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• BRIEF REPORT •

Treatment of rotaviral gastroenteritis with Qiwei Baizhu powder

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Abstract

AIM **To observe the effects of Qiwei Baizhu Powder (QWBZP) on rotaviral gastroenteritis in children and in animal models.**

METHODS **Enrolled patients were divided into two groups, and one group was treated with oral rehydration solution (ORS) and the other treat ed with oral liquid of QWBZP. Neonate mice were orally infected with 50 μL rotavirus suspension (4×10^8 PFU/mL) and treated with ORS or oral liquid of QWBZP, respectively.**

RESULTS **Eighty-three cases of rotaviral gastroenteritis treated with QWBZP revealed a better efficacy than that treated with ORS ($\chi^2 = 10.87$, $P<0.05$). The contents of sodium and glucose as well as number of patients with positive human rotavirus antigen in stool in QWBZP group were all less than that in ORS group. In a nimal models, QWBZP was found effective in treating rotavirus gastroenteritis in neonate NIH mice, as compared with control groups. In QWBZP group, the mortality of infected mice was decreased by 73.3%, the body weight of infected mice was increased, the contents of sodium and glucose as well as number of mice with positive rotavirus antigen in feces were significantly reduced, and the pathological changes such as damage of small intestinal mucosa and villi were also obviously alleviated.**

CONCLUSION **QWBZP has effects on improving the absorptive function of small intestine, shortening the duration of diarrhea and rotavirus shedding from stool and alleviating the pathological changes of small intestine induced by rotavirus.**

Subject headings gastroenteritis/drug therapy; rotavirus infections/drug therapy; Qiwei baizhu powder/therapeutic use; disease models, animal

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INTRODUCTION

Rotavirus is the most common cause of acute gastroenteritis in infants and young children all over the world[1-4]. Although rotaviral diarrhea is a self -limited disease, it caused 870 000 deaths per year in developing countries[5], even a small part of patients were involved in encephalopathy[6,7]. The primary treatment of this illness is oral or intravenous rehydration to modulate dehydration and electrolyte disturbances due to vomiting and wat ery diarrhea[8,9]. Based on the oral rehydration solution (ORS) recommen ded by World Health Organization (WHO)[10,11], reduced osmolarity ORS[8], addition of Lactobacillus GG to ORS[12,13], and rice-based solution[14] have been used to treat this disease. Also, oral immunoglobulins was used as antiviral therapy[15,16], and rotavirus candidate vaccines are developing[17], in which a oral tetravalant, rhesus rotavirus-based, human reassortant vaccine has been licensed in USA[18].

To seek more effective and cheaper drugs to treat rotaviral diarrhea from Chinese medicinal herbs, we found that a Chinese traditional medical prescription named Qiwei Baizhu Powder (QWBZP) had been employed to treat acute diarrhea in infants and children for nearly one thousand years in Traditional Chinese Medicine (TCM). QWBZP was written by a famous ancient Chinese pediatrician who named ZhongYang Qian and lived from 1035 to 1117. After Mr. Qian, many other ancient Chinese pediatricians demonstrated that QWBZP had good effects in shorting diarrhea and improving the symptom of thirst in their pediatric works. According to their description and our clinical experiences, we prepared oral liquid from QWBZP[19], and tested the effects of the oral liquid in treating rotaviral infection in clinical and experimental studies. This traditional Chinese prescription was shown to be effective in inhibiting replication of human rotavirus at monolayer of MA104 cells[20]. In the present study, we investigate the effects of QWBZP in treating rotaviral gastroenteritis in both clinic and animal models.

