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# Effects of Chaihu Jia Longgu Muli Decoction Combined with Dietary Intervention on Serum Antibody Profiles in Children with Tic Disorders

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## Abstract

**This study investigated the effects of Chaihu Jia Longgu Muli Decoction combined with dietary intervention on serum anti-streptolysin O (ASO) and food-specific IgG antibodies in children with tic disorders (TD). Thirty children with TD were divided into two groups of 15 for combined intervention and traditional Chinese medicine (TCM) treatment, respectively, and 30 healthy children were selected as controls. Both treatment groups received Chaihu Jia Longgu Muli Decoction for 3 months, with additional dietary intervention in the combined group. The ASO positivity rate in children with TD was 66.7% (20/30), which differed significantly from that in healthy controls ($P<0.05$). After treatment, serum ASO levels decreased from 345.0 ± 25.6 to 239.1 ± 20.0 ($t=3.36$, $P<0.05$), while no significant difference was observed between the two treatment groups ($P>0.05$). Although food-specific IgG antibody distributions were comparable before treatment ($P=0.418$), a significant between-group difference was observed after treatment ($\chi^2=6.930$, $P=0.031$). In the combined group, the total number of positive antibodies decreased by 41.5%, from 41 to 24, while the number of 3+ antibodies decreased from 11 to 1. These results suggest that treatment was associated with a reduction in ASO levels, while additional dietary intervention was associated with changes in food-specific IgG antibody profiles. However, the clinical significance of these antibody changes remains unclear and warrants further investigation.**

## Keywords

**Tic disorders; Chaihu Jia Longgu Muli Decoction; dietary intervention; anti-streptolysin O; food-specific IgG.**

## 1. INTRODUCTION

Tic disorders (TD) is a common neurodevelopmental disorder in children and adolescents, which is characterized by sudden, rapid, repeated, non rhythmic motor tic and/or vocal tic. According to the clinical manifestations, duration and diagnostic criteria, tic disorders mainly include temporary tic disorders, persistent (chronic) motor or vocal tic disorders, Tourette syndrome (TS) and other types [1,2]. The disease often starts in childhood, and its clinical manifestations are volatile. Some children can be accompanied by attention deficit hyperactivity disorder, obsessive-compulsive behavior and emotional problems, which have a certain impact on children's learning, social and family life.

At present, the pathogenesis of tic disorders remains incompletely understood. Previous studies have suggested that genetic susceptibility, abnormalities in neurotransmitter systems, immune-inflammatory responses, and environmental factors may contribute to disease development [2-5]. Among these factors, infection-related immune responses have attracted

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attention, particularly in relation to pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS) [10-12]. However, the relationship between streptococcal infection and tic disorders remains controversial, and evidence supporting a direct causal association is insufficient. Anti-streptolysin O (ASO) is an antibody produced in response to streptolysin O and may serve as a serological indicator of previous or recent streptococcal exposure. Nevertheless, an elevated ASO level alone cannot establish active infection or confirm that streptococcal infection is the cause of tic symptoms [12].

In addition to the immune response to infection, other links between diet and the gut microbiome in children's neuropsychiatric disorders have also been studied. Recently, researchers have investigated whether changes in the gut microbiome and dietary factors are related to tic disorders, but the specific mechanisms underlying these relationships remain unclear [6-8,14]. Some clinical studies have also used food-specific IgG tests to examine antibody responses to certain foods. The presence of food-specific IgG antibodies does not necessarily indicate food allergy or food intolerance. At present, clinical recommendations do not support the use of food-specific IgG testing as an independent diagnostic tool for food allergy or hypersensitivity [9,15]. Therefore, such results should be interpreted cautiously and considered in conjunction with dietary history and clinical manifestations.

According to traditional Chinese medicine (TCM), tic disorders are often classified within the theoretical categories of liver wind and convulsions. The disease is considered to involve multiple internal organs, particularly the liver, spleen, and heart, and its pathogenesis may be associated with wind, phlegm, and an imbalance of Yin and Yang. Chaihu Jia Longgu Muli Decoction, as mentioned in Shanghan Lun, is traditionally used to harmonize the Shaoyang and calm the spirit. According to the clinical features of tic disorders in children and the principles of TCM syndrome differentiation, a modified application of this classical formula may provide a theoretical basis for clinical treatment. Pharmacological studies in recent years have investigated its possible mechanisms in depression, but its effects in children with tic disorders have not yet been established [13].

