# A randomized controlled trial on the effect of dietary guidance on the treatment of Henoch-Schonlein purpura in children

Li Wang,[1] Chunyan Yin,[1] Meizhen Zhang,[1] Hua Mao,[1] Huixiang Hao,[1] Xiaoting Hu,[1] Wanli Xue [2]

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[1]Department of Pediatrics, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China
[2]Department of Nutrition and Food Safety Research, School of Public Health, Xi'an Jiaotong University, Xi'an, Shaanxi, China

**Correspondence to**
Dr Wanli Xue, Department of Nutrition and Food Safety Research, School of Public Health, Xi'an Jiaotong University, Xi'an, Shaanxi, China; xuewl@mail.xjtu.edu.cn

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## ABSTRACT

The amino acid-based formulae were extensively added to diet of children for the treatment of Henoch-Schonlein purpura (HSP), and the nutrition and growth situation of children were evaluated after giving new dietary intervention. Patients were randomly divided into restricted diet group (n=30) and dietary guidance group (n=30). Besides, 30 cases with bronchiolitis who had normal diet were selected as the control group. The dietary questionnaire was designed to record the types and intakes of various foods taken by children every day, and the intake levels of nutrients were analyzed. Physical examination, biochemical analysis of blood and urine routine were carried out to evaluate the effect of dietary guidance on their growth and development. The results showed that restricted diet group had lower levels of nutrient intake and the actual/recommended percentage. However, overall nutrient intake level of the dietary guidance group was higher, basically equal to the recommended intake level. Besides, the actual intake and actual/recommended percentage of nutrients of dietary guidance group were significantly higher than those of restricted diet group ($p<0.05$). Dietary guidance can improve nutrients and protein intake of children with HSP, and reduce the relapse of rash and incidence of complications.

## Significance of this study

**What is already known about this subject?**
- ► Strict diet control method has a good therapeutic effect on children with Henoch-Schonlein purpura (HSP).
- ► Eliminating the allergens in the diet and the suspected food formula is the main purpose of treatment of food allergy.

**What are the new findings?**
- ► The application of extensively hydrolyzed protein or amino acid-based formulae under dietary guidance can improve the intake of nutrients and protein in children with HSP.
- ► Dietary guidance is conducive to the healthy growth of children and can make the nutritional status, growth and development of children with HSP reach to normal.

**How might these results change the focus of research or clinical practice?**
- ► Dietary guidance can improve the therapeutic effect of HSP, reduce the recurrence rate of skin rash and reduce the occurrence of complications.

## INTRODUCTION

Anaphylactoid purpura, also known as Henoch-Schonlein purpura (HSP), is a vasculitis syndrome characterized by systemic vasculitis, with the highest incidence in the childhood.[1] Clinical features include non-thrombocytopenic purpura, accompanied by joint swelling and pain, abdominal pain, hematochezia, hematuria and proteinuria, which are prone to recurrent attack. HSP is mainly found in school-age children, and children younger than 10 years of age account for about 90% of the total patients.[2] At present, there is no unified and standardized treatment for HSP. Generally, symptomatic support treatment is the main therapy method and most of the children recover well after treatment. However, some of the children suffer from repeated disease and renal impairment, leading to end-stage renal disease several years later,[3] which affects their learning and quality of life, and even poses a threat to their life and health.

Recently, with the change of environment and diet structure, the incidence of HSP in children is on the rise.[4] It is reported that the incidence of HSP in children younger than 17 years of age ranges from 13/100,000 to 20/100,000. Besides, the incidence of HSP varies in different regions. In 2004, an investigation in the Netherlands found that the incidence of HSP in patients aged 0–18 years was approximately 6.1/100,000.[5] Kawasaki *et al*[6] reported that the average annual incidence of HSP in Japanese children was (3.6±1.0)/100,000 in 22 years. From 2007 to 2009 in Jiangxi Province, the incidence of HSP in children younger than 14 years of age was approximately 14/100000.[7]



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HSP is a complex process with a variety of different signaling pathways involving in multiple systems and factors. Nowadays, some achievements have been made in the study of the etiology and treatment of HSP, but the exact etiology and pathogenesis remain not completely clear, and the clinical manifestations of HSP are complex and diverse. More than half of children with HSP who are admitted have gastrointestinal symptoms and recurrent rashes.[8] Some scholars have found that 20.5% of children with HSP eat a specific food before onset, 90% of the allergens in food are protein,[9] which has the antigen specificity of glycoprotein, can withstand food processing and heating without damage, and is not easy to be digested in the gut. Infection and food allergy were the main etiological factors of HSP, and the dominant digestive clinical features were abdominal pains and vomiting.[10] Repeated exposure of children with HSP to allergens can lead to the recurrence of skin rash, aggravation of gastrointestinal bleeding and renal damage (even renal failure). As the gastrointestinal small vasculitis leads to vulnerable bleeding of gastrointestinal mucosal blood vessels, eating will increase the burden of gastrointestinal tract and aggravate mucosal bleeding. In clinic, it is very important to control the diet of children with HSP while receiving medicine and symptomatic treatment.[11] In management of conventional diet control, HSP is treated and prevented by forbidding the intake of all animal protein and most of plant protein. This diet management method is widely used in clinical practice.[12]