PATIENTS AND METHODS

Study population

All patients aged from 3 to 24 months (mean age 13.5±3.2 months) were observed at pediatric wards or out-patients service in both the hospital affiliated to Hunan Province Academy of Traditional Chinese Medicine and the Second Hospital of Shuangfeng County at Hunan Province in China from October 1993 to March 1996. Patients enrolled into the study were diagnosed based on clinical symptoms and laboratory tests in accordance with the diagnostic standard worked out by the Chinese Ministry of Health[21]. That was: the age of patients was less than 24 months, history of acute watery diarrhea less than 72 hours with or without upper respiratory symptoms, negative pathogenic bacteria in stool culture, positive of rotaviral antigen in stool samples. Any patient with negative rotaviral antigen or positive pathogenic

germs was excluded.

Preparation of oral liquid from QWBZP and oral rehydration solution

The oral liquid prepared from QWBZP was described as previously[19]. The prescription of Qiwei Baizhu Powder was composed of seven kinds plants or herbs as listed below: Panax ginseng C. A. May, 7.5 gm; Poriacocos (Schw.) Wolf, 15 gm; Atractylodes macrocephala Koidz, 15 gm; Glycyrrhiza uralensis Fisch, 3 gm; Pogostemon cablin (Blanco) Benth, 15 gm; Pueraria lobata (Willd.) Ohwi, 30 gm; and Viadimiria souliei (Franch.) Ling, 6 gm.Briefly, the seven medicinal materials were washed and dried. Among them, Glycyrrhiza was fried with a little honey. These medicinal materials were carefully weighed and grounded into powder. The seven kinds of powder were mixed together and decocted with eight-fold of water (w/w) until half the water was evaporated off. The volatile oil evaporated from these herbs was collected at the same time. The decoction was extracted and filtered through 50 μM hole of sieves, then clarified at 4℃ overnight. The supernatant was collected and mixed with the volatile oil, bottled in 200 mL per glass flask, sealed and sterilized. The bottled decoction were stored at 4℃ and used as oral liquid of QWBZP. Detected by high performance liquid chromatography (HPLC) or automatic analyzer (7170A type, Hitachi, Japan), the oral liquid contained 12.6mg/L gensenoside Rg^1, 95.3 mmol/L K^+, 50.6 mmol/L Cl^-, 37.4 mmol/L Na^+, 2.01 mmol/L Ca^{2+}, with pH 6.1. The oral rehydration solution was prepared according to the formulae recommended by WHO, and contained in mMol per liter, Na^+90, K^+20, HCO^3-30, Cl^-80 , glucose 110 with pH 7.5[2,10,11].

Treatment protocol

The enrolled patients were divided into two groups at random, one was ORS group, and the other was QWBZP group. There were 83 patients in QWBZP group, aged 3-24 months (mean age 13.6±3.5 months), with histories of watery diarrhea for 21 to 72 hours (mean history of diarrhea 53.5±12.4 hours), 50 boys and 33 girls, 65 moderate cases, and severe 18. And 72 cases in ORS group, aged 3-24 months (mean age 14.1±4.1 months), with histories of diarrhea for 19-72 hours (mean history 56.2±13.7 hours), 41 boys, 31 girls, 56 moderate cases, and 16 severe cases. Patients in QWBZP group were fed with the oral liquid of QWBZP, and ORS group were fed with oral rehydration solution for three days. Children aged less than 12 months were fed 5 mL of ORS or QWBZP each time, children aged 12-24 months were fed 10mL ORS or QWBZP each time. The total dose per day was 10-15 $mL \cdot kg^{-1} \cdot d^{-1}$. During the treatment, the children continued to have their mother's breast-milk or milk or their usual food, other treatment including antibiotics, and antimobility drugs were not used[2,21]. Their stool frequency was recorded. The children were observed until the cessation of diarrhea. If their symptoms such as diarrhea, vomiting, and dehydration became more severe after 24 hours of treatment in both groups, these patients would receive intravenous rehydration and other treatments, who were considered as inefficient cases statistically.

