

◎原 著

## Costs of drugs used for the treatment of asthma in relation to disease severity

Yoshiro Tanizaki, Fumihiro Mitsunobu, Yasuhiro Hosaki,  
Kozo Ashida, Masanori Hamada<sup>1)</sup>, Naofumi Iwagaki,  
Makoto Fujii, Shingo Takata

Division of Medicine, <sup>1)</sup>Division of Rehabilitation, Misasa Medical Center,  
Okayama University Medical and Dental School

**Abstract :** Costs of drugs used for the treatment for 1 year were examined in 32 patients with asthma in relation to disease severity. Asthma severity was classified as : 1) intermittent ; 2) mild persistent ; 3) moderate persistent ; 4) severe persistent. 1. The total cost of drugs used for each patient for 1 year was the highest (¥263,710) in patients of stage 4 (severe persistent) and the lowest (¥74,670) in those of stage 1 (intermittent). The costs of bronchodilators and antiallergics were predominant at all stages, and their cost increased significantly with increasing severity. 2. The costs of drugs such as antiallergics and bronchodilators were predominant, and the costs of drugs such as inhaled corticosteroids and mucolytics were considerably high in patients of all stages. 3. The costs of bronchodilators, inhaled corticosteroids, and antiallergics were the largest in patients of stage 4. The results suggested that the costs of drugs used for the asthma treatment tended to increase as the disease severity became stronger from stage 1 to stage 4, and the main drugs related to the increase in total costs were bronchodilators, antiallergics, and inhaled corticosteroids.

**Key words :** asthma, disease severity, costs, bronchodilators, corticosteroids, antiallergics

### Introduction

Asthma is one of the most popular respiratory diseases. In the onset mechanisms of asthma, IgE-mediated allergy plays an important role, in which an increase in the generation of leukotriene C4 (LTC4) related to bronchospasm<sup>1-3)</sup>, and

leukotriene B4 (LTB4) related to bronchial hyperresponsiveness<sup>4-6)</sup>, is observed. The leukocytes of the asthmatics generated significantly more LTB4 and LTC4 than those of controls. The leukocytes of patients with atopic asthma generated significantly more LTC4 than those of patients with nonatopic asthma. In addition, it has been reported that there is a significant

correlation between LTB<sub>4</sub> generation by leukocytes and the degree of bronchial hyperresponsiveness to methacholine<sup>6)</sup>. However, the pathogenesis of asthma becomes somewhat complex with aging. Our previous studies have shown that bronchial hyperresponsiveness decreases significantly as age at onset increases in patients without a family history, suggesting that the hyperresponsiveness shows a tendency to decrease with aging<sup>7)</sup>.

The process of development of drugs for the treatment of asthma has shown that asthma symptoms could be improved more easily with newly developed drugs such as inhaled corticosteroids and bronchodilators. However, the costs of drugs newly developed are considerably high, and the number of patients with asthma has been increasing in recent years. Because of high cost of newly developed drugs and an increase in number of patients with asthma, it has been suggested that the costs of medication for the treatment of asthma has been increasing.

In recent years, several pharmacoeconomic studies in asthma have been conducted in the USA<sup>8-10)</sup> and Europe<sup>11-14)</sup>. In the present study, the costs of drugs used for the treatment of asthma was studied in relation to disease severity.

### Subjects and Methods

The subjects of this study were 32 patients (18 females and 14 males) with asthma. Their mean age was 66.2 years (range 48-76 years). All patients were treated with antiasthmatic drugs such as bronchodilators, corticosteroids, antiallergics, mucolytics, antibiotics, and others (physiological saline, drugs for common cold, etc) at Misasa Medical Center for 1 year. The costs of drugs used for the treatment of asthma per patient for 1 year (from January to December in 2000) were calculated. The total costs of

all drugs and the cost of each drug were expressed throughout in ¥.

Asthma severity was evaluated according to international guidelines<sup>15)</sup>. Assessments of severity were classified as : 1) intermittent ; 2) mild persistent ; 3) moderate persistent ; 4) severe persistent. The costs of drugs used per patient for 1 year were compared among four stages.

Statistically significant differences of the mean were estimated using unpaired Student's t test. A p value of <0.05 was regarded as significant.

### Results

The total costs of drugs used for patients of stage 1 and 2 were significantly lower than in those of stage 3 and stage 4. The costs of drugs such as bronchodilators, corticosteroids, antiallergics, mucolytics, antibiotics, and others tended to increase as stage of asthma went up, as shown in Table 1. Of all drugs used for

Table 1. Costs of drugs used for treatment per patient for 1 year in relation to asthma severity

Drugs	Asthma stage			
	1	2	3	4
Bronchodilators	20,200	29,170	56,170	55,140
Corticosteroids	9,950	15,280	27,070	34,930
Antiallergics	30,570	56,440	111,170	130,210
Mucolytics	12,700	15,820	18,630	19,460
Antibiotics	820	3,420	9,480	20,780
Others	440	1,670	1,640	3,190
Total	74,670 <sup>ab</sup>	121,780 <sup>cd</sup>	224,160 <sup>ac</sup>	263,710 <sup>bd</sup>

Data are presented as mean ¥. a,b and d: p<0.001, c:p<0.01.

asthma treatment, the costs of antiallergics and bronchodilators were markedly large, and the costs of corticosteroids and mucolytics were considerably high in patients of all stages (Table 2).