Strict diet control method has a good therapeutic effect on children with HSP, but malnutrition, eating disorders, anorexia, wasting, weight loss, stunting and other adverse phenomena can be caused by long-term diet control management,[13] which can affect the normal growth and development of children, and have a serious impact on the health of these children.

Eliminating the allergens in the diet and the suspected food formula is the main purpose of treatment of food allergy, usually referring to eliminating the proteins in the food, which is the basis of the treatment of food allergy. The commonly used hypoallergenic formulas include amino acid-based formulae (AAF) and extensively hydrolyzed protein (eHF).[14] The hydrolyzed protein of the eHF is formed through the process of enzymolysis and heating, making it into several peptide segments. After these processes, the molecular weight of the peptide segments contained in it is lower than the original protein, and the structural sequence and spatial conformation of the protein have also changed, changing the antigenic determinant of the protein, thus reducing the antigenicity of the protein.[15] It has been proved that the eHF can effectively reduce the occurrence of protein allergy and support the normal growth and development of infants.[16 17] There is modest evidence that the onset of atopic disease may be delayed or prevented by the use of hydrolyzed formulas compared with formula made with intact cow milk protein, particularly for atopic dermatitis.[16] Hydrolyzed protein formula can improve gastric emptying and feeding tolerance, and enable a more rapid establishment of full enteral feeding in very low birthweight infants compared with standard preterm infant formula.[17]

However, there are few reports about the application of eHF (or AAF) in the diet treatment of children with HSP. Therefore, based on the conventional diet restriction scheme, the replacement treatment of protein deficiency was carried out in our study by using dietary nutrition analysis and adding hypoallergenic formulas. To evaluate the role and application of hypoallergenic formulas and dietary guidance in the diet treatment of HSP in children, a randomized controlled trial was performed.

## MATERIALS AND METHODS

### Subjects

From January 2014 to June 2015, 60 children with HSP hospitalized in the Second Affiliated Hospital of Xi'an Jiao Tong University were enrolled and analyzed in this single-center prospective study. These patients were randomly divided into the following two groups by using a computer to generate random numbers: restricted diet group (30 patients received only conventional restricted diet programs) and dietary guidance group (30 patients received dietary guidance diet programs based on the conventional restricted diet programs). Sodium hydrocortisone succinate (Tianjin Biochemical Pharmaceutical, 20160319) was used for intravenous drip injection, 5 mg/(kg·day), 2 times/day, and the amount was gradually reduced after the symptoms disappeared. The drug was stopped after 1 week, and the symptoms were treated. At the same time, diet was restricted or guide dietary was followed. Children of the two groups were followed up and dietary survey was performed at 1, 2 and 3 months after admission. In addition, 30 children with bronchitis who were hospitalized in our hospital from January 2014 to January 2015 were selected and included into the control group, and children with food allergy or intolerance were excluded. The children in control group had normal diet without restriction.

### Diet programs

#### *Conventional restricted diet programs*

The patients of restricted diet group received the following diet programs in this study:

1. It was forbidden to eat fish, shrimp, meat, eggs, milk, vegetables, fruits and spices, as well as raw, cold, hard and other stimulating food. Three meals a day included rice, noodles, steamed bread, porridge and some salt. Patients were advised to drink warm boiled water.
2. When the abdominal pain disappeared, no new rash appeared 7 days later, vegetables were added to the food. A small amount of one kind of vegetable was added first, and no new rash appeared 5 days later, then another vegetable was added. Generally, the vegetables were added in the following order: potato, cabbage, sweet potato, green vegetable, cauliflower, cabbage, cucumber, etc; a small amount of fruits can also be added in the following order: banana, apple, watermelon, pear, etc. The interval between the two kinds of vegetables or fruits must be >5 days, and the vegetables and fruits can be added alternately.
3. After adding vegetables or fruits without new rash for 1 month, a small amount of eggs and milk could be added. After adding eggs and milk without repeated disease for 2 months, a small amount of meat could be added in the food.

4. In the process of adding food, when skin rash, abdominal pain and other repeated symptoms occurred, it was necessary to stop eating the added food and restart after the situation was considered to be stable.

