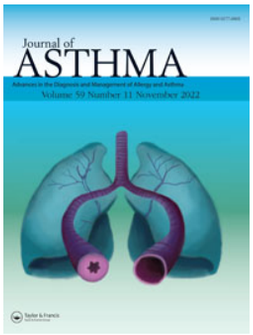

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Psychosocial factors and lack of asthma knowledge undermine child and adolescent adherence to inhaled corticosteroid

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ABSTRACT

Objective: This study aimed to evaluate inhaled corticosteroid (ICS) adherence and identify factors associated with nonadherence in pediatric asthma patients.

Methods: A total of 134 patients aged 8–18 years old were included. At the first visit, patient adherence, asthma knowledge, and outcome expectation data were collected and recorded. Depression, anxiety, and self-esteem were assessed using psychiatric questionnaires. After providing asthma education, reevaluation of adherence and asthma control was performed at one 3- to 6-month follow-up visit.

Results: The mean ICS adherence was 75.9 ± 27.5%. Fifty-seven patients (42.5%) were defined as having poor adherence (<75%). "Intentional" and "hectic lifestyle and forgetfulness" were the main reasons for missing ICS doses in mid-late adolescents and children, respectively. Asthma knowledge generally improved with age. Overall, 89% and 67.7% of patients could define symptoms and triggers of asthma, respectively; however, less than 25% understood how asthma affected their body and the chronic nature of asthma. Patients with ICS adherence <75% had unfavorable expectations from asthma treatment (odds ratio [OR]: 1.05, 95% confidence interval [CI]: 1.01–1.10), and a higher proportion of inhaled short-acting beta-agonist use before exercise (OR: 4.12, 95% CI: 1.27–13.36). Depression and anxiety were frequently found (27.5%) and 23.3%, respectively; $p > 0.05$). Significant improvement in ICS adherence ($p = 0.02$) and Asthma Control Test scores ($p = 0.02$) were observed at the follow-up visit.

Conclusions: Patient outcome expectations could be predictors of ICS adherence. Patient education regarding the mechanism and nature of asthma should be considered as an intervention for improving pediatric patient adherence. Psychological evaluation is warranted in pediatric patients with asthma.

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Introduction

Effective asthma treatment can be achieved with cooperative patient self-management; however, medication adherence is crucial (1). Adherence to inhaled corticosteroid (ICS) among children and adolescents has been reported to range from 30% to 70%, with the rate being lower among late adolescents (2). Some studies revealed that medication adherence <75–80% was associated with frequent exacerbation and worse asthma control. Moreover, the adherence rate decreased over time, and its value over 62.1% at 6-month follow-up was also found to be a strong determinant of asthma control (3).

Reduced ICS adherence is multifactorial. Studies conducted on African-American asthmatic adolescents showed that greater ICS knowledge was associated with higher medication adherence (>48%) and that misbelief and misperception about asthma and its treatment were common among adolescents (4,5). Various asthma education programs implemented among late adolescents and adults in Spain yielded reduced rates of exacerbation as well as reduced rates of work absenteeism (6). In part, a poor adherence behavior, based on the "problem behavior theory," may be influenced by personality factors such as low expectation of a successful outcome, stress, depression, and low self-esteem (7). Outcome expectations, which reflect patients' belief that certain management will help their asthma, were more favorable in American youths with high rates of medication adherence (8). In addition, psychiatric problems, including depression and anxiety disorder, demonstrated a negative effect

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on medication adherence and clinical outcomes (9–11). Apart from personality factors, environmental factors (e.g., family relations, living environment, social support) were involved in eliciting adolescents' behavior (7). The family socioeconomic status and parental years of schooling were found to be positively correlated with routine pediatric asthma management (12) and medical adherence (3), respectively. Considering the importance of long-term controller medication, simplifying the drug regimen to regular use once daily was expected to improve adherence to ICS (13,14). However, a range of regimens, including twice daily, every alternate day, and inhaled controller plus oral medication, have been prescribed in real-world practice, and their impact on ICS adherence still needs to be investigated. A systematic review analyzing four interventions—namely, provision of adherence education, use of electronic reminders, simplifying the regimen, and provision of an inhaler during school hours—showed a significant increase in adherence rate; nonetheless, the benefit with respect to a reduction in exacerbation rate was not clear (15).

Herein, considering that patients in each age group have distinct psychological developments (e.g., risk-taking behavior predominant in middle adolescents (16)), we were interested in evaluating the reasons for not using medications in the following three age groups: late children, early adolescents, and middle adolescents. Thai children are closely connected to their family, and their autonomy is framed and developed within a model that expects obedience to their parents' wishes (17). This tradition can either contribute to or prevent undesired poor adherence. Nevertheless, no study has evaluated asthma medication adherence and associated factors in Thai pediatric patients.

The primary objective of the present study was to evaluate ICS adherence among Thai and early-middle adolescents. Its secondary aims were to determine the reasons for suboptimal adherence and to identify psychosocial and disease-related factors that could significantly influence ICS adherence in children and adolescents.

