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Original Research Article

Efficacy of Jade Wind-Barrier Powder in adjuvant treatment for children with asthma, and its influence on IFN-γ, immunoglobulin and mucin

Huifen Wu, Pengfei Li, Jingying Guan, Jiaxuan Hong*
Department of Pediatrics, Hangzhou Xiaoshan Hospital of Traditional Chinese Medicine, Hangzhou, Zhejiang Province 311200, China

For correspondence:* ***Email:* *hjx_jiaxuan789@163.com;* ***Tel:*** *+86-13867170152*

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Abstract

Purpose: *To study the effects of Jade Wind-Barrier Powder on peripheral blood interferon-γ (INF-γ), immunoglobulin and sputum mucin in children with asthma.*
Methods: *Sixty-six children with asthma in remission stage were randomly separated into study and control groups. The control group was treated with budesonide formoterol powder inhaler, while the study group was orally administered Jade Wind-Barrier Powder. The therapeutic effects, and INF-γ, immunoglobulin and mucin levels in sputum, as well as pulmonary function parameters in both groups were determined. The number of acute relapses of asthma and duration of wheezing were counted in the patients. The relative effectiveness of Jade Wind-Barrier Powder in the treatment of asthma in the children was also assessed.*
Results: *The overall response rate (ORR) in the study group was 93.94 %, which was higher than in the control group (75.76 %, $p < 0.05$). Over the 6-month period of follow-up, the frequency of acute attacks of asthma in the study group was significantly lower while the duration of wheezing during attack was also shorter than in the control group. After treatment, pulmonary function indices in the study group were higher, whereas mucin 5AC (MUC5AC), mucin 5B (MUC5B) and mucin 1 (MUC1) levels in sputum were lower than in the control group ($p < 0.05$).*
Conclusion: *Jade Wind-Barrier Powder exerts therapeutic effect in children with asthma. However, further clinical trials across multi-centers are required to validate it its use in clinical practice.*

Keywords: *Asthma in children, Jade Wind-Barrier powder, Peripheral blood interferon-γ, Immunoglobulin, Mucin*

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INTRODUCTION

Asthma remains a common respiratory disease in childhood, with recurrent wheezing, cough, and shortness of breath as the main clinical manifestations, seriously affecting children's learning and life [1]. Asthma is divided into acute and remission phases. For treating asthma in remission, it is necessary to prevent and reduce acute episodes of asthma [2].

At present, there is still a lack of drugs for thorough treatment of asthma. In medicine, bronchodilators and glucocorticoids are utilized as the mainstream drugs for the treatment of asthma in clinical practice. However, inhaled corticosteroid (ICS) has restrictions in dose-dependent growth, and many parents have insufficient cognition of drugs, often leading to poor compliance in children with asthma towards conventional western medicine [3]. It shows great importance therefore, to seek a safer and more effective treatment, which promotes the stability of children with the asthma condition, as well as improve the prognosis and their quality of life.

Traditional Chinese Medicine (TCM) attributes asthma into the categories of "gasping syndrome" and "wheezing syndrome", and deems that the disease is located in the lung, with manifestations of upward adverse flow of phlegm and airway occlusion. TCM treatment attaches importance to the overall concept, and holds that the treatment of asthma in remission should focus on supplementing and ventilating lung qi, fortifying the spleen and boosting the kidneys [4]. Jade Wind-Barrier Powder, derived from Danxi's Mastery of Medicine in Yuan Dynasty, is a famous prescription for reinforcing vital energy and consolidating the constitution in traditional Chinese medicine, which has the effect of tonifying the lung, replenishing qi, and consolidating the exterior [5]. The aim of the present study was to determine the effectiveness of Jade Wind-Barrier Powder in children with stable asthma.

METHODS

Study subjects

A total of 66 children with asthma in remission admitted to Hangzhou Xiaoshan Hospital of Traditional Chinese Medicine from June 2021 to June 2022 were included in the study, and divided randomly into study and control groups, with 33 children in each group. The study group consisted of 16 males and 17 females aged 5 - 14 years (mean, 8.45 ± 2.16 years). Duration of asthma was 1 - 5 years (mean, 2.26 ± 0.36 years). The control group comprised 18 males and 15 females aged 5 - 13 years (mean, 8.74 ± 2.03 years) with duration of asthma of 1 - 5 years (mean, 2.13 ± 0.41 years). There was no significant difference in general profile between both groups ($p > 0.05$). All the procedures performed in the study were approved by the Ethics Committee of Hangzhou Xiaoshan Hospital of Traditional Chinese Medicine (approval no. 2022020), and followed the guidelines of 1964 Helsinki Declaration and its later amendments for ethical research involving human subjects [6].