*Dietary guidance diet programs*

1. Based on conventional restricted diet programs, the diet of children was recorded by weighing method and retrospective inquiry method, and then the dietary structure was analyzed by nutrition software (Nutrition Evaluation System, Shanghai Hui Cheng Consulting). According to the results of nutritional analysis, recommended nutrition intakes (RNI) of children[4] and nutritional standard,[5] as well as the results of allergen monitoring, AAF was added for the children with protein allergy, while the eHF was added for children without protein allergy.
2. In the whole process of dietary adjustment, as long as vegetables, fruits, eggs, milk and meat were added, the dietary investigation was carried out. The nutrient intake level of children was analyzed by nutrition software, and the intake amount of eHF (or AAF) provided by the software was applied in the programs.

AAF was added for the children with protein allergy, while the eHF milk (produced by Nestle) was added for children without protein allergy. The detection of protein allergens was carried out in accordance with the kit instructions (Biomerica, USA). Briefly, 2 mL of venous blood was extracted on an empty stomach to obtain serum, and the antibody level of IgG in serum was detected by ELISA using an automatic allergen detector.

## Detection indicators

*Nutrients*

The diet of children with HSP was investigated for three consecutive days each time. The actual daily intake of various foods was analyzed and calculated by nutrition software. The children in control group, restricted diet group and dietary guidance group were followed up and investigated at 1, 2 and 3 months after admission. After discharge, as long as the children of the dietary guidance group needed to add some food, they would be followed up for dietary investigation and nutritional analysis to develop a new diet plan and implement it.

*Physical examination*

Physical examination was carried out for all the children in our study, including height (cm), weight (kg), upper arm circumference (cm), skinfold thickness of triceps brachii (mm) and subscapular skinfold thickness (mm). Height and weight were used to calculate body mass index (BMI) as follows:

$$\text{BMI} = \text{weight (kg)}/\text{height}^2\ (\text{m}^2)$$

Age-specific and sex-specific BMI percentiles were used for weight status categories[6]: normal weight: 5th–85th BMI percentile; over weight: 85th–95th BMI percentile; obesity: >95th BMI percentile.

*Biochemical analysis of blood*

Biochemical analysis of blood was carried out for all the children in our study, including routine blood examination (white blood cell (WBC), red blood cell (RBC), hemoglobin (HB), platelet (PLT), lymphocyte number, hematocrit, mean corpuscular volume, total protein, albumin, globulin, etc), blood lipid (cholesterol and triglycerides), trace elements (Zn, Ca, Mg, Cu, Fe).

*Urine routine*

An amount of 10 mL urine was collected for urine routine by using Sysmex-1000 automatic urine, including appearance, pH value, urinary protein, urinary WBC count, urinary RBCs and urinary sediment microscopy.

*Evaluation of therapeutic effect and complications*

During the treatment, the following indicators were recorded and analyzed:

1. Time of complete skin rash disappearance: refers to the days from the appearance of rash to the complete disappearance of rash or no new rash.
2. Repeated rashes: purpura-like rashes appeared again in batches after the previous rashes were eliminated and cleared.
3. Recurrence of HSP: the children diagnosed with HSP had purpuric rash again at least 1 month after the disappearance of the rash.
4. Complications: children diagnosed with HSP will suffer from renal involvement if hematuria and/or albuminuria occur >2 days.[7]

## Statistical analysis

SPSS V.21.0 was used for data statistical analysis in this study. All measurement data were expressed as mean±SD, and counting data were expressed as n (%). The data before and after dietary intervention were examined by paired t-test, while counting data were examined by $\chi^2$ test. P value <0.05 was considered to be statistical significant.

# RESULTS

## Comparison of general clinical information of children

There were no significant differences in age and gender among the three groups (p>0.05).

In terms of physical examination, there were no significant differences in height, weight and BMI of children at admission (p>0.05). Besides, there were no significant differences in RBC, HB, serum albumin, serum prealbumin, Ca and Fe among the three groups (p>0.05) (table 1).

## Effect of dietary guidance on nutrient intake level of children with HSP

*Effect of conventional restricted diet programs on children of restricted diet group*

The results of dietary nutrition analysis showed that the overall nutrient intake level of children in the restricted diet group was low; the actual/recommended percentage of each nutrient intake gradually increased from 10% to 20% to 50% with the implementation of the restricted diet programs, and there were significant differences in the actual intake and actual/recommended percentage of each nutrient among three different time periods (p<0.05). However, the actual/recommended percentage of most nutrients intake at 3 months after admission was still <60% (figure 1).

