

ORIGINAL ARTICLE

Differences in the Prescription Patterns of Anti-asthmatic Medications for Children by Pediatricians, Family Physicians and Physicians of Other Specialties

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Background: Prescription patterns of anti-asthma medications in children vary among doctors in different disciplines and settings, and may reflect differences in treatment outcome. The purpose of this study was to analyze the prescribing patterns of anti-asthma drugs by pediatricians, family physicians and other practitioners.

Methods: Data for a total of 225,537 anti-asthma prescriptions were collected from the National Health Insurance Research Database for the period from January 1, 2002 to March 31, 2002. These medications included inhaled and oral adrenergics, inhaled and oral corticosteroids, xanthine derivatives, and leukotriene receptor antagonists prescribed by general pediatricians, family physicians and physicians in other disciplines.

Results: Oral β_2 -agonist was the most commonly prescribed drug used as monotherapy, with prescription rates of 70.4%, 46.9% and 58.0% by pediatricians, family physicians and other physicians, respectively. A xanthine derivative was the next most commonly prescribed monotherapy. Oral corticosteroid combined with oral β_2 -agonist, followed by oral β_2 -agonist combined with a xanthine derivative were the two most commonly prescribed dual-agent combined therapies by all three physician categories. The prescription rate for inhaled corticosteroid monotherapy was 7.8% by pediatricians, 5.6% by family physicians, and 8.0% by other physicians. The prescription rate for inhaled adrenergic was the highest in family physicians (14.9%), followed by the other physicians (7.2%), and was lowest in pediatricians (3.1%).

Conclusion: Pediatricians and family physicians appeared to share similar opinions on the medical management of children with asthma in that both most commonly prescribed oral β_2 -agonists and xanthine derivatives, either alone or in combination. Family physicians were least likely to prescribe an inhaled corticosteroid and most likely to prescribe an inhaled adrenergic agent. [*J Formos Med Assoc* 2006;105(4): 277-283]

Key Words: asthma, family medicine, insurance claims, pediatrics, prescription

Asthma has become more common in both children and adults around the world in recent decades.¹ The rate of asthma has increased as communities adopt Western lifestyles and become urbanized.² Similar changes in lifestyle and increasing rates of asthma have occurred in Taiwan, where the prevalence of asthma increased from 5.1% to 9.4% between 1985 and 1997.^{3,4} In 1989,

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a learning program for physicians named the Global Initiative for Asthma (GINA) program was begun in an effort to raise awareness among health care workers and the general public about the increasing rates of asthma and the need for standardized asthma care.⁵ According to GINA guidelines, several drugs are recommended either alone or in combination to treat asthma, including β 2-agonists (oral or inhaled form), corticosteroids (oral or inhaled form), xanthine derivatives, and leukotriene receptor antagonists.

It is often assumed that much of the leadership for defining optimal medical care for asthma emerges from the knowledge, attitudes, beliefs, and actual practice patterns of medical care specialists. Due to cultural differences, an inefficient and poorly functioning referral system, and comparatively convenient access to health care provided by the National Health Insurance system in Taiwan, asthma care in children is provided by a wider array of medical practitioners than is common in the West, including general pediatricians, family physicians and other physicians, such as those specializing in internal medicine. The differences in the quality of care and care preferences for asthmatic children provided by pediatricians, family physicians and other practitioners remain unclear. This study analyzed the prescribing patterns of anti-asthma drugs by pediatricians, family physicians and other practitioners using data obtained from the National Health Insurance Research Database.

Methods

Data source

The National Health Insurance Research Database served as the data source for this study. The information in each computerized claim form included patients' personal identification number (ID), age, gender, prescription dates, medical care institutions, drugs prescribed (the drug therapeutic code can be used to identify the drug dispensed), and the diagnosis relevant for the prescription and medical expense claims. Both per-

sonal and medical care institutions' IDs in the database were scrambled in compliance with the Personal Electronic Data Protection Law.

