

Effects of Family-Supported Healthcare on Children with Asthma

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Introduction: Healthcare is essential for asthma control, however, whether family-supported healthcare improves therapeutic effects in childhood asthma remains unclear.

Methods: The enrolled patients were randomly divided into control and intervention groups. The pulmonary function was evaluated by forced expiratory volume in 1 s as a percentage of forced vital capacity (FEV1/FVC) and fractional exhaled nitric oxide (FeNO). Asthma control and life quality were assessed via a childhood asthma control test and pediatric asthma quality of life questionnaire. Inflammatory cytokines interleukin-6 (IL-6) and interleukin-17 (IL-17) were determined by enzyme-linked immunosorbent assay.

Results: No significant differences existed in the basic characteristics of asthma children and their parents among two groups. The increase of FEV1/FVC was higher in the intervention group versus the control group ($76.47 \pm 10.76\%$ vs $69.76 \pm 8.88\%$, $p = 0.001$ at the time of post-intervention), and the decrease of FeNO was greater in the intervention group (30.43 ± 6.85 bbp vs 35.64 ± 6.62 bbp, $p = 0.003$ at the time of post-intervention). Family-supported healthcare highly improved asthma control and quality of life in childhood asthma post-treatment. Meanwhile, the inflammatory cytokines IL-17 (118.14 ± 25.79 pg/mL in intervention group vs 142.86 ± 28.68 pg/mL in control group, $p = 0.004$ at the time of post-intervention) and IL-6 (103.76 ± 23.11 pg/mL in intervention group vs 119.73 ± 22.68 pg/mL in control group, $p = 0.009$ at the time of post-intervention) significantly decreased by family-supported healthcare intervention. Importantly, acute exacerbation (80.8% in intervention group vs 95.7% in control group, $p = 0.030$) and rehospitalization cases (88.5% in intervention group vs 100% in control group, $p = 0.028$) also decreased by family-supported healthcare intervention.

Discussion: Family-supported healthcare improves pulmonary function and quality of life while alleviates inflammation, acute exacerbation, and rehospitalization in childhood asthma post-routine treatment.

Keywords: asthma, family-supported healthcare, pulmonary function, IL-6, IL-17

Introduction

Bronchial asthma, also known as asthma, is the most common chronic lung disease of childhood, with 420000 deaths worldwide, and developing countries account for over 80% of child deaths worldwide.^{1,2} Asthma is an incurable disease that requires careful management to be controlled. Uncontrolled asthma results in high healthcare costs, including acute ambulatory, emergency and in-patient hospital care. The Global Initiative for Asthma (GINA) regards asthma control as the absence of recurrent exacerbations.³ A recent study showed that 59.6% of asthma patients experienced at least one exacerbation post-therapy in a year, and almost one in three experienced three or more exacerbations.⁴ The life quality of asthma patients is significantly impaired including lethargy, sleep disturbance, decreased activity and poor concentration.

Simple asthma drugs, such as controllers like inhaled corticosteroids and relievers like short-acting bronchodilators, can be used to treat the symptoms of asthma. These drugs have been developed over time and are recognized as essential medicines by the World Health Organization.⁵ The fact that accessibility and availability are still major problems in low-income nations makes them one of the most crucial challenges. Reliever treatment, or salbutamol, was not listed as a necessary medication in 72% of low-income nations, according to a survey.⁶ Similarly, only 50% of all asthma patients

had access to a bronchodilator, and less than 20% had access to a corticosteroid inhaler in low-income countries.^{6–8} Moreover, the cost of asthma treatment is expensive,⁹ and the process of treatment is too long. Additionally, it is difficult to cure asthma. Therefore, parents, as the primary caregivers, often were under high levels of care burden and psychological barriers due to repeated exposure to the pressure of caring for their children.¹⁰ Herein, it remains a huge challenge to develop a feasible and professional nursing plan.

Due to frequent, persistent, and poorly controlled asthma attacks in children, they can negatively impact learning, social interaction, and mental health. Moreover, asthma's specificity and insufficient social support pose many challenges for parents, including insufficient knowledge and care skills. These factors directly reduce the quality of parental care and disease control for children. Therefore, asthma children's parents should learn and master relevant family preventive care and healthcare knowledge and apply them reasonably in daily life. As such, this study aims to investigate family preventive and healthcare for children with asthma and evaluate the effectiveness of family-supported healthcare in improving the therapeutic effect of asthma children with routine treatment.

Materials and Methods

Inclusion and Exclusion Criteria

Patients were included in the study if they met the following criteria: (1) The child met the diagnostic criteria in the 2016 edition of the Guidelines for the Diagnosis and Treatment of Childhood Bronchial Asthma; (2) The patient's condition was stable and they could cooperate with the study; (3) Family members voluntarily participated; (4) Children and families had certain cognitive, communication, and comprehension abilities; (5) Family members had clear consciousness.

Any patients who met the following criteria would be excluded from the study. Firstly, patients with acute exacerbation of asthma. Secondly, asthma patients with pneumonia, pulmonary tuberculosis, and congenital pulmonary hypoplasia. Thirdly, individuals with a recent history of infection. Fourthly, patients are accompanied by congenital respiratory failure or heart failure. Fifthly, children with mental and intellectual disabilities. Informed consent and hospital medical ethics approval were obtained for this study.

