# Ketotifen versus Inhaled Budesonide for Controlling Childhood Asthma

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***Background:*** *International asthma guideline recommends inhaled corticosteroids therapy for children of all ages as the first controller. However, in some less developed parts of the world, ketotifen, an old inexpensive medicine with antihistaminic and anti-allergic reactions, has been found to be the most favored prophylactic agents.*
***Objective:*** *To compare the efficacy and safety of ketotifen and inhaled budesonide in asthmatic children aged 8 months to 14 years at Banpong Hospital, located 80km south from Bangkok.*
***Material and Method:*** *Children who had been admitted with acute asthmatic attack in 2008 at Banpong Hospital and had > 3 episodes of wheeze with good response to nebulized bronchodilators were randomized into two groups. Ketotifen group (n = 16) were given oral ketotifen 0.5 mg or 1 mg twice daily depending on age. Budesonide group (n = 14) were given as inhaled budesonide 200 μg (MDI) twice daily. Caregivers recorded children's asthmatic symptoms and nebulized treatments in diaries every day. The enrolled children received these two treatment regimens and were followed up for 26 weeks.*
***Results:*** *Number of ER visits decreased significantly after both treatments ($p < 0.005$). The percentage of children with reduction in ER visits was comparable between ketotifen and budesonide ($p = 0.16$). Ketotifen group also demonstrated a reduction in days of hospital stay ($p < 0.05$). Budesonide treatment resulted in more symptom-free days ($p < 0.05$). Both medications were well tolerated and safe. The only demonstrated side effect of ketotifen was weight gain. The growth rate in height for both groups did not differ.*
***Conclusion:*** *Both ketotifen and inhaled budesonide are effective, safe, and well-tolerated in the prevention of asthma exacerbation in children particularly in the country with limited resource.*

***Keywords:*** *Budesonide, Ketotifen, Asthma, Children, Randomized control trial*

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Asthma is one of the most common chronic diseases in children worldwide[1,2]. The prevalence of asthma in Thai university students was initially reported to be 2.4% in 1975[3] and increased to 8.8% in 2002[4]. With the administration of the International Study of Asthma and Allergies in Childhood (ISAAC) phase I questionnaire, the prevalence of asthma in Bangkok children aged 6-7 years and 13-14 years was found to be 11.7% and 13.6%, respectively[5]. Accordingly, at least 1.8 million Thai children are expected to suffer from this disease. The symptoms of breathlessness together with chest tightness prevent children from exercising or playing and often cause them to visit the emergency room (ER) at night or hospital admissions and increases school absence.

At Banpong Hospital, Ratchaburi Province, which is a government community hospital in a rural area, 80 km south from Bangkok, the rate of ER visits and admissions of all 483 asthmatic children, aged less than 14 years, in 2008, were 25.7% and 18.8% respectively. Frequent hospitalizations in the patients are probably due in part to rare continual use of long-term prophylactic medications. By retrospectively reviewing the hospital records, the average cost of hospitalization was 3,114 $\pm$ 2,798 (range 865-28,648) baht per one admitted case.

To decrease ER visits and admission rate, chronic airway inflammation causing bronchial

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hyperresponsiveness and deterioration of lung function should be treated appropriately[6]. Asthma guidelines such as the Global Initiatives for Asthma (GINA) has recommended inhaled corticosteroids (ICS) therapy for children of all ages as the first controller[6]. Despite various international asthma guidelines, Vichyanond et al reported that among 174 Thai pediatricians, who responded to their questionnaires, ICS therapy was chosen only by 9.6%, whereas ketotifen was the most favored prophylactic agents being chosen by 90.4%[7]. This is perhaps due to the incorrect belief that inhaled corticosteroids are associated with more side effects than ketotifen. Moreover, ketotifen is less expensive and easier to administer by mouth comparing with ICS, which requires a spacer and training effort to achieve correct inhalation technique. Commercial standard spacers for metered dose inhalers also are not readily available especially in the rural areas. In the old version of Thai National Guideline for Diagnosis and Management of Childhood Asthma, ketotifen was noted to be included among the list of recommended prophylactic agents[8]. In Malaysia, the neighboring country situated to the south of Thailand, ketotifen was found to be the most common prescribed oral preventer treatment among 109 general practitioners as well[9].