**Table 1** Comparison of general clinical features of children before treatment

| | Control group | Restricted diet group | Dietary guidance group |
|---|---|---|---|
| Age (years) | 6.93±0.59 | 6.92±0.54 | 6.95±0.47 |
| Gender (male/female) | 13/17 | 16/14 | 12/18 |
| Height (cm) | 119.07±9.92 | 119.53±11.46 | 119.50±11.94 |
| Weight (kg) | 26.03±2.53 | 25.47±2.55 | 25.13±2.48 |
| BMI (kg/m$^2$) | 20.38±2.05 | 20.04±2.09 | 19.94±1.78 |
| RBC (10$^{12}$/L) | 4.44±0.41 | 4.52±0.32 | 4.40±0.24 |
| HB (g/L) | 132.27±11.16 | 134.50±7.51 | 137.42±8.11 |
| Albumin (g/L) | 45.50±4.10 | 44.57±3.25 | 47.17±3.59 |
| Prealbumin (mg/L) | 289.00±15.62 | 300.12±12.71 | 305.35±15.44 |
| Ca (mmol/L) | 1.87±0.18 | 1.92±0.16 | 1.86±0.17 |
| Fe (mmol/L) | 9.25±0.98 | 10.11±0.87 | 9.55±0.80 |

BMI, body mass index; HB, hemoglobin; RBC, red blood cell.

### *Effect of dietary guidance diet programs on children of dietary guidance group*

The analysis of dietary nutrition for 1, 2 and 3 months after admission showed that the overall nutrient intake level of the children in the dietary guidance group was high, basically equal to the recommended intake level. The actual intake of all nutrients reached 90%–110% of the RNI, especially the intake of calories and protein, and all the actual/recommended percentage of three time periods were >98%.

Our results showed that the intake levels and the actual/recommended percentage of several nutrients of 1 month after admission were lower than those of 3 months after admission with statistical difference ($p<0.05$). The actual/recommended percentage of most nutrients was in the range of 93%–101%, which were >75% of RNI. The level of nutrients of the dietary guidance group can meet the nutritional needs of children with HSP (figure 2).

### *Comparison of nutrient intake level of children among three groups*

The analysis of dietary nutrition for 1 month after admission showed that the actual/recommended percentage of most nutrients of the restricted diet group was in the range of 10%–20%, which was significantly lower than that of the control group ($p<0.05$). However, in the dietary guidance group, the overall intake level of nutrients was high, and the actual/recommended percentage of most nutrients was in the range of 90%–95%. The actual intake and actual/recommended percentage of nutrients of children in the dietary guidance group were significantly higher than those of children in the restricted diet group ($p<0.05$), but there were no significant differences between dietary guidance group and control group ($p>0.05$) (figure 3).

After 3 months of diet treatment, the overall nutrient intake level of children in the restricted diet group was significantly improved, but the overall level was still low, and the actual/recommended percentage of most nutrients was in the range of 40%–60%, which was still significantly lower than that of the control group ($p<0.05$). Three months after admission, the actual/recommended intake percentage of all nutrients of the dietary guidance group was in the range of 95%–105%, which was basically equal to RNI and significantly higher than those of the restricted diet group. Furthermore, there were no significant differences in the actual/recommended intake percentage of all nutrients between dietary guidance group and control group ($p>0.05$) (figure 4).

## Effect of dietary guidance on nutritional status of children with HSP

### *Effect of dietary guidance on the levels of trace elements in the whole blood of children with HSP*

In the restricted diet group, the levels of Zn, Ca, Cu and Fe of three time periods were lower than the normal reference range, suggesting that the levels of Zn, Ca, Cu and Fe of the restricted diet group were in a state of deficiency and insufficient intake. Compared with the control group, the levels

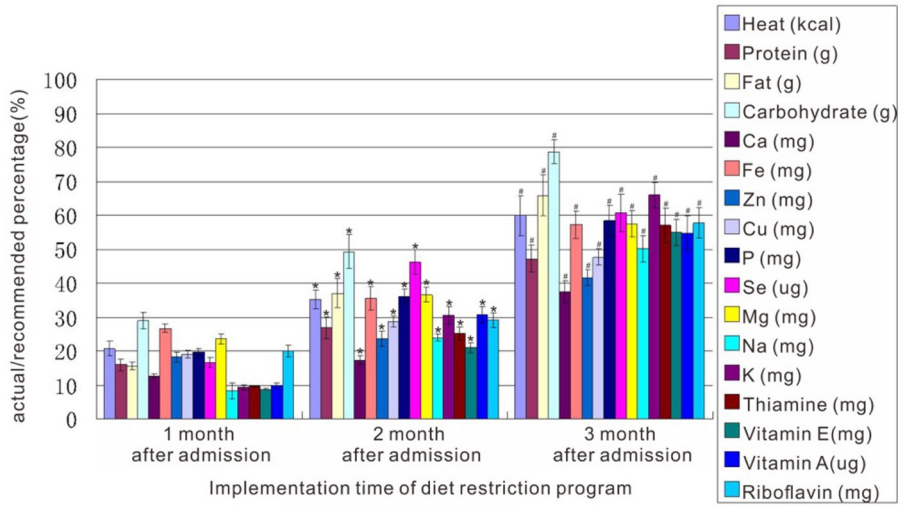


**Figure 1** The nutrient intake levels of children in the restricted diet group. *Compared with group of 1 month after admission, $p<0.05$; #compared with group of 2 months after admission, $p<0.05$.

