

Kampo Medicine - Current Research

Essentials of Pediatric Kampo Medicines (2)

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2. Kampo medicines with emotionally stabilizing functions

Among various crude drugs, even though there are certain differences in the strength of the effects, many drugs have emotionally stabilizing functions and if Kampo formulas contain several such crude drugs, they may correspondingly be expected to manifest such emotionally stabilizing actions. It is well-known that mind and body can only hardly be separated in children and any mental problem has a high tendency toward somatization. The relevant Kampo medicines act simultaneously on stabilizing the emotional state and improve the physical condition (for example, improve the gastrointestinal function) and are precisely for this reason well suited for children. Characteristics of these formulas include them being mild, not inducing drowsiness, dry mouth or gastrointestinal dysfunction or similar side effects. Therefore they are not suited for the relief of severe symptoms, but they can be considered to act by transforming both mind and body of the children little by little (providing relief). The use of psych mimetic drugs in pediatrics is currently more difficult than in adults. Kampo medicines therefore can probably considered to be easily applicable drugs for emotional and psychological problems.

Yokukansan, *kanbakutaisoto*, *saikokaryukotsuboreito* can be listed as representative tranquilizers that can be used in children.

Yokukansan (or *yokukansankahangechinpi*) is a formula that has been devised in ancient times for pediatric convulsive diseases and because of its sedative actions it is therefore indicated for conditions associated with irritability and easy excitation. *Kanbakutaisoto* and *saikokaryukotsuboreito* are thought to have mainly anti-anxiety action, but this may not always be taken literally. Based on experience is *kanbakutaisoto* the drug of first choice for pavor nocturnus

or episodic apnea and so is *yokukansan* for diaphragmatic tics.

In recent years the importance of developmental disorders in general practice has increased, in particular for pervasive developmental disorders or attention deficit hyperactivity disorder and the above mentioned three preparations are useful and reportedly have been found to be effective even in patients non-responsive to methylphenidate¹¹⁾. Apart from the mentioned preparations *orengedokuto*, *kamikihito* etc. can also be used.

* *Kanbakutaisoto*: anti-anxiety activity, improving gastrointestinal function

* *Saikokaryukotsuboreito*: sedative, anti-anxiety activity, anti-inflammatory activity

* *Yokukansan*: strongly sedative, improving gastrointestinal function, improving blood circulation, the original text recommends simultaneous application to mother and child.

3. Kampo medicines with gastrointestinal function improving actions

In Kampo medicine gastrointestinal function are expressed as "spleen/stomach = digestive system". The meaning of this term is thought not to be restricted simply to the gastrointestinal function, but includes the more comprehensive concept of maintaining the functioning of the entire body. Naturally, both aspects are closely related, but for the sake of convenience I would like to discuss here the following 2 separately.

1) Treatment of diseases of the gastrointestinal tract in a general sense

Basically, gastrointestinal symptoms representing problems in pediatric clinical practice include vomiting, diarrhea, constipation and abdominal pain. These may be caused by a variety of pathologic conditions and while, needless to say, their differential diagnosis and treatment is very important, Kampo medicines may prove to be helpful in cases difficult to treat with Western medications.

It has long been known that oral administration of Goreisan is markedly effective during the early phase of acute viral gastroenteritis presenting mainly as vomiting. Yet, in recent years the use of dissolved extract preparations as enemas or suppositories has also been reported. Regarding these application forms Yoshida¹²⁾ and others have published many reports, each of which indicates, a quick inhibition of the vomiting and improvement of the general condition had been achieved.

Like in adults too *daikenchuto* is effective for chronic constipation¹³⁾. Although it is not a cathartic, it promotes peristalsis by improving blood flow in the intestinal tract¹⁴⁾.

Shokenchuto warms the body and relaxes smooth muscle tone and therefore is used to treat recurrent umbilical colics, while *rikkunshito* is used for gastroesophageal reflux and thus has been variously studied in the field of pediatrics¹⁵⁻¹⁶⁾.

(1) For Vomiting

*Vomiting in the early phase of acute gastroenteritis: Goreisan

*Gastroesophageal reflux (GER): *rikkunshito*
Slightly increasing peristalsis of the stomach results in an alleviation of the vomiting.

(2) For diarrhea

*In case of prolonged diarrhea following acute gastroenteritis: *ninjinto*, *shinbuto*

By warming the abdominal cavity the decreased functioning improves and *shinbuto* simultaneously improves also the water metabolism.

*Prescription for diarrhea in the absence of any organic causes: *keihito*

This formula is similar to the above mentioned but even milder.