The Routine Treatment and Healthcare for Patients

The study was approved by Zibo Central Hospital, and written informed consents were obtained from the parents or legal guardian. This study was performed in strict accordance with the Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects. Patients were randomized into the control group and intervention group. Post-discharge, both groups received standardized anti-asthma treatment including inhaled glucocorticoids and β_2 receptor blockers. The control group received routine care and education on asthma risk factors, daily living environment, medication guidance, light diet, and allergen avoidance from an education manual. Emphasis was placed on standardized, rational drug use. Regular phone follow-ups assessed patient disease and medication changes, and parents were reminded of outpatient follow-ups.

The Principle for Family-Supported Healthcare

The intervention group received family-supported healthcare along with routine care and education. The detailed principles were as follows. Initially, a home care and healthcare platform were established. Before discharge, a detailed plan for the child's diet, daily life, and health activities post-discharge was developed after communication and exchange between the responsible nurse and parents. Meanwhile, media communication platforms including the WeChat group, WeChat official account and TikTok account were established to push relevant asthma knowledge once a week, and all parents were trained on the method of application, functions and history reviewing. Additionally, question consultation time was scheduled from 19:00 to 21:00 every Saturday when management persons answered questions for parents of asthma children through the WeChat group. After discharge, an electronic information document was established for the patient, including the detailed home address, contact information, disease information, etc. Secondly, parents were trained with professional skills. Before discharge, parents were trained with professional

knowledge, intervention skills and appreciation of the importance of family therapy. The parents were instructed to measure body temperature, and observe cough and wheezing. Meanwhile, they should master the correct method of nebulization inhalation, and accurately maintain and clean the atomizer. Additionally, they were able to use medication correctly and provide emergency treatment during acute attacks. The medication dose was modified based on the patient's condition. Parents and children were told about the significant repercussions of altering or quitting medicine without authorization, which improved medication compliance.

An asthma family diary was created under the collaboration between parents and children which recorded the times of coughing and wheezing during the day and night; conscious feeling of suffocation, amount of activity, frequency of medication, etc. This data was consulted by specialized nurses and clinical physicians to adjust intervention plans in case of need. Thirdly, environmental improvement was conducted. Sick children's living environment should be kept clean and well-ventilated. Bedclothes and bedding should be clean and dry, regularly cleaned and mites removed. Pets should be minimized at home, and furry toys avoided. Smoking was prohibited. The parents should pay attention to air quality and weather. In spring and summer when pollen and willow catkins are flying, asthma patients should wear masks or hats when going out, or avoid going out. They should avoid going out or engaging in outdoor activities on hazy days, and avoid staying in public places with high pedestrian traffic and poor air conditions. Fourthly, healthcare in daily life was scheduled. Children should have regular routines, such as going to bed and waking up early. The child was guided to engage in jogging, walking or fitness exercises for more than 30 minutes each time, at least 3 times weekly. Fifthly, psychological support was employed. The psychological pressure of the child and parents was monitored, and parents were assisted in understanding the children's psychological changes during treatment. Standardized and reasonable health education was provided to parents and enable them to accurately understand the disease and eliminate the burden of family care.

The Detection of FEV1/FVC and FeNO

The intervention period was three months. The lung function indicators of children's asthma from two groups were measured at their first visit (before intervention) and 3 months after intervention, respectively. The indicator included forced expiratory volume in the first second/forced vital capacity (FEV1/FVC), and fractional exhaled nitric oxide (FeNO).

The Evaluation of Asthma Control Using the Childhood Asthma Control Test

Asthma control was evaluated in children pre- and post-intervention using the Childhood Asthma Control Test (C-ACT) table designed by Professor Nathan in the United States in 2006. C-ACT mainly included four aspects over the past 4 weeks, with a maximum score of 5 points per aspect and 25 points total. Asthma hinders daily activities (5 points); the times that patients experience difficulty breathing (5 points); difficulty sleeping or waking up early due to asthma symptoms such as difficulty breathing, chest tightness, and pain (5 points); evaluation of asthma control over the past 4 weeks (5 points). A total score of less than 20 indicated that asthma had not been controlled, with a score of 20–24 indicating good control and 25 indicating complete control. The coefficient of Cronbach's α in the test scale was 0.847, indicating good reliability and validity.

The Quality of Life

Children's asthma quality of life was assessed using the pediatric asthma quality of life questionnaire (PAQLQ), developed by Canadian biostatistician and epidemiologist Juniper. The scale used a 7-point scoring system (1–7 points), with 23 items across three dimensions: activity (5 items), symptom (10 items), and emotion (8 items). The total score was 171 points. Higher total scores mean higher quality of life. The coefficient of scale Cronbach's α was 0.859, indicating good reliability and validity.

The Detection of IL-6 and IL-17

Before and 3 months after the intervention, 3 mL of fasting venous blood was collected from children who woke up in the morning, followed by centrifugation. The obtained serum was used to measure the concentrations of inflammatory factors IL-6 and IL-17 in the serum with a commercial kit (Abcam, Cambridge, MA).