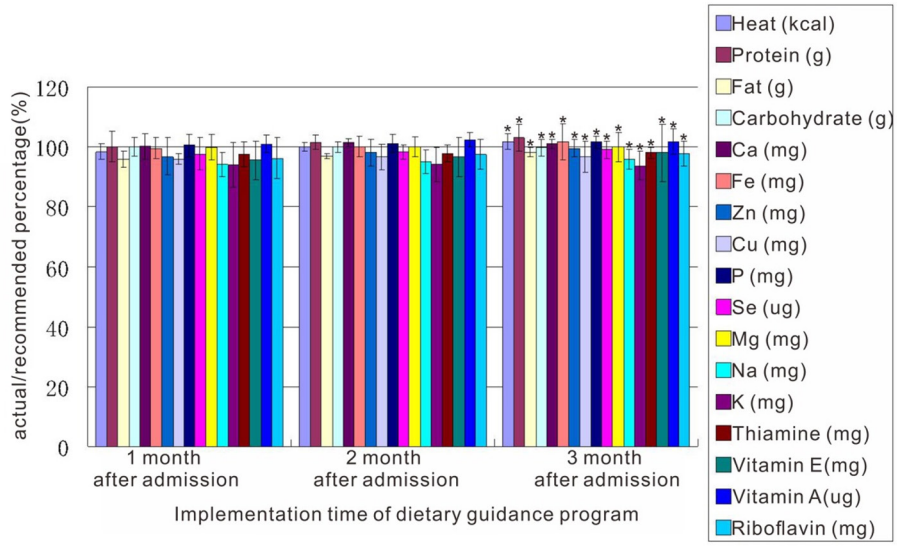


**Figure 2** The nutrient intake levels of children in the dietary guidance group after admission. *Compared with group of 3 months after admission, p<0.05.

of Zn, Ca, Cu and Fe in the whole blood of the restricted diet group were significantly lower (p<0.05). The levels of trace elements in the whole blood of the children in the dietary guidance group reached the normal reference range, and the levels of Zn, Ca, Cu and Fe were significantly higher than those of the children in the restricted diet group (p<0.05). Our study showed there were no significant differences in the levels of trace elements between dietary guidance group and control group (p>0.05) (table 2).

### *Effect of dietary guidance on indicators of routine blood examination of children with HSP*

Three months after admission, the value of RBC and HB of children in the restricted diet group were lower than the normal reference range, and were also significantly lower than that of children in the control group (p<0.05). Compared with restricted diet group, the value of RBC and HB in the dietary guidance group were significantly higher (p<0.05), reaching the levels of the control group with no statistical difference (p>0.05). In addition, there were no significant differences in the levels of WBC and PLT among three groups (p>0.05) (online supplemental table 1).

According to the value of HB, the degree of anemia is classified as the following three grades: HB >120 g/L is normal, 90–120 g/L HB is mild anemia, 60–90 g/L HB is moderate anemia and HB <60 g/L is severe anemia. Furthermore, our study showed that in the restricted diet group, there were only 9 children (30%) with HB in the normal range, 14 children (46.47%) with mild anemia, 7 children (23.33%) with moderate anemia. In the dietary

