Evaluation of asthma control by inhaled corticosteroids in general practice in Thailand

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Summary

Background: **Inhaled corticosteroid (ICS) is the main treatment of asthma but the clinical data of its efficacy is limited. This study aimed to evaluate the therapeutic efficacy of ICS alone or combined with controllers other than LABA for persistent asthma in Thailand.**

Methods: **This cross-sectional study involved 1,206 patients with persistent asthma and was conducted at 38 hospitals across Thailand between May and November, 2009. Patients were enrolled if they were >12 years old, had persistent asthma, receiving ICS with/without controllers other than long-acting beta2-agonists (LABA) for at least 3 months, and smoked <10 packs-year.**

Results: **Of 1,206 patients, 78.4% were females, age 49.4 ± 13.8 years old, 89.3% were non-smokers, the median duration of illness was 11 years, the median duration of ICS treatment was 20.4 months, and the mean dose of ICS was 738 ± 258 microgram per day. The top three medications prescribed in combination to ICS were short-acting beta2- agonist inhalers, theophylline, and short-acting beta2- agonist tablets. The mean Asthma Control Test (ACT) score was 19.2 ± 4.4. The percentage of successful asthma control (ACT ≥ 20) was 53.5% (95%CI: 50.7 to 56.3). The rate per patient per year of emergency room visits and all urgent health care visits were 0.98 and 1.28.**

Conclusions: **In clinical practice, patients using ICS alone or combined with theophylline or short-acting b2 agonists had a low percentage of asthma control and a high number of urgent care visits. ICS either alone or combined with theophylline or short-acting b2 agonists is not sufficient.** ***(Asian Pac J Allergy Immunol 2015;33:21-25)***

Keywords: *asthma, Asthma Control Test, controlled, inhaled corticosteroid, real clinical practice*

Abbreviations

ACT	=	Asthma Control Test
CI	=	confidence interval
ER	=	emergency room visit
GINA	=	Global Initiative for Asthma
ICS	=	Inhaled corticosteroids
LABA	=	Long-acting beta2-agonist
PEFR	=	Peak expiratory flow rate

Introduction

The Global Initiative for Asthma guidelines (GINA) recommends the use of inhaled corticosteroids (ICS) as a controller for patients with persistent asthma and short-acting beta 2-agonists (SABA) as a reliever.[1] For patients inadequately controlled by ICS the addition of long-acting beta 2 agonists (LABA) to ICS is recommended. Another option is to combine leukotriene modifiers with ICS. Alternatively the addition of sustained-release theophylline to ICS may be considered. In Thailand, LABA is not available as a monotherapy while ICS/LABA as a fix-combination is also not widely used due to its high costs.

In Thailand, the burden of asthma is high.[2-4] The current Thai asthma guideline recommends the use of ICS, but the ICS use is still low. In 2005, a nationwide questionnaire survey was conducted of 272 Thai physicians who were involved in routine asthma practice. Only 46.8% of them prescribed ICS for the management of mild persistent asthma.[5]

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Currently, there are no published data regarding asthma control in Thailand.

ICS is considered to be the most potent and effective anti-inflammatory medication currently available for the achievement and maintenance of control of persistent asthma.[6] Previous studies have shown that the efficacy of asthma control measures depends on several factors.[1,7-9] One important factor is that the efficacy of ICS on asthma control should be determined based on standardized, controlled settings.[1,10] At present, the efficacy of ICS treatment in asthma still needs to be addressed.

Because a variety of treatment options is available, it is difficult to assess the effect of ICS alone in real clinical practice under uncontrolled conditions. Once patients' asthma symptoms become uncontrolled with ICS alone, the patients will receive a combination treatment of ICS and other controllers such as LABA. In Thailand, LABA is not yet widely used because of its cost. This setting provided the opportunity to evaluate the efficacy of ICS in real clinical practice, either alone or in combination with controllers other than LABA.