Data collection

Data were collected on all prescriptions for all patients younger than 16 years old during the period from January 1, 2002 to March 31, 2002. Prescribed drugs were classified according to the Anatomical Therapeutic Chemical (ATC) classification system to facilitate international comparison. Medications were grouped into the following six categories: inhaled adrenergics (i.e. α - and β -adrenoreceptor agonists, selective β 2-adrenoreceptor agonists), oral β 2-agonists, inhaled corticosteroids, xanthine derivatives, oral corticosteroids, and leukotriene receptor antagonists.

Patient subgroups

Asthmatic patients were selected based on a diagnosis (International Classification of Diseases [ICD], Ninth Revision, Clinical Modification ICD-9-CM code 493.xx) of asthma as a principal or secondary condition made at an outpatient visit. A maximum of three outpatient diagnoses could be listed.

Three subgroups of patients within the 0–16-year-old group were studied. The first subgroup consisted of patients who had visited pediatricians who were restricted to pediatric practice by the National Health Insurance system. The second group consisted of those who had visited family physicians who were restricted to family medicine practice by the National Health Insurance system. The last group of patients had visited other health care providers who were neither pediatricians nor family physicians, including other specialists, such as internal medicine specialists, or ear, nose and throat specialists.

Statistical analysis

All analyses were performed using SAS version 8.2 for Windows (SAS Institute Inc, Cary, NC, USA). We used standard methods for analyzing contingency tables. For 2×2 tables, p values were based on the continuity-adjusted Pearson chi-

square test. All p values of less than 0.05 indicated statistical significance.

Results

A total of 225,537 prescriptions were written during the 3-month study period. Pediatricians wrote the highest number of prescriptions among the three categories of health care providers. They were also least likely to prescribe a single medication only compared with family physicians and other care providers, and were most likely to prescribe more than two medications (Table 1).

The frequency distribution of single medication use by pediatricians, family physicians and other care providers is shown in Table 2. Oral β 2-agonist was the most frequently prescribed monotherapy by pediatricians (70.4%), followed by xanthine derivatives (16.9%), inhaled corticosteroids (7.8%), and inhaled adrenergics (3.1%). Family physicians most frequently prescribed oral β 2-agonist (46.9%), followed by xanthine derivatives (30.1%). The percentage of prescriptions for inhaled adrenergics by family physicians was higher than that by pediatricians (14.9% vs. 3.1%; $p < 0.05$), while the percentage of inhaled

corticosteroids prescribed by family physicians was lower (7.8% vs. 5.6%; $p < 0.05$). Among all other care providers, oral β 2-agonist (58.0%) and xanthine derivatives (23.6%) were the two most frequently prescribed drugs, followed by inhaled adrenergics (7.2%) and inhaled corticosteroids (8.0%). The percentage of outpatient visits with leukotriene receptor antagonist prescription was $< 2.5\%$ in all care provider groups.

The frequency distribution of combining two medications in prescriptions by pediatricians, family physicians and other physicians is shown in Table 3. Oral β 2-agonists combined with a xanthine derivative was the most common combination therapy prescribed by pediatricians, family physicians and other physicians. The second most commonly prescribed combination by all three groups was oral corticosteroid combined with oral β 2-agonist. Oral corticosteroid combined with a xanthine derivative was the third most commonly prescribed two-drug combination by family physicians (14.6%), while inhaled corticosteroid combined with an oral β 2-agonist (7.0%) was the third most common prescription among pediatricians, and an inhaled adrenergic agent combined with an oral β 2-agonist was the third most common (9.2%) among the other physicians.