Materials and methods

Participants

We enrolled participants aged 8–18 years who had (i) physician-diagnosed asthma according to the Global Initiative for Asthma 2018 (GINA 2018) (1) and (ii) were actively treated with either ICS or ICS/long-acting beta-agonists (LABA) for more than 3 months. Subjects were excluded if they had underlying chronic diseases, such as severe cardiovascular, liver, or renal disease, pulmonary disorder other than asthma, inability to understand the study questionnaires, and/or facial or hand deformities that complicated the use of inhaler devices (Figure 1). Patients were classified as late children (8–9 years), early adolescent (10–14 years), or middle-to-late adolescent (15–18 years).

Study design

This single-center prospective study was conducted at the Pediatric Allergy Clinic of the Division of Allergy and Immunology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. A total of 134 participants were recruited from April 2019 to January 2020 during their scheduled visit to the clinic. Written informed consent was obtained from both parents/caregivers. Subjects aged 8–18 years provided assent after the caregivers consented to the children's participation. After evaluating asthma control, as defined by Asthma Control Test (ACT) scores (18,19), the same specialist physician interviewed all patients to assess their medical adherence and reasons for patients' suboptimal adherence, asthma knowledge, and asthma outcome expectations. Subsequently, under the supervision of a child and adolescent psychiatrist, patients completed the Children's Depression Inventory (CDI) (20,21), Screen for Child Anxiety Related Emotional Disorders (SCARED) (22), and Rosenberg Self Esteem Scale (23,24) questionnaires to evaluate depression, anxiety, and low self-esteem, respectively. Patients' clinical and sociodemographic data and caregivers' socioeconomic background, including sex, age, marital status, educational level, and monthly income, were collected. After providing asthma education and correcting any misunderstanding of patients regarding asthma-related details, reevaluation of medication adherence and asthma control was performed at one 3- to 6-month follow-up visit (for details on ICS adherence measurement, the interview questions and psychological questionnaires are available in the Supplementary Appendix). The study protocol was approved by the Siriraj Institutional Review Board (SIRB) (approval no. 903/2561).

Reasons behind suboptimal adherence

There are three types of non-adherence: erratic (understanding the treatment plan, but the complexity of the treatment and their lives interfere), unwitting (unintentional due to poor understanding of the disease and its treatment), or deliberate (altered asthma therapy based on reasoning) (2,3).

