Kampo Medicine - Current Research

Effects of Goreisan in Pediatric Acute Gastroenteritis

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Introduction

Pediatric acute gastroenteritis is a general term that describes disorders in infants and small children presenting the sudden onset of acute vomiting and diarrhea as primary symptoms. The condition is most commonly due to viral infection, but occasional instances of bacterial infection and food poisoning are also known. Although the majority of these viral infections in infants and small children have been attributed to rotaviruses, noroviruses have also recently been found to be extremely common. Infection typically follows a single-peak or double-peak pattern from winter into spring each year.

Rotavirus-induced gastroenteritis ordinarily presents with vomiting, followed by persistent watery diarrhea, with a fever that lasts for 1 to 3 days. Vomiting and fever are common in the early stage of the disease, and these symptoms, along with the subsequent diarrhea, normally resolve without treatment within a week. However, dehydration can develop, and if left untreated can result in death. In addition, even after the diarrhea resolves, several weeks can be required for full recovery of the intestinal mucosa, and the child's condition may be complicated by the development of secondary lactose intolerance. As a rule, gastroenteritis due to a norovirus is characterized primarily by vomiting, and diarrhea is relatively mild.

This condition is treated primarily by stopping the vomiting and by treating dehydration. The usual treatment is domperidone (Nauzelin®) by oral administration or as a suppository, together with fluid supplementation. Since the early-stage disease is characterized primarily by vomiting, oral intake can be problematic, making it difficult to give either medication or fluids by mouth. Recent findings suggest that early treatment with *goreisan* (Wuling san, 五苓散) can provide dramatic relief in many cases. These findings are supported by considerable research and numerous case reports. This treatment is now becoming widely accepted in Japan.

Research done to date is introduced below, with a summary of the methodologies used.

Research To Date

Goreisan is referenced in the classic Chinese texts "Shang Han Lun (Discussion of Cold-induced Disorders)" and "Jin Gui Yao Lue (Essentials from the Golden Cabinet). Mention is made in several chapters. Specifically, Article 74 of the “Shang Han Lun” states that "... when the patient is thirsty but vomits when he or she drinks water, the condition is termed 'Water Reverse'. The primary treatment is *goreisan*." This applies to pediatric acute gastroenteritis. Such applications have been researched for over 50 years and are used primarily in the field of pediatric medicine.

Like other Kampo medication, *goreisan* is given primarily by oral administration. However, because it is often prescribed for patients who are vomiting, and because of the importance of rapid effectiveness, physicians also frequently prepare and administer *goreisan* in the form of a suppository or enema in children.

In 1987, Morishima published research on the use of *goreisan* Enemas in the treatment of pediatric vomiting where oral administration was complicated by vomiting or other difficulties[1]. This is the first reported case of the use of *goreisan* by a route other than oral

administration. Subsequently, in 1995, Koga and colleagues investigated the administration of *goreisan* extract in suppository form. Of 45 patients between 1 and 8 years of age who had acute gastroenteritis or viral gastroenteritis related diarrhea and vomiting and presented the primary complaint of vomiting (28 boys and 18 girls), the researchers found that *goreisan* suppositories were effective in 36 patients (78.3%) and somewhat effective in 6 patients (13.0%). During the same period and season in the following year, those researchers used Western medical treatment without *goreisan*. They monitored patient progress during both years, and reported that, in children experiencing the same extent of vomiting, intravenous fluid support was required 6 times more frequently without *goreisan* than when *goreisan* was included in the treatment regimen[2].

The use of *goreisan* as a suppository was developed out of necessity because of the difficulty of effectively administering oral medications to patients who are prone to vomiting. The original instructions for the treatment of "Water Reverse" conditions called for the oral administration of extremely small amounts of *goreisan* liquid very gradually, in order to control vomiting. However, current research indicates that internal administration can provide equivalent effectiveness. These two studies are the pioneering works in the field.

Ongoing Research

(1) Study by Fukutomi et al.[3]

Fukutomi and colleagues selected 211 children age 6 months to 11 years (mean 3.7 ± 2.3 years) who came to the hospital with the primary complaint of vomiting and in whom acute gastroenteritis was suspected. The researchers dissolved *goreisan* extract 2.5 g in 20 mL of warm physiological saline solution, and administered the resulting liquid by catheter as an enema. If the enema stopped the vomiting, the treatment was considered to be effective. If the vomiting continued but lessened in severity, treatment was considered somewhat effective, and if the vomiting continued to the point of dehydration requiring supplemental i.v. fluids, the treatment was considered to be ineffective. The overall efficacy rate for the *goreisan* enema was 82.9%. Efficacy by age range was as follows: 80.0% at 0 years of age, 80.0% for 1-year-olds, 85.7% for 2-year-olds, 82.1% for 4-year-olds, 86.5% for 5-year-olds, 88.2% for 6-year-olds, 80.0% for 7-year-olds, and 83.3% for 8-year-olds. The *goreisan* enema was effective in all treated children 9 years of age or above (the number of patients in this age group was very small).