Diagnostic criteria of traditional Chinese and Western medicine

The diagnostic criteria used were based on the relevant criteria in the Guidelines for the Diagnosis and Prevention of Bronchial Asthma in Children of the Chinese Society of Pediatrics [7], as well as well as the diagnostic and therapeutic criteria stipulated in Pediatric Diseases in Traditional Chinese Medicine [8].

Inclusion criteria

Patients met the relevant diagnostic criteria of Chinese and Western medicine; were in the remission stage of asthma: the child's clinical symptoms and signs have disappeared, pulmonary function indices including forced expiratory volume in 1 s (FEV1) or peak expiratory flow rate ≥ 80 % predicted value, and maintained for 3 months or more; children aged 5 to 14 years; disposed to cooperate during the relevant examination and treatment; the children's parents must have signed the informed consent.

Exclusion criteria

Patients who are allergic to the test drug as well as those suffering from other serious systemic diseases.

Treatments

Based on the Guidelines for the Diagnosis and Prevention of Bronchial Asthma in Children [7], children in the control group were given budesonide formoterol powder inhaler (80/4.5 ug, AstraZeneca Pharmaceutical Co. Ltd, Switzerland, product batch no. LAPR), 1 inhalation each time twice a day for a total of 3 courses in a 4-week period.

The study group received Jade Wind-Barrier Powder based on the control group. The prescription composition was as follows: 30 g divaricate saposhniovia root, 60 g astragalus and 60 g atractylodes. These medical materials were boiled in water and decocted with gentle fire for 20 min. The same materials were decocted twice, and 400 mL of liquid medicine was obtained, to be taken twice in a warm state (200ml in the morning and evening, respectively). The medicine was administered orally for 4 weeks as a course with a total of 3 courses.

Evaluation of parameters/indices

After 3 courses of medication intervention in both groups, the efficacy of the treatments was statistically analyzed.

(1) After follow-up for 6 months, the frequency of asthma exacerbations and the duration of wheezing symptoms during asthma attacks were counted in both groups.

(2) According to the relevant criteria in the Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine [9], the efficacy index = (pre-treatment score - post-treatment score) /pre-treatment score × 100 %. It was divided into cure (TCM clinical symptoms and signs disappear or basically disappear, efficacy index ≥ 95 %), marked response (TCM clinical symptoms and signs are substantially improved, 70 % ≤ efficacy index < 95 %), moderate response (TCM clinical symptoms and signs are improved, 30 % ≤ efficacy index < 70 %) and no response (TCM clinical symptoms and signs did not notably improve or even aggravated, efficacy index < 30 %).

(3) Pulmonary ventilation function was compared between both groups before and after treatment. Forced expiratory volume in the first second (FEV1), peak expiratory flow (PEF), percentage of predicted forced expiratory volume in the first second (FEV1-Pred %), and percentage of predicted maximum expiratory flow (PEF-Pred %) were measured utilizing the Master Screen IOS spirometer (Jaeger, German).

(4) Peripheral blood interferon-γ (IFN-γ) and immunoglobulin levels were compared between both groups. Before and after treatment, 5 mL of peripheral blood was collected from the children to determine the conventional Ficoll gradient centrifugation. Peripheral blood mononuclear cells (PBMCs) were collected, and IFN-γ levels were measured using an avidin-biotin system-enzyme-labeled immunosorbent assay (ABC-ELISA), and the kit was purchased from Shenzhen Jingmei Biotech Co., Ltd. Immunoglobulin A (IgA) and immunoglobulin G (IgG) levels were measured by immunoturbidimetry, and the kits were purchased from Yilikang Biotechnology Co. Ltd.

(5) Before and after treatment, sputum samples were collected from the children, and was induced by nebulization with 3 % hypertonic saline, treated with 0.1 % dithiothreitol, and filtered. Then, the sample was centrifuged at 3000 r/min for 5 min, and the supernatants were taken to detect mucin 5AC (MUC5AC), mucin 5B (CMUC5B), and mucin 1 (MUC1) levels by enzyme-linked immunosorbent assay (ELISA). The kits were purchased from Shanghai Ji Ning Biotechnology Co. Ltd.

Statistical analysis

The data were processed with SPSS 19.0 statistical software. Measurement data are presented as mean ± SD while independent sample t-test was applied to compare the means between the two groups. Paired t-test was adopted for comparison of the means before and after treatment, while enumeration data were presented as numbers/percentage. χ^2 test was used to compare both groups. $P < 0.05$ indicated statistical significance.

RESULTS

Treatment outcomes

The overall response rate (ORR) in the study group was higher than in the control group ($p < 0.05$). The results are stated in Table 1.

Frequency of acute asthma attacks and duration of wheezing

The frequency of asthma exacerbations in the study group was less than in the control group, while the duration of wheezing during asthma attacks was shorter than in the control group ($p < 0.05$). The results are displayed in Table 2.

