

Utility of therapeutic strategy based on the modified Pulmonary Index Score for childhood asthma exacerbation

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ABSTRACT

Background: There are no validated quantitative tools for assessing asthma exacerbation, which may cause significant variation in determining the severity of exacerbation across caregivers. A modified Pulmonary Index Score (mPIS) has been proposed as a quantitative indicator of the severity of childhood asthma exacerbation. However, the utility of mPIS as a treatment decision-making tool has not been investigated.

Objective: The aim of the present study was to clarify the utility of therapeutic strategies based on mPIS in children hospitalized for asthma exacerbation.

Methods: This was a case-control study of patients admitted to our hospital between 2010 and 2015. In addition to the conventional therapy based on Japanese guidelines, treatment adaptation by using mPIS began in 2013. Children admitted after 2013 were regarded as being in the case group and those before 2012 were the control group. The length of the hospital stay and the duration of continuous isoproterenol inhalation therapy (CIT) were compared as clinical outcomes.

Results: The targeted number of patients was 346 (182 cases and 164 controls). The mean $\pm$ standard error age was 3.5 ± 0.2 years in the case group and 3.4 ± 0.2 years in the control group. Male patients constituted 64.3% of the case group and 60.4% of the control group. The mean $\pm$ standard error length of hospital stay was significantly shortened in the case group (8.1 ± 0.2 days versus 9.6 ± 0.2 days, $p < 0.001$). The mean $\pm$ standard error duration of CIT was also shortened in the case group (2.3 ± 0.1 days versus 3.9 ± 0.3 days, $p < 0.001$).

Conclusion: An mPIS-based therapeutic strategy may have reduced the length of hospital stay by enabling timely adjustments to clinical interventions and enabling caregivers to perform a more-accurate assessment of asthma exacerbation.

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Asthma is a common and potentially serious chronic disease that imposes a substantial burden on patients, their families, and the community. It causes respiratory symptoms, limitations of activity, and flare-ups that at times require urgent health care. Management of asthma exacerbations and adequate control are milestones for optimal routine clinical practice. Most childhood asthma guidelines recommend classifying an exacerbation by using qualitative indicators, including patient dyspnea and other objective findings,^{1–5} which may cause significant variation in deciding the level of exacerbation across caregivers. The modified Pulmonary Index Score (mPIS) is a quantitative indicator for the level of respiratory distress for childhood asthma.⁶ Introduction of the mPIS score in a clinical setting enables caregivers to

have a more accurate assessment of asthma exacerbation, which standardizes the degree of a patient's respiratory distress across caregivers.^{7,8}

Incorporation of mPIS in a clinical setting is likely beneficial, but the impact of treatment decisions on patient outcomes based on that score has not been investigated. We began to use mPIS to assess a patient's level of exacerbation in 2012 and developed an mPIS-based decision-making flowchart in 2013. The aim of the present study was to clarify the utility of therapeutic strategies based on mPIS in patients hospitalized for asthma exacerbation by comparing patients before and after adaptation of this method.

METHODS

This was a case-control study. The participants were the children admitted to Showa University Hospital between 2010 and 2015 due to asthma exacerbation. Children admitted after 2013 and treated by using the mPIS-based flowchart were regarded as "cases" and those hospitalized before 2012 and treated with conventional therapy were regarded as "controls." Patients with severe physical disorders, mental retardation, and congenital malformation syndromes were excluded. Patients who did not use methylprednisolone, (*i.e.*, mild exacerbation) were also excluded.

