

Kampo Medicine - Current Research

Efficacy of Goshuyuto for Migraines

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1. Introduction

Migraine is a disease that has been around the world dating far back to the ancient times and it occurs periodically. The patients with migraine have to go through a considerably difficult time coping with the severe symptoms it produces: Once a migraine attack takes place, it can almost interfere with patients' day-to-day life. In recent years, migraine treatment has greatly been advanced and with the availability of triptan preparations, migraines have become a far better controllable disease than before. Even then, currently the complete and total effect cannot be expected from modern medications.

On the other hand, migraines are considered to be a disease easy to care for in Kampo medicine. The reason is that though migraines, having many types, are triggered by a variety of factors, Kampo medicine is the medicine capable of doing right things for each of triggers and types with pinpoint precision. To cure the pains, many prescriptions are ready for use. Hereunder, a few experiences in Japan of a typical prescription *goshuyuto* (*goshuyuto*, Wu-Zhu-Yu-Tang, 呉茱萸湯) are introduced.

2. Case Study on *Goshuyuto* for Migraines

A case report on *goshuyuto* for a migraine was first made in Japan about 200 years ago by Nangai Yoshimasu (1750-1813) as follows:

Patient: An adult male, age unknown, had always migraines. A heavy headache attack occurred on a certain day with vomiting, disabling him to speak. He continuously slapped his neck by his hand. It looked like a puppet, giving a weird impression. People around him did not know that his behavior was from a headache and they thought he went out of order. Nangai Yoshimasu saw the behavior and knew that

he did not go made such behavior and it was a furious headache. Yoshimasu hurriedly prepared two doses of *goshuyuto* and administered him. After the use of them, the headache disappeared.

Since this reported, the use of *goshuyuto* has become a kind of common sense and many cases have been reported till now. Some clinicians discussed a variety of conditions in which *goshuyuto* was effective and according to the tips gained from the discussions and handed down orally, the prescription has been applied.

Following are the cases of interest:

Case Report 1:

The patient was a 29-year old female. In her high school days, headache began to develop by the triggers of stresses and the crowd. Headache always started in the muscles of the left shoulder, spreading to the back of the entire head from the left back side of the head, leading to a pain behind the eyes and then making her to feel like vomiting. . An attack occurred especially before the onset of menstruation and persisted for about a day. The patient had cephalic CT scans but nothing abnormal was detected. The analgesic drugs she used to take, although initially effective, gradually became less effective and unworkable, so Kampo treatment was started. With the administration of *goshuyuto*, mild headaches were experienced only 2-3 times before the onset of menstruation and severe agonizing headaches disappeared completely. Thereafter, not only has an attack not occurred before the onset of menstruation, but also menstrual pains and constipation have been improved.¹⁾

This is a representative case report on *goshuyuto*. In case the analgesic drug initially effective becomes ineffective, like this case, the treatment by a medical specialist is required. However, *goshuyuto* is effective in many of such cases.

Case Report 2:

The patient was a 49-year old female with a medium build. Since two years before, the patient sometimes had experienced paroxysmal attacks of severe headache. Before and after the attack, the patient always had a stomach disorder, or distended

stomach or pain in the stomach. She felt like vomiting but did not throw up. The nuchal region and the broad of the back became stiff. Appetite slightly decreased. The epigastric region was often distended with a heavy sensation in the region and hands and feet became cold. There were no significant changes in two-times stools. Pulse was deep and slow. The tongue had a moderate coating of white moist furs. The abdominal strength was slightly flaccid. Mild resistance and tenderness on pressure were felt in the epigastric region and clapotage was demonstrated. These symptoms were diagnosed as the conditions (*sho*) of *goshuyuto*, and thus the one-week doses were given. After a week, discomfort in the epigastric region dissipated. After three weeks of administration, medication was discontinued. Although it has passed one year since then, a headache attack has not recurred.²⁾

Headaches that have indications for *goshuyuto* are generally associated with underlying internal cold caused by a lack of yang Qi, to which external influences are added to develop an attack. This case had several symptoms considered indications for *goshuyuto*, which will be described later in this paper. It may be a marked improvement that since three weeks medication, no headache episode has been experienced for a year.

