The relationship between changes in peak expiratory flow and asthma exacerbations in asthmatic children

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Research Article

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Abstract

Background

Asthma is one of the most common chronic airway diseases in children. The aim of this study is to analyze whether children with asthma have changes in PEF before an acute asthma exacerbation and to evaluate the relationship between peak expiratory flow (PEF) and asthma exacerbation.

METHODS

Basic information (including sex, age, atopy, BMI, etc.) and clinical information of asthmatic children registered in the Electronic China Children's Asthma Action Plan (e-CCAAP) from 1 September 2017 to 31 August 2021 were collected. Subjects with 14 consecutive days of PEF measurements were eligible. Subjects in this study were divided into an exacerbation group and a control group. We analyzed the relationship between changes in PEF% pred and the presence of asthma symptoms.

Result

A total of 194 children with asthma who met the inclusion criteria were included, including 144 males (74.2%) and 50 females (25.8%), with a male-to-female ratio of 2.88:1. The mean age of the subjects was 9.51 ± 2.5 years. There were no significant differences in sex, age, allergy history, BMI distribution or baseline PEF between the two groups. In children with and without a history of allergy, there was no significant difference between the variation in PEF at 14 days. Children who showed only a decline in PEF had a significantly greater decline in PEF than the rest of the population. The most common cause of acute exacerbations of asthma is upper respiratory tract infection. Among the causes of acute exacerbations of asthma, the variation in PEF caused by air pollution was significantly higher than that of other causes (P < 0.05). In acute exacerbations, the decrease in PEF was significantly greater in the exacerbation group than in the control group. In children with asthma symptoms, there was a decrease in PEF approximately 1.34 days before the onset of symptoms.

Conclusion

Children with asthma show a decrease in PEF 1.34 days before the onset of asthma symptoms. We recommend that asthmatic children who show a decrease in PEF should step-up asthma therapy. The most common cause of acute exacerbations of asthma was upper respiratory tract infections, and the variation in PEF caused by air pollution was significantly higher than that caused by other factors.

Background
In many countries, childhood asthma is a major public health problem. Papi, Brightling, Pedersen, & Reddel (2018). As of 2018, there were approximately 350 million people with asthma worldwide (including children, adolescents and adults). The Third National Epidemiological Survey of Childhood Asthma in China found that the prevalence of asthma among urban children aged 0–14 years was 3.02% in 2010, compared with 1.09% and 1.97% in 1990 and 2000, respectively. Liu CH. In China, the incidence of childhood asthma is increasing at a rate of more than 50% per decade. According to the national report in China, the overall prevalence of asthma in adults is 4.2% (95% CI 3.1–5.6), representing 45.7 million people Huang et al. (2019).

A global multicenter study showed high rates of poorly controlled asthma in children (6–7 years), adolescents (13–14 years), and adults (≥ 19 years), with particularly high rates in children Garcia-Marcos et al. (2023). The Global Initiative for Asthma (GINA) states that the key to asthma management is the prevention of acute exacerbations and that early identification of asthma exacerbations and timely intervention can reduce the burden of disease. However, asthma exacerbations usually occur without any signs, and many children with asthma can breathe normally for weeks or months between exacerbations. Individuals and families do not have an accurate perception of symptoms. We need objective parameters to describe the severity of asthma. Peak expiratory flow (PEF) is an objective pulmonary parameter measured by an instrument that gives a true picture of a child's airways. GINA recommends PEF testing and regular follow-up for children over the age of 5 with asthma prior to diagnosis and initiation of controller therapy.

It has been shown that patients' perceptions of asthma symptoms or the severity of exacerbations vary and that difficulties with physical sensations and emotional expression are often associated with severe asthma, even fatal acute asthma attacks Serrano et al. (2006). In children, the need for additional objective parameters to describe the status and severity of asthma is reinforced by the poor perception of asthma symptoms and the fact that children often have difficulty expressing themselves. Studies have shown that FEV1 does not change significantly in most school-aged children, regardless of whether they have an acute asthma attack, and FEV1 is not associated with asthma severity as defined by symptoms Bacharier et al. (2004); Paull, Covar, Jain, Gelfand, & Spahn (2005); Spahn, Cherniack, Paull, & Gelfand (2004). A study in adults suggests that peak expiratory flow (PEF) may be a useful method for monitoring trends in asthma exacerbations and quantifying asthma control history Reddel (2006). Several studies have shown the effectiveness of peak expiratory flow-based asthma education and self-management programs in reducing emergency department visits and hospitalizations due to asthma exacerbations Beasley, Cushley, & Holgate (1989); Ignacio-Garcia & Gonzalez-Santos (1995); Lahdensuo et al. (1996).