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Point		0	1	2	3
Heart rate (/min)	< 3 year	<120	120-140	141-160	>160
	≥ 3 year	<100	100-120	121-140	>140
Respiratory rate (/min)	< 6 year	≤ 30	31-45	46-60	>60
	≥ 6 year	≤ 20	21-35	36-50	>50
Accessory muscle use		None	Mild	Moderate	Severe
I/E ratio		2:1	1:1	1:2	1:3
Wheezing		None	End expiratory only	Both I/E wheeze + good aeration	Both I/E wheeze + bad aeration
Oxygen saturation (%)		≥ 96	93-95	90-92	<90

Figure 1. The mPIS consists of six factors; heart rate, respiratory rate, accessory muscle use, inspiratory-to-expiratory flow ratio, the degree of wheezing, and oxygen saturation. The sum of the score indicates the severity. mPIS = modified Pulmonary Index Score; I/E = inspiratory-to-expiratory ratio.

Age, sex, a previous diagnosis of asthma by physicians, administration of continuous inhalation of isoproterenol therapy (CIT), and administration of aminophylline were examined as background factors.

The Definition of Asthma

Asthma was diagnosed based on Japanese pediatric guidelines for the treatment and management of asthma (JPGL).⁵ Briefly, children with respiratory distress with wheezing that responded to short-acting β -agonist (SABA) inhalation and diagnosed by a physician or had an episode of recurrent wheezing were treated as asthma exacerbation. The episodes of wheezing and a physician's diagnosis of asthma were obtained from the parents at admission. A radiograph was obtained in all patients to exclude other respiratory diseases.

mPIS

The mPIS is shown in Fig. 1. The mPIS is a scoring system to assess the severity of asthma exacerbation.⁶ The score consists of six factors with each factor graded on four levels (0–3 points). The six factors are as follows: heart rate, respiratory rate, accessory muscle use, inspiratory-to-expiratory flow ratio, the degree of wheezing, and oxygen saturation. The sum of the score shows the severity; the severest score is 18 points. The scores of mPIS ≥ 6 –9 points and ≥ 10 points are indications of moderate and severe exacerbation, respectively. General pediatricians scored mPIS at admission and then at least two times a day during admission.

Primary and Secondary End Points

The primary end point was the difference in the length of hospital stay before and after introduction of the therapeutic criteria, and the secondary end point was the difference in the duration of CIT. Subgroup analysis was performed to compare the length of hospital stay by the presence or absence of CIT.

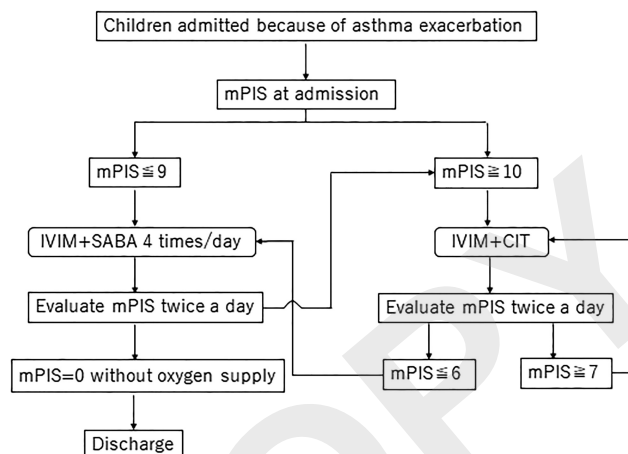


Figure 2. The mPIS-based therapeutic strategy. CIT was started when mPIS reached ≥ 10 and terminated once the score dropped to ≤ 6 points. mPIS = modified Pulmonary Index Score; IVIM = intravenous injection of methylprednisolone; SABA = short-acting β -agonist; CIT = continuous inhalation of isoproterenol therapy.