The Information of the Enrolled Patients

A total of 184 children with asthma were evaluated in this study. Of these, 25 cases did not meet the criteria and 31 children or their guardians were unwilling to participate. Therefore, 128 children were included and randomly divided into an intervention group and a control group using a random logarithmic table, with 64 cases in each group.

Statistical Analysis

All statistical analysis was performed using SPSS software, version 26.0. The statistical data was shown with mean \pm standard deviation (SD), and all p values were shown in the table and corresponding figures. P less than 0.05 indicated the significance of the test. The comparison of the basic information was done by the Mann–Whitney test or Chi-square test or Fisher's exact test. The comparison of treatment effect in two groups was conducted using the mixed model of ANOVA followed by Tukey's multiple comparisons tests.

Results

The Research Flow of This Study

As shown in [Figure 1](#), 128 children were enrolled after the initial screening and divided into two groups with 64 cases in each group. Subsequently, both groups underwent a three-month intervention. During this period, four cases were lost to follow-up in the control group, and eight actively withdrew. Finally, 52 cases were included in the analysis. There were 5 cases of loss of contact in the intervention group and 12 cases of active withdrawal. Finally, 47 cases were included in the analysis.

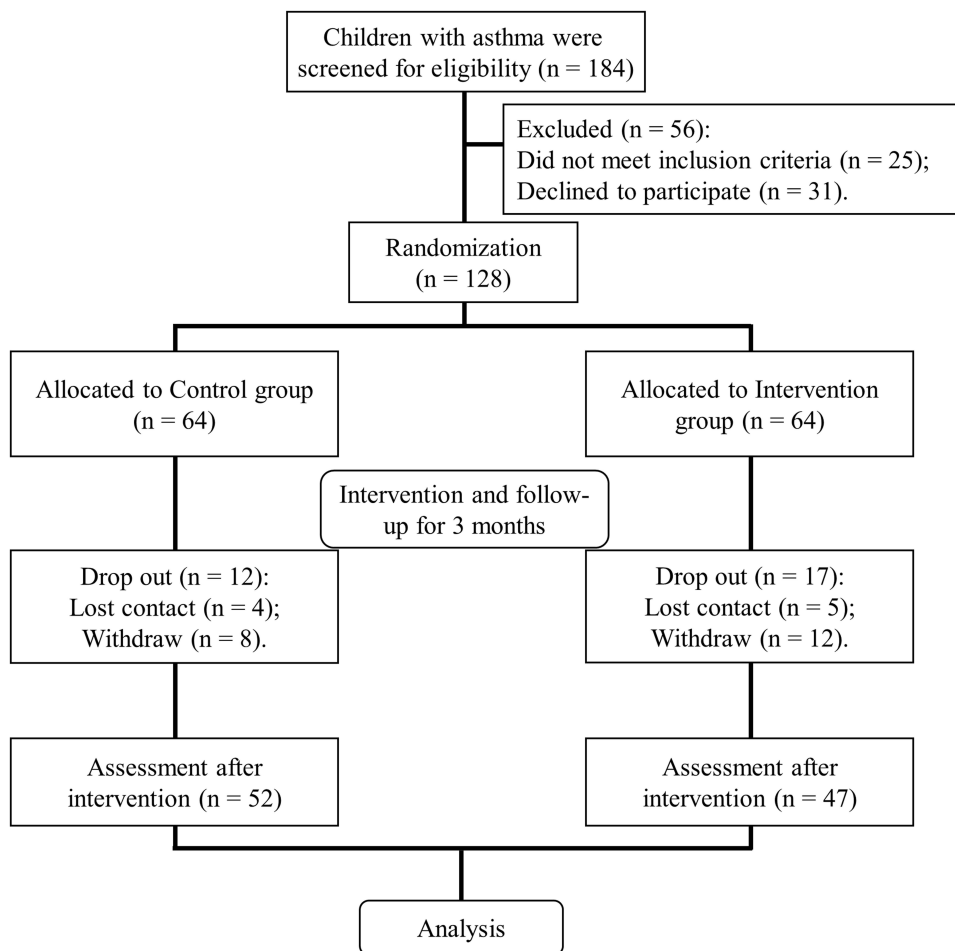


Figure 1 The research framework of this study.

The Demographic and Clinical Characteristics of Analyzed Children and Their Parents

To exclude potential risk factors affecting the effect of family-supported healthcare, the potential risk factor involving the age, gender, course of asthma and education status of the parents was compared between the two groups. The analysis showed that the average age was 7.49 in the control group and 7.67 in the intervention group, which demonstrated that there was no significant difference in age between the control group and the intervention group (Table 1). Furthermore, it was found that there were 30 boys and 22 girls in the control group, while there were 26 boys and 21 girls, which proved that the gender distribution was comparable in the two groups (Table 1). Moreover, the course of asthma was also compared in the two groups and the result showed that the average course of asthma was 2.95 in the control group and 3.06 in the intervention group, indicating no significant difference (Table 1). Additionally, the education status of the parents was also compared and the result showed that the number of parents with college and above was 25 in the control group and 26 in the intervention group (Table 1), which implied that the education level of parents was similar. Taken together, it was concluded that there is no difference in the basic information of the parents.