Ketotifen has antihistaminic and anti-allergic actions. It can inhibit not only the release of inflammatory mediators but also bronchospasm by reducing calcium uptake in mast cells and smooth muscle[10]. Evidence from randomized controlled trials indicates that ketotifen alone or in combination with other co-interventions improves control of asthma and wheezing in children with mild to moderate asthma[11]. Therefore, the present study was undertaken to scientifically assess the efficacy and safety of ketotifen comparing with inhaled budesonide for controlling childhood asthma.

## Material and Method

### *Patients*

All patients, aged less than 14 years, who were admitted with asthmatic attack at Banpong Hospital in 2008, were reviewed. Only patients with a lifetime history of three or more episodes of dyspnea and wheezing with good response to nebulized short acting beta-2 agonist were included in the present study. Patients who received ketotifen or any corticosteroids in the preceding 3 months and patients with other chronic illnesses were excluded. Baseline characteristics of each patient were recorded.

The present study was approved by Banpong Hospital Ethics Committee with approval coding number R 09/2552. Written informed consent was signed by parents of each patient and an assent form was agreed by patients 7 years old and above.

### *Study design*

The present study was conducted during February to September 2009. It consisted of a 1-week screening period, a 1-week to 2-week run-in period during which patients did not receive systemic or inhaled corticosteroids or ketotifen, followed by a 26-week treatment period.

Following completion of the run-in period, patients who fulfilled the criteria were randomly allocated to treatment with either ketotifen (TM Fen® syrup; T Man Pharma Ltd, Part, Bangkok, Thailand or Ketotifen® tablet; Government Pharmaceutical Organization, Bangkok, Thailand) or inhaled budesonide (Aeronide®; Aero Care Co, Ltd, Bangkok, Thailand). For ketotifen group, 0.5 mg twice daily was given to patients below 3 years of age and 1 mg twice daily for patients at the age of 3 and above. For the budesonide group, inhaled budesonide 200 μg twice daily was administered via non-valved face mask spacers (Thai Kid Cone Spacer®; Ramathibodi Hospital, Bangkok, Thailand) in patients below 5 years old and via non-valved mouth piece spacers (Aerohaler®; Aero Care Co, Ltd, Bangkok, Thailand) in patients at the age of 5 and above.

The parents were instructed to complete a diary every day, whether or not their child had asthmatic symptoms and received any nebulized bronchodilator at the hospital. During the 26-week treatment period, patients were asked to visit the clinic at 2-4 week interval for physical examination, assessing adverse events, checking the medications and diaries.

### *Efficacy and safety assessments*

For baseline data, the hospital records of enrolled patients were reviewed for number of ER visits and the number and days of hospital admissions during 26 weeks prior to receiving either ketotifen or inhaled budesonide.

Over the 26-week treatment period, six efficacy variable outcomes were evaluated. These included number of ER visits, days to first ER visit, number and days of hospital admissions, days of school absence, and symptom free days. The first four variables were obtained from the hospital and diary records. Days of school absence were asked from the parents at the

follow-up clinic. Symptom-free days were verified from the diary record. Symptom-free day was defined as a day without any of the following asthmatic symptoms including cough or difficult breathing either in daytime or nighttime, difficulty breathing during playing, or receiving nebulized rapid-acting bronchodilator at the hospital.

Data on adverse events were obtained from history taking and physical examination at clinic visits. Any discontinuation of treatment caused by adverse events was recorded. Weights and heights were measured. Each patient was evaluated for weight gain and sedation, which were the most common side effects of ketotifen[11] and for hoarseness and oral candidiasis, which were local side effects of inhaled budesonide[12,13].