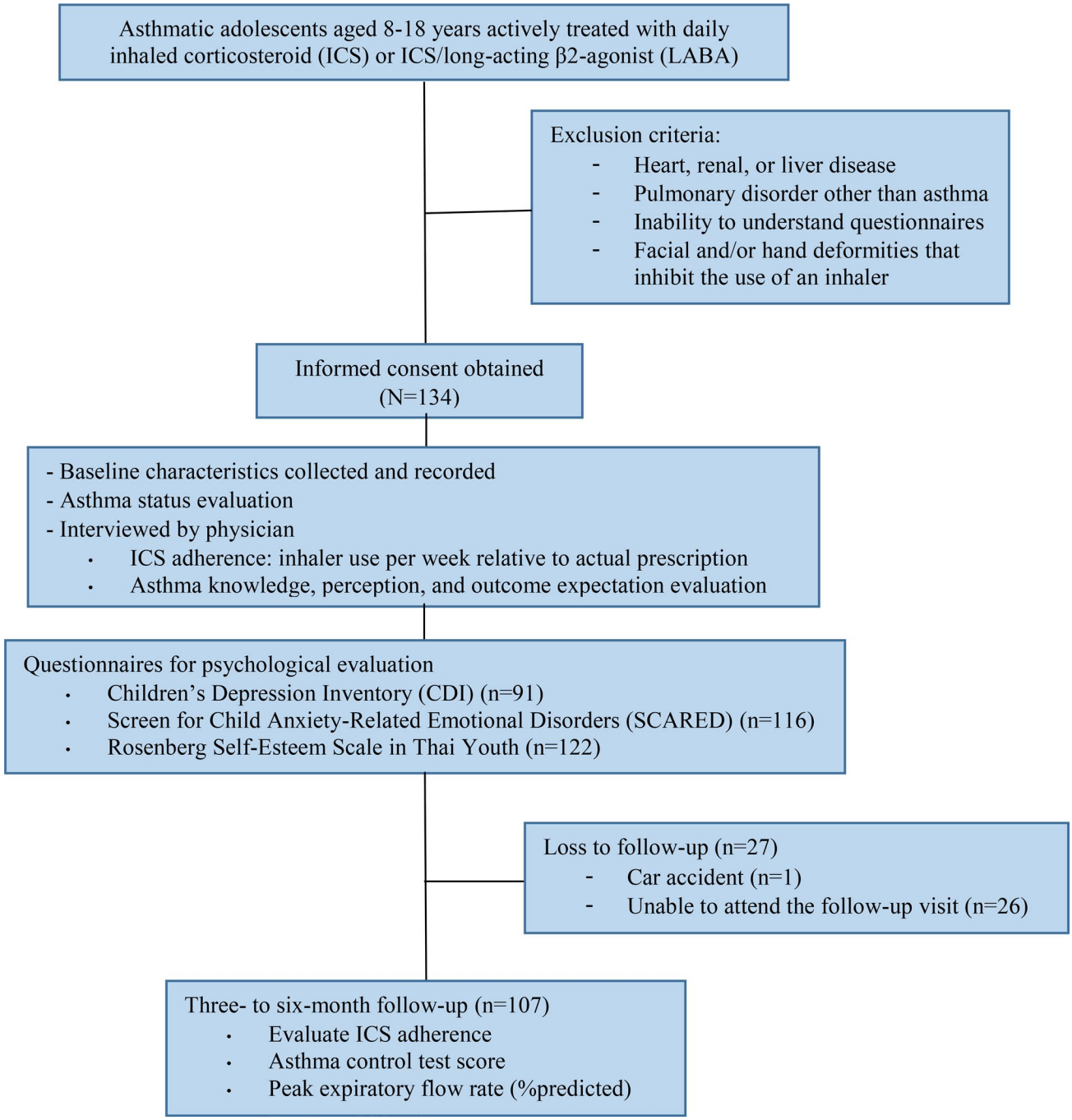

Figure 1. Flow diagram of patient enrollment and the study protocol.

Asthma knowledge

Two domains of asthma-related knowledge—namely, disease-related knowledge and treatment-related knowledge—were evaluated through interview using five open-ended questions for each of the two domains. The interview questions were developed based on the GINA guideline (1) and the Caretaker Expectations Regarding the Management of Pediatric Asthma Scale (25). Patients were also asked to demonstrate their inhalation technique and to indicate which canister was used for control and which one was for relief.

Outcome expectation

A visual analog scale (VAS) was used to evaluate the patient's perception of how much his/her treatment helped his/her asthma in five different settings. The

far left (0 cm) indicated no help at all, and the far right (10 cm) the best possible help in treating asthma (score for each line: 0 to 10).

Statistical analysis

To determine the ICS adherence rate, we calculated the sample size using the ICS adherence rate at the time of the initial visit from a previous study that reported a standard deviation of 25.4 (26). With a margin of error (E) of 4.5 and the accepted level of significance of 0.05, the calculated minimum sample size was 123 subjects. All statistical analyses were performed using SPSS version 23 software (SPSS, Inc., Chicago, IL, USA). The adherence rate and other continuous variables and scores are reported as mean ± standard deviation. Numerical categorical data are reported as numbers and percentages. Association between variables and the medication adherence rate was analyzed using Student's t test for continuous variables and Fisher's exact test or chi-square test for categorical variables. Variables with a $p < 0.1$ were included in multivariate logistic regression analysis to identify independent factors. The mean differences in ICS adherence, ACT score, and peak expiratory flow rate between baseline and follow-up were analyzed using a paired samples t test. Statistical significance was set at $p < 0.05$.

Results

Patient demographic and socioeconomic data

Of the 134 enrolled patients, 39, 68, and 27 patients were categorized into childhood, early adolescent, and mid-late adolescent groups, respectively. The average age of all participants was 11.6 ± 2.9 years, and 70.1% were males. The mean asthma duration was 8.1 ± 3.7 years, and 88.1% of patients also had allergic rhinitis. Among all caregivers, 81.3% were the child's mother, and 41% had an educational level of bachelor's degree or higher. One-third of patient families reported earning less than 20,000 Thai baht (THB)/month (equivalent to approximately 612 USD/month).

Most participants had controlled asthma (mean C-ACT score: 24.2 ± 2.7, mean ACT score: 23.5 ± 2.2), and mild (39.3%) to moderate (51.9%) severity according to GINA criteria (1). Seventy-four (55.2%) and 60 (44.8%) patients were treated with ICS and a fixed-dose combination of ICS/LABA, respectively. Of the 134 included patients, 62.7% were prescribed once daily medication, and 64.2% used a metered dose inhaler (MDI). Forty-three patients (32.0%) were on oral controller medication (either leukotriene receptor antagonist or theophylline), and 13 (9.8%) patients received subcutaneous immunotherapy. Patient characteristics and asthma treatments are described in Table 1.

Adherence to inhaled controller medication

The overall adherence rate was 75.9%±27.6%, and subgroup analysis by age showed similar results among groups (78%, 74.3%, and 77% in the late childhood, early adolescence, and middle-late adolescence groups, respectively).

The reasons for suboptimal ICS adherence reported by the 91 patients who indicated having missed an ICS dose are shown in Figure 2. Intentional non-adherence due to a feeling that the burden of treatment was greater than the benefit of treatment was reported by 66.7% of early adolescents and by 83.3% of mid-late adolescents. Unlike adolescents, children unintentionally missed their ICS doses. The proportion of children who reported forgetfulness and a hectic family lifestyle as reasons for missing an ICS dose was 40 and 40%, respectively.

Knowledge about asthma and its treatment

Overall, there was no significant difference in any knowledge item between the good and poor adherence groups.

Concerning disease-related knowledge, 89.2% of participants knew about asthma symptoms, and 67.7% knew what triggers them. In contrast, only 12.2% knew that asthma affects the airway, and only 25.6% understood the chronic and incurable nature of asthma, but that it could be controlled.