(3) For constipation

*The below mentioned *keishikashakuyakuto* decreases smooth muscle tone, or used with added rhubarb having laxative action in the formula: *keishikashakuyakudaioto*

*A formula particularly for warming the intestinal tract and improving blood flow to increase peristalsis: *daikenchuto*.

(4) For abdominal pain

*Formula for warming the body and simultaneously relieving smooth muscle tone: *shokenchuto*, *keishikashakuyakuto*

Used for example for recurrent umbilical colics, irritable bowel syndrome.

2) Treatment of digestive organs and not directly related symptoms and diseases using the "Kampo medical concept of digestive function"

Maintaining the function of the body depends according to Kampo medical concepts on respiratory function (lung), digestive function (spleen and stomach) and the genetic life force (kidney). In developing children the digestive function is viewed as particularly important among these. In this case digestive function refers not simply to the functions of the digestive organs in the Western medical sense, but is presumed to mean the energy production system related to food ingestion in general. In Kampo medicine impairment of digestive functions for any reasons is thought to easily cause secondary generalized dysfunction or else functional disorders of various parts of the body. Thus, therapy has the meaning of rectifying the digestive functions as causative factors in order to bring about improvement of symptoms / diseases not directly related to the digestive organs. This is a typical Kampo concept and can be simplified in everyday language as 'harmonizing the gastrointestinal tract → recovering health → possibility that diseases may improve'. Representative preparations are *shokenchuto*, *rikkunshito* and *hochuekkito*. Preparations improving this kind of decreased body functions are called "Qi supplementing formula" and represent a characteristic of Kampo treatment.

Shokenchuto is the most frequently used formula and the preparation of first choice from infants to children in the first grades of elementary school,

where it is directed at generalized symptoms like cold sensitivity and lack of vitality as secondary manifestations of eating too little, recurrent abdominal pain, soft stools and similar gastrointestinal symptoms. *Rikkunshito* improves the general conditions like lack of appetite, abdominal distension as well as systemic symptoms like bowel mobility disorders or lassitude, while *hochuekkito* is indicated in cases of easy fatigability, heaviness of arms and legs etc. as well as marked generalized malaise. These two preparations are often used for comparatively older children, like higher grade elementary school students. Moreover, by "improving the digestive functions" they could possibly provide an effective supplementary therapy in cases, where the patients present with diseases other than those of the digestive organs, like for example allergic diseases, infections and similar conditions marked by derangement of immune functions. Within the scope of the author's research no substantial amounts of results could be found regarding this kind of Kampo medical application, but there is a close correlation with the already earlier mentioned concept of treating perianal abscesses with *juzendaihoto* and atopic dermatitis with *hochuekkito*¹⁷⁾ and the like.

**Shokenchuto*: Warms the body and relieves excessive tension of the intestinal tract. In cases of generalized symptoms like sensitivity to cold and lack of vitality as secondary manifestations of eating too little, recurrent abdominal pain, soft stools and similar gastrointestinal symptoms. It is the formula of first choice from infants to children in the lower grades of elementary school.

**Hochuekkito*: Slightly warms the body and improves a generalized hypotonic state. Used for patients who fatigue easily, wish to lie down and complain of generalized malaise including heaviness of arms and legs.

**Rikkunshito*: Slightly warms the body and improves in particular a hypotonic intestinal tract and the water metabolism. If lack of appetite,

abdominal distension and similar symptoms of stagnant peristalsis are observed, or in case of lassitude.

(Many Kampo medicines used for other purposes than improving digestive function too obviously or casually include crude drugs acting on decreased digestive functions and therefore are often used for secondary treatment regimens. I believe this confirms, that the importance of the digestive function had been recognized since ancient times.)

4. Kampo medicines with sedative actions

Some Kampo medicines have an affinity for the respiratory tract and some formulas have been used for the treatment of respiratory disorders. Naturally, in cases of respiratory failure or similar severe diseases various modern Western medical therapies are far more effective, but some Kampo medicines have unique antitussive properties and can be used as antitussives in children.

In pediatrics the first preparations that come to mind are *shoseiryuto*, *makyokansekito* and *bakumondoto*. In conjunction with their antitussive activity these preparations have different actions on the respiratory tract. *Shoseiryuto* inhibits airway secretions while also having a warming effect. *Makyokansekito* too inhibits airway secretions, but is considered to have more marked anti-inflammatory actions. Conversely, *bakumondoto* promotes airway secretions and thus has a moistening effect.