Many international guidelines recommend the provision of a written asthma action plan (WAAP) to guide patients in recognizing and responding to worsening asthma symptoms to reduce acute asthma exacerbations EPR; Society. Almost all written asthma action plans (WAAPs) include long-term monitoring of PEF as an objective indicator of asthma control.
To help healthcare professionals, children and families self-manage asthma and achieve good asthma control, we implemented the China Children's Asthma Action Plan (CCAAP) and published an expert consensus on the clinical application of the CCAAP (in Chinese with an English abstract)Kunling & Jing.

This study was based on the China Children's Asthma Action Plan. We collected the children's PEF values and combined them with the children's symptoms to determine their asthma status.

**Methods**

**China Children's Asthma Action Plan (CCAAP)**

CCAAP classifies the asthma status into "green zone", "yellow zone" and "red zone". Symptoms, PEF or a combination of both were used as criteria to determine the status of asthma.

**Green zone**

regular use of controller medications and good asthma control.

**Identification of the Green Zone**

asthma condition is stable, patients without coughing, wheezing, chest tightness, shortness of breath, etc. In addition, have restful night’s sleep, normally to study, exercise, and play with their friends. PEF% pred ≥ 80%.

**Yellow Zone**

Uncontrolled or partially controlled or unstable asthma with exacerbations. We need to identify symptoms in a timely manner and take measures to control symptoms, prevent exacerbations, and reduce emergency department visits.

**Identification of the Yellow Zone**: A child is in the yellow zone if he or she shows any of the following signs: (1) Frequent coughing, especially at night or in the morning or after exercise. (2) Wheezing, shortness of breath, breathing with rales in the lungs. (3) Coughing or choking that wakes them up at night, affecting their sleep. (4) Weakness, shortness of breath or coughing and wheezing after activity. (5) Bronchodilator use ≥ 2 times/week. (6) Chest tightness, prolonged inhalation/exhalation or decreased PEF. (7) PEF% pred between 60% and 80%.

**Red Zone**: severe asthma exacerbation requiring emergency care and immediate medical treatment.

**Identification of the Red Zone**: A child is in the red zone if he or she shows any of the following signs: (1) Severe coughing, difficulty breathing, or appearance of the three depressions sign. (2) Difficulty walking and talking and inability to lie flat. (3) Nasal flaring and cyanosis of the lips. (4) Crying, dysphoria, lack of energy, and drowsiness. (5) PEF% pred < 60%.
Subjects

Asthmatic children who registered in the electronic China Children's Asthma Action Plan (e-CCAAP) from 1 September 2017 to 31 August 2021 and recorded PEF measurements for at least 14 consecutive days were eligible. We retrospectively analyzed their acute asthma exacerbations and PEF% pred. Basic information included sex, age, allergy history, and basic medications. History of allergy was defined as positive for ≥ 1 inhaled allergen (dust mites, mold, cockroaches, pets, spring/fall pollen, other allergens) or positive for ≥ 1 food allergen (milk, egg, wheat, nuts, seafood, soybeans, peanuts, other allergens). In our study, PEF reduction was defined as PEF% pred ≤ 80%. Subjects were divided into an exacerbation group or a control group according to asthma symptoms and PEF% pred. The characteristics of the control group were PEF% pred > 80% and no onset of asthma symptoms. The exacerbation group can be divided into three subgroups: 1) onset of asthma symptoms after a decrease in PEF (PEF + symptom group). 2) only a decrease in PEF (PEF group). 3) onset of asthma symptoms only (symptom group).

Inclusion Criteria:

1. Registered in the electronic China Children's Asthma Action Plan (e-CCAAP).
2. Age ≥ 6 and ≤ 18 years.
3. Children diagnosed with asthma by physicians.
4. The PEF measurements were recorded for at least 14 consecutive days.