Methods

This study was a hospital-based, cross-sectional, epidemiological, multi-center study. All general and community hospitals in every province across Thailand were contacted to obtain information regarding the average number of asthma patients seen per day and the availability of the ICS/LABA combination. Only hospitals with no ICS/LABA in the hospital medication list were invited to participate. Patients were enrolled if they were 12 years old or older, had persistent asthma, were receiving ICS without LABA for at least 3 months, and smoked less than 10 packs of cigarettes per year.

Participating physicians consecutively enrolled asthma patients who met the above inclusion criteria. Data collection was conducted between May and November 2009. The patients were interviewed by research associates who worked independently from the physicians. The Asthma Control Test (ACT) score was obtained and the peak expiratory flow rate (PEFR) was measured in all patients.

Patients were classified as controlled based on an ACT score of 20 or greater.[11] The PEFR was used as supplemental data for asthma control outcomes. A PEFR of more than 80% was defined as controlled asthma according to the GINA guideline.[1] The predicted PEFR for the Thai population was based on the formula suggested by Dejsomritrutai et. al.[12] The asthma control rate was also calculated based on an ACT score of 20 or more plus a PEFR more than 80% of the predicted value.

This study was conducted in full conformity with Good Clinical Practice (GCPs), including the International Conference on Harmonization (ICH) Guidelines, and in general, consistent with the most recent version of the Declaration of Helsinki. The study was approved by: Joint Research Ethics Committees (JREC). (JREC Reference No: 016/51 Date Approval: 1 October 2008)

Statistical Methods

The results from the asthma registry were used as the basis for the sample size calculation. A sample size of 1,210 was needed to detect a percentage of achieving control of asthma of 26.9% with a precision of plus or minus 2.5%.

The percentage of asthma control was calculated by the number of controlled patients divided by the total number of patients multiplied by one hundred. The 95% confidence intervals (95%CI) were estimated based on normal approximation of binomial distribution. For exploratory purposes, the proportion of hospitalization of patients with and without controlled asthma were compared using the chi-squared test. All analyses were performed using STATA version 10 (StataCorp, College Station, TX). A p-value of less than 0.05 was considered as statistically significant.

Results

Characteristics of patients and treatments at date started ICS

Thirty-eight hospitals participated in the study. A total of 1,220 asthma patients being treated with ICS were screened and 14 patients were excluded as per the inclusion/exclusion criteria. Of the 1,206 patients, 78.4% were female with an average age of 49.4 ± 13.8 years old; 89.3% were non-smokers, the median duration of asthma was 11.0 years, the median duration of ICS treatment was 20.4 months with a mean dose of 738 microgram per day (Table 1). The vast majority (86%) of the patients were given a short acting beta 2-agonist as metered-dose inhaler (MDI) in combination with ICS, while theophylline was combined with ICS in 51% of patients (Figure 1).

Table 1. Characteristics of the patients (n = 1,206)

Characteristics	N=1206
Age (years), mean (SD)	49.4 (13.8)
Sex, % female	78.4%
Smoking status, % smokers	10.7%
Age at onset of asthma symptom (years), mean (SD)	33.8 (17.3)
Duration of illness (years), median (min:max)	11.0 (0.2 : 78.1)
Duration under ICS treatment (months) , median (min:max)	20.4 (0.3 : 144.6)
Dose of ICS (microgram/day), mean (SD)	738 (258)

SD=standard deviation; min=minimum; max=maximum; ICS = inhaled corticosteroid

Asthma control assessments

The mean ACT score for the 1,206 patients was 19.2±4.4 (Table 2). Patients with an ACT ≥ 20 made up 53.5% (95%CI: 50.7 to 56.3) of the sample. Patients having an ACT ≥ 20 with a predicted PEFR ≥ 80% constituted 36.7% (95%CI: 33.5 – 39.8).