Laboratory tests

Before and during the observation, blood and stool samples of patients were collected for detection of glucose, electrolytes, hematocrit, antigen of rotavirus, and pathogenic bacteria including Salmonella, Shigella, Vibrio cholerae, and enteropathogenic Escherichia coli. Stool was placed in Eagle's medium complemented with 5% bovine serum, 5 U/mL penicillin and 5 μg/mL streptomycin, and frozen until examined for rotavirus antigen by enzyme-linked immunosorbbent assay (ELISA). The monoclonal antibody against human rotavirus was supplied by Dr. Zhu SH, Laboratory of Immunology at Medical College of Zhejiang University, Hangzhou)[22-24] or under direct electron microscopy[25]. Concentration of glucose in stool, and contents of electrolytes in serum and stool were measured by automatic analyzer. hematocrit was tested by microtube method.

Evaluation of curative effect

The curative effect was classified into three categories: ① cured: all of symptoms disappeared, normal appetite and stool, negative rotaviral antigen in stool, normal value of laboratory tests; ② efficient: stool output and frequency were obviously decreased, appetite improved, index of laboratory tests improved; and ③ inefficient: stool output and frequency as that before treatment, dehydration was not improved or even worse, rotavirus antigen was positive or negative.

METHODS IN ANIMAL MODELS

Cells and virus

MA_{104} cells, a cell line derived from fetal rhesus monkey kidney, were obtained from Prof. Hong T, Institute of Virology, Chinese Academy of Preventive Medicine. The cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM , Gibco Inc., USA) complemented with 10% fetal bovine serum, 5U/mL penicillin, 5ìg/mL streptomycin, and 10mmol/L HEPES. Human rotavirus (HRV) Wa strain was kindly granted by Dr. Qian Y, Laboratory of Virology at Capital Pediatric Institute of China through the authority of Dr. Kapikian AZ, National Institute of Allergy and Infectious Diseases, NIH of USA. The virus was replicated at the monolayer of MA_{104} cells[26-29]. When the viral titer was raised to 10^8 PFU/mL after several passages, the viral suspension was stored at -80℃ and employed to inoculate animals.

Animal infection

Pregnant dam mice (NIH strain, supplied by Experimental Animal Department at Hunan Institute of Medicinal Industry) were fed in sterile cages. The new born pups were maintained in germfree isolators at 20℃ room temperature and fed with sterilized milk in germfree conditions. The neonate mice were divided into 4 group at 2 days of age. The four groups were normal group, infected group, ORS group, and QWBZP group. Pups in the later three groups were orally inoculated with 50 μL of cold viral suspension of 4×10^8 PFU/mL human rotavirus according to the METHODS as described for mice[30-34]. Neonate mice in normal group were not inoculated. Pups in each group were maintained in isolated room after division.

Treatment

After 24 hours of inoculation, the pups in ORS group and in QWBZP group were fed with 0.1 mL of ORS or 0.1 mL oral liquid of QWBZP each time, respectively, 4 times per day for

three days. The total dose was 0.5 mL, or about 150 mL·kg^{-1}·d^{-1}. Pups in normal group and infected group were fed with sterilized distilled water at the same dose as other two groups. Aside the oraltherapy, all pups in the four groups were fed with 0.1 mL sterilized milk, three times per day.

Observation and laboratory tests

After inoculation, the intake of food, body weight, activity, and number of death of the pups in all four groups were carefully recorded daily until 10 days after inoculation. For the observation of the intake of food, when fed with 0.1 mL milk, there was a white round lump in the stomach of pup to be seen through the transparent skin. If the digestive function and absorptive function of neonate mouse were normal, the white lump in the stomach of pup gradually became smaller and smaller after feeding. If the digestive and absorptive functions were decreased, the white lump in stomach did not become smaller, in contrast, the a bdomen of the pup became distended. In this condition, the next feed of milk was not needed. For assessment of diarrhea, when the abdomen of pup was gently pressed[35,36], the watery stool or loose yellow stool was shedding fro m the anus of the pup. The blood samples and stool specimen were collected before the treatment and at day 4 and 7 after infection for the analysis of serous electrolytes, glucose, and hematocrit, and rotaviral antigen, electrolyte, and glucose in stool. The METHODS of analysis was described in clinical study.