Table 1. Anti-asthma medications prescribed by various types of physicians

Number of prescribed medications	Pediatricians	Family physicians	Other physicians
One medication, n (%)	64,211 (34.6)	3405 (45.8)	14,653 (45.2)
Two medications, n (%)	74,026 (39.9)	3260 (43.8)	11,145 (34.4)
> Two medications, n (%)	47,472 (25.6)	771 (10.4)	6594 (20.4)
Total prescriptions, n	185,709	7436	32,392

Table 2. Frequency distribution of medications prescribed as monotherapy

	Pediatricians	Family physicians	Other physicians
Inhaled adrenergic agent, %	3.1	14.9	7.2
Inhaled corticosteroid, %	7.8	5.6	8.0
Oral β 2-agonist, %	70.4	46.9	58.0
Xanthine derivative, %	16.9	30.1	23.6
Oral corticosteroid, %	0	0.8	1.2
Leukotriene receptor agonist, %	1.8	1.7	2.0
Total prescriptions, n	64,211	3405	14,653

Table 3. Frequency distribution of prescriptions of combined therapies using two medications

	Pediatricians		Family physicians		Other physicians	
	OBA+XAN	40.6%	OBA+XAN	48.4%	OBA+XAN	34.5%
	OCS+OBA	36.4%	OCS+OBA	28.0%	OCS+OBA	29.3%
	ICS+OBA	7.0%	OCS+XAN	14.6%	IBA+OBA	9.2%
	IBA+OBA	5.9%	IBA+XAN	1.7%	OCS+XAN	7.5%
	OCS+XAN	3.3%	IBA+ICS	1.6%	ICS+OBA	4.8%
	Other	6.8%	Other	5.7%	Other	14.7%
Total prescriptions, <i>n</i>		74,026		3260		11,145

IBA = inhaled adrenergic agent; ICS = inhaled corticosteroid; OBA = oral β 2-agonist; OCS = oral corticosteroid; XAN = xanthine derivative; Other = remaining possible two-drug combinations.

The frequency distribution of prescriptions combining three or more medications by pediatricians, family physicians and other physicians are shown in Table 4. Combination of an oral corticosteroid, oral β 2-agonist and a xanthine derivative was the most common combination of three or more drugs prescribed by all three physician groups. The second most common combination of three or more drugs varied among the three types of physicians, with inhaled adrenergic agent plus oral corticosteroid plus oral β 2-agonist plus a xanthine derivative most commonly prescribed by pediatricians (13.5%), and inhaled adrenergic agent plus oral corticosteroid plus oral β 2-agonist most commonly prescribed by family physicians (8.8%) and other care providers (21.8%). Family physicians who used a combination of three or more drugs showed a marked preference for the combination of oral corticosteroid plus oral β 2-agonist plus a xanthine derivative.

Discussion

This study found that oral β 2-agonist was the most commonly prescribed monotherapy by pediatricians, family physicians and other types of physicians treating children with asthma in Taiwan. Previous studies in other countries found similar results. Grant et al reported that oral β 2-agonists were the most commonly prescribed type of medication, with 80.8% of primary care physicians reporting that they were most likely to prescribe them in patients < 5 years old with moderate persistent asthma.⁶ A retrospective analysis of 28,000 asthmatic patients treated in five managed care settings by Buchner et al found that the use of bronchodilators without inhaled anti-inflammatory therapy was the dominant pattern of pharmacologic therapy.⁷ As in this study, they also found that oral β 2-agonist was the most commonly prescribed therapy in all regimens. Oral forms of therapy are easier for patients to use and do not

Table 4. Frequency distribution of prescriptions of combined therapies using three or more medications

	Pediatricians		Family physicians		Other physicians	
	OCS+OBA+XAN	33.3%	OCS+OBA+XAN	54.7%	OCS+OBA+XAN	23.0%
	IBA+OCS+OBA+XAN	13.5%	IBA+OCS+OBA	8.8%	IBA+OCS+OBA	21.8%
	ICS+OCS+OBA	12.2%	IBA+OCS+OBA+XAN	6.7%	IBA+OCS+OBA+XAN	11.5%
	IBA+OCS+OBA	12.1%	IBA+OBA+XAN	5.6%	IBA+OBA+XAN	8.7%
	IBA+OBA+XAN	8.8%	ICS+OBA+XAN	5.6%	IBA+ICS+OCS+OBA	6.2%
	Other	20.3%	Other	18.6%	Other	28.8%
Total prescriptions, <i>n</i>		47,472		771		6594