Exclusion Criteria:

1. PEF values with significant deviations.
2. The information is incorrect.

Analysis

Statistical analyses were performed using SPSS Statistics version 22.0. Continuous and categorical variables are presented as the mean ± standard deviation (x±sd) or number (percentage). We analyzed the differences in the demographic characteristics between the two groups by using a χ² test and two-sample t tests for proportions and continuous data, respectively. Comparisons of nonnormally distributed data were performed using the Mann–Whitney U rank test. A two-tailed p value of 0.05 was considered to be statistically significant.

Result

Baseline Characteristics

The baseline characteristics of the two groups are summarized in Table 1. A total of 194 subjects were included in this study. Of the 194 subjects, there were 144 males and 50 females, with a male to female
The mean age was 9.51 ± 2.5 years. There were 162 subjects in the exacerbation group. Of the 162 subjects, 98 were in the PEF + symptom group, 13 in the PEF group and 51 in the symptom group. There were 32 subjects in the control group. The number of subjects in the PEF + symptom group was significantly higher than that in the other groups (P < 0.05). The mean ages of the four groups were 9.56 ± 2.08, 10.69 ± 2.39, 9.41 ± 3.03, and 9 ± 2.78 years, respectively. The baseline PEF was significantly higher in the PEF group than in the other three groups (P = 0.014). With the exception of baseline PEF, there were no statistically significant differences in baseline characteristics between the two groups (Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exacerbation group(n = 162)</th>
<th>Control group(n = 32)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PEF + symptom group(n = 98)</td>
<td>PEF group(n = 13)</td>
<td>Symptom group(n = 51)</td>
</tr>
<tr>
<td>Gender</td>
<td>77 (78.6%)</td>
<td>1184.6%</td>
<td>37 (72.5%)</td>
</tr>
<tr>
<td>male</td>
<td>21 (21.4%)</td>
<td>2 (15.4%)</td>
<td>14 (27.5%)</td>
</tr>
<tr>
<td>female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD, y</td>
<td>9.56 ± 2.08</td>
<td>10.69 ± 2.39</td>
<td>9.41 ± 3.03</td>
</tr>
<tr>
<td>6–9</td>
<td>49 (50%)</td>
<td>4 (30.8%)</td>
<td>35 (68.6%)</td>
</tr>
<tr>
<td>10–14</td>
<td>41 (41.8%)</td>
<td>6 (46.2%)</td>
<td>13 (25.5%)</td>
</tr>
<tr>
<td>15–18</td>
<td>8 (8.2%)</td>
<td>3 (23.1%)</td>
<td>3 (5.9%)</td>
</tr>
<tr>
<td>Allergy history</td>
<td>64 (65.3%)</td>
<td>10 (76.9%)</td>
<td>38 (74.5%)</td>
</tr>
<tr>
<td>Yes</td>
<td>34 (34.7%)</td>
<td>3 (23.1%)</td>
<td>13 (25.5%)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline PEF(l/min, ±2SD)</td>
<td>237.73 ± 75.93</td>
<td>270.08 ± 83.04</td>
<td>239.53 ± 100.69</td>
</tr>
<tr>
<td></td>
<td>69 (70.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline Medication</td>
<td>15 (15.3%)</td>
<td>8 (61.5%)</td>
<td>37 (72.5%)</td>
</tr>
<tr>
<td>LABA + ICS</td>
<td>14 (14.3%)</td>
<td>1 (7.7%)</td>
<td>8 (15.7%)</td>
</tr>
<tr>
<td>ICS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>others*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Impact of allergy history on PEF

LABA: Long Acting β 2 Agonist, ICS: inhaled corticosteroids.
The distribution of food allergens or inhalation allergens in this study is shown in Table 2. There were no statistically significant differences between the groups for food and inhalation allergens. In children with a history of allergy, the mean PEF variation was less than that in children without a history of allergy, and their PEF decrease was less than that in children without a history of allergy when there was an onset of asthma symptoms, but the difference in PEF changes between these two groups was not statistically significant (P = 0.206).