Proper dietary management is important to provide all the necessary nutrients for the healthy growth and development of children. Dietary patterns may affect the composition and metabolism of gut microbiota and have therefore been linked to various aspects of neurodevelopment and mental health [6,14]. Based on this background, the present study investigated the effects of Chaihu Jia Longgu Muli Decoction combined with dietary intervention on serum ASO levels and food-specific IgG antibody profiles in children with tic disorders, aiming to provide preliminary clinical observations of this combined intervention.

## 2. METHODS

### 2.1. Research object

30 children with tic disorder who met the inclusion criteria were selected, and 30 healthy children were selected as the healthy control group. Children with tic disorder were divided into combined intervention group and simple Chinese medicine treatment group according to the treatment scheme, with 15 cases in each group.

General data such as age, gender, course of disease, clinical manifestations and related medical history were collected. The general information of each group should be filled in according to the original case record.

### 2.2. Diagnostic Criteria

The diagnosis of tic disorders was established according to the diagnostic criteria described in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-

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5-TR), with reference to relevant clinical guidelines [1,2,16]. Diagnoses were determined based on the children's clinical manifestations, age at onset, symptom duration, and disease course.

## 2.3. Inclusion Criteria

(1) It met the diagnostic criteria of tic disorder;

(2) Age meets the preset range of this study [to be added];

(3) Complete clinical data, able to cooperate with the completion of treatment and serological testing;

(4) The guardians of the children were informed and agreed to participate in the study.

## 2.4. Exclusion Criteria

(1) Patients with severe diseases of the heart, liver, kidneys, or other major organs;

(2) Patients with severe neurological disorders or other diseases that may interfere with the study results;

(3) Patients with a confirmed acute infection shortly before enrollment that may significantly affect serological test results;

(4) Patients with known contraindications to any of the medications used in the study;

(5) Patients with incomplete clinical data or those unable to complete the prescribed treatment course.

## 2.5. Treatment Methods

### 2.5.1 Chaihu Jia Longgu Muli Decoction

Both treatment groups received Chaihu Jia Longgu Muli Decoction for 3 months. The prescription was based on the classical formula recorded in Shanghan Lun, with appropriate modifications according to the children's clinical manifestations and traditional Chinese medicine syndrome differentiation. The main ingredients included Bupleurum (Chaihu), Scutellaria baicalensis (Huangqin), Pinellia ternata (Banxia), Ginseng (Renshen), Poria (Fuling), Cinnamon twig (Guizhi), Fossilized bone (Longgu), Oyster shell (Muli), Rhubarb (Dahuang), Ginger (Shengjiang), Jujube (Dazao), and other components as clinically indicated. The herbal medicines were obtained from the hospital pharmacy and prepared in granule form. The medication was administered orally according to the hospital's established clinical protocol. The treatment duration was 3 months.

### 2.5.2 Combined Intervention Group

In addition to Chaihu Jia Longgu Muli Decoction, children in the combined intervention group received individualized dietary intervention for 3 months. Dietary adjustments were made according to each child's dietary habits and clinical conditions, with attention to nutritional balance and intervention compliance.

### 2.5.3 Traditional Chinese Medicine Treatment Group

Children in the TCM treatment group received Chaihu Jia Longgu Muli Decoction alone for 3 months, without additional dietary intervention.

## 2.6. Detection of Serological Indicators

### 2.6.1 ASO Detection

The peripheral venous blood was collected before treatment and 3 months after treatment, and the ASO level was detected after serum separation. Immunoturbidimetric method was used for detection, and the specific detection steps were carried out in accordance with the test reagent instructions and laboratory standard operating procedures. The ASO test results of each

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group before and after treatment were recorded, and whether the test results were positive was judged according to the laboratory reference range.