Case Report 3:

The patient was a 55-year old female. The patient had the problem of high blood pressure on a daily basis and made visits to our hospital. Sometimes, she was plagued by headaches. As seen in many women of about her age, blood pressure numbers were not stable. At a certain night of November 1983, I received a telephone call from her family, saying that the patient had come down with a headache since daytime, at nightfall began to have a severe pain and now was suffering from vomiting. I made a house call, taking cerebral vascular disorder into account. Her sensorium was clear and her response was also clear without motor paralysis and stiff neck. So I breathed a little easier. When I asked her the type of the pain, she replied that at nightfall the pain became a pulsating type of throbbing sting with the appearance of violent

nausea. While answering, she seemed to have nausea attacks and frequently threw up some gastric-fluid-like substance into a washbowl. To my query of whether she felt cold in the hands and feet, she said she felt them considerably cold. On the basis of these findings, I thought *goshuyuto* might be the application targeting cold in the extremities, headache, and vomiting, and gave her on site a dose of the extract dissolved in half a cup of hot water. I always have some doses of *goshuyuto* extract in my bag with me when I make a patient's house call. It may be unbelievable but vomiting stopped before me and in about five minutes, such rampant headache was reduced to only a fraction of the intensity she felt originally. And she was able to rise from the recumbent position and sit on the floor.³⁾

This is the case that showed a rapid relief of headache after the administration of *goshuyuto* on a potion basis. It is very rare that such a marked effect was obtained in day-to-day clinical practice. It may not be extremely rare but it does not mean that any patient shows such an effect. The person who is as responsive as this patient will not have a migraine recurrence by taking this medication for a long period of time, like several months to one year. In other words, migraines can be cured.

Case Report 4:

The patient was a parous female of 27 years old. Before becoming pregnant, the patient used to have headaches. In the 13th week of pregnancy, she had a headache attack disabling her to do family work. She did not take analgesics thinking of adverse influences of the drug on her fetus. She was given *goshuyuto* on the moment. On her way home, she fell asleep in the train. She also had a good night sleep and when she woke up, she found the headache disappeared. Attention is called to it that during the period of pregnancy, the medication should not be administered without careful consideration.⁴⁾

In many of women with migraine, a sharp decrease in the frequency of the attack due to pregnancy has generally been observed together with relief of migraine symptoms. However, this is

not applicable to any woman. Indeed, the research by Ratinahirana et al. reports that cases of frequency and symptoms became worse in pregnant woman represented 6.8%.⁵⁾ Moreover, the research by Maggioni et al. reports that improvements in women experienced pregnancy twice or more were not as good as in the first time pregnancy.⁶⁾

Although not many headaches get worse with pregnancy, they are not scarce. In any event things are significantly serious to the people who suffer from headaches. Kampo medication offers only a few choices but they can be expected to yield safe and high efficacy. One of these choices is *goshuyuto*, on which other cases were reported.

3. Clinical Study on *Goshuyuto* for headaches

Many clinical experiences similar to the above have been reported and it has become a kind of common knowledge in Japan that *goshuyuto* is effective for migraines. However, details of this medication have not been elucidated as to under what environments migraines occur in what types of persons and efficacy percentages. Thus, some researchers have conducted clinical studies on these points. The studies included tension headaches as well as migraines. So, though the efficacy of migraine has not thoroughly been elucidated in these studies, the data are very useful from a clinical view point. Introduced hereunder are representative studies.

1) Study by Maeda et al.: Efficacy of *Goshuyuto* for Chronic Headache⁷⁾

Goshuyuto Extract was administered to 147 patients with chronic headache (Male 46, Female 101) to assess the overall improvement, general safety, and usefulness. The details of the cases are: vascular headache 47 cases, muscle-contraction headache 46, and combined headache 54. Overall improvement comprises: markedly improved 16 cases (10.9%), improved 61 (41.5%), slightly improved 54 (36.7%),

and remained unchanged 16 (10.9%). Usefulness consists of: extremely useful 18 cases (12.2%), useful 61 (41.5%), slightly useful 53 (36.1%), and not useful 15 (10.2%). The cases that achieved useful and higher effects for each type of headache are: vascular headache 61.7%, muscle-contraction headache 47.8%, and combined headache 48.1% with many cases of improvement in vascular headache. Production of effects was seen in 51.7% of cases within two weeks.