IBA = inhaled adrenergic agent; ICS = inhaled corticosteroid; OBA = oral β 2-agonist; OCS = oral corticosteroid; XAN = xanthine derivative; Other = remaining possible three-drug combinations.

require physicians to spend additional time as would be required to demonstrate how to use inhaled preparations. This convenience may be one of the factors responsible for the high rate of prescription of oral β 2-agonists.

According to GINA guidelines, xanthine derivatives serve as an adjunctive therapy that can be added to regimens of patients whose asthma is not completely controlled by inhaled β -agonist and inhaled corticosteroids. This study found that xanthine derivatives were widely used in the treatment of bronchial asthma, being prescribed in 22.7% of patients. In a population-based longitudinal analysis conducted between 1984 and 1993, Goodman et al measured trends in all pediatric uses of medications for asthma.⁸ Oral theophylline use declined 10-fold to only 0.25% of prescriptions in the pediatric population during the study period. The relative efficacy of theophylline therapy has been established for several decades.⁹⁻¹¹ However, because of its narrow therapeutic range, the dosage must be individualized in order to optimize the treatment based on the measurement of serum theophylline concentration. If theophylline therapy is to be used safely, clinicians must be quite familiar with numerous factors that alter clearance of this drug, and they must be prepared to use an appropriate dosage and monitor serum concentrations.¹²

In this study, the prescription rates for leukotriene receptor antagonists were very low. Because the marketing of leukotriene receptor antagonists in Taiwan only began in the winter of 2001, i.e. just before the beginning of the study period, these low rates may be partly attributable to lack of awareness of this new treatment option by many physicians.

Among the two-drug combination therapies, an oral β 2-agonist combined with a xanthine derivative, and oral corticosteroid combined with an oral β 2-agonist were the most frequently prescribed by all three categories of physicians. These results are in agreement with a study by Eggleston et al.¹³ Their data, obtained by parental questionnaire, revealed that adrenergic agonists were prescribed in 221 of 396 (56%) asthmatic children,

either as monotherapy (34%) or in combination with theophylline (22%). Lozano et al found that the most common asthma medication regimens used by children with asthma in the USA were oral β 2-agonist (15.4%), β 2-agonist plus theophylline (10.4%), theophylline (6.1%) and β 2-agonist plus corticosteroid (2.7%).¹⁴ Thus, oral β 2-agonist, theophylline and oral corticosteroid are the most commonly prescribed drugs in both Taiwan and abroad, although the percentage of prescriptions involving each of these agents was higher in this study than in the previous studies.

The use of oral corticosteroid monotherapy was very low in this study. Oral corticosteroid, however, was commonly included in combined therapy with two or more drugs. The use of oral corticosteroid combined with an oral β 2-agonist was the second most common dual-drug therapy, ranging from 28.0% to 36.4% among the different groups of physicians treating asthmatic children. Oral corticosteroid was included in all of the three most commonly prescribed combination regimens involving three or more agents by all three physician groups. Thus, oral corticosteroid plays an especially large role in combination therapies for asthma in children. According to GINA guidelines, oral corticosteroid should be prescribed for severe persistent symptoms or as a burst in patients with acute asthma attack. Whether the use of oral corticosteroid in this study's patients represents excessive treatment on a regular basis that is outside of the recommended guidelines remains to be clarified. Our data may suggest the need for more extensive trials of inhaled anti-inflammatory therapy prior to the introduction of oral corticosteroid.