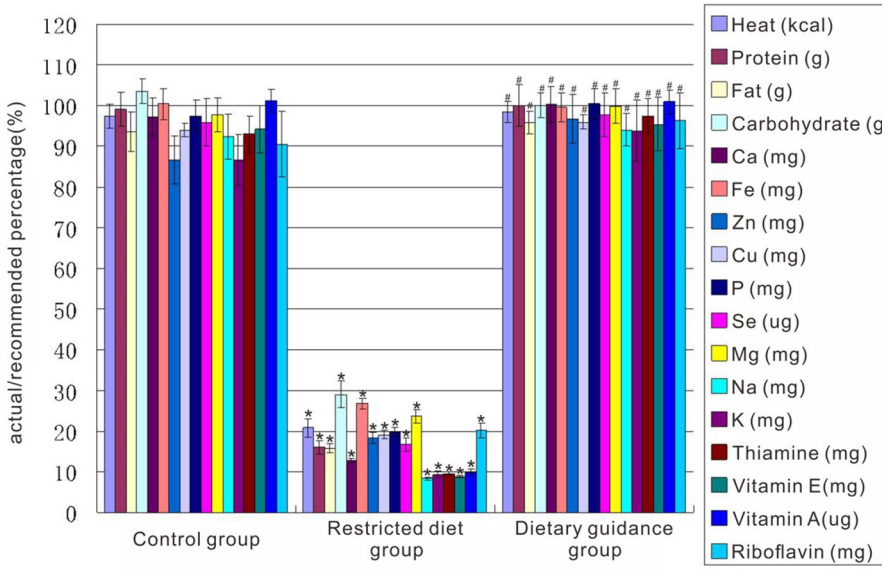


**Figure 3** Comparison of nutrient intake levels of children among three groups 1 month after admission. *Compared with control group, p<0.05; #compared with restricted diet group, p<0.05.

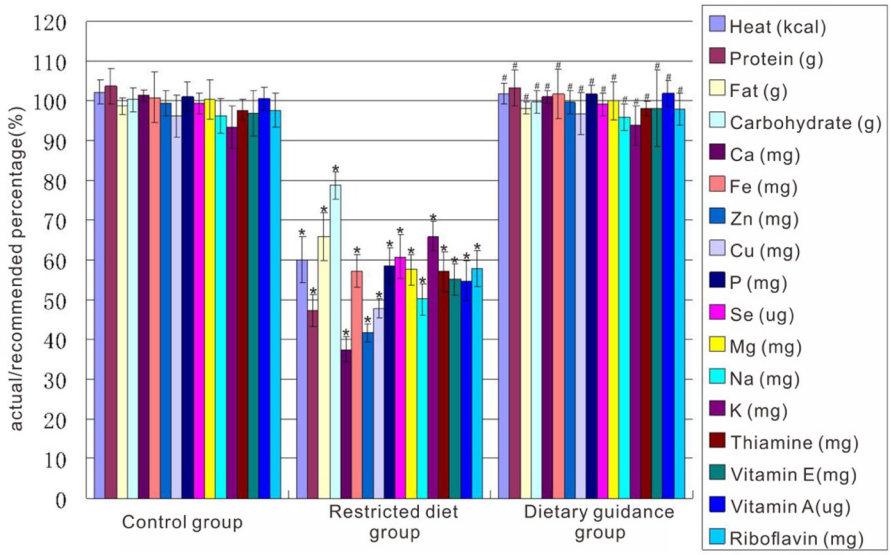


**Figure 4** Comparison of nutrient intake levels of children among three groups 3 months after admission. *Compared with control group, p<0.05; #compared with restricted diet group, p<0.05.

guidance group, there were 26 children with HB (86.67%) in the normal range, 4 children (13.33%) with mild anemia, no children with moderate or severe anemia. These results suggested that the detection rate of anemia in the dietary guidance group was significantly lower than that in the restricted diet group (p<0.05) (online supplemental table 2).

### *Effect of dietary guidance on indicators of blood biochemical test of children with HSP*

Our study demonstrated the levels of serum triglyceride, cholesterol, prealbumin, total protein, albumin and globulin in the children of the restricted diet group increased gradually at 1, 2 and 3 months after admission, which were still significantly lower than those in children of the control group (p<0.05). Compared with the restricted diet group, the levels of serum triglyceride, cholesterol, prealbumin, total protein, albumin and globulin in the children of dietary guidance group were significantly increased (p<0.05), but there were no significant differences between dietary guidance group and control group (p>0.05) (online supplemental table 3).

### Effect of dietary guidance on the growth of children with HSP

Three months after the treatment of restricted diet, the weight, upper arm circumference, skinfold thickness of triceps brachii, subscapular skinfold thickness and BMI of the children in the restricted diet group were significantly lower than those of children in the control group (p<0.05), except that there was no significant difference in height between restricted diet group and control group (p>0.05). However, 3 months after the treatment of dietary guidance, there were no significant differences in these indicators between dietary guidance group and control group (p>0.05) (online supplemental table 4).

According to the value of BMI, the physical condition of children is classified as the following four grades: 18.5–23.9 is normal, <18.5 is chronic malnutrition, 24.0–27.9 is overweight and >28 is obesity. Three months after the treatment, our study showed that in the restricted diet group, there were 13 children (43.33%) with BMI in the normal range, 17 children (56.67%) were chronic malnutrition and there were no overweight children or children with obesity. In the dietary guidance group, there were 24 children