### *Statistical analysis*

A sample size of 63 patients per treatment group was estimated to have 95% confidence ($\alpha = 0.05$) and 80% power of the test ($\beta = 0.20$). Categorical variables are expressed as percentages and compared between the two groups using the Chi-square test or Fisher's exact test where appropriate. Continuous variables are expressed as mean or median and range and compared between the two groups using the Student's t-test or Mann-Whitney U-test where appropriate. Wilcoxon signed-rank test was used to compare continuous variables of before and after treatments. All tests were two-tailed. Differences were considered to be statistically significant at $p < 0.05$. SPSS version 10 statistical software was used for statistical analysis.

## Results

### *Subjects*

Ninety-one patients, aged less than 14 years, were admitted with an asthmatic attack at Banpong Hospital in 2008. Thirty-three patients had at least three episodes of dyspnea and wheezing with good response to inhaled short acting beta-2 agonist. Of the 33 patients enrolled, no patients received either ketotifen or corticosteroids in the preceding three months. No patients had other serious chronic illnesses except asthma. Then they were randomly assigned to ketotifen (n = 18) or inhaled budesonide (n = 15) (Fig. 1). Two patients in the ketotifen group moved to other provinces and were lost to follow-up. One patient in the budesonide group was excluded because she refused to use a spacer. Thus, the final numbers of patients in ketotifen and budesonide groups were 16 and 14 respectively.

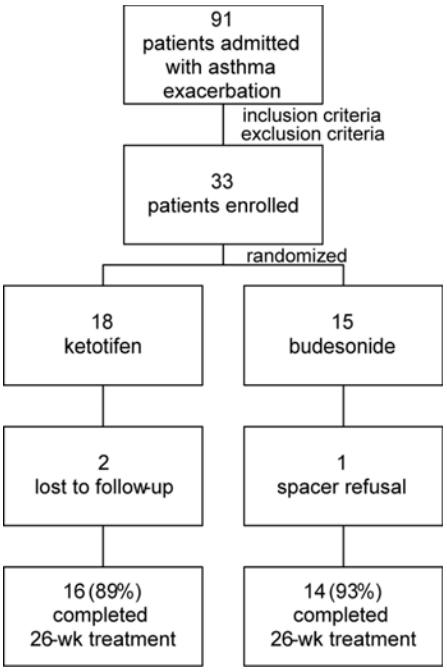


**Fig. 1** Study profile

As shown in Table 1 the baseline socio-demographic characteristics including age, sex, weight, height, education and occupation of parents, and family income were comparable in the two groups. The proportion of patients living with smokers at home was higher in the budesonide group. Climate change was the most common precipitating factor complained of by parents in both groups. There were no significant differences in the other environmental and precipitating factors between the two groups.

### *Efficacy and safety*

Table 2 shows three variables including number of ER visits, number and days of admissions in the duration of 26 weeks before and after treatment was initiated. Before treatment, number of ER visits in the ketotifen group was significantly higher than the budesonide group. Number of ER visits significantly decreased after treatment in both groups. Days of hospital stay significantly decreased only in the ketotifen group.

Table 3 shows the percentage of patients who had reduction in ER visits and hospitalization. The decrease of one or more times of ER visits and admissions of each patient was recorded. Such reductions were collected and calculated as percentage of patients for

**Table 1.** Baseline sociodemographic characteristics of patients getting ketotifen or budesonide, numbers in parentheses are percentages

