blood pressure suggested the  
possibility of a lesion involving the brain stem.  
Connection to a respirator due to hypoxia.

December 13: Consciousness: JCS II-2.

December 14: The CT showed low density areas  
          (LDA) in the left cerebellar hemisphere, while  
          LDAs of the brain stem were indistinct.  
          Ventricular distention, development  
          hydrocephalus. For the hydrocephalus a  
          decompression through suboccipital craniotomy  
          was performed and the ventricles drained.  
          Postsurgical development of hiccup.  
          Consciousness: JCS II-2.

December 17: Drinking of cold water and  
          compression of the eye balls was tried as

          treatment for the hiccup, but did not stop it.

Consciousness: JCS II-3.

December 19: Begin of acupuncture treatment  
          for the refractory hiccup. Following the  
          treatment the hiccup stopped for 3 to 4 hours.  
Consciousness: JCS II-3.

December 20: Second acupuncture treatment.  
          Following the treatment the hiccup stopped for 3  
          to 4 hours.

At night, the GABA receptor agonist Baclofen was  
          administered.

December 21: Third acupuncture treatment.  
          Following the treatment the hiccup stopped and  
          did not recur later. Consciousness: JCS II-3.

December 25: The hiccup had not recurred since  
          the last treatment on December 21. Today the  
          acupuncture treatment was discontinued.

(200G + 1) On January 4 apnea developed, so that  
          for the purpose of assistive respiration the use of  
          a continuous positive airway pressure (CPAP)  
          apparatus was started.

January 8: A "central alveolar hypoventilation  
          syndrome" was newly diagnosed. Consciousness:  
          JCS II-3.

January 15: The patient was again referred  
          from the neurosurgery department. The purpose  
          this time was improvement of the central  
          alveolar hypoventilation.

February 5: SPO<sub>2</sub> (percutaneous arterial  
          oxygen saturation) had reached a good and stable  
          level. Later the patient was transferred to a  
          different hospital.

[ Results of the acupuncture treatment ]

          This is a case, in which cerebellar infarction led  
          to the development of hydrocephalus. When a  
          suboccipital craniotomy was performed for the  
          decompression of the hydrocephalus "refractory  
          hiccup" developed unexpectedly and put the  
          attending physician at a loss regarding its  
          treatment. This attending physician heard from  
          other physicians, that acupuncture treatment may  
          be effective for "refractory hiccup" and thus referred

the patient to the research department for oriental medicine. Over a period of 6 days following surgery and until the start of the acupuncture treatment the hiccup had continued constantly, but after both the first and second treatment session stopped for a period of 3 to 4 hours. Conceivably the function of inhibitory mechanisms for hiccup may have been impaired due to the brain stem lesion. Therefore we suggested on the day of the second acupuncture treatment to the attending physician to administer drugs activating inhibitory systems descending from the brain stem. In that same night Baclofen was prescribed<sup>1)</sup>. The synergistic effects of the acupuncture treatment and Baclofen stopped the hiccup on the day of the third acupuncture treatment. On the day of the third acupuncture treatment the refractory hiccup was cured and the treatment therefore discontinued. No recurrences of the hiccup occurred later.

### [ Case No. 3 ]

[ Name ] Mr. J  
 [ Age, sex ] 70 years, male  
 [ Occupation ] scaffolding man  
 (construction worker)  
 [ Chief complaint ] headache, feeling of  
 weakness, dark orange  
 colored urine  
 [ History ] hypertension  
 On December 16 (200J-1) left-sided sudden deafness  
 On December 23 (200J-1) lacunar infarction (no  
 paralysis)  
 [ Allergy history ] none  
 [ Smoking/drinking ] Smoking:30 cigarettes  
 /day x 50 years  
 Drinking: ca. 0.36 /day  
 [ Family history ] no appreciable disease  
 [ Present illness ] Since 2 months earlier  
 development of headache and weariness. Since 2  
 two weeks earlier passing of dark orange colored  
 urine. While blood tests performed in a different  
 hospital on December 16 showed BUN: 24, Cr: 1.51,  
 similar tests performed today (200J, February 3)

showed BUN: 69.8, Cr: 7.55 and thus led to an emergency referral visit.

Today: emergency hospital admission  
 [ Diagnosis ] necrotizing crescentic glomerulonephritis,  
 refractory hiccup (side effect of a steroid pulse therapy)  
 [Acupuncture therapy]

PC6 (Naikan / Neiguan) and ST36 (Soku Sanri / Zusanli), depth of needle insertion 3 mm, low frequency electrical stimulation at 2 Hz, duration of electrical stimulation: 20 min.

During the hospital stay one treatment per day, 5 per week.

[ Clinical course ]

February 3: Admission of behalf of the department of nephrology.

February 5: Performance of a kidney biopsy. Electronmicroscopic examination.

February 10: Initiation of a steroid pulse therapy for three days.

February 11: The hiccup started on the second day of the steroid drip infusion.