**Table 2** Comparison of levels of trace elements in the whole blood of children with HSP

| | 1 month after admission | | 2 months after admission | | 3 months after admission | | |
|---|---|---|---|---|---|---|---|
| Elements | Restricted diet group | Dietary guidance group | Restricted diet group | Dietary guidance group | Restricted diet group | Dietary guidance group | Control group |
| Zn (μmol/L) | 61.20±5.12* | 106.77±10.12† | 62.45±5.6* | 162.45±15.6† | 64.56±4.7* | 164.56±14.7† | 134.12±7.92 |
| Ca (mmol/L) | 1.01±0.08* | 1.91±0.15† | 1.21±0.06* | 2.11±0.16† | 1.34±0.12* | 2.24±0.16† | 1.87±0.18 |
| Mg (mmol/L) | 1.18±0.17 | 1.78±0.17 | 1.76±0.12 | 1.86±0.11 | 1.46±0.17 | 1.58±0.13 | 1.52±0.15 |
| Cu (μmol/L) | 7.9±0.12* | 14.9±1.22† | 10.01±0.61* | 18.01±1.51† | 11.2±0.70* | 20.2±1.70† | 23.56±2.33 |
| Fe (mmol/L) | 5.43±0.48* | 10.45±0.88† | 5.79±0.02* | 11.56±0.79† | 6.21±0.76* | 10.21±0.37† | 9.25±0.98 |

*Compared with control group, p<0.05.
†Compared with restricted diet group, p<0.05.

(80.00%) with BMI in the normal range, 3 children (10%) were overweight, 1 child (3.33%) had obesity and only two children (6.67%) had chronic malnutrition. Compared with control group, the detection rate of chronic malnutrition in the restricted diet group was significantly higher ($p<0.05$). There was no statistical difference in the detection rate of chronic malnutrition between dietary guidance group and control group ($p>0.05$) (online supplemental table 5).

### Effect of dietary guidance on the treatment and complications of children with HSP

Our study demonstrated that the time of complete skin rash disappearance of children in the dietary guidance group was significantly lower than that of children in the restricted diet group (11.25±1.05 days vs 18.5±1.75 days, $p<0.05$). In the dietary guidance group, 6 children (20%) had repeated rashes, which was significantly less than that in the restricted diet group (14, 46.67%) ($p<0.05$). There were two children with rash recurrence in the dietary guidance group, which was significantly less than that in the restricted diet group (eight children) ($p<0.05$). In the restricted diet group, 19 children suffered from renal involvement, including 13 children had hematuria and 6 children had hematuria combined with proteinuria. However, 11 children of dietary guidance group (8 children had hematuria and 3 children had hematuria combined with proteinuria) suffered from renal involvement, and the incidence was significantly lower than that of the restricted diet group (36.67% vs 63.33%, $p<0.05$) (online supplemental table 6).

## DISCUSSION

Nutrition is the material basis of growth and development of children. Children aged 4–10 years are in the rapid growth period of physical development, and more nutrients are required. The reasonable intake of energy and various nutrients, especially protein, palys an important role in these processes. The nutritional deficiency caused by insufficient intake of protein and/or heat energy, namely protein energy malnutrition (PEM), is short for malnutrition. In this study, no matter 1 month, 2 months or 3 months after admission, the nutritional intake levels of children in the diet restriction group were relatively low. Although the overall nutrient intake level of children in the restricted diet group showed an increasing trend, most of the nutrient intake level only increased to >50% of RNI at 3 months after admission, which was unable to meet the normal nutritional needs of children. In particular, the intake level of calories and protein has been at a low level in the whole process of the implementation of the diet restriction program, and lack of intake is more likely to lead to PEM. These results suggested that the dietary structure of the conventional restricted diet programs is very unreasonable for children with HSP, and the long-term protein deficiency and low nutrient level are likely to lead to PEM in these children, which was not conducive to the recovery of children with HSP. This report is also consistent with the contemporary study.[13]

Recently, more and more attention has been paid to the important role of diet in human health and disease recovery.[18] Dietary survey is one of the important means to investigate the dietary structure of the population, which is also a common method to evaluate the nutrition of patients. The analysis of dietary nutrition in different periods after admission showed that the overall nutrient intake levels of children in the dietary guidance group were relatively high, and the actual intake level of most nutrients reached 90%–110% of RNI. In order to avoid increasing the burden on the gastrointestinal tract of children with HSP, their food intake was slightly below normal. The actual/recommended percentage of each nutrient of dietary guidance group can reach 93%–101% (>75% of the RNI), which can meet the needs of nutrition of children. Interestingly, the intake level of calories and protein has been kept at a high level during the implementation of the dietary guidance diet programs. In the dietary guidance group, the actual/recommended percentage of intake in the three time periods was >98%, which was basically equal to those of control group. These results suggested that the nutritional intake of children in the dietary guidance group was sufficient for children with HSP, which was not easy to cause PEM. In the limited diet, children with HSP mainly rely on carbohydrate energy supply, avoiding the intake of vegetables, fruits and eggs, milk, poultry and meat. Furthermore, the deficiency of nutrition levels in the restricted diet programs were analyzed by dietary survey, and children with HSP were instructed to intake proper amount of eHF or AAF, which made up for the deficiency of various nutrients in the limited diet, supplemented the nutrients required by children, and promoted the recovery of the children with HSP.