Based, in part, on evidence that intervention will prevent or reduce airway damage and result in beneficial long-term effects on asthma morbidity, GINA guidelines emphasize the use of inhaled anti-inflammatory agents, particularly corticosteroid. In this study, family physicians demonstrated the lowest prescription rate of inhaled corticosteroid (5.6%). This rate is lower than in studies from other countries. Halterman et al studied a total of 1025 American children with physician-

diagnosed asthma, and found that only 26% of those with moderate to severe asthma had taken a maintenance medication.¹⁵ In Germany, Beimfohr et al found that 16.3% of asthmatic children had used inhaled corticosteroid.¹⁶ In Great Britain, Warner found that 39% of asthmatic children were prescribed inhaled corticosteroid.¹⁷ In Taiwan, many parents are concerned about the side effects of inhaled corticosteroids that are to be used as controller medications for at least 3 months. Such concerns may affect a physician's intention to prescribe inhaled corticosteroid. In addition, the quality of the interaction between physicians, parents and children affects treatment efficiency. Another study found that significantly fewer children aged 3–5 years old received any controller medication compared to older children ($p < 0.001$).¹⁸ Further analysis of data for the different age groups in this study revealed that family physicians were less likely to prescribe inhaled corticosteroid than pediatricians (2.3% vs. 4.8%) in children younger than 5 years.

In this study, family physicians had the highest prescription rate for inhaled adrenergics (14.9%). In patients younger than 5 years old, the percentage of outpatient prescriptions of inhaled adrenergic was higher than expected at 7.6%. A previous population-based study in Taiwan found that inhaled adrenergics were prescribed in 10.7% of children.¹⁹ As a symptom reliever, an inhaled adrenergic is the most effective of the bronchodilators, especially in terms of its β -agonist effect.²⁰ Because of their quick onset and short duration of action, inhaled β -agonists are apt to be improperly used and may be a risk factor for asthma death.^{21,22} GINA guidelines and the findings of some previous studies^{23,24} remind us that frequent preventive treatment with β -adrenergic agents is still an indication for concomitant therapy with anti-inflammatory drugs.

Recent studies indicated that the addition of β -agonist to the regimen of symptomatic patients with a low to moderate dosage of inhaled steroid improved lung function and increased the number of symptom-free days and nights.^{25,26} It was also

recommended that inhaled corticosteroid plus long-acting inhaled β_2 -agonist be prescribed for patients with persistent asthma during the moderate to severe stages of the disease. This study found that combined treatment using both inhaled corticosteroid and β -adrenergic agents was prescribed at $< 1\%$ of outpatient visits in all three physician groups. This may be due to the lack of familiarity with newer treatment concepts or underestimation of asthma severity in pediatric patients.

Several limitations of this study should be noted. This study was a retrospective analysis of claims data as opposed to prospective referral data. Assessment of illness severity was not possible because of the exclusive use of computerized prescription drug data on dispensed medications and physicians' diagnosis ICD codes. Thus, patients could not be classified into the four severity groups to evaluate whether the prescribing patterns followed GINA guidelines. In addition, the findings reflect how asthma care was provided at only one outpatient visit for each patient. How prescription patterns change over the course of illness in patients remains unclear. Determination of the extent of the pediatric asthma care burden assumed by pediatricians and family physicians in Taiwan also remains unclear and would require longitudinal follow-up study.

In conclusion, this study found that oral β_2 -agonist and xanthine derivatives were the most commonly dispensed asthma monotherapies in pediatric asthma in Taiwan, regardless of the type of practitioner seen at the clinic. Oral corticosteroid combined with oral β_2 -agonist, and oral β_2 -agonist combined with a xanthine derivative were the two most common dual-drug therapies. The prescription patterns of pediatricians and family physicians generally suggested that they shared similar opinions on the medical management of children with asthma, except for the use of anti-inflammatory controller drugs, for which the prescription rate of inhaled corticosteroid was higher among pediatricians than among family physicians (7.8% vs. 5.6%). With regard to a symptom reliever, however, the prescription rate of inhaled

adrenergics by pediatricians was far lower than by family physicians (3.1% vs. 14.9%).

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