February 12: Initiation of dialysis. Hiccup did not stop since the day before. Administration of Metoclopramide for the treatment of the hiccup remained without effect.

February 13: Request of acupuncture treatment for "refractory hiccup". Hiccup stopped during the acupuncture treatment.

February 14: Kidney dialysis. No hiccup (-) since the day before. Today the acupuncture treatment is discontinued.

February 15: No hiccup (-)

February 16/18: Kidney dialysis.

February 20: The second 3-day steroid pulse therapy begins. Kidney dialysis.

February 22: Hiccup starts on the third day of the steroid drip infusion. The steroid pulse therapy leads to an improvement of the kidney function. Later, kidney dialysis is discontinued.

February 23: The hiccup continues since the day before. Acupuncture treatment is requested again. Hiccup stops during the acupuncture treatment.

February 24: No hiccup (-) since the acupuncture treatment on the day before. Today the acupuncture treatment is discontinued.

February 25/26: No hiccup (-)

March 25: Cr value has improved to 4.3.  
Today: discharge.

#### [ Results of the acupuncture treatment ]

This is a case, in which the hiccup recurred. The initial occurrence of the hiccup and its later recurrence have in common, that both instances occurred during the steroid drip infusion. Nausea, heartburn and hiccup are listed as adverse effects of the steroid pulse therapy on the digestive organs. After the second steroid pulse therapy this treatment form was not repeated and there were no further recurrences of the hiccup. This suggests that in this patient the refractory hiccup may conceivably have been a drug induced hiccup<sup>2)</sup>. The hiccup in this patient did not respond to the administration of the antiemetic drug Metoclopramide, but during the electrical stimulation of the needles applied during the acupuncture treatment an immediate response was observed and the hiccup stopped. Both during the initial occurrence and the recurrence of the hiccup a single electroacupuncture treatment led to the cessation of the hiccup.

#### [ Therapeutic results of the treatment of 10 patients with refractory hiccup ]

As described in Table, we used acupuncture to treat over a 4-year period from 2005, 9 men and one women with refractory hiccup. Diseases of the digestive tract were the most frequent causative disorder and had been responsible for the hiccup in 6 patients, among which it developed in 5 patients following surgery for cancers of digestive organs. This incidence was followed in frequency by 3 patients with cerebral stroke. Apart from diseases of the digestive organs and cerebrovascular disorders refractory hiccup developed in one patient as a side effect of steroid pulse therapy.

Except for patient B, who had impaired liver

functions, Metoclopramide was administered, but had no effect on the hiccup. Moreover, attempts of drinking cold water or compressing the eyeballs also failed to stop the hiccup. Attempts at using electroacupuncture treatment for these 10 patients with refractory hiccup caused the cessation of the hiccup in all patients. The number of treatment sessions until the hiccup stopped was in patients, in whom the effect appeared quickly, just one treatment and required in patients with a slow response 5 sessions of electroacupuncture treatment. The hiccup recurred in the three patients H / I / J. In patient H aspiration occurred after a cerebral infarction. Aspiration during the drinking of alcohol invariably leads to the occurrence of hiccup and once this has started may continue for 3 to 7 days. During this last half year the number of days without hiccup were for this patient rather few in number. Since he started to visit the clinic affiliated with our research institute as an outpatient and received electroacupuncture treatment the hiccup stopped.

As described under [ Case No. 3 ] the hiccup in patient J was caused by a steroid pulse therapy. Both the initial occurrence and the recurrence of the hiccup were cured by just one electroacupuncture treatment. In patient I the initial occurrence of hiccup developed following the surgical resection of a rectal cancer and was alleviated after 3 electroacupuncture treatments. The recurrence of the hiccup occurred immediately after a rupture of the abdominal wall required emergency surgical intervention on the twelfth day after the initial surgical resection of a rectal cancer. The hiccup in this case proved to be rather unresponsive to the treatment and required a total of 11 electroacupuncture treatments.

All patients except patient G, who suffered from disturbances of the consciousness, experienced the acupuncture treatment as "comfortable" (pleasant).

#### Discussion

Hiccup is an involuntary spasm of the

respiratory muscles, mainly the diaphragm. The reflex arch for the hiccup uses the afferent pathways of the phrenic and vagal nerves originating from the esophagus, stomach and diaphragm, while the phrenic and vagal nerves descending towards the respiratory muscle groups and diaphragm serve as efferent pathways. Also, there appears to be a still unidentified singultus center in the brain stem<sup>1)</sup>. Usually areas in the parietal lobe, hypothalamus and the reticular activating system of the medulla act to inhibit descending singultus activities<sup>1)</sup>. The frequent occurrence of hiccup in newborn is presumably due to the immaturity of these inhibitory function<sup>2)</sup>.