The Pulmonary Function

To evaluate the pulmonary function of pediatric asthma patients after family-supported healthcare, the FEV1/FVC and FeNO were analyzed. Before treatment, the average FEV1/FVC was 56.428 in the control group and 56.152 in the intervention group; after treatment, the average FEV1/FVC increased to 69.756 in the control group and 76.456 in the intervention group. This finding demonstrated that both groups had elevated FEV1/FVC after the intervention, more prominently in the intervention group (Figure 2A). FeNO, a biomarker of airway inflammation, can be used as an index to evaluate asthma management's efficacy.¹¹ Therefore, the level of FeNO was detected in both groups. Before treatment, the average level of FeNO was 40.503 in the control group and 41.338 in the intervention group; after treatment, the average level of FeNO was 35.642 in the control group and 30.43 in the intervention group (Figure 2B). This finding indicated that family-supported healthcare more drastically reduced FeNO level than routine treatment. Collectively, it was concluded that the healthcare improved the pulmonary function better than routine treatment.

Table 1 Demographic and Clinical Characteristics of Analyzed Children and Their Parents

Characteristics	Study group		p value
	Control group (n = 52)	Intervention group (n = 47)	
Age (years)	7.49 ± 1.18	7.67 ± 1.23	0.371
Course of asthma	2.95 ± 0.61	3.06 ± 0.67	0.528
Gender			
Boy	30 (57.7%)	26 (55.3%)	0.841
Girl	22 (42.3%)	21 (44.7%)	
Education status of the parents			
Junior high school and below	10 (19.2%)	7 (14.9%)	0.745
Senior high school	17 (32.7%)	14 (29.8%)	
College and above	25 (48.1%)	26 (55.3%)	

Notes: Values were presented as mean ± SD or n (percentage, %). p values were derived from Mann-Whitney test or Chi-square test or Fisher's exact test.

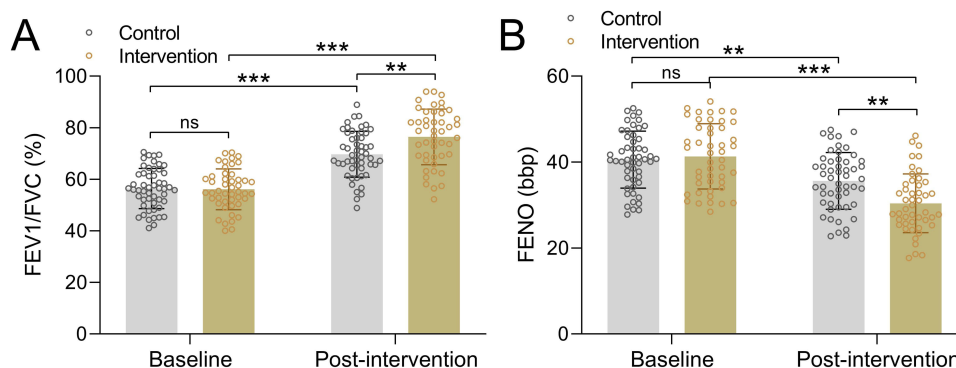


Figure 2 Comparisons of forced expiratory volume in 1 s as a percentage of forced vital capacity (FEV1/FVC, **A**) and fractional exhaled nitric oxide (FeNO, **B**) between the two groups at baseline and after the intervention of 3 months. N = 52 for the control group and n = 47 for the intervention group. Data were shown with mean \pm SD. **Notes:** **p < 0.01, ***p < 0.001 and ns means no significance from the mixed model of ANOVA followed by Tukey's multiple comparisons tests.

The Evaluation of Asthma Control and Life Quality

The C-ACT was developed to assess asthma control globally in children.¹² Thus, the C-ACT of two groups was evaluated before and after treatment. Analysis showed that the average score of the control group was 16.788 before treatment and 20.346 after treatment (Figure 3A). The average score of the intervention group was 16.532 before treatment and 21.681 after treatment (Figure 3A). This indicated that the C-ACT was comparable between groups pre-treatment but better post-treatment, especially in the intervention group. The PAQLQ was applied to assess the effect of treatment on the quality of life improvement.¹³ Analysis showed no difference between two groups pre-treatment, with an average score of 123.327 for the control group and 122.064 for the intervention group. However, post-treatment, the scores of both groups increased to 135.673 and 146.213 respectively, with greater improvement in the intervention group (Figure 3B). It can be concluded that family-supported healthcare improved asthma control and quality of life in patients receiving routine drugs.

The Detection of Inflammatory Factors

IL-6 has long been viewed as a general marker of inflammation. Elevated serum IL-6 levels were reported in asthmatic patients versus normal populations.¹⁴ Tang et al reported that IL-17 and IL-6 levels correlated with the severity of asthma.¹⁵ Therefore, the levels of IL-17 and IL-6 were analyzed to evaluate the effect of healthcare on the improvement of asthma. It was revealed that the average level of serum IL-17 was 185.734 pg/mL in the control group and 189.447 pg/mL in the intervention group before treatment; after treatment, it was 142.862 pg/mL in the control group and 118.140 pg/mL in the intervention group (Figure 4A). This finding demonstrated that the level of serum IL-17 decreased in two groups after treatment, with a greater decrease in the intervention group. Similarly, the average level of serum IL-6 was 150.366 pg/mL in the control group and 146.286 pg/mL in the