2.6.2 Food Specific IgG Detection

Enzyme linked immunosorbent assay (ELISA) was used to detect the food specific IgG antibody in children's serum. According to the test results, the positive levels of different food related antibodies were recorded, including 1+, 2+and 3+. At the same time, the number of antibodies with different positive levels in each group and the number of food types involved in positive antibodies in the test results of each child were counted.

The specific test food type, reagent manufacturer, test steps and positive judgment standards shall be supplemented according to the actual test reagents and laboratory operation records.

### 2.7. Observation Indexes

(1) The positive rate of ASO was compared between tic disorder children and healthy control group;

(2) The changes of ASO level in children with tic disorder before and after treatment were compared;

(3) Aso levels were compared between the combined intervention group and the simple Chinese medicine treatment group after treatment;

(4) The grade distribution of food specific IgG positive antibodies before and after treatment was compared between the two groups;

(5) The distribution of food types involved in food specific IgG positive antibodies before and after treatment in the two treatment groups was compared.

### 2.8. Statistical Methods

Statistical analyses were performed using SPSS software. The normality of continuous variables was assessed before analysis. Normally distributed data were expressed as mean ± standard deviation. Independent-samples t-tests were used for comparisons between groups, while paired-samples t-tests were used for comparisons before and after treatment within each group. Non-normally distributed data were analyzed using appropriate nonparametric tests. Categorical data were expressed as numbers and percentages and compared using the chi-square test or Fisher’s exact test, as appropriate. A two-sided P value of less than 0.05 was considered statistically significant.

For food-specific IgG antibody levels, antibody counts and patient counts were distinguished, and appropriate statistical methods were selected according to the actual data structure.

## 3. RESULTS

### 3.1. Comparison of ASO Test Results Between Tic Disorder Children and Healthy Control Group

The positive rate of ASO in children with tic disorder was 66.7% (20g30). The difference between the two groups was statistically significant (P<0.05). The results suggest that some children with tic disorder have positive expression of serological indicators related to streptococcal infection, but streptococcal infection cannot be directly identified as the cause of tic disorder.

### 3.2. Comparison of ASO Levels in Children with Tic Disorder Before and After Treatment

The level of ASO in children with tic disorder decreased after treatment, and the difference was statistically significant (t=3.36, P<0.05). There was no significant difference in ASO level

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between the combined intervention group and the simple Chinese medicine treatment group after treatment (t=0.57, P>0.05). See Table 1 for specific results.

**Table 1.** Comparison of ASO levels in children with tic disorder before and after treatment

| Group | n | ASO level |
|---|---|---|
| Before treatment | 30 | 345.0 ± 25.6 |
| After treatment | 30 | 239.1 ± 20.0 |
| t value | — | 3.36 |

Note: after treatment, the ASO level in the combined intervention group was compared with that in the simple Chinese medicine treatment group, t=0.57,P＞0.05.

The mean, standard deviation and specific cases of the two groups need to be supplemented according to the original data.

### 3.3. Comparison of Food Specific IgG Positive Antibody Levels Between the Two Groups Before Treatment

Before treatment, the distribution of food specific IgG positive antibodies in 1+, 2+and 3+levels in the combined intervention group and the simple Chinese medicine treatment group were 17, 13, 11 and 12, 7, 13, respectively. There was no significant difference between the two groups ($\chi^2$=1.746, P=0.418), suggesting that the distribution of positive antibody levels in the two groups before treatment was comparable. The results are shown in Table 2.

**Table 2.** Comparison of food specific IgG positive antibody levels between the two groups before treatment

| Group | 1+ | 2+ | 3+ | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| Combined intervention group | 17 | 13 | 11 | 1.746 | 0.418 |
| Chinese medicine treatment group | 12 | 7 | 13 | \ | \ |

Note: the data in the table are the number of antibodies of each positive grade, not the number of children; The specific statistical units and statistical methods need to be further verified in combination with the original data.