Urgent health care visits due to asthma in the 3 months before the survey date

Among a total of 1,206 patients, 67 patients (5.6%) had a recent history of hospital admission at least once. There were a total of 91 occasions of admission, 83 occasions in the medical ward and 8 occasions in the ICU. Thus, the admission rate was 0.30 per patient per year (95% CI: 0.24 – 0.37). There were 178 patients (19.3%) who visited an emergency room (ER) at least once with a total of 297 occasions (ER visit rate = 0.98 per patient per year; 95%CI: 0.88 – 1.10). Overall, there was a total of 387 urgent health care visits (ER or hospitalization). Thus, the rate of all urgent health care visits due to asthma was 1.28 per patient per year (95%CI: 1.16 – 1.42).

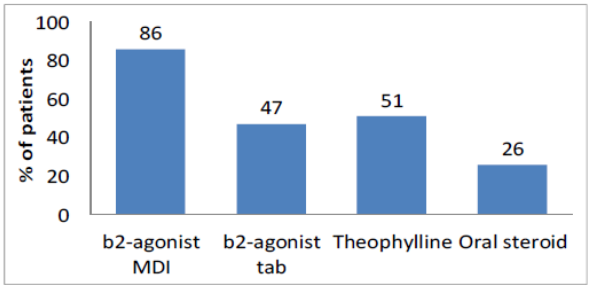

Figure 1. Numbers of patients according to medications prescribed in combination with inhaled corticosteroid.

Comparison of urgent health care visits between controlled and uncontrolled asthma patient groups based on ACT

Overall, the percentage of urgent health care visits was statistically higher in patients with uncontrolled asthma than those with controlled asthma. Patients having a history of urgent health care visits (either ER or hospitalization) at least once during the previous 3 months was 33.3% in the asthma uncontrolled group versus 8.7% in the asthma controlled group (95% CI: 20.19 to 29.12, $P < 0.001$) (Table 3). The asthma uncontrolled group had a significantly higher ER visit rate than the asthma controlled group (25.0% versus 5.9%, $P < 0.001$). Of note, the ER visit rate in the asthma controlled group was still high (5.9%).

Discussion

The present study demonstrates that the control of persistent asthma by ICS alone or in combination with controllers other than LABA is insufficient in real clinical practice. About 50% of the patients were controlled at the level of ACT ≥ 20 and about 30% of patients were maintained at the level of ACT≥20 with a PEFR ≥80 %predicted. Nonetheless, clinical burdens, such as hospitalizations or emergency room visits, remain high even in well-controlled patients. The mean ACT score in this study was 19.2±4. This was considered as the best scenario for the general asthma population in Thailand as only patients who had used ICS for at least 3 months were enrolled. The patients in this study appeared to receive adequate treatment since they received moderate doses of ICS and the mean duration of treatment was 20.4 months. Moreover, more than half of them received other controllers.

In clinical controlled trial, 65% of the patients achieved asthma control by using inhaled fluticasone.[13] Addition of LABA to ICS improved asthma control to 71%.[13] But in real life practice, our study showed much lower asthma control rates than in the clinical controlled study. This might be due to the difference in of the potency of different inhaled corticosteroids used, differentces in inhaler devices and most importantly might be due to compliance of the patients.[14] In a clinical controlled trial compliance is usually better than in real-life practice. However another study with the same methodology found that 86.5% (95% CI: 84.1-88.9%) of the patients achieved asthma control by using ICS/LABA.[15] This implies that ICS alone is not enough to control asthma.