| | Ketotifen group (n = 16) | Budesonide group (n = 14) | p-value |
|---|---|---|---|
| Age distribution, n (%) | | | 0.94 |
| < 5 years | 8 (50) | 7 (50) | |
| 6-10 years | 5 (31.2) | 5 (35.7) | |
| 11-14 years | 3 (18.8) | 2 (14.3) | |
| Age (years) mean ± SD | 6.2 ± 3.6 | 6.1 ± 3.3 | 0.92 |
| Male:Female | 9:7 | 8:6 | 0.96 |
| Weight (kg) mean ± SD | 20.0 ± 9.7 | 19.7 ± 8.8 | 0.71 |
| Height (cm) mean ± SD | 113.2 ± 25.3 | 112.0 ± 22.9 | 0.89 |
| Education-father, n (%) | | | 0.87 |
| Primary | 7 (43.7) | 6 (42.9) | |
| Secondary | 6 (37.5) | 6 (42.9) | |
| Others | 3 (18.8) | 2 (14.2) | |
| Education-mother, n (%) | | | 0.42 |
| Primary | 8 (50.0) | 5 (35.7) | |
| Secondary | 7 (43.8) | 5 (35.7) | |
| Others | 1 (6.2) | 4 (28.6) | |
| Occupation-father, n (%) | | | 0.79 |
| Employee | 10 (62.5) | 8 (57.2) | |
| Agriculture | 2 (12.5) | 3 (21.4) | |
| Others | 4 (25) | 3 (21.4) | |
| Occupation-mother, n (%) | | | 0.38 |
| Employee | 8 (50.0) | 4 (28.6) | |
| Agriculture | - | - | |
| Others | 8 (50.0) | 10 (71.4) | |
| Family income (baht/month), n (%) | | | 0.20 |
| < 5,000 | 3 (18.8) | 4 (28.6) | |
| 5,000-15,000 | 6 (37.5) | 8 (57.2) | |
| 15,000-25,000 | 5 (31.2) | 1 (7.1) | |
| > 25,000 | 2 (12.5) | 1 (7.1) | |
| Environment, n (%) | | | |
| Smokers at home | 7 (43.7) | 12 (85.7) | 0.02 |
| Nearby factory | 6 (37.5) | 7 (50.0) | 0.49 |
| Pets (dogs or cats) | 12 (75.0) | 12 (85.7) | 0.46 |
| Kapok mattress | 6 (37.5) | 7 (50.0) | 0.49 |
| Precipitating factors, n (%) | | | |
| Climate change | 13 (81.3) | 13 (92.9) | 0.35 |
| Exercise induced | 11 (68.8) | 6 (42.9) | 0.15 |
| Rhinitis | 9 (56.3) | 9 (64.3) | 0.65 |
| Smoke | 8 (50.0) | 3 (21.4) | 0.11 |
| Dust | 11 (68.8) | 5 (35.7) | 0.07 |
| Pets (dogs or cats) | 5 (31.2) | 5 (35.7) | 0.80 |

each group. The decrease of one or more days of hospital stay of each patient was collected and calculated as percentage as well. Although the ketotifen group had a higher percentage of patients with reduction in ER visits and hospitalization, there were no statistically significant differences between the two treatment groups.

Table 4 shows six efficacy outcomes obtained over the 26-week treatment period. There were significantly more symptom-free days in the budesonide group compared to the ketotifen group. However, there were no significant differences between the two groups for other five efficacy outcomes.

**Table 2.** Comparison of ER visits and hospital admissions in the duration of 26 weeks before and after patients receiving ketotifen and inhaled budesonide, presented as median (range)

| | Ketotifen group (n = 16) | | | Budesonide group (n = 14) | | |
|---|---|---|---|---|---|---|
| | Before | After | p-value | Before | After | p-value |
| Number of ER visits | 4* (1-8) | 1 (0-4) | 0.001 | 2* (0-8) | 0.5 (0-4) | 0.005 |
| Number of admissions | 0 (0-3) | 0 (0-1) | 0.10 | 0 (0-3) | 0 (0-2) | 0.56 |
| Days of hospital stay | 0 (0-13) | 0 (0-2) | 0.04 | 0 (0-11) | 0 (0-7) | 0.41 |

* Comparison of number of ER visits before treatment with ketotifen vs. budesonide was analyzed by Mann-Whitney U-test (p = 0.014)

**Table 3**. Number of patients who had reduction in ER visits, frequency of admission and days of hospital stay after receiving ketotifen or budesonide, presented as n (%).

| | Ketotifen group (n = 16) | Budesonide group (n = 14) | p-value |
|---|---|---|---|
| Patients with reduction in: | | | |
| Number of ER visits | 15 (93.8) | 10 (71.4) | 0.16 |
| Number of admissions | 5 (31.3) | 2 (14.3) | 0.40 |
| Days of hospital stay | 5 (31.3) | 2 (14.3) | 0.40 |