The above is a case series using *goshuyuto*. Despite the low level of evidence, efficacy of the medication is clearly demonstrated. The medication tends to be more effective for vascular headaches (migraines). However, since headaches that were originally migraines must have been included in other types of headache, this medication may be said to be more effective for migraines.

2) Study by Odaguchi et al.: Study on the administration of *goshuyuto* in the same dose to patients with chronic migraine.⁸⁾

The subjects participated in this study were 49 persons who, in principle, took some medicine once a month for headache attacks due to chronic primary headache (male/female=6/43, age 43±14), and scores were given to improvement in the severity of headache, improvement in the frequency of headache episodes, improvement in the cold sensation, improvement in menstrual pains, and improvement in stiff shoulders, which were then divided on the basis of given standards into two groups – Responder Group (R-Group 36 patients) and Non Responder Group (N-Group 13). And then the patients in the two groups were equally administered *goshuyuto* Extract in the same dose of 7.5g x 3/day for a month and the exact test of a contingency table was performed.

The results indicated that R-Group had significantly high points in “do not get motion sickness” (R-Group 34 patients, N-Group 8: P=0.01) among subjective findings and “have tenderness in the paraumbilical region” (R-Group 15 patients and N-Group 1: P=0.04) among objective findings. The study also indicated that R-Group tended to show

higher points in the finding of subjective cold sensation, finding of discomfort with pain when pressed in the epigastric region (“kyokyo-kuman”), facial hot flushing, and non-finding of tenderness in the sigmoid region. The findings that exceeded 0,5 in both sensitivity and peculiarity were subjective cold sensation, menstrual pains, hard epigastrium with a sensation of heaviness (“shinka-hikou”), and tenderness in the region between umbilicus and epigastric fossa, whereas non-findings that exceeded 0,5 in both sensitivity and peculiarity are perspiration, irregular menstruation, weak abdominal power, and flaccid lower abdomen.

This study investigated to find differences in the signs and symptoms between the patients group that obtained efficacy (Responder Group) of *goshuyuto* and the patients group that had poor efficacy (Non-Responder Group) and is a groundbreaking study as a step forward for clarifying the whole picture of *goshuyuto*. The results prominently appear in subjective symptoms and abdominal diagnostic findings, offering clues for future applications of the medication.

3) Study by Hayashi et al.: Clinical Study on *Goshuyuto* for Chronic Headache⁹⁾

Goshuyuto was administered to 32 patients with chronic headache with the result of efficacy at 34.4%. However, factors associated with the efficacy of *goshuyuto* (level of $p < 0.05$) were not recognized and the medication may not be said to be specifically effective for any one of migraine, tension headache and combined headache.

This study investigated more than 100 items of subjective and objective signs and symptoms to elucidate the *sho* of *goshuyuto* and multivariable analysis was conducted. The methodology was quite objective, eliminating views from the angle of Kampo medicine to a maximum extent. The result from this methodology was that there were almost

no signs and symptoms associated with *goshuyuto*. The study by Oda et al. was conducted from somewhat Kampo point of view, whereas as this study excluded unfair views favoring Kampo medicine when possible, it may be natural that the results differ between the two studies. This is an aspect of *goshuyuto*. In addition, although the result showed that efficacy was not related to the type of headache, some of tension headaches and combined headaches may have progressed to migraines.

4. Target in the use of *goshuyuto* for migraine

Goshuyuto first appeared in “Shang han lun”. The section of “kechchin” disease (power to stay alive almost extincts) of the prescription text has the description meaning “*goshuyuto* is applied for the conditions of feel like vomiting but nothing is brought up, throw up liquids, person with headache...” The medication is now applied referring to the description. Traditional Chinese medicine uses the medication for vomits caused by excessive fluids in the cold stomach, whereas in Japan, the medication is an important prescription applied for migraines as a first choice medicine. *goshuyuto* is beneficial, in theory, for headaches caused by cold evil invading into the condition lacking yang Qi or heat energy, which reversely flows upward through the liver meridian. It may be extremely difficult to grasp signs and symptoms that can clinically support this theory.

Most recently, the study by Odagukuchi et al. has made substantial progress in elucidating indications for *goshuyuto* and has made a clear distinction between responders and non responders to *goshuyuto* by investigating subjective and objective findings in detail. The content of the investigation shows that the characteristics of *goshuyuto* appear in the subjective symptoms and abdominal *sho*. Especially abdominal *sho* confirms the content of the findings described in