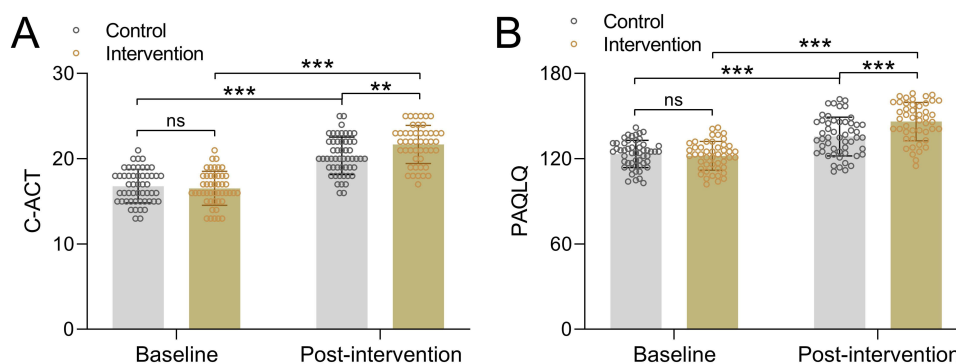


Figure 3 Comparisons of C-ACT (**A**) and PAQLQ (**B**) between the two groups at baseline and after intervention of 3 months. N = 52 for the control group and n = 47 for the intervention group. Data were shown with mean \pm SD. **Notes:** **p < 0.01, ***p < 0.001 and ns means no significance from the mixed model of ANOVA followed by Tukey's multiple comparisons tests.

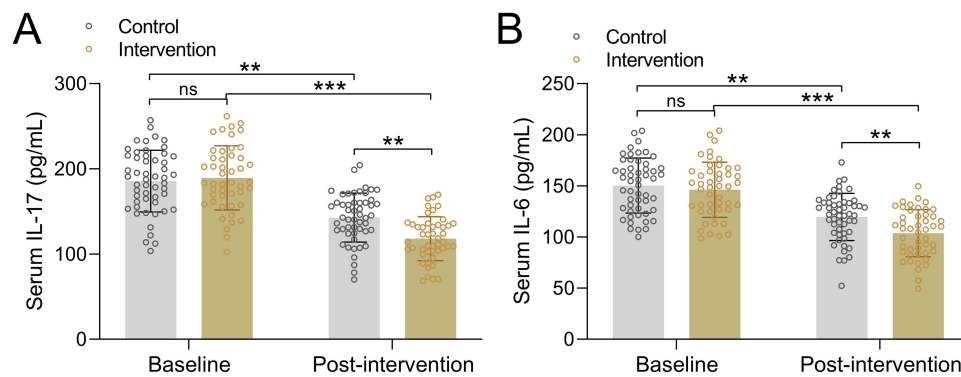


Figure 4 Comparisons of serum IL-17 (A) and IL-6 (B) between the two groups at baseline and after the intervention of 3 months. N = 52 for the control group and n = 47 for the intervention group. Data were shown with mean \pm SD.

Notes: **p < 0.01, ***p < 0.001 and ns means no significance from the mixed model of ANOVA followed by Tukey's multiple comparisons tests.

intervention group before treatment. After treatment, the average serum IL-6 level was 119.730 pg/mL in the control group and decreased to 103.759 pg/mL in the intervention group (Figure 4B). This result demonstrated that serum IL-6 decreased in two groups post-treatment, with a greater decrease in the intervention group. Together, intervention treatment inhibited inflammation, with family-supported healthcare having a better inhibitory effect on IL-17 and IL-6. This finding indicates that family-supported healthcare enhanced the improvement of inflammation in asthma patients treated with routine drugs.

The Evaluation of Acute Exacerbation Time and Rehospitalization Time

To further evaluate the improvement of healthcare in asthma, acute exacerbation and rehospitalization were analyzed during the 3-month intervention. The results showed an acute exacerbation incidence of 19.2% in the control group versus 4.3% in the intervention group, indicating healthcare significantly reduced acute exacerbation incidence (Figure 5A). Similarly, the rehospitalization incidence was 11.5% in the control group with no cases in the intervention group, suggesting that healthcare significantly reduced rehospitalization incidence (Figure 5B). Collectively, family-supported healthcare effectively reduced acute exacerbation and rehospitalization frequency in pediatric asthma patients.

Discussion

Asthma is defined as reversible airflow obstruction in the condition of airway inflammation, characterized by variable symptoms like wheezing, breathlessness, chest tightness, and cough.^{16,17} Asthma incidence and severity across all age