Of all participants, 57.7 and 41.5% believed controller use and trigger avoidance to be the main principles of treatment, respectively. Moreover, 67.2 and 78.4% were able to distinguish between regular inhalers and reliever, respectively, and 102 (76.0%) patients could correctly perform the inhaler technique using their own device. Only 15.4% were able to correctly explain what to do when they had an attack.

The patient knowledge results in the three age groups (8 to <10 years, 10 to <15 years, and 15 to <18 years) are shown in Figure 3A and 3C. The same trend of results was observed among groups, and the proportion of patients who gave correct answers

Table 1. Baseline participant and caregiver characteristics.

Characteristics	Total ($N=134$)	Adherence < 75% ($n=57$)	Adherence>75% ($n=77$)	p value
Age (years), mean ± SD	11.6 ± 2.9	11.8 ± 3.1	11.5 ± 2.8	0.50
Children (8 to ≤10 years) ($n=39$)	8.5 ± 0.5	8.5 ± 0.5	8.5 ± 0.5	0.66
Early adolescents (10 to ≤15 years) ($n=68$)	11.6 ± 1.4	11.4 ± 1.5	11.7 ± 1.4	0.36
Mid-late adolescents (15 to ≤18 years) ($n=27$)	16.2 ± 1.1	16.3 ± 1.1	16.2 ± 1.1	0.76
Male sex, n (%)	94 (70.1%)	38 (66.7%)	56 (72.7%)	0.45
Body mass index (kg/m^2), mean ± SD	20.7 ± 19.5	20.4 ± 4.9	20.9 ± 6.0	0.63
Caregiver characteristics				
Age (years), mean ± SD	43.5 ± 8.3	43.2 ± 8.0	43.7 ± 8.4	0.73
Relationship, *n* (%)				
Mother	109 (81.3%)	50 (87.7%)	59 (76.7%)	***0.04***
Father or other family members	25 (18.7%)	7 (12.3%)	18 (23.4%)	
Educational level, *n* (%)				
Primary-elementary school	25 (18.6%)	6 (10.5%)	19 (24.7%)	0.07
High school	23 (17.2%)	9 (15.8%)	14 (18.2%)	
Vocational degree	31 (23.1%)	12 (21.1%)	19 (24.7%)	
Bachelor degree or higher	55 (41.0%)	30 (52.6%)	25 (32.5%)	
Family income (per month), *n* (%)				
<2 0,000 Thai baht Thai baht	47 (36.2%)	15 (26.8%)	32 (43.2%)	0.09
2 0,000–5 0,000 Thai baht	48 (36.9%)	20 (35.7%)	28 (37.8%)	
5 0,000–1 00,000 Thai baht	25 (19.2%)	15 (26.8%)	10 (13.5%)	
>1 00,000 Thai baht	10 (7.7%)	6 (10.7%)	4 (5.4%)	
Asthma status				
Age of asthma onset (years), mean ± SD	3.5 ± 2.9	3.9 ± 2.9	3.1 ± 2.8	0.11
Allergic rhinitis, *n* (%)	118 (88.1%)	52 (91.2%)	66 (85.7%)	0.33
Snoring, *n* (%)	32 (23.9%)	46 (80.7%)	57 (74.0%)	0.37
Food allergy, *n* (%)	30 (22.2%)	14 (24.6%)	16 (20.8%)	0.60
Atopic dermatitis, *n* (%)	12 (8.9%)	5 (8.8%)	7 (9.0%)	0.95
Asthma symptom control by ACT score				
C-ACT, mean ± SD	24.1 ± 2.7	23.2 ± 3.3	24.8 ± 1.8	***0.01***
ACT, mean ± SD	23.7 ± 2.0	23.4 ± 2.5	23.9 ± 1.5	0.42
Well-controlled asthma justified by C-ACT or ACT (≥20), *n* (%)	127 (94.8%)	53 (93.0%)	74 (96.1%)	0.17
Asthma symptom control by GINA				
Well-controlled asthma, *n* (%)	111 (82.8%)	43 (75.4%)	68 (88.3%)	0.15
Partially-controlled asthma, *n* (%)	18 (13.4%)	11 (19.3%)	7 (9.1%)	
Poorly-controlled asthma, *n* (%)	5 (3.7%)	3 (5.3%)	2 (2.6%)	
Severity of asthma				
Mild, *n* (%)	53 (39.6%)	24 (42.1%)	29 (37.7%)	0.22
Moderate, *n* (%)	70 (52.2%)	26 (45.6%)	44 (57.1%)	
Severe, *n* (%)	11 (8.2%)	7 (12.3%)	4 (5.2%)	
Pulmonary function				
PEFR (L/min), %predicted, mean ± SD	91.4 ± 14.1	91.6 ± 13	91.4 ± 14.9	0.94
Spirometry ($n=85$)				
FEV1 (%predicted), mean ± SD	89.1 ± 12.9	91.3 ± 11.9	87.6 ± 13.4	0.19
FEV1/FVC (%), mean ± SD	87.1 ± 6.6	88.0 ± 6.4	86.5 ± 6.7	0.30
Asthma medication				
Inhaled controller, *n* (%)				
ICS	74 (55.2%)	33 (57.9%)	41 (53.2%)	0.59
ICS/LABA	60 (44.8%)	24 (42.1%)	36 (46.8%)	
Combination oral and inhaled controller, *n* (%)	43 (32.1%)	17 (29.8%)	26 (33.8%)	0.44
Subcutaneous immunotherapy, *n* (%)	13 (9.8%)	7 (12.3%)	6 (8.0%)	0.41
Omalizumab, *n* (%)	1 (0.8%)	1 (1.8%)	0 (0.0%)	
Inhaler regimen prescribed, *n* (%)				
Once daily	84 (62.7%)	37 (64.9%)	47 (61.0%)	0.33
Twice a day (1 × 2)	37 (27.6%)	12 (21.1%)	25 (32.5%)	
Twice a day (2 × 2)	3 (2.2%)	2 (3.5%)	1 (1.3%)	
Device, *n* (%)				
MDI	86 (64.2)	35 (61.4)	51 (66.2)	0.56
DPI	48 (35.8)	22 (38.6)	26 (33.8)	
Correct inhaler technique	102 (76.1%)	40 (70.2%)	62 (80.5%)	0.17
Adherence rate, mean ± SD	75.9 ± 27.5	49.9 ± 23.1	95.2 ± 7.2	–