METHODS of statistics

All quantitative data in the study were presented as $\bar{x}\pm s$, and compared by Student's *t* test between two group or by analysis of variance (ANOV) among three groups or more than three groups. The dichotomous data were compared with Chi-square test.

RESULTS

Effects of antidiarrhea

After treatment for 3 days, 71 cases in QWBZP group and 45 cases in ORS group had formed stool, and their symptoms of vomiting, diarrhea, dehydration, and fever disappeared. As seen in Table 1, the cured cases in QWBZP group we re more than that in ORS group ($\chi^2 = 10.87$, $P<0.01$) , while the inefficient cases in QWBZP group were less than that in ORS group ($\chi^2 = 5.85$, $P<0.05$). From these cured cases, the duration from beginning of treatment to stop of diarrhea was 25.9±13.5 hours in QWBZP group, and 41.8±19.3 hours in ORS group. The duration of cessation of diarrhea in QWBZP group was shortened as compared with ORS group (t = 5.86, $P<0.01$). The results showed that the curative effect of QWBZP in treating rotaviral diarrhea was better than that of ORS.

Table 1 The curative effect of QWBZP and ORS

Group	Total cases	Cured cases	Efficient cases	Inefficient cases
ORS	72	45	15	12
QWBZP	83	71	8	4

Changes of electrolytes in serum and sodium and glucose in stool

Hematocrit and serum electrolytes of patients were all improved in the two groups after treatment, but as seen in Table 2, more improvedment were shown in QWBZP group. Contents of sodium and in stool samples of patients were not changed in ORS group, but remarkably reduced in QWBZP group as seen in Table 3. The results showed that QWBZP had the effects in reducing the contents of sodium and glucose in stool and promoting the absorptive function of small intestine to intake sodium and glucose from intestinal cavity.

Table 2 Changes of electrolytes in serum and hematocrit after treatment ($\bar{x}\pm s$)

Treatment	Cases	Time point	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)	Hematocrit (%)
ORS	72	Before treatment	146.4±9.4	3.9±0.2	98.5±5.0	50.6±4.6
		After treatment	140.6±7.3[a]	4.1±0.3	102.4±6.7	45.7±3.8[a]
QWBZP	83	Before treatment	145.7±8.6	3.8±0.2	101.0±5.4	51.2±4.4
		After treatment	141.2±8.1[a]	3.9±0.3	103.5±4.8	46.1±5.8[a]

[a]$P<0.05$ *vs* the same group before treatment.

Table 3 Changes of sodium and glucose in stool after treatment (mmol/L, $\bar{x}\pm s$)

Treatment	Cases	Time point	Sodium	Potassium	Chloride	glucose
ORS	72	Before treatment	25.3±4.1	18.5±3.4	11.7±2.6	0.9±0.2
		After treatment	26.8±4.7	11.7±4.1	13.0±3.1	1.0±0.4
QWBZP	83	Before treatment	26.2±4.3	17.3±3.5	12.4±2.5	0.9±0.3
		After treatment	11.5±3.6[a,b]	10.4±2.8[a,b]	6.8±2.7[a,b]	0.2±0.1[a,b]

[a]$P<0.05$ *vs* the same group before treatment; [b]$P<0.05$ *vs* ORS group.

The clearance of rotaviral antigen in stool

There were positive rotaviral antigen or rotaviral particals in stool samples of all patients in two groups. After 3 days of treatment, 13 cases became positive for rotavirus in QWBZP group, 45 cases in ORS group. Significant difference was seen between the two groups ($\chi^2 = 30.47$, $P<0.01$). The result indicted that treatment with QWBZP can shorten the duration of rotavirus excretion from stool.