**Table 4.** Efficacy variable outcomes of ketotifen and budesonide groups during the 26-week treatment period, presented as median (range)

| | Ketotifen group (n = 16) | Budesonide group (n = 14) | p-value |
|---|---|---|---|
| Number of ER visits | 1 (0-4) | 0.5 (0-4) | 0.10 |
| Days to first ER visit | 94.5 (12-182) | 167 (10-182) | 0.16 |
| Number of admissions | 0 (0-1) | 0 (0-2) | 0.48 |
| Days of hospital stay | 0 (0-2) | 0 (0-8) | 0.23 |
| Days of school absence | 3 (0-9) | 0.5 (0-12) | 0.13 |
| Symptom-free days | 138 (12-175) | 160.5 (124-182) | 0.02 |

**Table 5.** Weight and height gain over the 26-week treatment period in patients getting ketotifen and budesonide, presented as mean $\pm$ SD

| | Ketotifen group (n = 16) | Budesonide group (n = 14) | p-value |
|---|---|---|---|
| Weight gain (kg) | 3.5 $\pm$ 1.5 | 2.2 $\pm$ 1.4 | 0.02 |
| Height gain (cm) | 4.8 $\pm$ 2.4 | 4.8 $\pm$ 2.1 | 0.94 |

Neither adverse events nor any early discontinuation of treatment related to its side effects were observed at clinic visits. No parents of patients in the ketotifen group reported sedative effect, drowsiness or other behavioral changes. The results of weight and height gain are shown in Table 5. Weight gain was significantly higher in the ketotifen group, whereas, height gain did not differ significantly between the two groups. There were no hoarseness and oral candidiasis noted in the budesonide group. Only one boy aged 2-years in the budesonide group complained of unpleasant smell of inhaled budesonide. Nevertheless,

he could complete the whole study with his mother's encouragement.

**Discussion**

The result of the present study in children with asthma shows that ketotifen and inhaled budesonide have comparable efficacy in reducing asthma exacerbation as indicated by the decrease in number of ER visits. In addition, only ketotifen treatment reduces days of hospital stay. Budesonide treatment on the other hand resulted in more symptom-free days. Both medications were well tolerated and were safe. The only minor side effect of ketotifen is weight gain most likely due to ketotifen's appetite-stimulating properties. It is also noted that inhaled budesonide at the dose of 400 μg per day given for 26 weeks did not affect growth rate in height as compared with ketotifen treatment.

The present study was conducted in a community hospital, which serves a local population of 160,000 in Banpong district. There is no any other government hospital nearby. More than half of the presented patients came from low-income families. When they had asthma exacerbation, they usually came to the ER at Banpong Hospital, where they could receive health care coverage subsidized by the government. Of 33 enrolled patients, only three (< 10%) could not complete the 26-week study. The high success rate may be due to the patients' homes located not far from the hospital. The farthest one took less than half an hour by motorcycle to the hospital. If the patient failed to follow-up, the first investigator could easily reach the patients by phone or even directly visited at their houses. More importantly, the authors were fortunate to receive good cooperation from the patients' families without any incentive requirement. Prior to the present study, ICS had rarely been prescribed, not only for the enrolled patients but also in routine clinical practice. Despite Thai National Guideline for management of childhood asthma published in 2000 strongly recommended prophylactic therapy[8], very few pediatricians followed this guideline[7]. At Banpong Hospital, the pediatricians considered that ICS was too difficult to administer especially in children. It required more time to teach young children and parents how to inhale properly. Commercial spacers were too expensive and not easily obtained. In spite of understanding the inhalation technique, children's compliance and the proper use of inhaler devices at home were still unpredictable. Furthermore, ketotifen had hardly ever been used as a long-term therapy. It was used only as needed when the patients had allergic symptoms. Previous epidemiological studies in Thailand found that lower respiratory tract infection with wheezing was found more frequently in the rainy season (July-October)[14] and the incidence of RSV infection peaked in July and August[15], which may result in frequent wheezing and hospitalizations. Therefore, the present study period was selected to cover the peak months of wheezing associated illnesses in order to avoid the seasonal bias on efficacy outcome variables.