Table 1: Comparison of treatment outcomes between both groups [n (%)]

Group	n	Recovered	Marked response	Moderate response	No response	Overall response rate
Study	33	20（60.61）	5（15.15）	6（18.18）	2（6.06）	31（93.94）
Control	33	13（39.39）	6（18.18）	6（18.18）	8（24.24）	25（75.76）
χ^2		--	--	--	--	4.243
P-value		--	--	--	--	0.039

Table 2: Comparison of the frequency of acute asthma attacks and duration of wheezing between both groups (mean ± SD, n = 33)

Group	Frequency of acute attack (N)	Wheezing duration (day)
Study	3.01±0.53	4.36±0.73
Control	4.16±0.64	6.61±0.85
T	7.950	11.536
P-value	<0.001	<0.001

Table 3: Comparison of pulmonary function between both groups before and after treatment (mean ± SD, n = 33)

Group	Time	FEV1-Pred%	PEF-Pred%
Study	Pre-treatment	94.15±7.15	89.54±8.41
	Post-treatment	103.64±8.05	95.14±8.05
	t	-7.173	-3.910
	P-value	<0.001	<0.001
Control	Pre-treatment	94.74±7.26	90.02±8.81
	Post-treatment	96.66±7.79	90.41±8.16
	t	-1.466	-0.264
	P-value	>0.05	>0.05
	t	3.579	2.371
	P-value	<0.001	<0.05

Table 4: Comparison of IFN-γ and immunoglobulin levels in the peripheral blood between both groups before and after treatment (mean ± SD, n = 33)

Group	Time	IFN-γ (ng/L)	IgA (g/L)	IgG (g/L)
Study	Pre-treatment	46.55±11.05	0.74±0.18	7.23±1.45
	Post-treatment	63.67±12.32	1.11±0.21	10.17±1.79
	t	-8.417	-10.900	-10.425
	P	<0.001	<0.001	<0.001
Control	Pre-treatment	45.89±10.85	0.72±0.19	7.19±1.64
	Post-treatment	46.12±11.46	0.76±0.22	7.26±1.73
	t	-0.118	1.121	-0.239
	P	>0.05	>0.05	>0.05
	t	5.992	6.611	6.715
	P	<0.001	<0.001	<0.001

Pulmonary function

After treatment, the FEV1-Pred % and PEF-Pred % levels in the study group were higher than before treatment ($p < 0.05$). The FEV1-Pred % and PEF-Pred % levels in the control group were not significantly different from the values before treatment ($p > 0.05$). However, after treatment, FEV1-Pred % and PEF-Pred % levels were more elevated in the study group than in the control group, icance ($p < 0.05$). The results are shown in Table 3.

IFN-γ and immunoglobulin levels in peripheral blood

After treatment, the IFN-γ, IgA and IgG levels in the study group were higher than before treatment, ($p < 0.05$). On the other hand, IFN-γ, IgA and IgG levels in the control group, pre- and post-treatment, were not significantly different ($p > 0.05$). After treatment, however, IFN-γ, IgA and IgG levels in the study group were higher than in the control group ($p < 0.05$). The results are shown in Table 4.

Mucin levels in sputum

After treatment, the MUC5AC, MUC5B and MUC1 levels in the sputum of both groups were lower than before treatment ($p < 0.05$). However, the levels of all the mucins in sputum in the study group were lower than in control group ($p < 0.05$). The results were displayed in Table 5.

DISCUSSION

Surveys have shown that there are an estimated 334 million asthma patients worldwide, and in recent years, the prevalence of childhood asthma has been on the rise [10]. With the increasing attention paid to asthma prevention and treatment by the Global Initiative for Asthma (GINA) [11], the clinical control of asthma has increased, but due to incomplete disease cognition of parents, asthma control still has not reached the ideal level.

Table 5: Comparison of mucin levels (μg/mL) in sputum between both groups before and after treatment (mean ± SD, n = 33)

Group	Time	MUC5AC	MUC5B	MUC1
Study	Pre-treatment	0.53±0.11	1.21±0.15	1.13±0.23
	Post-treatment	0.24±0.06	0.76±0.21	0.61±0.17
	t	19.600	14.361	14.936
	P-value	<0.001	<0.001	<0.001
Control	Pre-treatment	0.57±0.12	1.24±0.17	1.16±0.21
	Post-treatment	0.44±0.04	1.03±0.19	0.94±0.18
	t	9.335	6.702	6.481
	P-value	<0.001	<0.001	<0.001
	t	15.933	5.477	7.657
	P-value	<0.001	<0.001	<0.001

Aerosol inhalation of bronchodilators and glucocorticoids can play an anti-inflammatory and anti-asthmatic role, with quick effect and good efficacy. However, long-term use of glucocorticoids may weaken body resistance and limit children's growth and development.