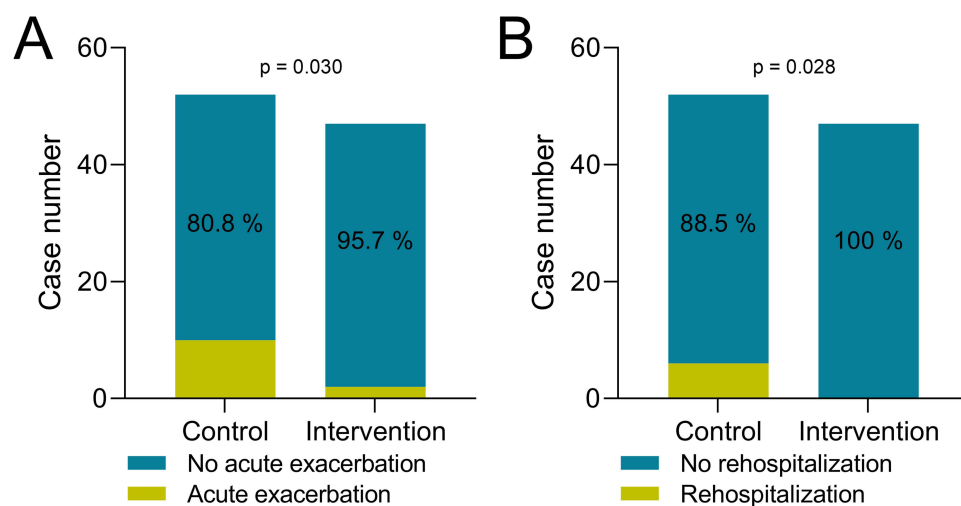


Figure 5 Comparisons of acute exacerbation times (A) and rehospitalization time (B) during the intervention of 3 months between the two groups. Fisher's exact test.

groups continue to make it a major global health concern. An estimated 235–334 million people worldwide have asthma, causing about 250,000 deaths yearly.¹⁸ Asthma management aims for symptom control and reducing exacerbation risk so patients can live normally. However, poor asthma control affects 30%–50% of school-aged children and adolescents in developed countries.^{19,20} Poor asthma control often results from modifiable factors like poor inhaler technique²¹ and low adherence to treatment.²² Thus, asthma self-management is crucial for adequate control and efficient healthcare use.²³ Recently, asthma has been viewed as a special illness affecting families and society, not just individuals. The family's response directly affects disease outcomes, behavior, and quality of life of children with asthma. Therefore, family-supported healthcare interventions for asthma are attracting special attention.²⁴ This study adopted family-supported healthcare interventions to increase parents' professional knowledge about asthma and improve the level of asthma control, and enable continuous, long-term, standardized prevention and health management post-discharge, positively promoting asthma control.

In our comprehensive study, a family-supported healthcare and care plan was formulated, with the initial establishment of a home care and healthcare platform. Subsequently, the development of parental professional skills was undertaken, adhering to an intricate process. Furthermore, the living environment was factored into the plan, undergoing improvements. A wide array of detailed standards for daily life healthcare and psychological backing was also outlined. Through rigorous healthcare intervention, it was found that FEV1/FVC and FeNO levels significantly increased in the intervention group, when compared with the control group. This prominent rise indicates that healthcare could positively enhance the therapeutic effect for children afflicted with asthma. Following this, the enhancement of quality of life in the intervention group was markedly more distinct than in the control group, painting a clear picture of the intervention's efficacy. Consequently, these results validate our hypothesis that healthcare interventions can elevate the therapeutic efficacy and notably improve the quality-of-life post-treatment for asthma children.

Specific biomarkers can guide diagnosis, and treatment, and predict treatment responses.²⁵ IL-6 is a typical cytokine with roles in immune response, inflammation, hematopoiesis and the endocrine and nervous systems.²⁶ IL-6 is produced by innate immune cells, B cells, and some CD4 effector Th cells. In addition, IL-6 is secreted by non-leukocytes such as endothelial cells, fibroblasts, astrocytes, epithelial cells and some malignant cells.²⁷ IL-6, produced rapidly and transiently in response to infections and tissue injuries, promotes host defense by stimulating acute phase responses, hematopoiesis, and immune responses. Therefore, IL-6 is a general inflammation marker. Increasing evidence shows IL-6 is a key cell signaling mode in asthma-related pathways and may act as an asthma biomarker.²⁸ Our analysis found that the baseline of IL-6 was high in two groups before treatment, but it decreased more significantly in the intervention group after treatment, indicating an association between IL-6 and asthma.

IL-17 was initially demonstrated to be produced by activated CD4⁺ T cells. IL-17 can induce lung structural cells to secrete proinflammatory cytokines and chemokines, thereby triggering neutrophil infiltration.²⁹ Notably, lung resident IL-17-producing TH2 cells persist as the dominant IL-17 producers during chronic allergic airway inflammation.³⁰ IL-17 expression increases in the lung, sputum, bronchoalveolar lavage fluid, and sera of asthma patients, correlating positively with airway hyper-responsiveness severity.³¹ Numerous studies also suggest IL-17 in asthmatic airways relates to asthma severity.^{32,33} Our comprehensive analysis showed that the level of serum IL-17 was elevated in two study groups before treatment, a finding that was consistent with previous research. Moreover, the level of IL-17 was found to be significantly decreased post-treatment, particularly, it declined more in the intervention group as compared to the control group. These findings, in a nutshell, provide evidence that inflammatory cytokines such as IL-17 tend to be elevated in asthma patients, and sympathetically, the inflammation can be better alleviated when proper healthcare interventions are provided by family and healthcare professionals.