A possible cause of hiccup is a weakening of the inhibition exerted from higher brain levels on the singultus reflex arch, stimulation of the neural pathways of that singultus reflex arch, or else direct stimulation of the diaphragm. Among the central nervous systems cerebral infarction, cerebral hemorrhage, brain tumors and similar disorders resulting in disturbances of the brain stem may be a cause of hiccup. Lesions in the thoracic or abdominal cavities may also result in stimulation of afferent and efferent pathways of the singultus reflex arch or the diaphragm. In particular cancer of the digestive organs or ablative surgeries are likely to result in hiccup<sup>2)</sup>.

Metoclopramide is used as an antiemetic for the treatment of hiccup caused by diseases of the digestive tract. A side effect of Metoclopramide is blockage of the D2 receptors located on parasympathetic nerves, leading to an augmentation of the motility of the digestive tract. Here Metoclopramide is administered in the hope, that it will alleviate the hiccup through a reduction of the digestive tract motility<sup>1)</sup>. For hiccup caused by diseases of the central nervous system the GABA receptor agonist Baclofen is frequently administered. The relevant mechanism of action here is considered to be an inhibition of the efferent portion of the singultus reflex arch<sup>1)</sup>. Moreover, Baclofen acts also on the brain stem and activates inhibitory systems for descending pain pathways.

Needle stimulation of St36 (Soku Sanri, Zusanli) and other points on the legs and arms is known to promote the motility of the digestive tract through enhanced parasympathetic dominance<sup>3,4)</sup>. PC6 (Naikan / Neiguan) reportedly has both antiemetic effects and activates inhibition of descending pain pathways via endogenous opioids<sup>5)</sup>. Thus, while the mode of action of Soku Sanri and Naikan differs slightly from those mediating the effects of Metoclopramide or Baclofen, we chose these two acupoints for the treatment of drug-resistant, refractory hiccup, because the results are similar.

Based on clinical experiences gained over a 4-year period since 2005 from the treatment of 10 patients with drug-resistant, refractory hiccup, we found electroacupuncture stimulation at 2 Hz of Soku Sanri and Naikan useful. The mechanisms of their effectivity has not been established, but Soku Sanri and Naikan apparently act to promote the motility of the digestive tract and conceivably have inhibitory effects on the singultus reflex arch as well. Moreover, experiencing the acupuncture treatment as "comfortable" (pleasant) by the patients may also be considered an important factor contributing to the cure of hiccup.

## Conclusion

Electroacupuncture stimulation at 2 Hz of Soku Sanri and Naikan is considered to be useful for drug-resistant, refractory hiccup.

## References

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## Results of acupuncture treatment for refractory hiccup

	Name	Age	Disease	Cause of the hiccup	Day of treatment begin; Duration of the hiccup until start of acupuncture treatment	Number of acupuncture treatments until the cure of the hiccup	Number of acupuncture treatments	Outcome
A year, May 8 Admission to surgery ward	A	57	Rectal cancer, terminal stage (systemic metastases)	Not recorded	June 8 5 days	2	3	June 13 Death
B year, February 24 Admission to surgery ward	B	52	Rectal cancer (liver metastases)	Development following resection of rectal cancer	March 20 10 days	4	13	December 28 Discharge
C year, December 21 Oriental medicine ambulance	C Female	30	Reflux esophagitis (since 2 years) Aerophagia (since 2 years)	Not recorded	December 21 1 month	1	3	Next January 18 Discontinued
D year April 23 Admission to digestive surgery ward	D	64	Esophageal cancer	Development following resection of esophageal cancer	July 9 3 days	5	5	July 31 Discharge
E year, September 14 Admission to the neurology ward	E	68	Cerebral infarction	Not recorded	September 27 7 days	1	3	October 18 Transferred
F year, August 18 Admission to surgery ward	F	67	Gastric cancer	Occurred after surgery	December 5 3 days	4	5	December 16 Discharge
G year, December 11 Admission to neurosurgery ward	G	73	Cerebral infarction 3 days later ventricular distention hydrocephalus	Development after cerebral decompression	December 19 2 days	3	3	Next February 5 Transferred
H year, April 18 Oriental medicine ambulance	H	66	Cerebral infarction (previous year on November 20) Aspiration (previous year October)	Occurs upon aspiration induced intensive choking	April 18 6 months Stopped occasionally for 1-2 days	2 1 1	15	In July: based on suspicion of hemorrhage into multiple organs the attending physician ordered to discontinue treatment
I year, January 29 Admission to surgery ward	I	70	Rectal cancer	① Following rectal cancer resection ② After resurgery following abdominal wall rupture	① February 9 8 days ② February 17 1 day	① 3 ② 11	① 3 ② 11	April 3 Discharge
J year, February 3 Admission to nephrologic ward	J	70	Glomerular nephritis	After steroid pulse therapy	① February 13 3 days ② February 22 2 days	① 1 ② 1	① 1 ② 1	March 25 Discharge

Over a 4-year period since 2005 we treated 10 patients with drug-resistant, refractory hiccup with acupuncture. These patients included 9 men and one woman. Recurrences were observed in the patients H / I / J.