Conventional Therapy

According to JPGL, patients were hospitalized if the severity of exacerbation remained more than moderate after two or three treatments with SABA inhalation and an intravenous injection of methylprednisolone (IVIM) (1 mg/kg/dose). Children with a recurrent history of severe exacerbations were hospitalized even if an exacerbation improved to mild. The patients with moderate exacerbation received intermittent SABA inhalation (four times a day) and 3–4 mg/kg/day of IVIM, and those with severe exacerbation received CIT instead of SABA inhalation. In addition to those treatments, until 2012, intravenous aminophylline injection had been positively considered as one of the treatment options for severe asthma. Once the severity of exacerbation was reduced to moderate, CIT was stopped and intermittent SABA inhalation was started. When the severity of exacerbation improved to mild, IVIM and SABA inhalation were stopped. The patients were discharged if they had no symptoms 1 day after stopping IVIM and SABA inhalation.

mPIS-Oriented Therapeutic Strategy

The decision-making flowchart for asthma exacerbation since 2013 is shown in Fig. 2. Based on a clinical history review in 2012, the criteria that activated treatment were as follows: mPIS of ≥ 6 –9 for admission and treating moderate exacerbation (IVIM and intermittent SABA inhalation) and mPIS ≥ 10 for severe exacerbation treatment (CIT). CIT was continued for at least 12 hours after induction and was deactivated once the score dropped to ≤ 6 points. The score for permission to discharge was set to 0 points without the supply of oxygen, IVIM, and intermittent SABA inhalation.

Table 1 Comparison of characteristics between the case and control groups

Characteristics	Case Group (n = 182)	Control Group (n = 164)	p
Age, mean $\pm$ SE, y	3.5 $\pm$ 0.2	3.4 $\pm$ 0.2	0.896
Boys, no. (%)	117 (64.3)	99 (60.4)	0.452
Asthma diagnosis ever: yes, no. (%)	86 (47.3)	82 (50.0)	0.610
CIT treatment: yes, no. (%)	66 (36.2)	56 (34.1)	0.681
Aminophylline treatment: yes, no. (%)	9 (4.9)	19 (11.6)	0.014

Aminophylline treatment: yes, no. (%) = 4.

SE = Standard error; CIT = continuous inhalation of isoproterenol therapy.

Statistical Analysis

The differences between groups in continuous variables were assessed by using the Mann-Whitney U test. Differences between the groups in categorical data were examined by using the Fisher exact test or the Pearson χ^2 test, depending on the sample size. To exclude confounders, stepwise multiple regression analysis was performed with the length of hospital stay as the objective variable and with age, sex, history of asthma diagnosis by physicians, administration of CIT, and administration of aminophylline as explanatory variables. *P* values of <0.05 were regarded as significant. All analyses were performed with IBM SPSS software, v24.0.0 (IBM Corp. Armonk, NY).

Ethical Considerations

The study was designed in accordance with the Declaration of Helsinki and the guidelines for the ethics of an epidemiology investigation from the Ministry of Health, Labor and Welfare, and the Ministry of Education, Culture, Sports, Science and Technology in Japan. We obtained approval from the ethics committee of Showa University School of Medicine (Showa-2437).

RESULTS

Descriptive and Outcome Data

There were 375 admissions for asthma exacerbation during the whole period. Sixteen children (4.3%) were excluded because of severe physical disorders, mental retardation, or congenital malformation syndromes. Thirteen children (3.5%) were excluded because there was no methylprednisolone use. The remaining 346 patients (92.2%) satisfied the eligibility criteria and were included in the study. A comparison of background factors and treatment conditions between case and control groups is shown in Table 1. The number of the children in the case and the control groups were 182 and 164, respectively. There was no significant difference between the groups in mean $\pm$ standard error age (3.5 $\pm$ 0.2 years versus 3.4 $\pm$ 0.2 years, *p* = 0.896), sex (117 [64.3%] versus 99 [60.4%] male patients, *p* = 0.452), previous diagnosis of asthma by physicians