Although it has been established that family-supported healthcare could improve therapeutic effects and enhance asthma control. There are still some unresolved issues to be addressed. First, our work did not discuss which specific intervention worked against childhood asthma. The specific intervention measures of the intervention group mainly included environmental improvement, daily life care, and psychological support for the children. We think that these intervention measures have different focuses, and it is the combination that has produced the effect. From a perspective of study design, it is hard to distinguish which intervention exerts the most important effects. Thus, this work can not provide a very specific family health care plan that can be immediately promoted in clinical practice, but emphasizes the importance of family health care, which can be further optimized later in the future work. Second, the education level

was associated with asthma management in adults, as demonstrated in a study by Wambiya et al.³⁴ However, whether the education level of parents affects the improvement of healthcare in asthma control in children within an intervention group requires further research utilizing a more extensive subpopulation sample. Third, there are other inflammatory cytokines associated with asthma rather than IL-6 and IL-17. Therefore, identifying and studying a greater number of inflammatory cytokines represents a significant avenue for future research. Last, data on the specific medications, such as the doses, used by the children at home was not collected.

Conclusion

The current work systematically analyzed the benefits of family-involved care for children with asthma, including asthma control, quality of life, lung function, acute exacerbation rate, rehospitalization rate, and inflammatory factor indicators in the serum of children. Our study demonstrated that family-supported healthcare significantly improved the pulmonary function of childhood asthma. Consequently, asthma control and life of quality of childhood asthma were also enhanced by the healthcare intervention. Importantly, the inflammatory IL-17 and IL-6 were also significantly decreased more by the family-supported healthcare. These findings highlight the key role of family participation in the care of children with asthma and provided a basis for the clinical prevention and treatment of children with asthma.

Abbreviations

FEV1/FVC, forced expiratory volume in 1 s as a percentage of forced vital capacity; FeNO, fractional exhaled nitric oxide; C-ACT, childhood asthma control test; PAQLQ, pediatric asthma quality of life questionnaire; interleukin, IL; GINA, Global Initiative for Asthma.

Disclosure

The authors report no conflicts of interest in this work.

References

- Centers for Disease C, Prevention. Vital signs: asthma prevalence, disease characteristics, and self-management education: United States, 2001--2009. *MMWR Morb Mortal Wkly Rep.* 2011;60(17):547–552.
- Trikamjee T, Comberati P, Peter J. Pediatric asthma in developing countries: challenges and future directions. *Curr Opin Allergy Clin Immun.* 2022;22(2):80–85. doi:10.1097/aci.0000000000000806
- Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee Report. *Allergy.* 2004;59(5):469–478. doi:10.1111/j.1398-9995.2004.00526.x
- Kirenga BJ, de Jong C, Mugenyi L, et al. Rates of asthma exacerbations and mortality and associated factors in Uganda: a 2-year prospective cohort study. *Thorax.* 2018;73(10):983–985. doi:10.1136/thoraxjnl-2017-211157
- Hanley Nadeau E, Toronto CE. Barriers to Asthma Management for School Nurses. *J School Nurs.* 2015;32(2):86–98. doi:10.1177/1059840515621607
- Babar Z-U-D, Lessing C, Mace C, Bissell K. The availability, pricing and affordability of three essential asthma medicines in 52 low- and middle-income countries. *Pharmacoeconomics.* 2013;31(11):1063–1082. doi:10.1007/s40273-013-0095-9
- Ait-Khaled N, Auregan G, Bencharif N, et al. Affordability of inhaled corticosteroids as a potential barrier to treatment of asthma in some developing countries. *Int J Tuberc Lung Dis.* 2000;4(3):268–271.
- Meghji J, Mortimer K, Agusti A, et al. Improving lung health in low-income and middle-income countries: from challenges to solutions. *Lancet.* 2021;397(10277):928–940. doi:10.1016/s0140-6736(21)00458-x
- Godard P, Chanez P, Siraudin L, Nicoloyannis N, Duru G. Costs of asthma are correlated with severity: a 1-yr prospective study. *Eur Respir J.* 2002;19(1):61–67. doi:10.1183/09031936.02.00232001
- Wang G, Wang F, Gibson PG, et al. Severe and uncontrolled asthma in China: A cross-sectional survey from the Australasian Severe Asthma Network. *J Thorac Dis.* 2017;9(5):1333–1344. doi:10.21037/jtd.2017.04.74
- Xie Z, Chai M, Gu W, Yuan H. Changes in fractional exhaled nitric oxide, exhaled carbon monoxide and pulmonary function during the acute attack, treatment and remission phases of pediatric asthma. *Transl Ped.* 2020;9(6):784–794. doi:10.21037/tp-20-351
- Sommanus S, Direkwattanachai C, Lawpoolsri S, Sitcharungsi R. Accuracy of childhood asthma control test among Thai childhood asthma patients. *Asian Pac J Allergy Immun.* 2018;36(3):152–158. doi:10.12932/ap-300517-0094
- Elizabeth C, Suzanna S, Tim CF, Shek LP, Mital R, Bee Wah L. Pediatric asthma quality of life questionnaire: validation in children from Singapore. *Asian Pac J Allergy Immun.* 1999;17(3):155–161.
- Pan R, Kuai S, Li Q, Zhu X, Wang T, Cui Y. Diagnostic value of IL-6 for patients with asthma: a meta-analysis. *All Asthma Clin Immun.* 2023;19(1):39. doi:10.1186/s13223-023-00794-3
- Tang X, Sun W, Xu H, Liu W, Wang T, Liu H. The Changes in the Levels of IL-6, IL-17, and IL-21 in the Acute Stage of Childhood Asthma. *Clin Lab.* 2013;59(2013):1381–1387. doi:10.7754/Clin.Lab.2013.121246
- Erzurum SC, Gaston BM. Biomarkers in Asthma. *Clin Chest Med.* 2012;33(3):459–471. doi:10.1016/j.ccm.2012.06.007