A p values <0.05 indicates statistical significance.

SD, standard deviation; C-ACT, childhood asthma control test; ACT, asthma control test; GINA, Global Initiative for Asthma; PEFR, peak expiratory flow rate; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; ICS, inhaled corticosteroid; ICS/LABA, inhaled corticosteroid/long-acting beta-agonist; MDI, metered-dose inhaler; DPI, dry powder inhaler.

generally increased with age, except for treatment knowledge relating to recognition of the first sign of an attack, and how to follow the instructions when having an attack.

Asthma outcome expectation

The average total outcome expectation score was 39.3 ± 8.6 out of 50. Of all items, patients had the

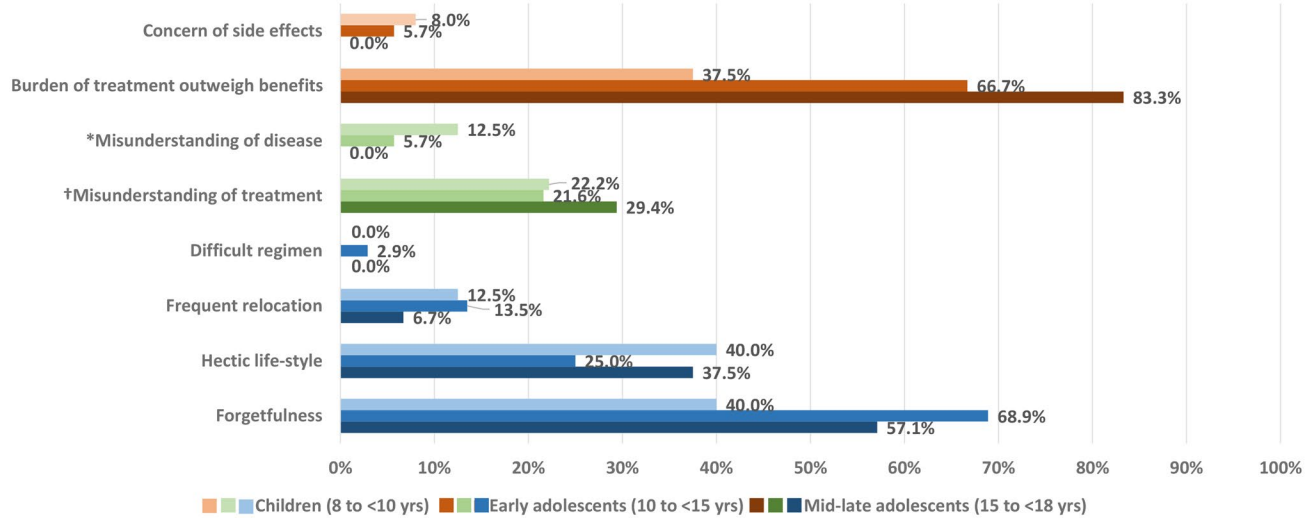

Figure 2. Reasons for suboptimal inhaled corticosteroid adherence. The percentage of 91 patients who reported missing ICS doses due to suboptimal adherence to ICS. Erratic causes (blue), unwitting causes (green), and deliberate causes (red). Light, medium, and dark colors represent the reasons given by children, early adolescents, and middle-late adolescents, respectively. ICS, inhaled corticosteroid. *Misunderstanding of diagnosis and/or prognosis. †Misunderstanding of prescribed doses and/or drug schedules.

highest expectation from following as instructed when having an attack (mean score: 8.5 ± 1.7). In contrast, patients had the least expectation from coming to an appointment (mean score: 7.1 ± 2.6) (Figure 4).

Psychological evaluation

At baseline, no significant difference was observed between the low (<75%) and high (≥75%) adherence groups for the prevalence of symptoms of mood disorders and self-esteem (depression: 31.1% vs. 24.5%; anxiety: 26.5% vs. 20.9%; and low self-esteem: 1.9% vs. 8.6%), or for the average scores (depression: 12.3 ± 5.5 vs. 10.2 ± 6.5, $p = 0.11$; anxiety: 22.5 ± 10.7 vs. 20.5 ± 10.3%, p = 0.30; and low self-esteem: 19.5 ± 3 vs. 19.9 ± 4.1, $p = 0.58$).