Accordingly, in patients presenting with copious thin white sputum, for example asthmatic bronchitis, *shoseiryuto* is used, but in patients with infective inflammation, presenting mainly as copious amounts of yellow sputum like for example in acute bronchitis or pneumonia, *makyokansekito* is considered, while in slightly dry conditions with little sputum but continuing cough *bakumondoto* is used as a rule. *Bakumondoto* reportedly has the same antitussive effect as dextromethorphan¹⁸⁾.

A trial is considered worthwhile, when the effects of the general antitussive drugs seems to be insufficient. Moreover, *saibokuto* is used for psychogenic cough.

**Makyokansekitō*: Anti-inflammatory, strong expectorant effect, in cases of copious yellow sputum.

**Shosaikoto*: Since it acts mainly as an expectorant, it is used for copious amounts of thin, white sputum, and frequently also for allergic rhinitis (in cases of large amounts of airway secretions the combination of *makyokansekitō* and *shosaikoto* enhances the antitussive effect).

**Bakumondoto*: Is suited for chronic, dry (no – little sputum) cough, since it moistens the airway and has relatively strong antitussive effects.

**Saibokuto*: Combined formulation composed of *shosaikoto* and *hangekobokuto*. In the past is was frequently used during the intermissions in cases of pediatric bronchial asthma¹⁹. It is also effective for psychogenic cough and tic-like cough.

Chronic paranasal sinusitis is in routine pediatric care often related to cough, but equally often no effective Western medical pharmaceutical therapies can be found. In these cases Kampo medicines can provide a useful therapeutic means. *Kakkontokasenkyoshini* and *shiniseihaito* can be listed as therapeutic agents for the treatment of chronic paranasal sinusitis. Theoretically, *shiniseihaito* is used for conditions with more marked inflammation and has reportedly been useful in cases where low-dose macrolide therapy had been ineffective²⁰.

When nasal obstruction is prominent in cases of paranasal sinusitis

**Kakkontokasenkyoshini*: Slightly warming, improving blood flow.

**Shiniseihaito*: Moistens and cools, helps discharge viscous nasal secretions (viscous nasal discharge, sputum; yellow).

5. Kampo medicines with growth and development supplementing functions

In Kampo medicine there are formulas to aid the growth and development of children. The world's oldest pediatric textbook published during the Sung dynasty: "Xiao er yao zheng zhi jue" (around 1107) lists *rokumigan* as a representative formula, that seems to have been used for inherently weak children. Although it is naturally not possible to change the congenital disposition, there can possibly be conditions associated with decreased activity, or where greater maturity can be expected to lead to a remission of symptoms. Also, combined use of Kampo medicines with actions improving digestive functions like *hochuekkito* and the like make the treatment even more effective.

* *Rokumigan*: In cases were delayed growth / development or decreased activity is observed, or else in cases of decreased activity due to chronic disease etc.

6. Kampo medicines with actions regulating water metabolism

Water comprises approximately 60% of the human body. Regulating functions related to any insufficiencies, excesses or imbalances are very important for the body. Sudden loss of water resulting in dehydration, renal or cardiac failure may be associated with severe edema and acute encephalopathy can cause cerebral edema etc. Needless to say, these conditions represent an important therapeutic topic in modern medicine. However, even not so severe conditions resulting in only minimal insufficiencies, excesses or uneven distributions are known to cause systemic or local symptoms. In pediatric primary care diseases associated with even minimal excesses or uneven distributions may cause headache, vertigo, lethargy, malaise, nausea, loss of appetite and similar symptoms are treated. The actions are not simply restricted to promotion of miction, but are considered to concentrate more on a balancing of the water distribution. In Kampo medicine the water

distribution has since ancient times been regarded as important and several corresponding Kampo medicines have been formulated. Also, even if water regulation is not the primary target of the used formulas, many of them contain water regulating crude drugs.

Representative preparations used in pediatrics are *goreisan*, *choreito*, *ryokeijutsukanto*, *hangebyakujutsutenmato* etc.

**Goreisan*: The most frequently used formula, for nausea during the early phase of gastroenteritis, headache related to atmospheric pressure etc.

**Choreito*: Simultaneously with promoting water excretion it cools the body or for inflammations of the lower urinary tract like cystitis; in combination with *orengedokuto* it is used for atopic dermatitis associated with much exudate.

**Chokeijutsukanto*: In cases of marked malaise, difficulties getting up in the morning and orthostatic regulation disorders etc.

**Hangebyakujutsutenmato*: For orthostatic regulation disorders²¹⁾ characterized by vertigo, loss of appetite etc.

Adverse reactions of Kampo medicines

1. Main side effects caused by the drug components

Care is required when combining 2-3 formulas, because many Kampo medicines contain licorice and therefore could cause pseudohyperaldosteronism. Naturally, their use in patients with hyperaldosteronism, myopathies or hypokalemia is contraindicated.