The taste of the oral liquid QWBZP

Compared with ORS, the oral liquid of QWBZP tastes slightly sweat and free from bitterness. So the oral liquid was easy to be drunk for infants and young children. In contrast, ORS was so bitter, which often induced vomiting maleings the patients refus to drink. Furthermore, the appetite, the intake of food, the activities, and nutrition of patients in QWBAZ group were considerably improved. No side-effect was presented during

the treatment with QWBZP.

The endpoint of diarrhea and mortality of mice

The neonate mice were ill with decreased digestive function (the white lump in stomach was not decreased after 4-8 hours of feeding with milk), abdominal distension, and watery diarrhea at 48 hours of rotaviral inoculation. Dehydration occurred after 3 days of rotavirus infection with the presence of dry, loose, and wrinkly skin, in activities. Symptoms of prostration, cyanosis, and weight loss appeared at day 4 after inoculation. All of the pups in infected group (15/15), 10 mice in ORS group (10/15), 4 mice in QWBZP group (4/15) died during the observation. But still 1 mouse died in the normal group. The surv ivals in QWBZP group were more than that in the infected group ($\chi^2 = 17.37$, $P<0.01$) and in ORS group ($\chi^2 = 4.82$, $P<0.05$). The diarrhea in survived mice stopped at day 6-12 after inoculation. The diarrhea in QWBZS group stopped at day 5-10 (7.4±1.3 days), and in ORS group at day 8-12 (9.9±1.8 days) after infection. There was significant difference between the two groups (t = 2.79, $P<0.05$).

Changes of body weight

The body weight of mice in all four groups are shown in Table 4. The body weight of mice in infected group was not increased, but that in QWBZP group was increased after three days of treatment. The result indicated that treatment with QWBZP could rectify dehydration and improve nutrition of mice infected with rotavirus.

Table 4 Changes of body weight of mice after inoculation (g, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	2.2±0.2	2.8±0.4	5.1±0.6
Infected	5	2.1±0.3	2.2±0.2	2.3±0.4
ORS	5	2.2±0.2	2.4±0.3	3.6±0.5[a]
QWBZP	6	2.1±0.3	2.7±0.4[a]	4.8±0.5[b]

[a]$P<0.05$, [b]$P<0.01$ *vs* infected group.

Changes of laboratory value

As shown in Tables 5-9, contents of sodium and glucose in stool samples from the mice in QWBZP group were both decreased in comparison of infected group and ORS group at day 4 and 7 after inoculation. Hematocrit of mice in QWBZP and ORS groups were also improved. Content of sodium and glucose in blood were not changed in all four groups after treatment. These results suggested that QWBZP had effects in promoting the absorption of sodium and glucose after rotavirus infection.

Table 5 Changes of content of fecal sodium (mmol/L, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	9.5±0.6	10.2±0.8	9.3±1.2
Infected	5	10.1±1.1	22.9±2.2[a,b]	24.7±1.9[a,b]
ORS	5	9.7±0.9	26.5±1.3[a,b]	15.7±1.9[c,d]
QWBZP	6	10.4±1.1	11.6±1.4	11.2±1.1

[a]$P<0.001$, [b]$P<0.01$ *vs* QWBZP group. [c]$P<0.001$, [d]$P<0.01$ *vs* the same group before treatment.

Table 6 Changes of content of glucos in stool (mmol/L, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	0.1±0.2	0	0.1±0.1
Infected	5	0	1.1±0.3[a]	1.3±0.4[a]
ORS	5	0	1.2±0.4[a]	1.2±0.3[a]
QWBZP	6	0.1±0.1	0.2±0.2	0.1±0.1

[a]$P<0.01$ *vs* QWBZP group.