Factors associated with low ICS adherence (<75%)

In univariate analysis, adherence <75% was significantly associated with the use of the reliever before exercise ($p = 0.02$) (Figure 3D), lower C-ACT score ($p = 0.01$), and having the mother as the main caregiver ($p = 0.04$) (Table 1). A lower outcome expectation score for the following was also significantly associated with poor adherence: recognition of the first sign of an attack ($p = 0.03$), coming to an appointment ($p = 0.01$), following as instructed when having an attack ($p = 0.01$) (Figure 4), and total score (37.1% vs. 40.9%, $p = 0.01$) (Table 2).

Further multivariate analysis that included related factors that yielded significant results ($p < 0.1$) in univariate analysis revealed lower total outcome expectation score (adjusted odds ratio [OR]: 1.05, 95% confidence interval [CI] 1.01–1.10) and patient use of reliever before exercise (adjusted OR: 4.12, 95% CI 1.27–13.36) to be factors independently associated with low ICS adherence (<75%) (Table 2).

Adherence at the 3- to 6-month follow-up visit

A total of 107 patients (36, 50, and 21 patients from the child, early adolescent, and mid-late adolescent groups, respectively) attended the 3- to 6-month follow-up appointments. After asthma education and correction of patient knowledge and misunderstanding from the first visit, we found a significant increase in average ICS adherence to 83 ± 25.1% (t_{107} 2.3, 95% CI 1.0–13.2). The average ACT score in all three age groups was also increased (t_{107}2.7, 95% CI 0.2–1.1) (Table 3).

Discussion

Adherence to inhaled controller medication

In this study, the mean ICS adherence in Thai asthmatic children and adolescents was 75%, which is

Figure 3. Percentage of patients who gave correct responses to interview questions related to asthma knowledge. (A,B) Patients' disease-related knowledge. (C,D) Patients' treatment-related knowledge. Panels A and C show the percentage of patients compared among three different age groups (children <11 years, early adolescents 11–13 years, and middle-late adolescents 14–18 years). Panels B and D show the percentage of patients with an adherence rate ≥75% and that with an adherence rate <75%. *P* values are based on chi-square analyses, and items with a *p* values <0.05 were considered to be significantly associated with adherence <75%.

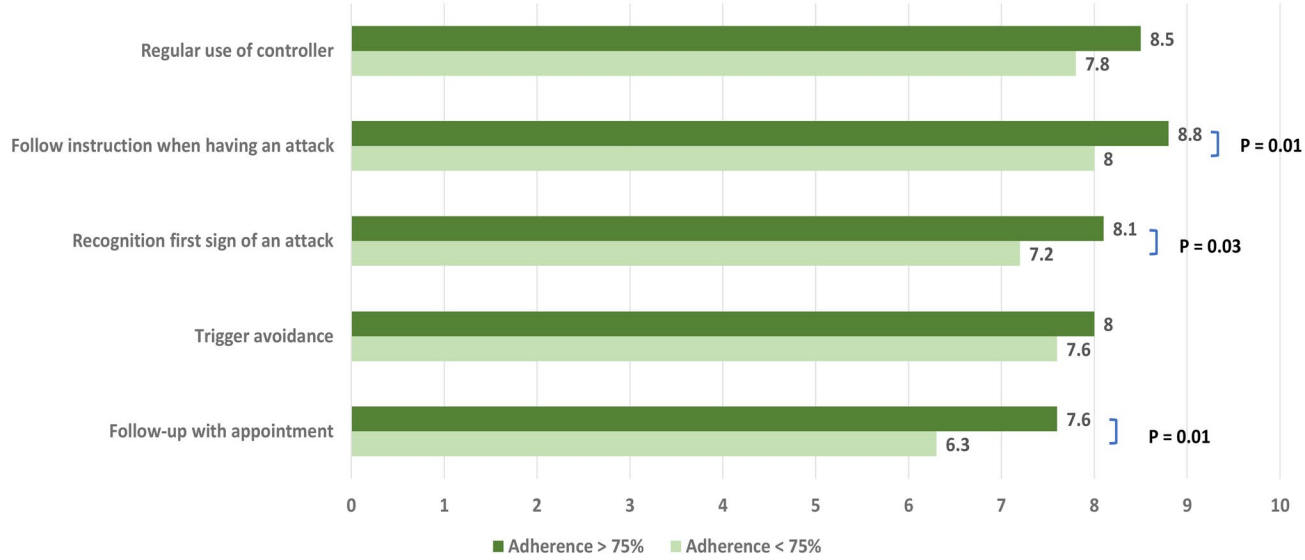

Figure 4. Asthma outcome expectation rating scale. Rating scale from 0 to 10, evaluating to what extent the patients felt their asthma symptoms were relieved by each treatment item. Scores are rated by patients with adherence ≥75% (dark green) and those with adherence <75% (light green). *p* values are based on chi-square analyses, and items with a *p* values <0.05 are considered to be significantly associated with adherence <75%.