Role of ketotifen in asthma has been described in pediatric literatures for more than three decades[16]. A Cochrane systematic review involving 26 randomized, double blind, controlled trials in 1,826 subjects aged 4 months to 18 years recently suggested that ketotifen alone or in combination with other co-interventions improves control of asthma and wheezing in children with mild and moderate asthma[11]. The efficacy of ketotifen alone is again confirmed by the results of the present study. In that review, ketotifen was given orally at a dose not less than one mg daily, which is the same dose as the present study. It should be noted that ketotifen made in Thailand was used because it was not expensive. The maximum cost of ketotifen either syrup or tablet at Banpong Hospital for all ages was only 60 baht (less than 2 US dollars) per month. This may be the main reason why Thai physicians still prefer ketotifen to other drugs in controlling asthma.

The beneficial effect of ketotifen to prevent asthma exacerbation was previously studied in two placebo-controlled trials[17,18], which reported very large and similar treatment effects. The overall relative risk is 0.31 (95% CI 0.19 to 0.59) indicating a highly significant beneficial effect of ketotifen in preventing exacerbations[11]. In the present study, it was found that ER visits due to asthma exacerbation were significantly decreased in 15 out of 16 patients after taking oral ketotifen for 26 weeks. Thus, the results are consistent with those two studies. In addition, the results also showed a significant decrease in hospitalization as indicated by the reductions in days of hospital stay.

Treatment guidelines state that ICS are the most effective controller therapy, and are therefore the recommended treatment for asthma for children for all ages[19]. The results of the present study support this recommendation. Patients in the budesonide group not only had the reduction in ER visits but also had more symptom-free days compared with ketotifen group. Budesonide was chosen to use in the present study because it is the only inhaled drug made in Thailand

that recently approved by the Thai FDA. The cost of inhaled budesonide 400 μg per day was only 66 baht (approximately 2 US. dollars) per month. If the patients did not have to pay for spacers, the cost of inhaled budesonide would be a little more expensive than the cost of oral ketotifen.

To the authors' knowledge, this is the first study to compare ER visits of asthmatic children between ketotifen and inhaled budesonide treatments. In the past, Hoshino et al compared the effects of ketotifen 2 mg per day and inhaled beclomethasone dipropionate (BDP) 400 μg per day on bronchial mucosa and asthma symptoms in 32 asthmatic adults. They found that ketotifen and BDP exerted anti-inflammatory activity in the bronchial mucosa but BDP demonstrated better clinical responses than ketotifen[20]. In terms of therapeutic efficacy, inhaled BDP and budesonide were found to have equal potency in the treatment of asthma[21]. The present study demonstrated a better clinical outcome of inhaled budesonide as shown by greater symptom-free days compared with ketotifen. However, a significant decrease in admission rate was not found in those receiving inhaled budesonide. One reason could be that drug deposition in the respiratory tract after inhalation from a metered-dose inhaler (MDI) via a spacer in children was less than that observed in adults[22]. Additionally non-valved plastic spacers made in Thailand were used, from which the drug deposition has never been investigated. Nevertheless, the findings partly support the clinical efficacy of these spacers when using with inhaled budesonide in order to reduce asthma exacerbation in children.

The finding that the growth rate in height of patients treated with inhaled budesonide 400 μg per day for 26 weeks did not differ significantly with those treated with ketotifen strengthens the safety of inhaled budesonide on growth of asthmatic children. In the ketotifen group, it is not surprising to see significantly more weight gain. Several placebo-controlled trials reported the same findings with various magnitudes[23,24]. No patients in both groups withdrew from the present study due to side effects suggests that both drugs were well tolerated.

The present study has certain limitations. One limitation is the severity of asthma in patients is unknown. To overcome this limitation, the number of ER visits in the duration of 26 weeks before patients entering the present study was compared. It was found that patients in the ketotifen group had significantly more frequent ER visits, suggesting more severe asthma in the ketotifen group than the budesonide group. Then the proportion of patients with reduction in ER visits after treatments was compared and found that both groups did not differ from each other for reduction in ER visits. Another limitation is the sample size was too small to demonstrate more differences in clinical outcomes between the two treatment regimens.