### Table 2
Distribution of allergens

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exacerbation group(n = 162)</th>
<th>Control group(n = 32)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PEF + symptom group(n = 98)</td>
<td>PEF group(n = 13)</td>
<td>Symptom group(n = 51)</td>
</tr>
<tr>
<td><strong>Food allergens, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soybeans</td>
<td>1(1.02%)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Seafood</td>
<td>1(1.02%)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Egg</td>
<td>5(5.1%)</td>
<td>0(0.0)</td>
<td>7(13.73%)</td>
</tr>
<tr>
<td>Milk</td>
<td>8(8.16%)</td>
<td>3(23.08%)</td>
<td>7(13.73%)</td>
</tr>
<tr>
<td>Wheat</td>
<td>1(1.02%)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Other allergens</td>
<td>82(83.68%)</td>
<td>10(76.92%)</td>
<td>37(86.27%)</td>
</tr>
<tr>
<td><strong>Inhalation allergens, n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dust mites</td>
<td>44(44.9%)</td>
<td>6(46.15%)</td>
<td>24(47.06%)</td>
</tr>
<tr>
<td>Mold</td>
<td>6(6.12%)</td>
<td>2(15.38%)</td>
<td>3(5.88%)</td>
</tr>
<tr>
<td>Pets</td>
<td>1(1.02%)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Spring/Fall pollen</td>
<td>4(4.08%)</td>
<td>2(15.38%)</td>
<td>3(5.88%)</td>
</tr>
<tr>
<td>Cockroaches</td>
<td>1(1.02%)</td>
<td>2(15.38%)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Other allergens</td>
<td>42(42.86%)</td>
<td>3(23.08%)</td>
<td>21(41.18%)</td>
</tr>
</tbody>
</table>

### Changes in PEF over 14 days in included subjects

As shown in Fig. 1, the change in PEF% pred over 14 days in the exacerbation group (PEF + symptom group, PEF group, Symptom group) and the control group. The variation in PEF% pred was significantly greater in the PEF group than in the other groups.

### Analysis of triggers in the exacerbation group
As shown in Fig. 2 and Table 3, in the exacerbation group, the most common trigger for an acute exacerbation of asthma was upper respiratory tract infection. The proportion of acute exacerbations of asthma caused by upper respiratory tract infections was significantly higher than that caused by other triggers. Changes in PEF% pred for acute exacerbations of asthma caused by different triggers are shown in Fig. 3.

Acute exacerbations due to air pollution have significantly higher variations in PEF% pred than other triggers. Acute exacerbations of exercise-induced asthma had significantly less variating changes in PEF% pred than other triggers.

### Table 3 Triggers in the Exacerbation Group

<table>
<thead>
<tr>
<th>Triggers</th>
<th>PEF+ symptom group</th>
<th>PEF group</th>
<th>Symptom group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n=162</strong></td>
<td><strong>n=98</strong></td>
<td><strong>n=13</strong></td>
<td><strong>n=51</strong></td>
</tr>
<tr>
<td><strong>Triggers ,n(%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>44 (44.9%)</td>
<td>8 (61.5%)</td>
<td>25 (49.0%)</td>
</tr>
<tr>
<td>Allergen exposure</td>
<td>7 (7.1%)</td>
<td>0 (0.0%)</td>
<td>3 (5.9%)</td>
</tr>
<tr>
<td>Exercise</td>
<td>5 (5.1%)</td>
<td>1 (7.7%)</td>
<td>6 (11.8%)</td>
</tr>
<tr>
<td>Air pollution</td>
<td>6 (6.1%)</td>
<td>1 (7.7%)</td>
<td>2 (3.9%)</td>
</tr>
<tr>
<td>Climate change</td>
<td>8 (8.2%)</td>
<td>0 (0.0%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>Cigarette exposure</td>
<td>2 (2.0%)</td>
<td>1 (7.7%)</td>
<td>1 (2.0%)</td>
</tr>
<tr>
<td>Other triggers</td>
<td>26 (26.6%)</td>
<td>2 (15.4%)</td>
<td>13 (25.4%)</td>
</tr>
</tbody>
</table>

### Time to PEF changes before exacerbation

We performed a retrospective analysis of children who developed asthma symptoms after the onset of PEF changes. Ninety-eight subjects (50.5%) developed symptoms after a decrease in PEF% pred, significantly more than those who did not develop asthma symptoms after a decrease in PEF% pred (6.7%). We found that most children with asthma have changes in PEF approximately 1–3 days before the onset of asthma symptoms. Statistically, the time from PEF change to symptom onset was 1.34 days [95% CI, 1.19, 1.49].