Table 2. Univariate and multivariate analyses of factors independently associated with inhaled corticosteroid adherence <75%.

Variables	Adherence < 75% (*n* = 57)	Adherence ≥ 75% (*n* = 77)	Univariate analysis *p* value	Adjusted OR (95% CI)	*p* value
Patient outcome expectation total score (0–50)	37.1 ± 8.4	40.9 ± 8.4	0.01	1.05 (1.01–1.11)	*0.03*
Patient use of reliever before exercise	12 (21.1%)	6 (7.8%)	0.02	4.12 (1.27–13.36)	*0.047*
Mother as caregiver	50 (87.7%)	59 (76.7%)	0.04	4.1 (0.33–50.77)	0.85
Caregiver education – high school or higher	51 (89.5%)	58 (75.3%)	0.07	2.65 (0.68–10.26)	0.16
Family income higher than 20,000 THB/month	41 (73.2%)	42 (56.8%)	0.09	1.42 (0.28–7.12)	0.67

Data are presented as mean ± standard deviation or numbers and percentages.
Variables with a *p* values <0.1 from univariate analysis, were included in the multivariate analysis.
A *p* values <0.05 indicates statistical significance.
OR, odds ratio; CI, confidence interval; SD; THB, Thai baht.

high compared to the results of previous studies (i.e., 30% to 70%) (2). One possible explanation for this difference among studies is an overestimation of patient and/or parent self-report. A study that measured the mean adherence rate using four methods, including self- and/or parent-report, pharmacy records, electronic monitoring, and canister weight, reported the highest adherence rate from patient-/parent-report, followed by the three other methods (97.9%, 70, 51.5%, and 46.3%, respectively) (27). Accordingly, they suggested canister weight and electronic monitoring were more reliable measurement methods. Although self-report adherence appears to be less accurate, we attempted to improve the reliability of responses by using non-judgmental questions during the interview, such as "Many patients don't use their inhaler as prescribed. Within the last 4 weeks, how many days per week did you use your inhaler? Not at all, 1, 2, 3, or more than 3 days per week?" (1). In case of questionable adherence by report, the interviewer rechecked the history of medication refill to ensure that the patient's report was reliable. Another explanation for the high adherence rate is that we conducted this study in the setting of a specialist clinic in a university hospital where patients were systematically taken care of by an asthma care team.

Reasons behind suboptimal ICS adherence

Most adolescents (10–18 years) reported that they did not use an inhaled controller because they felt that their symptoms were already well controlled. In contrast, poor adherence among children resulted from forgetfulness or a hectic lifestyle, which they mostly defined as going to school early and coming home

Table 3. Paired samples *t* test analysis of the mean differences in inhaled corticosteroid adherence and asthma status between baseline and the 3–6 months follow-up.

Variables	Baseline	3- to 6-months follow-up	Paired *t* test, *p* value	(95% CI for mean difference)
ICS adherence, mean ± SD	75.9 ± 27.5	84.5 ± 24.2	t_{107} 2.5; ***0.02***	(1.5, 14.0)
Age 8–11 years	74.0 ± 30.9	83.6 ± 23.9	t_{61} 2.3; ***0.02***	(1.3, 17.9)
Age >11 years	80.4 ± 22.5	85.7 ± 24.9	t_{46} 1.1; 0.28	(–4.5, 15.2)
ACT score, mean ± SD	23.6 ± 2.2	24.3 ± 1.4	t_{46} 2.4; ***0.02***	(0.1, 1.2)
C-ACT score, mean ± SD	24.2 ± 2.7	25.4 ± 5.6	t_{61} 2.1; ***0.04***	(0.03, 1.5)
PEFR, L/min, mean ± SD	91.0 ± 14.2	90.8 ± 14.6	t_{107} 0.9; 0.40	(–3.0, 1.2)
Age 8–11 years	91.1 ± 13.8	89.3 ± 13.3	t_{61} –1.2; 0.25	(–4.9, 1.3)
Age > 11 years	92.4 ± 14.4	92.8 ± 16.2	t_{46} 0.3; 0.78	(–2.3, 3.0)

A *p* values <0.05 indicates statistical significance.
ICS, inhaled corticosteroid; SD, standard deviation; ACT, asthma control test; C-ACT, childhood asthma control test; PEFR, peak expiratory flow rate.

late, leading to difficulties in complying with the morning-evening regimen at home while with parents. This result is consistent with the findings of a recent review on problems that cause poor adherence and on how to improve adherence in school-aged children (5–12 years) and adolescents (12–17 years) (28). In children, spending time at school with a lack of ability to self-manage and self-monitor influenced lower controller compliance, which made this group more prone to exacerbation. In adolescents, becoming independent (autonomy) and developing a risk-taking behavior (experimenting) during the period when cognitive processing is shifting from concrete to abstract thinking could lead to untimely discontinuance of ICS (28,29).