Compared with conventional western medicine treatment, TCM treatment is safer, as it emphasizes the overall treatment view, thus improving the body immune function and enhancing the effect of asthma control. Jade Wind-Barrier Powder is a classic prescription for increasing vital energy and consolidating the body. It is mainly composed of three herbs: Astragalus membranaceus, Atractylodes macrocephala Koidz and Divaricate Saposhniovia Root. Astragalus membranaceus has the effect of consolidating exterior and replenishing qi, invigorating qi to elevate yang, then removing stasis and dredging arthralgia. Atractylodes macrocephala Koidz fortifying the spleen to boost qi, thus removing dampness and inducing diuresis. Divaricate Saposhniovia Root functions to dispel pathogenic wind from the muscles, thus eliminating dampness and relieving pain, and it also demonstrates great efficacy in treating xogenous wind-cold, spleen deficiency as well as dampness syndrome [12].

The integration of the three drugs exert the effect of expelling evil and strengthening vital energy, harmonizing nutrient-blood, and invigorating spleen and vital qi. This study discovered that the addition of Jade Wind-Barrier Powder to conventional western medicine can effectively reduce the number of acute attacks of asthma in children, and shorten the duration of wheezing during asthma attacks, and its overall response rate is higher than that of the control group. It is thus suggested that Jade Wind-Barrier Powder effectively maintained the stability of asthma, and reduced acute attacks as well as its clinical symptoms in children.

Additionally, this study found that after intervention with Jade Wind-Barrier Powder, serum IFN-γ and immunoglobulin (IgA, IgG) levels in the study group increased, and there were prominent differences in the levels after treatment compared with the control group. IFN-γ is an inflammatory substance involved in the pathological process of asthma, and has immune regulatory functions which promote Th1, inhibit Th2 cell responses, inhibit bronchial epithelial cell proliferation, and play a negative regulatory role in the development of asthma [13,14]. It has been shown that the expression of IFN-γ signaling pathway continues to decrease in children with bronchial asthma, and plays an essential role in improving the clinical symptoms of asthma and suppressing airway inflammation[15].

Immune factors are critical factors leading to asthma, and studies have shown that IgA, IgG, and IgM levels in asthmatic patients were decreased to some extent, suggesting that humoral immunity participates in the pathogenesis of asthma [16]. After treatment, the serum levels of IFN-γ, IgA and IgG in the study group increased, implying that Jade Wind-Barrier Powder sufficiently regulated the immune function of children with asthma in remission.

Airway mucus hypersecretion is a critical pathophysiological alteration of asthma, and is mainly manifested by increased sputum and evident proliferation of goblet cells. Mucin is a prominent component of mucus. Mucins in the airways are dominated by MUC5AC, MUC5B, as well as MUC1. When mucin level increases, the adhesion of airway mucus also elevates, mucociliary clearance ability is lowered, and the risk of airway microbial infection rises, which adds to the probability of an asthma attack. Elevated mucin levels also triggers airway obstruction, limiting airflow and gas exchange, and causing lung function decline[17]. In the present study, MUC5AC, MUC5B and MUC1

levels in the sputum of the study group were lower than before treatment; furthermore, FEV1-Pred % and PEF-Pred % levels of the pulmonary function indicators were higher than before treatment, suggesting that the addition of Jade Wind-Barrier Powder reduced sputum viscosity and improved the pulmonary ventilation function of children.

As reported in modern pharmacological studies [18], Jade Wind-Barrier Powder enhances human immune function and inhibits the release of sensitizing active substances from mast cells. It has also been discovered that *Astragalus membranaceus* in Jade Wind-Barrier Powder has bidirectional regulatory function, interacts with *Divaricate saposhniovia* root and *Atractylodes macrocephala* Koidz, regulates body immunity, and reduces body inflammatory response [19,20]. This may be the reason why Jade Wind-Barrier Powder improves body immunity and inflammatory response, as well as pulmonary ventilation function in children with asthma.

CONCLUSION

The Jade Wind-Barrier Powder regulates the immune function of children with asthma in remission, reducing airway mucus viscosity and improving pulmonary function. It also reduces the frequency of acute attacks of asthma and symptom severity, and is effective in treating asthma in children. However, the sample size of the studies included in this paper is too small, and this is a single-center study. Therefore, there may also be bias in the experimental data, and hence further multi-center studies with a large sample size are required to confirm the reliability of the conclusions reached in this study.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Huifen Wu and Jiaxuan Hong designed the study and carried them out; Huifen Wu, Peifei Li, Jingying Guan supervised the data collection, analyzed and interpreted the data; Huifen Wu and Jiaxuan Hong prepared the manuscript for publication and reviewed the draft of the manuscript. All authors read and approved the manuscript for publication.

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