### 3.4. Comparison of Food Specific IgG Positive Antibody Grade Distribution Between the Two Groups after Treatment

After treatment, the levels of 1+, 2+and 3+in the food specific IgG positive antibodies in the combined intervention group were 15, 8 and 1 respectively, and those in the simple Chinese medicine treatment group were 11, 7 and 9 respectively. The number of 3+positive antibodies in the combined intervention group was significantly reduced, and the difference in the distribution of positive antibodies between the two groups after treatment was statistically significant ($\chi^2$=6.930, P=0.031). The results are shown in Table 3.

**Table 3.** Comparison of food specific IgG positive antibody level distribution between the two groups after treatment

| Group | 1+ | 2+ | 3+ | $\chi^2$ value | P value |
|---|---|---|---|---|---|
| Combined intervention group | 15 | 8 | 1 | 6.930 | 0.031 |
| Chinese medicine treatment group | 11 | 7 | 9 | \ | \ |

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Note: the data are presented as the number of positive food-specific IgG antibodies at each level. The distribution of antibody levels differed significantly between the two groups after treatment ($\chi^2$ = 6.930, P = 0.031).

### 3.5. Comparison of the Distribution of Food Types Involved in Food Specific IgG Positive Antibodies between the Two Groups before Treatment

Before treatment, 5 cases, 3 cases and 7 cases of children with one, two, three or more food related positive antibodies were detected in the combined intervention group; There were 5 cases, 5 cases and 5 cases in the simple Chinese medicine treatment group. The distribution of food species involved in the two groups of food related positive antibodies was relatively close. The results are shown in Table 4.

**Table 4.** Distribution of food types involved in food specific IgG positive antibodies in the two groups before treatment

| Number of IgG-positive food items | Combined intervention group (n=15), n (%) | Chinese medicine treatment group (n=15), n (%) |
|---|---|---|
| 1 | 5 (33.3%) | 5 (33.3%) |
| 2 | 3 (20.0%) | 5 (33.3%) |
| ≥3 | 7 (46.7%) | 5 (33.3%) |
| Total | 15 (100%) | 15 (100%) |

Note: the data are presented as the number and percentage of patients. The number of positive food items was counted for each patient. Percentages were recalculated based on 15 patients in each group.

### 3.6. Comparison of the Distribution of Food Types Involved in Dood Specific IgG Positive Antibodies Between the Two Groups after Treatment

After treatment, 2 cases in the combined intervention group did not detect food specific IgG positive antibody, 6 cases detected a food related positive antibody, 4 cases detected two kinds, and 3 cases detected three or more kinds. In the pure Chinese medicine treatment group, 1 case did not detect positive antibodies, 5 cases detected one kind, 6 cases detected two kinds, and 3 cases detected three kinds or more. The results are shown in Table 5.

**Table 5.** Distribution of food types involved in food specific IgG positive antibodies in the two groups after treatment

| Number of positive food types | Combined intervention group (n=15) | TCM treatment group (n=15) |
|---|---|---|
| 0 | 2(13.3%) | 1(6.7%) |
| 1 | 6(40.0%) | 5(33.3%) |
| 2 | 4(26.7%) | 6(40.0%) |
| ⩾3 | 3(20.0%) | 3(20.0%) |
| Total | 15(100%) | 15(100%) |

Note: the data are presented as the number and percentage of patients. The number of food-specific IgG-positive food items was counted for each patient. Percentages were recalculated based on 15 patients in each group.

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### 3.7. Changes in the Number of Food Specific IgG Positive Antibodies in the Combined Intervention Group Before and After Treatment

Among the food specific IgG positive antibodies in the combined intervention group before treatment, the levels of 1+, 2+and 3+were 17, 13 and 11, respectively, with a total of 41; After treatment, there were 15 cases, 8 cases and 1 case, a total of 24 cases. After treatment, the total number of positive antibodies decreased by 17, with a decrease rate of 41.5%. Among them, 1+decreased by 2, 2+decreased by 5, and 3+decreased by 10, suggesting that the number of high-grade positive antibodies in the combined intervention group decreased significantly after treatment.

It should be pointed out that the above decline rate is a descriptive index calculated based on the total number of positive antibodies, not the decline rate of the number of children, nor can it be directly equivalent to the improvement of clinical food intolerance.