### Discussion

In our study, we found that children with asthma had a decrease in PEF 1.34 days before the onset of asthma symptoms, which may be an early sign of an acute exacerbation of asthma. A randomized controlled trial in children aged 7–14 years with moderate asthma showed that the PEF threshold was
70% of the optimum for increasing inhaled steroids and 50% of the optimum for starting prednisone therapy based on the PEF action plan. There was a significant decrease in PEF approximately 1 day prior to step-up treatment Wensley & Silverman (2004). A study in adults showed that asthma exacerbations were characterized by a gradual decrease in PEF over a few days, followed by more rapid changes over 2 to 3 days Tattersfield et al. (1999). Many countries’ asthma action plans advocate increasing the dose of inhaled corticosteroids (ICS) or initiating "yellow zone" therapy at the early signs of an exacerbation to avoid an acute exacerbation or reduce the severity and to prevent the need for oral steroids or hospitalization. In this study, some of the subjects had a significant decrease in PEF but had no asthma symptoms. This suggests that we may delay treatment if symptoms are used as an early sign of an acute exacerbation of asthma. PEF decreases before the onset of symptoms, and as soon as a decrease in PEF is detected during daily PEF monitoring, we can initiate "yellow zone" therapy. In our study, children in the PEF group had the greatest decrease in PEF% pred, which may be related to the fact that they had a higher PEF at baseline.

This study found that the most common trigger of acute asthma exacerbations in children was upper respiratory tract infections. Infection is the main trigger for acute exacerbations of asthma in children of all ages, followed by exposure to allergens Dondi et al. (2017). In the United States, childhood asthma morbidity decreased during the novel coronavirus epidemic compared with other periods, which may be related to reduced pathogen exposure due to the use of masks Ulrich, Macias, George, Bai, & Allen (2021). The study by Anneclaire et al. also found that the likelihood of children's asthma worsening increased as pollen levels increased De Roos et al. (2020). Some studies found that houses that have been painted in the past 1 year are also a risk factor for acute exacerbations of asthma Saif, Janecki, Wanner, Colin, & Kumar (2021). We need individualized action plans to improve the management of asthma, and avoiding infections and allergens are very important measures.

Doctors, teachers and parents need to be involved in improving asthma control in children. Natasha et al. showed that asthmatic students, teachers, and family members were involved in the study together to teach them how to identify asthma symptoms based on the Asthma Action Plan (AAP) and actions for each area. By the end of the study, all students accurately identified symptoms, AAP areas, and action steps McClure et al. (2018). When we promote our asthma action plan, we can consider a combined hospital-school-home model.

The advantage of this study is the simplicity and economy of long-term PEF monitoring through an electronic platform, with subjects from all over China participating in this study. Subjects can monitor the PEF anytime and anywhere, which greatly improves their compliance. The limitations of this study are as follows. First, as a retrospective study, some recall bias is inevitable. Second, PEF measurements are related to the child's ability to breathe calmly and regularly, measurements taken at home or at school are highly arbitrary, and even PEF measurements taken under different circumstances can vary greatly.

**Conclusion**
In children with asthma, the PEF% pred decreased 1.34 days before the onset of asthma symptoms. Therefore, we recommend starting "yellow zone" treatment when the PEF % pred decreases during long-term PEF monitoring to prevent acute exacerbations of asthma. The most common trigger for acute exacerbations of asthma is upper respiratory tract infections. Acute exacerbations due to air pollution have significantly higher variations in PEF% pred than other triggers.

**Abbreviations**

PEF  
peak expiratory flow  
CCAAP  
China Children's Asthma Action Plan

**Declarations**

**Ethics approval and consent to participate**

The study was approved by Beijing Children's Hospital ethical committee, and written informed consent was exempted

**Consent for publication**

Not applicable.

**Availability of data and materials**

All data generated or analysed during this study are included in this published article.

**Competing interests**

The authors declare that they have no competing interests.

**Funding**

Not applicable.

**Author's contributions**

xiongbin Chen proposed the study and wrote the first draft. kunling Shen guided the design of the study and helped to draft the manuscript. All authors read and approved the final manuscript.

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Author's information

xiongbin Chen is the first author of this paper, and Kunling Shen is corresponding author.

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Figures
Figure 1
Changes in PEF

Figure 2
Triggers in the Exacerbation Group

Upper respiratory tract infection
Allergen exposure
Exercise
Air pollution
Climate Change
Cigarette exposure
Other triggers
Figure 3

Changes in PEF with different triggers