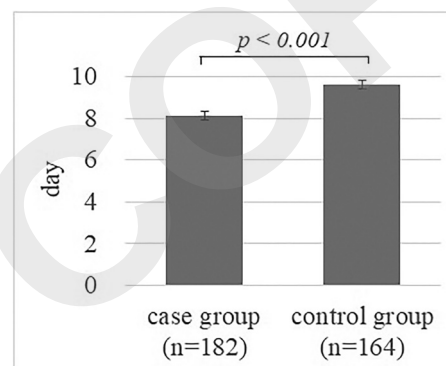


Figure 3. The difference in the length of hospital stay (primary outcome in this study). The length of hospital stay was significantly shortened in the case group (8.1 $\pm$ 0.2 days versus 9.6 $\pm$ 0.2 days, *p* < 0.001).

before admission (86 [47.3%] versus 82 [50.0%], *p* = 0.610), and prevalence of CIT treatment (66 [36.2%] versus 56 [34.1%], *p* = 0.681). Prevalence of aminophylline treatment was higher in the control group (9 [4.9%] versus 19 [11.6%], *p* = 0.014).

Main Results

A comparison of the length of hospital stay between the case and control group is shown in Fig. 3. Compared with the patients before the flowchart was introduced, the length of hospital stay was significantly decreased in case group (8.1 $\pm$ 0.2 days versus 9.6 $\pm$ 0.2 days, *p* < 0.001). A comparison of the CIT duration between the case and the control groups is shown in Fig. 4. Compared with the patients before the flowchart was introduced, the duration of CIT was also significantly decreased in case group (2.3 $\pm$ 0.1 days versus 3.9 $\pm$ 0.2 days, *p* < 0.001). The comparison of the length of hospital stay by the presence or absence of CIT is shown in Table 2. The length of hospital stay was significantly shortened in the case group in both patients who received CIT and those who did not. The results of uni- and multivariate analyses of the shortening of hospitalization days by the new therapeutic strategy are shown in Table 3. Even after adjustment for age, sex, previous asthma diagnosis, CIT, and am-

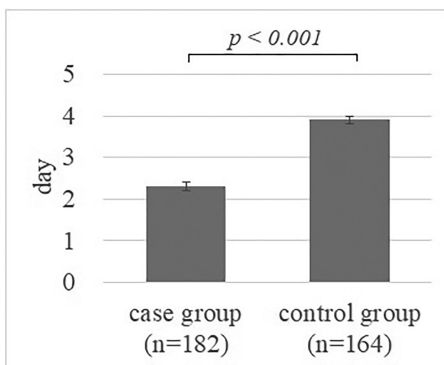


Figure 4. The duration of continuous inhalation of isoproterenol therapy (secondary outcome in this study). The duration of continuous inhalation of isoproterenol therapy was significantly shortened in the case group (2.3 ± 0.1 days versus 3.9 ± 0.3 days, $p < 0.001$).

inophylline administration, the length of hospital stay was significantly shortened in the case group.

DISCUSSION

Main Findings

The introduction of an mPIS-based therapeutic strategy for asthma exacerbation may have substantially reduced the length of hospital stay and duration of CIT. Both the length of hospital stay and the duration of CIT were shortened by ~1.5 days.

Limitations

These were several limitations to this study. First, there was a significant difference in the frequency of the aminophylline administration between the case and control groups. Because a concern was raised that aminophylline usage may induce seizure in an infant, JPGL 2012⁹ gave a recommendation to refrain from its administration and to provide alternative treatments to infants. This recommendation may have caused the significant difference in the asthma treatment between the groups. To address this issue, we conducted a *post hoc* analysis on children hospitalized after 2012 when there was still a significant difference in the hospital stay between the case ($n = 184$) and control ($n = 65$) groups (8.3 ± 0.2 days versus 9.4 ± 0.4 days, $p = 0.008$). Hence, the impact of the difference on the aminophylline usage should be insignificant.