## 4. DISCUSSION

The results showed that 66.7% of children with tic disorders had elevated serum anti-streptolysin O (ASO) levels compared to those of healthy children. Previous research has proposed that infection-related immune responses may be involved in the acute neuropsychiatric symptoms of some children, particularly in pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS) [11, 12]. However, the causal relationship between streptococcal infection and common tic disorders remains unclear. Although high ASO levels may be due to past or current streptococcal infection, a single test is not conclusive. The 2025 clinical report of the American Academy of Pediatrics also indicated that ASO and anti-DNase B should not be used alone for the diagnosis of PANS or to determine whether an infection caused neuropsychiatric symptoms [12].

Serum ASO levels were reduced to a certain extent after treatment ($t=3.36$, $P<0.05$), but there was no further significant difference between the combined intervention and the TCM treatment groups following treatment ($t=0.57$, $P>0.05$). Therefore, no additional effect of dietary intervention on the reduction of ASO was demonstrated. Changes in ASO levels may also be due to the natural course of the disease and the time since the previous infection; therefore, further research is needed.

Chaihu Jia Longgu Muli Decoction originates from Zhang Zhongjing's Shanghan Lun and is generally used to regulate the Shaoyang and soothe the nerves. The original materials for these herbs are generally used to reduce heat and regulate the body's Qi. The above therapeutic ideas may offer some theoretical support for the treatment of certain children with tic disorders, such as those with restlessness, sleep problems, and mood swings. Recently, pharmacological research has investigated the relevant mechanisms of depression via meta-analysis and network pharmacology [13]. However, these findings provide only indirect pharmacological evidence and have not established its efficacy in children with tic disorders.

There was no significant difference in the distribution of 1+, 2+, and 3+ antibody levels for food-specific IgG antibodies between the two treatment groups before treatment ($P=0.418$). After treatment, the corresponding numbers were 15, 8, and 1 in the combined intervention group and 11, 7, and 9 in the TCM treatment group, with a significant between-group difference ($P=0.031$). The total number of positive antibody findings in the combined group decreased from 41 to 24 (41.5%), while 3+ findings decreased from 11 to 1. The above modifications indicate changes in food-specific IgG antibody profiles after combined treatment; however, their clinical significance remains unclear. Food-specific IgG positivity is not always associated with food allergy or intolerance. The 2023 European Academy of Allergy and Clinical Immunology (EAACI) guidelines do not recommend isolated food-specific IgG testing for the diagnosis of IgE-

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mediated food allergy [9], and recent professional recommendations have also discouraged its use as a diagnostic tool for food hypersensitivity [15]. Therefore, these tests should be interpreted as preliminary serological findings and cannot be used to diagnose food allergies or intolerances.

Regarding the distribution of food types associated with positive IgG tests, no positive antibodies were detected in the 2 children of the combined intervention group and the 1 child of the TCM treatment group after treatment. Meanwhile, 7 and 9 children, respectively, had positive findings for two or more food types. These descriptive changes should not be interpreted as evidence of food allergy or intolerance. Based on an individual's dietary history and clinical conditions, dietary adjustments should be made to provide adequate nutrition and support normal growth.

Overall, serum ASO levels decreased after treatment, and food-specific IgG antibody profiles changed in the combined intervention group. However, these findings do not establish a causal relationship between antibody changes and tic disorders or demonstrate additional clinical benefits from dietary intervention. The small sample size and short treatment period were important limitations of this study. Further multicenter, prospective studies with larger samples, standardized TCM prescriptions and dietary interventions, and comprehensive clinical and laboratory assessments are needed to clarify the clinical significance of these findings.

## 5. CONCLUSION

This study found that serum ASO levels decreased after treatment in children with tic disorders, although no statistically significant difference was observed between the combined intervention group and the traditional Chinese medicine treatment group. In addition, the combined intervention group showed changes in the distribution of food-specific IgG antibody levels after treatment. However, these findings do not establish the additional clinical benefits of dietary intervention or demonstrate a causal relationship between food-specific IgG antibodies and tic disorders. Further multicenter, prospective studies with larger sample sizes and standardized intervention protocols are needed to clarify the clinical significance of these findings.

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