Table 2. Asthma control status of patients according to ACT and PEFR

Measurements	Percentage
Mean ACT score (SD)	19.2 (4.4)
ACT ≥ 20	53.5
95% CI	50.7 to 56.3
PEFR ≥ 80%	54.8
ACT ≥ 20 and PEFR ≥ 80%	36.7
95%CI	33.5 to39.8

SD = standard deviation; ACT = Asthma Control Test; CI = confidence interval; PEFR = peak expiratory flow rate

In general asthma patients, in whom ICS is less utilized, it is more likely to have much lower ACT scores. Recent studies on the ACT assessment of asthma control in real clinical practice in patients treated with ICS have shown consistently low asthma control values. For example, asthma control in a survey in Sweden was 40.2%.[16] In Pakistan, the mean ACT was 17.71±4.41.[17] In a developed country such as the US, in a study in 2007 involving 134,401 households representative of the US population, the prevalence of controlled asthma was 59%.[18] This Thai study is the only one that has reported the percentage of asthma control among patients who use ICS and it consistently indicates suboptimal effectiveness in real world clinical practice.

In the present study, exacerbations of asthma requiring urgent health care visits were still high. Overall, the prevalence of urgent health care visits was statistically higher in the uncontrolled asthma patients group than those with controlled asthma. Even in the controlled patients group, the urgent health care visits were still high at 8.7%. These data suggested that using ICS alone is not sufficient.

The methods of this study overcame many limitations. Firstly, the sample selection of this study was conducted by well-trained research associates from a single research organization who worked independently from the attending physicians at the study hospitals. It was done consecutively, without any follow-up arrangements, and under uncontrolled conditions. Assessments of asthma control using the ACT scores were also done by this well-trained personnel group resulting in highly standardized outcomes. This design made the results less likely to introduce either selection or information biases. It also reflects real world clinical practice. Secondly, all 38 study hospitals were selected because they had no combination therapy with inhaled corticosteroids (ICS) and long-acting beta 2-agonists (LABA). Thus, this study should provide the percentage of asthma controlled by the ICS exclusively as a single therapy. This was done so that the results could allow conclusions about the sufficiency of ICS as a single therapy or the necessity of moving to the ICS/LABA combination therapy. Thirdly, about 90% of the sample were non-smokers. The remaining smoked less than 10 packs per year. This minimized chance of including COPD patients in the study.

This hospital-based study has some limitations; the estimated percentage of asthma control might be distorted due to selection bias, i.e. patients who suffer from asthma symptoms were more likely to visit the hospital than those who did not. It is believed, however, that this possibility is minimal in the present study for the following reasons. Asthma treatment in Thailand is provided to patients with minimal charges under the universal health insurance coverage scheme of the National Health Security Organization policy. The patients pay only 1 USD for each hospital visit under this health insurance policy. So, asthma patients visit hospitals on a regular basis, as required by the attending physicians, rather than when they suffer from asthma symptoms. This bias was also minimized by the hospital-based design. Receiving clinical data

Table 3. Percentage of hospitalization during the period of 3 months comparing the asthma controlled and uncontrolled groups.

Urgent health care visits	Uncontrolled Group (n = 561)	Controlled Group (n= 645)	Difference	95%CI	*P* -value
Admissions	8.7	2.8	5.94	3.28 to 8.60	< 0.001
Emergency room (ER) visits	25.0	5.9	19.06	15.05 to 23.08	< 0.001
urgent health care visits (ER or hospitalization)	33.3	8.7	24.65	20.19 to 29.12	< 0.001

including the histories of asthma symptoms and treatments from medical records provided more reliable data.

Another limitation of the study is that information regarding hospitalization and ICS use were obtained by interviewing the patients at the survey date. This required the patients to recall what happened during the period of 3 months prior to the survey date. Although recalling remarkable events such as hospitalizations can be reliable, recalling the number of the hospitalizations within a period of 3 months might be difficult for some patients.

In conclusions, in real clinical practice, about half of patients using ICS alone or combined with theophylline or short-acting b2 agonists had their asthma controlled. The clinical burdens such as the rate of hospitalizations or emergency room visits, however remains high even in patients with controlled asthma. This indicates that using ICS either alone or combined with theophylline or short-acting b2 agonists, is not sufficient.

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Conflict of interests

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