The content of trace elements in human body exhibits a very close association with health, which is particularly important for growth and development of children.[19] In our study, in the restricted diet group, the levels of Zn, Ca, Cu and Fe of three time periods were lower than the normal reference range, and were significantly lower than that of the control group, especially the level of iron, which decreased more significantly. These results suggested that the levels of Zn, Ca, Cu and Fe of children in the restricted diet group were in a state of deficiency and insufficient intake, which may be related to the limited nutrient intake level of children in the restricted diet group. The levels of trace elements of children in the dietary guidance group reached the normal reference range, and the levels of Zn, CA, Cu and Fe in the three time periods were significantly higher than those of children in the diet restriction group, which may be related to the reasonable intake of trace elements provided by eHF or AAF.

Because of the lack of protein intake, the metabolism of protein in the body is in a negative balance, which results in the decrease of concentration of protein. In this study, due to the strict restriction of protein intake in the restricted diet group, the levels of serum triglyceride, cholesterol, prealbumin, total protein, albumin and globulin in the children of the restricted diet group increased gradually at 1, 2 and 3 months after admission, which were still significantly lower than those in children of the control group. Compared with the restricted diet group, the levels of serum triglyceride, cholesterol, prealbumin, total protein, albumin and globulin in the children of dietary guidance group were significantly increased. These results showed that the children in diet guidance group are better than those in diet restriction group in terms of body nutrition evaluation, and the diet nutrition guidance is reasonable and effective in

the application of eHF or AAF, which can meet the protein needs of children with HSP and promote their growth. Our report is also consistent with the research that eHF and AAF can effectively reduce protein allergy and support normal growth and development of infants.[16]

In addition, the weight, upper arm circumference, skinfold thickness of triceps brachii, subscapular skinfold thickness and BMI of children in the restricted diet group decreased significantly after 3 months of restricted diet treatment, especially the changes of weight and BMI were the largest, 56.67% of children with HSP were in state of chronic malnutrition. Physical development of children is the main indicator of their health.[20] Malnutrition can lead to wasting, dwarfism, stunting and other diseases, and also affect brain development and intellectual development of children. On the basis of the conventional diet restriction treatment, the children in the dietary guidance group were supplemented with a proper amount of eHF or AAF to make up for the deficiency of various nutrients. Three months after the treatment of dietary guidance, there were no significant differences in these indicators (weight, upper arm circumference, skinfold thickness of triceps brachii, subscapular skinfold thickness and BMI) between dietary guidance group and control group, suggesting that the growth and development level of children with HSP reached the level of normal children. The detection rate of chronic malnutrition in dietary guidance group was only 10%, which was close to the detection rate of malnutrition in Chinese adolescent.[21] In summary, our study indicated that the diet structure of dietary guidance group was reasonable and long-term application was beneficial to the growth and development of children with HSP.

In this study, on the basis of forbiddance of eating fish, shrimp, meat, eggs, milk, vegetables and fruits, the eHF or AAF were added to the children of the dietary guidance group to make the level of various nutrients of diet of children with HSP consistent with the RNI through dietary nutrition analysis. The results showed that the time of complete skin rash disappearance of children in the dietary guidance group was significantly lower than that of children in the diet restriction group, and the number of children with repeated and relapsed rashes was also significantly less than that of children in the diet restriction group. The reasons for these findings may be related to the fact that the children in the diet guidance group evaded the allergen protein and the suspected allergic substances. Besides, the incidence of renal involvement in dietary guidance group was significantly lower than that of the restricted diet group. The renal impairment caused by recurrence of HSP is more serious than that caused by initial HSP,[22] and with the increase of frequency of recurrence, the renal impairment was more and more serious, resulting in poor prognosis of children.[23] Avoiding the inducement of recurrence and reducing the frequency of recurrence are the key to the treatment of HSP. Therefore, after the application of the eHF or AAF, the intake of nutrients is sufficient, the nutritional status of the body is good, thus the overall immunity of the body is improved, which is more conducive to the elimination of the rash and the reduction of recurrence of HSP, further promoting the recovery of children with HSP and reducing the occurrence of other complications.

In conclusion, the application of eHF or AAF under dietary guidance can improve the intake of nutrients and protein in children with HSP, which is conducive to the healthy growth of children and can make the nutritional status, growth and development of children with HSP reach to normal. Besides, dietary guidance can reduce the recurrence rate of skin rash and reduce the occurrence of complications.

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**ORCID iD**
Wanli Xue http://orcid.org/0000-0003-2025-4588

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