Second, even though episodes of recurrent wheezing and response to SABA during treatment were included for the diagnosis of asthma, it was not possible to exclude asthma-like respiratory diseases, *e.g.*, acute bronchiolitis, exclusively. Because children with these diseases generally have a poor response to typical asthma treatment,¹⁰ the difference in hospital stay among children with a confirmed asthma diagnosis may be smaller than our findings. Third, because this was a retrospective study, caregivers varied from year

to year. To minimize the differences in scoring mPIS, caregivers were trained to be able to evaluate asthma exacerbation accurately. Consistency in mPIS across caregivers was high⁶; score differences between caregivers were probably minimal. Fourth, the number of readmission and CIT reintroduction could not be evaluated because of unavailability of data.

Interpretation

Adding an mPIS-based therapeutic strategy to conventional therapy may have improved clinical outcomes. The reduction in the length of hospital stay was only 1.5 days. However, because a large number of children are admitted for asthma exacerbation in Japan, even a small reduction may bring substantial economic benefits.¹⁴ The impact of assessment scores for asthma exacerbations on clinical outcomes, such as hospital stay and financial cost, was also reported by Nkoy *et al.*¹² They used a composite score for eight quality measures and showed a reduction in median length of hospital stay by 4 hours and a median cost by \$113 per hospitalization. Decreasing the length of hospital stay may lead to a reduction of an otherwise outsized proportion of health-care costs.

The mPIS-based therapeutic strategy may allow timely intervention in asthma exacerbation. In addition to reducing the CIT period, the variation in the CIT period was lower in patients in the case group. This decrease in variation may suggest that the physicians were able to select treatments with confidence by using a quantitative indicator for the severity of exacerbation. Hence, mPIS may provide a modernistic perspective for classifying asthma exacerbations. As shown in Table 2, the CIT group had a greater reduction of length of hospital stay than that in the non-CIT group (-2.6 days versus -1.0 days). Therapeutic strategies based on mPIS may be more effective in severe asthma exacerbation due to the timely and consistent intervention and termination of the treatment. The mPIS system is a useful scoring system to readily assess respiratory conditions. Several scoring systems to evaluate asthma exacerbation have been proposed.^{13–15} We adopted mPIS because the scoring system is easy to administer daily, does not require a respiratory function test, and is highly correlated among caregivers.

Generalizability

Our hospital is a tertiary emergency medical facility, and patient characteristics may have differed from general hospitals. In fact, 122 children (35.2%) required CIT treatment, which may mean that children required intensive medical care.^{6,7} However, a significant reduction of the length of hospital stay was found, even in patients with non-CIT treatment. Therefore, the mPIS system may improve clinical outcomes in general hospitals as well.

Table 2 Comparison in the length of hospital stay by the presence or absence of CIT

	Case Group (n = 182)	Control Group (n = 164)	p
Non-CIT group			
Hospital stay, mean $\pm$ SE, days	7.7 $\pm$ 0.2	8.7 $\pm$ 0.2	<0.001
No. patients	116	108	
CIT group			
Hospital stay, mean $\pm$ SE, days	8.9 $\pm$ 0.4	11.5 $\pm$ 0.5	<0.001
No. patients	66	56	

SE = Standard error; CIT = continuous inhalation of isoproterenol therapy.

Table 3 Univariate and multivariate analysis of the shortening of hospitalization days by new therapeutic strategy

	Univariate Analysis (95% CI)	p	Multivariate analysis (95% CI)*	p
Shortening of hospitalization, days	-1.54 (-0.95 to -2.14)	<0.001	-1.49 (-0.93 to -2.05)	<0.001

CI = Confidence interval.

*Adjusted for age, sex, previous diagnosis of asthma, administration of continuous inhalation of isoproterenol therapy, and administration of aminophylline.

CONCLUSION

Appropriate interventions based on mPIS may have decreased the length of hospital stay and CIT duration. Recently, the Japanese Pediatric Society of Allergy published guidelines for childhood asthma, which includes mPIS as a qualitative indicator for asthma exacerbation severity.⁵ Based on our data, we strongly recommend the management of asthma exacerbation by using this score. In the future, the appropriate mPIS cutoff points to activate and deactivate treatment should be reviewed by using data for adverse events.

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