Determining asthma outcome

In this study, we could not demonstrate a significant association between high adherence (≥75%) and good asthma control (ACT score >19). However, the average C-ACT score was significantly higher in the high adherence group than in the low adherence group ($p = 0.01$). This might be due to the small number of patients with not well-controlled asthma in our study as categorized by ACT score (5.2%) or GINA criteria (13.4% for partially controlled, and 3.7% for uncontrolled). These results are in stark contrast to studies where more than half of the recruited patients had uncontrolled asthma (26,30).

Knowledge on asthma and its treatment

The influence of patient asthma-related knowledge on ICS adherence was inconclusive because different methods were used to measure outcomes (4,5,31). In our study, specialist physician interviews using open-ended questions were employed to ensure patient comprehension of each question. From our data, patients were generally able to explain the symptoms and triggers of asthma, and they were able to distinguish their regular inhaler from the inhaler used for relief. Most patients were in good compliance with the inhaler and treatment regimens. In contrast, fewer patients understood the simple pathophysiology of the disease, and that asthma is not only a come-and-go disease. This suggests that physicians may have paid less attention to pathogenesis and asthma prognosis when educating patients about asthma, and this may have adversely affected medication adherence. To support this presumption, we closed this knowledge gap via education and correction of misunderstandings, and significant improvements in both adherence and ACT scores were observed at the 3- to 6-month follow-up visit compared to baseline.

Factors affecting ICS adherence

Our multivariate analysis revealed unfavorable patient outcome expectation scores and patient reports of using reliever before exercise as factors significantly associated with poor ICS adherence. Parental educational level, family income, and relationship of caregiver, all of which had a *p* values less than 0.01 from univariate analysis, did not show significant differences in multivariate analysis. Concerning outcome expectation, our findings are similar to those in a study on patients aged 11–17 years that found a lower youth asthma outcome expectation score to be a significant predictor of adherence problems (8). The results of our study are also similar to those in a study on adults that investigated modifiable socio-behavioral predictors of adherence. Favorable attitude (perception of the risks/benefits of ICS) was associated with greater adherence ($p = 0.01$), but lower educational achievement and lower household income were not (31). Other studies found poor socioeconomic status and educational achievement of caregivers to be associated with adolescent non-adherence (3,32,33), which was the opposite of what we found

in our study. It is likely that disease education and health literacy, rather than a high degree of educational achievement, facilitated more effective treatment in our population (34). Interestingly, we found that patients who reported using reliever before exercise or exertion and who rated higher expectation scores for following instruction when having an attack had a significantly lower rate of regular ICS controller use. This might suggest that some asthmatic patients tend to rely on reliever use when they are going to have an attack instead of using ICS regularly (35).

Depressive and anxiety symptoms are more prevalent among asthma patients (36,37). In the general population of Thai adolescents, the prevalence of depression and anxiety was 15–34% and 7–17%, respectively, depending on the assessment tools used (38–41). The prevalence of depressive symptoms in our study was within the range found in general adolescents; however, our population demonstrated a somewhat higher frequency of anxiety. This could be due to the mild and less troublesome severity of asthma in our patients. Similar to previous studies, we did not find an association between ICS adherence and either depression or anxiety (4,31). Further face-to-face interviews with psychologists to improve the accuracy of depressive and anxiety disorder diagnosis should be performed in future studies.

After providing proper asthma education, we reevaluated ICS adherence at the 3- to 6-month follow-up visits. We demonstrated a significant improvement in ICS adherence, C-ACT scores, and ACT scores. These results suggest that providing asthma knowledge in areas with poor or insufficient understanding may help facilitate better adherence and asthma control. As recommended in the EAACI guidelines, pediatric allergists should begin to transition allergy and asthma patients aged 11–13 years toward self-efficacy, and they should shift their focus of communication from the parent to the patient. Motivational interviewing and peer-led interventions improve asthma symptoms, asthma-related quality of life, and asthma knowledge, all of which reduce asthma-related doctor visits and school absence (42). However, further clinical trial studies using a standard patient asthma education protocol are needed to establish its clinical importance related to medication adherence and asthma outcomes.

This study had some limitations. First, the vast majority of patients enrolled in this study lived in Bangkok, which is a large urban metropolis. It is possible that an urban lifestyle could influence patient adherence differently than a rural lifestyle, and this could affect the generalizability of our findings to children and adolescents living in rural areas. As such, future studies are needed in a larger study population, and in a population in which urban dwellers and rural dwellers are both appropriately represented. Second, the ICS adherence evaluation using patient-reported data could affect the reliability of the results.

Conclusion

Self-reported ICS adherence among Thai children and adolescents was quite high, and patient knowledge of how and when to use ICS was also high. School-aged children spend most of their time at school; therefore, regular ICS scheduled early in the morning and in the late evening with the help of parents would be difficult. Thus, direct communication about asthma management with children rather than with the parent alone, and the implementation of a school-based asthma management program could help to improve adherence. Unlike children, adolescents deliberately did not use ICS because of the possible misconception that "controlled asthma" is a term that means the same as "outgrowing asthma." Concerning disease-related knowledge, patients knew the least about disease pathogenesis and asthma prognosis. Improved patient education that emphasizes this information may improve their adherence and disease control. Lastly, heightened physician awareness of depression and anxiety is encouraged since these conditions seem to be more prevalent among those with asthma than in the normal population.

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