The researchers also investigated the efficacy of *goreisan* in relation to the number of times the child had vomited before being brought to the hospital. They found that better results were achieved in cases where fewer vomitings had occurred. Symptoms before coming to the hospital were vomiting in 72 cases (34.1%), and vomiting and fever in 87 cases (41.2%). Where fever was noted, it was measured at 37.5°C to 38°C in 35.6% of patients, 38°C to 38.5°C in 56.3%, and more than 38.5°C in 8.0% of cases. Additional symptoms included abdominal pain in 32.2%, and upper respiratory inflammation such as cough and nasal drip in 11.8% of cases.

(2) Study by Yoshida[4]

Yoshida used *goreisan* suppositories, already widely accepted for pediatric applications by Kampo pediatric specialists in a double-blind randomized clinical trial (DB-RCT). For the comparator drug he used *hochuekkito* (Bu-Zhong-Yi-Qi-Tnag, 補中益気湯) suppositories prepared by the same method. Targeted subjects

were 34 children (21 boys and 13 girls age 1 to 9 years, mean age 3.9 years) who had vomited at least 3 times in the 24-hour-period before coming to the hospital, and who presented with nausea and/or vomiting. The children were treated with numbered suppositories using the double-blind method. Thirty minutes after administration, the children were given water to drink, and the effectiveness of treatment was evaluated on the basis of whether or not this induced nausea and/or vomiting.

There was no statistically significant difference between the *goreisan* suppository group of 16 children (10 boys and 6 girls) and the Hochu-ekki-to group of 18 children (11 boys and 7 girls) with regard to age, sex, number of vomitings, presence or absence of diarrhea, or underlying disease. Within the *goreisan* group, treatment was effective in 12 patients (75%), somewhat effective in 2 patients, and ineffective in 2 patients. In the Hochu-ekki-to group, treatment was effective in 5 patients (28%), somewhat effective in 2 patients, and ineffective in 11 patients.

(3) Study by Hashimoto[5)]

Hashimoto treated acute gastroenteritis patients with *goreisan* enema (297 children) or *saireito* enema (263 children). The mean number of days before coming to the hospital was 1.2±4.2 for the *goreisan* group and 1.0±1.0 for the *saireito* group. The study showed no significant difference in the efficacy rate between the two groups (*goreisan* 84.8%, *saireito* 85.6%). There was also no significant difference in the efficacy rate with regard to patient age, fever, or number of vomitings.

These findings indicate that *goreisan* can be highly effective against pediatric acute gastroenteritis. The reports show an efficacy rate of 75% to 84%, proof of the usefulness of *goreisan* in treating this condition.

Administration was either by suppository or by enema. Since the results showed no significant difference between these two methods, medical practitioners should feel free to choose the method that is easiest for them and for their patients.

The Yoshida study (DB-RCT) was performed using *hochuekkito* as the comparator drug. That prescription, which is classified as a Qi Tonic prescription, is not considered to be effective in treating diarrhea from conditions such as infectious enteritis. This study, performed with the consent of patients and guardians, showed that *hochuekkito* was ineffective while *goreisan* was highly effective, as expected. The study by Hashimoto used prescriptions of *goreisan* and *saireito. Goreisan* is included within the formulation of *saireito* as an ingredient, so these two prescriptions were essentially the same. Results for these two prescriptions were nearly identical, as would be expected.

Closing Remarks

As long as dehydration can be prevented, pediatric acute gastroenteritis, due to rotavirus or norovirus infection, is not a particularly serious condition. However, most patients improve quickly if given early treatment with *goreisan* extract in the form of a suppository or enema. Out of consideration for the child's symptoms and the worry and strain on the parents, it is obviously important to relieve this condition as soon as possible.

Additionally, in the developing nations where modern medical procedures such as intravenous

drip might be unavailable, these prescriptions and treatment methods could provide an extremely important tool for reducing mortality. It is our hope that this research will prove useful to those ends.

Reference

1) Morishima A: Effectiveness of *goreisan* enema in the treatment of pediatric vomiting. Kampo medical treatment 6:30-32, 1987
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4) Yoshida M: Effectiveness of *goreisan* suppository in the treatment of pediatric vomiting. Toyo Igaku 28(3) 36-38, 2000
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