Table 7 Changes of content of glucos in serum (mmol/L, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	4.4±1.2	3.9±1.4	4.1±1.2
Infected	5	4.2±0.9	3.8±1.3	4.3±0.9
ORS	5	4.4±0.8	4.6±1.4	4.5±1.7
QWBZP	6	4.1±1.6	4.5±1.5	4.8±1.6

Table 8 Changes of content of serous sodium (mmol/L, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	140.6±7.8	142.1±8.6	141.7±8.4
Infected	5	141.8±9.6	143.5±9.9	142.3±8.7
ORS	5	142.5±8.8	145.8±7.6	144.7±9.2
QWBZP	6	140.6±7.5	141.6±8.6	142.4±8.5

Table 9 Changes of hematocrit after treatment (%, $\bar{x}$±s)

Group	*n*	Days post-inoculation		
		1 d	4 d	7 d
Normal	4	42.1±5.6	41.3±4.2	40.5±4.4
Infected	5	43.5±4.8	52.2±5.4[a]	54.2±5.1[a]
ORS	5	42.7±5.2	46.7±3.4	46.5±3.7
QWBZP	6	43.9±5.5	45.7±4.7	43.4±4.1

[a]$P<0.05$ *vs* normal group.

Reduction of rotavirus shedding from stool

There were 2 mice with positive rotaviral antigen in stool in QWBZP group (2/1 5), 9 mice with positive rotaviral antigen in infected group (9/15), and 10 mice with positive rotaviral antigen in ORS group (10/15) at day 4 after inoculation. No mouse with positive rotaviral antigen was seen in the normal group. The mice with rotaviral antigen positive in QWBZP group were less than that in infected group ($\chi^2 = 8.1$, $P<0.01$) and in ORS group ($\chi^2 = 13.3$, $P<0.01$).

Histological changes of intestine

Main morphological changes seen at day 4 after rotavirus infection were villous shorting and exfoliation, irregular construction of small intestinal mucosa with infiltration of lymphocytes, thinned intestinal wall. At day 7 after inoculation, the villi of small intestine became rarer and the intestinal wall became thinner. The pathological changes in ORS group were the same as that in infected group at day 4 after inoculation, and at day 7, the pathological changes were obviously moderated in comparison with that in infected group, but more severe than that in QWBZP group. Compared with control groups, the villi and mucosa construction of small intestine were alleviated at day 4 after in oculation, and were nearly normal at day 7 after rotaviral infection. These results suggested that QWBZP had the effect in protecting intestinal

mucosa against the damage induced by rotavirus infection.

DISCUSSION

The results of this study clearly indicated that treatment with the oral liquid of QWBZP significantly shortened the duration of diarrhea and rotavirus shedding from stool, reduced the contents of sodium and glucose in stool samples as compared with ORS treatment in clinic. In animal models, treatment with QWBZP remark ably reduced rotavirus antigen in feces, decreased the mortality of infected mice, reduced the contents of sodium and glucose in stool, and alleviated the damage of small intestinal mucosa and villi. These results suggested that QWBZP had the effects in improving in absorptive function, protecting intestinal mucosa against in jury induced by rotavirus infection, and enhancing the clearance of rotavirus from stool. Another noteworthy finding in this study during clinical observation w as that the less bitter taste of the liquid of QWBZP was easily accepted by children as compared with ORS.