17. Pearce N, Ait-Khaled N, Beasley R, et al. Worldwide trends in the prevalence of asthma symptoms: Phase III of the international study of asthma and allergies in childhood (ISAAC). *Thorax*. 2007;62(9):758–766. doi:10.1136/thx.2006.070169
18. Kim H, Ellis AK, Fischer D, et al. Asthma biomarkers in the age of biologics. *Allergy Asthma Clin Immunol*. 2017;13(1):48. doi:10.1186/s13223-017-0219-4
19. Liu AH, Gilsenan AW, Stanford RH, Lincourt W, Ziemiecki R, Ortega H. Status of asthma control in pediatric primary care: results from the pediatric asthma control characteristics and prevalence survey study (ACCESS). *J Pediatr*. 2010;157(2):276–281.e273. doi:10.1016/j.jpeds.2010.02.017
20. de Blic J, Boucot I, Pribil C, Robert J, Huas D, Marguet C. Control of asthma in children: still unacceptable? A French cross-sectional study. *Respir Med*. 2009;103(9):1383–1391. doi:10.1016/j.rmed.2009.03.006
21. Gillette C, Rockich-Winston N, Kuhn JA, Flesher S, Shepherd M. Inhaler technique in children with asthma: A systematic review. *Acad Pediatr*. 2016;16(7):605–615. doi:10.1016/j.acap.2016.04.006
22. Gray WN, Netz M, McConville A, Fedele D, Wagoner ST, Schaefer MR. Medication adherence in pediatric asthma: a systematic review of the literature. *Pediatr Pulmonol*. 2018;53(5):668–684. doi:10.1002/ppul.23966
23. Guevara JP. Effects of educational interventions for self management of asthma in children and adolescents: systematic review and meta-analysis. *BMJ*. 2003;326(7402):1308. doi:10.1136/bmj.326.7402.1308
24. Netz M, Fedele DA, Sweenie R, Baker D, Light M, McQuaid EL. Asthma management responsibility, control, and quality of life among emerging adolescents. *J Pediatr Psychol*. 2020;45(1):40–49. doi:10.1093/jpepsy/jsz069
25. Licari A, Castagnoli R, Brambilla I, et al. Asthma endotyping and biomarkers in childhood asthma. *Pediatr Allergy Immunol Pulmonol*. 2018;31(2):44–55. doi:10.1089/ped.2018.0886
26. Kaur S, Bansal Y, Kumar R, Bansal G. A panoramic review of IL-6: structure, pathophysiological roles and inhibitors. *Biorg Med Chem*. 2020;28(5):115327. doi:10.1016/j.bmc.2020.115327
27. Hirano T. Interleukin 6 and its Receptor: Ten Years Later. *Int Rev Immunol*. 2009;16(3–4):249–284. doi:10.3109/08830189809042997
28. Poynter ME, Irvin CG. Interleukin-6 as a biomarker for asthma: hype or is there something else? *Eur Respir J*. 2016;48(4):979–981. doi:10.1183/13993003.01597-2016
29. Jovanovic DV, Di Battista JA, Martel-Pelletier J, et al. IL-17 stimulates the production and expression of proinflammatory cytokines, IL-beta and TNF-alpha, by human macrophages. *J Immunol*. 1998;160(7):3513–3521. doi:10.4049/jimmunol.160.7.3513
30. Wang Y-H, Voo KS, Liu B, et al. A novel subset of CD4+ TH2 memory/effector cells that produce inflammatory IL-17 cytokine and promote the exacerbation of chronic allergic asthma. *J Exp Med*. 2010;207(11):2479–2491. doi:10.1084/jem.20101376
31. Molet S, Hamid Q, Davoineb F, et al. IL-17 is increased in asthmatic airways and induces human bronchial fibroblasts to produce cytokines. *J Allergy Clin Immunol*. 2001;108(3):430–438. doi:10.1067/mai.2001.117929
32. Al-Ramli W, Prefontaine D, Chouiali F, et al. T(H)17-associated cytokines (IL-17A and IL-17F) in severe asthma. *J Allergy Clin Immunol*. 2009;123(5):1185–1187. doi:10.1016/j.jaci.2009.02.024
33. Bullens DMA, Truyen E, Coteur L, et al. IL-17 mRNA in sputum of asthmatic patients: linking T cell driven inflammation and granulocytic influx? *Respir Res*. 2006;7(1):135. doi:10.1186/1465-9921-7-135
34. Ilmarinen P, Stridsman C, Bashir M, et al. Level of education and asthma control in adult-onset asthma. *J Asthma*. 2021;59(4):840–849. doi:10.1080/02770903.2021.1871742

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