The main component of ephedra herb is ephedrine and thus could possibly cause palpitation, tachycardia or similar symptoms when used together with sympathomimetic drugs. Also, a mild state of excitation may cause in some patients insomnia and occasionally digestive symptoms like loss of appetite may also develop.

Shosaikoto is known to cause in adults interstitial pneumonia, but this reaction has almost not been reported in children. The most frequently reported adverse reaction in children is *saireito* induced

cystitis. Presumably this is an influence of components of the *shosaikoto* portion within *saireito*²²⁾, but has not been reported in relation to treatment with *shosaikoto* alone. Many extract preparations use lactose, so that they should not be used in cases of lactose intolerance²³⁾. There is no sizable amount of reports from the field of pediatrics dealing with allergies to crude drugs. In any case, Kampo medicines are generally considered to have few side effects^{22,23)}.

Table 3 Children's doses according von Harnack

Age conversion (when defining adult as 1)				
12 years	7 years 6 months	3 years	1 year	6 months
2/3	1/2	1/3	1/4	1/5

2. Could mistaking the indication be a factor possibly aggravating diseases?

Strictly speaking this does not refer to adverse reactions, but in case the indication has been mistaken, the possibility of an aggravation of the symptoms cannot be ruled out. An elementary distinction would be between heat and cold properties. Among Kampo medicines some warm and some cool the body, so that prolonged use of strongly cooling agents in patients sensitive to cold, or conversely agents warming the body in patients sensitive to heat could possibly result in adverse reactions and should therefore be kept in mind.

Application outside the recommended children's dose and indication

Since Kampo medicines are covered by the insurance 30 years have passed, but explanatory booklets about generally used Kampo medicines still include the remark, that "safety for children has not been established" (there is no experience). Thus Kampo medicines have like many Western medications necessary for children many pediatric pharmaceutical off-label problems. Currently, no solution seems to be in sight yet.

For the same reasons given above the children's doses for Kampo extract preparations too are still not listed in those explanatory booklets. Generally, they are calculated according to the von Harnack method based on body surface (Table 3), or by conversion of body weight, but occasionally the dose has to be increased depending on the pathologic condition, so that those values cannot be much more than rough estimates.

Moreover, it should be noted, that the daily dose of extract formulas may vary depending on the manufacturer and the type of Kampo medicine. Basically the drugs are administered in 3 fractions daily, but it is also possible to use 2 fractions. Principally, they are taken before meals, but there is not much differences, when they are taken after meals²⁴.

Instructions for taking Kampo medicines

Since many Kampo medicines have unique tastes and smells, they are in particular during early infancy difficult to administer. That is why treatment sometimes requires ingenious contrivances. Here I would like to briefly address some administration methods and refer the reader for further details to other references^{25,26}.

1) Increasing the motivation of children and family to take the drugs

First, I start by explaining to both the child(ren) and their guardians "what kind of Kampo medicines there are and what they are for" to help them understand the matter. In the late phase of infancy the children too are already capable of comprehending the outline of the involved concepts and after providing gentle explanations the children can often be unexpectedly compliant. Fundamentally, I am creating a motivation for taking the medicine.

2) Concrete application methods

Due to individual differences whether a patient can or cannot take the medicine at hand, the administration too has to be adjusted on a case by case basis. Generally the following methods are tried.

(1) Adjusting the way the medicine is taken

* Crush it and administer it as a liquid dissolved in warm water.

* For infants prepare a paste with warm water and apply this with your finger to the upper jar.

* After the late phase of infancy have the child take some cold water in the mouth, add the extract preparation and have it swallow it all at once.

* Wrap it in a wafer.

(2) Mix with something that is easy to swallow

* Yoghurt, milk, malt extract, juice, ice cream etc.

3) Change the path of administration

Regarding the application of Goreisan experiences with rectal application have accumulated (enemas, suppositories), but the above mentioned problems with off-label application are a reality.

Conclusions

In this article I tried to describe the application of Kampo extract preparations as the basics of pediatric Kampo as simple as possible, while at the same time trying to maintain the essential concepts of Kampo. This remains, however, very elementary and deepening one's understanding of other Kampo medicines, and further studies are required to ascertain whether these can be combined with other extract preparations or decoctions and thereby therapeutic effects possibly be further improved to treat still more complex diseases.

Kampo does not stand in opposition to Western medicine. By fully exploiting the characteristics of Kampo medicines within the framework of integrated medicine, complementing Western medicines, I believe we can broaden its application in pediatrics.

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