Usefulness of Japanese herbal Kampo medicine Goreisan for Chiari Malformation type1 with Syringomyelia

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Introduction

The natural history of Chiari malformation type 1 (CM-1) and syringomyelia is unpredictable. Spontaneous resolution of syringomyelia without surgery has been reported and the strategy for the remaining syringomyelia after surgery was unclear. The purpose of this study was to investigate the efficacy of Goreisan for symptoms and size of syringomyelia associated with CM-1. Goreisan is a Japanese herbal Kampo medicine and most popular Kampo in treatment of prevention of postoperative recurrence of chronic subdural hematoma in Japan.
Materials and methods

Three women with syringomyelia due to Chiari malformation type 1 were enrolled in this study. The mean age was 47.3 years (range: 38-59 years) and the mean levels of syringomyelia was 14.3 levels (range: 12-17 vertebral levels). Goreisan (TJ-17, Tsumura, Japan) was used 7.5 or 5.0 g per day for two remaining syringomyelias after surgery and one mild expanded syringomyelia without surgery. The mean follow-up periods from using Goreisan was 23 months (range: 22-25 months). The size of syringomyelia was evaluated by T2-weighted axial images (TE/TR = 65/3722 msec, FOV 38 cm, slice thickness 4 mm, Signa HDxt 1.5T, GE Healthcare, Waukesha, WI) by one neurosurgeon and three radiological technichians using CTL TOP coil obtained T2-weighted sagittal images (TE/TR = 105/3250 msec, FOV 38 cm, slice thickness 4 mm).
Results

The size of syringomyelia with CM-1 in all cases decreased, significantly in nonoperative case. Furthermore, Goreisan was effective for their headache and unchanging for sensory disturbance in the arm.

Figure 1: Pre- and post-administeral MR images of the cervico-thoracic spine in the non-operative case. This 42-year-old woman presents with severe neck pain after moving and numbness in her left forearm. (A, B, C, D): T2-weighted sagittal images show syringomyelia from C3 to T5. (E, F, G, H): T2-weighted axial images reveal that the syringomyelias with mixed intensity extend into the left posterior horn at the T2 level. The size of the syringomyelia is a little larger (B, F) at the beginning of administering Goreisan than before one year. They are smaller at 6 months (C, G) and 9 months (D, H) after administering Goreisan.
Figure 2 Post-administeral MR images of the cervico-thoracic spine in the operative case. This 58-year-old woman presents with numbness in left upper arm. (A, B, C): T2-weighted sagittal images show syringomyelia from C2 to T5. (D, E, F): T2-weighted axial images reveal the syringomyelias at the C4 level. (G, H, I): T2-weighted axial images reveal the syringomyelias extend into the left posterior horn at the T2 level. The size of the syringomyelia at 14 months (C, F, I) after administering Goreisan is a little larger, $682 \text{ mm}^2$, than $677 \text{ mm}^2$ at 2 months (A, D, G) and $657 \text{ mm}^2$ at 9 months (B, E, H) after administering Goreisan.

Figure 3 Pre- and post-administeral MR images of the cervico-thoracic spine in the operative case. This 38-year-old woman presents with neck pain, sensory disturbance in right arm. (A, B, C): T2-weighted sagittal images show syringomyelia from C2 to T4. T2-weighted axial images reveal that the syringomyelias extend into the right posterior horn at C4-5 level (D, E, F), and C6-7 level (G, H, I). The size of the syringomyelia at 12 months (C, F, I) after administering Goreisan is a little smaller, $641 \text{ mm}^2$, than $678 \text{ mm}^2$ at the beginning of Goreisan (A, D, G) and $699 \text{ mm}^2$ at 6 months (B, E, H) after administering Goreisan.
Discussion

Indications of surgery for patients with Chiari malformation type 1 (CM-1) and syringomyelia are controversial issues because the natural history of nonsurgical and postoperative syringomyelia associated with CM-1 is incompletely understood. Some cases of spontaneous resolution of symptoms and syringomyelia in adult were reported (1, 2). In symptomatic patients without surgery, mild symptoms, such as headaches and nausea, often improved, whereas ataxia and sensory disturbance tended not to improve spontaneously. Most asymptomatic patients with CM-1 remained asymptomatic (93.3%), even in the presence of syringomyelia (3). In children with syringomyelia associated with CM-1, a reduction in tonsillar descent was substantially more common than an increase. Radiological changes on MR images did not correlate with neurological examination findings, symptom progression, or the need for future surgery (4). Decision making of surgery or conservative therapy might be challenging, however, an anxiety for worsening symptoms by increasing size of syringomyelia led us to using Goreisan not surgery.

Goreisan, a Japanese herbal Kampo medicine, is a mixture of five herbs including Alismatis Rhizoma, Poria, Polyplus, Atractylodis Lanceae Rhizoma, and Cinnamomi Cortex. Previous studies have suggested Goreisan had a potential mechanism of hydrostatic modulation and inhibition of aquaporin-4 (AQP-4) caused by Poria, Polyplus, Atractylodis, and Lanceae Rhizoma (5,6).
Aquaporins are protein channels providing water transport across cell membranes. Among them, AQP4 is the most abundant in the central nervous system and is involved in all aspects of bulk water movement. In the brain and spinal cord, AQP4 is expressed primarily in astroglia, most abundantly in membranes at the tissue-blood or tissue-CSF interfaces, including astrocytic end-feet surrounding capillaries, the glia limitans, and ependyma (7). Since AQP4 can provide bidirectional transport, it can allow transport in or out, depending on the circumstances. Indeed, in the brain AQP4 has been shown to play a dual role. During cytotoxic edema where the blood-brain barrier is intact, it provides a route for water influx, facilitating edema (8). However, during vasogenic edema, it is responsible for water elimination (9).

The AQP4 expression in syringomyelia have been studied. During initial presyrinx state in rabbits, there was an increase in spinal cord water content and downregulation of AQP4 expression (10). As the edema resorbed, AQP4 expression increased, although it did not reach the baseline level. The downregulation of AQP4 was concluded the main reason for edema formation. This means that AQP4 plays a major role in the elimination of extracellular water from the spinal cord (10). However, during the late stage of syrinx formation in rats, a decrease in AQP4 expression in the communicating (11) and noncommunicating syringomyelia (12) without statistical significance. The results of this study indicate that AQP4 most likely does not play a major role in chronic syringomyelia.
Its slight downregulation during the initial stage of syrinx formation is possibly a compensatory mechanism. This effect is not present during the late stage of syringomyelia, and AQP4 is most likely not involved in the pathophysiology of syrinx cavity formation. Loss of integrity of the barrier with liquid entering the interstitial space of the spinal parenchyma may contribute to enlargement of the canal and progression of syringomyelia. In nonoperative case, syringomyelia for 8 years was already in chronic stage, however, Goreisan effected to reduce the syringomyelia size. Goreisan might have other mechanisms in reduction of syringomyelia associated with CM-1. In two postoperative cases, the effect of Goreisan was not enough for reduction of syringomyelia because some inflammation postoperatively might cause the remained syringomyelia.

It should be acknowledged that the measurements of syringomyelia size were performed using T2-weighted images not T1-weighted image. Therefore the syringomyelia size might include the interstitial edema (13) and the size of interstitial edema not true syringomyelic cavity might be reduced in this case. More cases using Goreisan for syringomyelia associated with CM-1 will be needed to evaluate these mechanism in the future.
Summary points

Japanese herbal Kampo medicine Goreisan was effective for symptoms such as headache and syringomyelia associated with Chiari malformation type 1.

references
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