The authors conclude that ketotifen and inhaled budesonide made in Thailand are useful and inexpensive in management of asthma in children. Both of them are effective and well tolerated in the prevention of asthma exacerbation in children aged less than 14 years. These findings should reassure pediatricians in less developed countries that ketotifen and inhaled budesonide, which is commonly recommended by all international guidelines, are beneficial controller therapy for childhood asthma.

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## ยากิน ketotifen เปรียบเทียบกับยาสูด budesonide ในการควบคุมโรคหืดหลอดลมในเด็ก

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**ภูมิหลัง**: International asthma guideline แนะนำการใช้ยาสูดคอร์ติโคสเตียรอยด์เป็นยาตัวแรก ในการควบคุมโรคหืดหลอดลมในเด็กทุกช่วงอายุ อย่างไรก็ตาม สำหรับประเทศกำลังพัฒนา ketotifen ซึ่งเป็นยาเก่าแก่ ราคาไม่แพง มีฤทธิ์ต้านฮิสตามีนและต้านปฏิกิริยาภูมิแพ้ยังถูกใช้มากที่สุดในการป้องกันโรคหืดหลอดลม

**วัตถุประสงค์**: เพื่อเปรียบเทียบประสิทธิผลและความปลอดภัยของยากิน ketotifen และยาสูด budesonide ในผู้ป่วยเด็กโรคหืดหลอดลม อายุ 8 เดือน ถึง 14 ปี ในโรงพยาบาลบ้านโป่งที่อยู่ห่างจากกรุงเทพมหานครไปทางใต้ 80 กิโลเมตร

**วัสดุและวิธีการ**:ทำการศึกษาไปข้างหน้าในปี พ.ศ. 2552 คัดเลือกผู้ป่วยเด็กโรคหืดหลอดลมที่นอนในโรงพยาบาลเนื่องจากโรคหืดหลอดลมกำเริบในปี พ.ศ. 2551 มีประวัติ หอบ 3 ครั้ง ขึ้นไป และตอบสนองดีต่อยาขยายหลอดลมชนิดพ่นฝอยละออง สุ่มผู้ป่วยเป็น 2 กลุ่ม กลุ่มที่รับยากิน ketotifen 16 คน และกลุ่มที่รับยาสูด budesonide 14 คน ผู้ดูแลเด็กจดอาการหอบหืด และการไปพ่นยาที่โรงพยาบาลในสมุดบันทึกทุกวัน นัดตรวจติดตามอาการนาน 26 สัปดาห์

**ผลการศึกษา**: พบว่าผู้ป่วยทั้ง 2 กลุ่ม ต่างมีจำนวนครั้งที่มาห้องฉุกเฉินลดลง ($p < 0.005$) โดยทั้ง 2 กลุ่ม มีจำนวนผู้ป่วยที่มีจำนวนครั้งที่มาห้องฉุกเฉินลดลงไม่แตกต่างกัน ($p = 0.16$) กลุ่ม ketotifen มีจำนวนวันนอนโรงพยาบาลน้อยกว่า ($p < 0.05$) กลุ่ม budesonide มี symptom-free days มากกว่า ($p < 0.05$) ผู้ป่วยสามารถใช้ยาทั้งสองชนิดได้ดีและมีความปลอดภัย ผลข้างเคียงที่พบมีเพียงน้ำหนักที่เพิ่มขึ้นตลอดช่วงเวลาที่ทำการศึกษา ในกลุ่ม ketotifen มากกว่ากลุ่ม budesonide อย่างมีนัยสำคัญทางสถิติ ในขณะที่ส่วนสูงที่เพิ่มขึ้นของผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกัน

**สรุป**: ทั้งยากิน ketotifen และยาสูด budesonide มีประสิทธิผลดี ปลอดภัย และใช้ได้ดีในการป้องกันการกำเริบของโรคหืดหลอดลมในเด็กโดยเฉพาะอย่างยิ่งในประเทศกำลังพัฒนาที่มีทรัพยากรอันจำกัด