According to the epidemiology, only 0% to 20 % of summer diarrhea cases were rot avirus associated, while 70% to 80% of winter diarrhea cases were due to rotavirus[11,37], and 55.9% of all hospitalized diarrheal children were associated with rotavirus and significantly clustered during winter months in China[38]. Resides vomiting, watery diarrhea, and dehydration, most patients with rotaviral diarrhea had upper respiratory symptoms such as fever, cough, and sneeze[39]. These clinical manifestations of rotavirus diarrhea were similar to one type of acute diarrhea named “cold diarrhea” in TCM. The “cold diarrhea” is thought to be caused by cold weather, cold wind, or cold food, which mostly occurred in winter or cold climates. The “cold diarrhea” was first described by Mr. Qian ZY. Qian said in his pediatric work: “If their diarrhea is caused by cold and wind , the children will have vomiting, fever, cough, sleepiness, thirst, and diarrhea with yellow watery stool. The patients need to drink decoction of Qiwei Baizhu Powder for quenching their thirst”. Following Mr. Qian, many other ancient Chinese pediatricians treated acute diarrhea in children with QWBZP. They recorded the effects of QWBZP in anti-diarrhea, quenching thirst, and improvement of appetite in detail. In our clinical practice, we observed that treatment wit h QWBZP not only shortened the duration of diarrhea and rotavirus shedding, but also improved the condition of nutrition and appetite of the ill patients. Therefore treating rotaviral diarrhea with QWBZP yielded better results than with ORS. The theory of TCM considered that the digestive and absorptive function in young children was immature, so children were susceptible to diarrhea. Treatment for acute diarrhea in childhood with QWBZP can improve the digestive and absorptive function and quench thirst induced by vomiting and diarrhea through the effect of “Bupi” of this prescription.

Following infection of rotavirus, the duodenal biopsies showed a patchy irrgulalarity of mucosal surface, shorting and bunting of the villi, distorting microvilli of absorptive cell[40]. As a consequence of virus replication in the cytoplasm and viral shedding, the infected cell at the surface of villilysed and the villious tip became atrophic[2,11,41], and the villious surface was replaced by immature cells migrating from the crypts[42]. The destruction of mature enterocytes and replacement of immature crypt cells result in reduced levels of disaccharidase and xylose absorption[43], and decrease in the absorptive surface of the small bowel. So diarrhea caused by rotavirus is mainly due to decreased absorption[11,44]. Clinical studies demonstrated that the stools of rotavirus diarrhea contained higher contents of sodium and glucose than normal[45]. In our observation in both clinic and animal models, we found that the contents of sodium and glucose in feces in ORS group or infected group were higher than that in QWBZP group. The result indicated that treatment with QWBZP could promote the absorption of sodium and glucose. The mechanism of ORS on rehydration was based on glucose-facilitated sodium transport[46], while the mechanism of QWBZP on treating rotavirus diarrhea would be more complex and involved in improving the digestive and absorptive function, protecting intestinal mucosa cells from damage induced by rotavirus, and clearance of rotavirus.

More recently, some studies identified that the non-structural protein 4 (NSP4) of rotavirus is a viral enterotoxin, which induced diarrhea by stimulating chloride secretion through a calcium-depedent signaling pathway after binding to the pulative receptor on the intestinal epithelium[34,44,47-50]. So the rotavirus diarrhea is caused by reduction of absorption as well as secretory hyperactivity[2,44,48]. The therapeutical method to improve the absorptive function to enhance the intake of sodium and glucose, therefore, plays an important role in cessation of diarrhea. That may be the reason why the efficacy of QWBZP is better than ORS. Indeed, a lot of studies in TCM in recent years demonstrated that some of medicinal herbs contained in QWBZP have effects of enhancing absorption of D-xylose.

As rotavirus diarrhea in children, rotavirus infection in animal models is also a self-limited disease[36,51]. But in our study, most of infected mice died of severe diarrhea and dehydration without treatment of QWBZP. This result might be due to different METHODS of feeding. In our study, we fed neonate mice with sterilized milk orally, Guerin-Danan, *et al* let the infected pups return to their dams and allowed to suckle[36]. Because breast milk contains IgA antibodies against rotavirus and trypsin inhibitors, which will provide protection to breast-fed infants[52]. Furthermore, it is well known that nutrition in breast milk was more easily absorbed than that in other milk. Treatment with QWBZP can promote the intake of nutrition through improvement of digestive and absorptive function. Therefore, the body weight was increased and most infected mice survived in the QWBZP group as compared with the infected group as well as ORS group.

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