Table 2. Total costs of each drug used for the treatment per patient for 1 year in all stages

Drugs	Costs ( ¥)	%
Bronchodilators	38,946	23.2
Corticosteroids	20,712	12.4
Antiallergics	81,708	48.8
Mucolytics	17,251	10.3
Antibiotics	7,094	4.2
Others	1,765	1.1
Total	167,476	100.0

The proportion of the cost of bronchodilators in total drugs in each asthma stage was the largest in patient with stage 1 and the lowest in those of stage 4 (Fig. 1 a). However, the proportion of the cost of bronchodilators used in

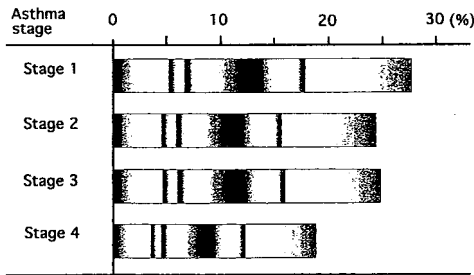


Fig.1a. The proportion of the cost of bronchodilators against total drugs in each asthma stage

patient of all stages was the largest in those of stage 4 (Fig. 1 b). The proportion of the cost

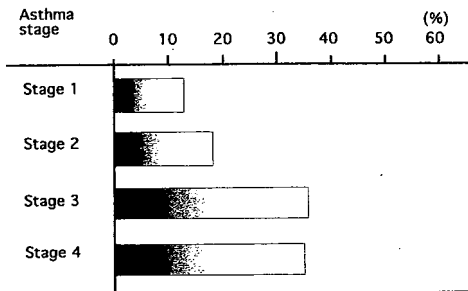


Fig.1b. The proportion of the cost of bronchodilators used in patients of all stages

of corticosteroids in total drugs in each asthma stage was not different among patients of four stages (Fig. 2 a). In contrast, the proportion of the cost of corticosteroids used in patients of all

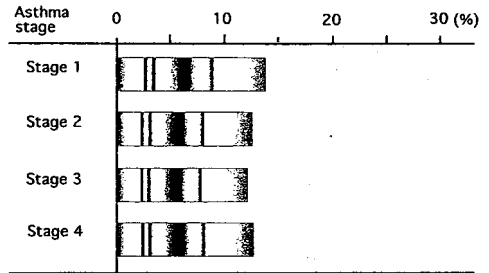


Fig.2a. The proportion of the cost of corticosteroids against total drugs in each asthma type

stages was the largest in those of stage 4, and the lowest in those of stage 1 (Fig. 2 b). The

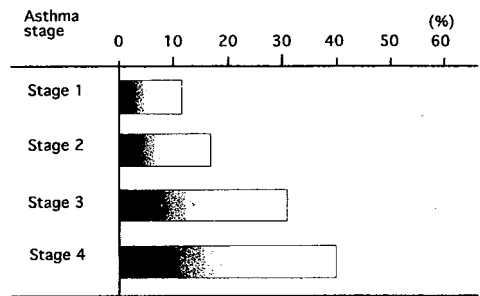


Fig.2b. The proportion of the cost of corticosteroids used in patients of all stages

proportion of the cost of antiallergic agents in total drugs in each asthma stage tended to increase as the asthma stage went up from 1 to 4 (Fig. 3 a). The proportion of the cost of antiallergics used in patients of all stages was

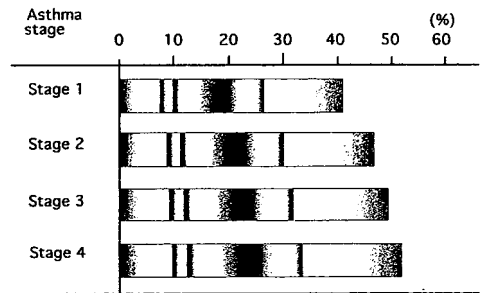


Fig.3a. The proportion of the cost of antiallergics against total drugs in each asthma type

the largest in those of stage 4, and showed a tendency to decrease as the asthma stages went down (Fig. 3 b).

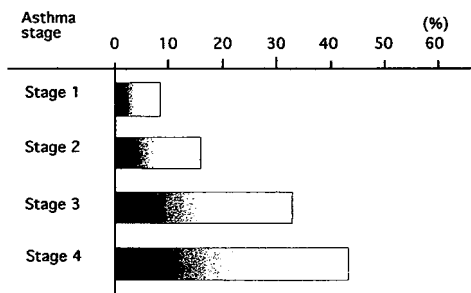


Fig.3b. The proportion of the cost of antiallergics used in patients of all stages

The proportion of the cost of mucolytics in total drugs in each asthma stage was the largest in patients of stage 1 and the lowest in those of stage 4 (Fig. 4). In contrast, the proportion of

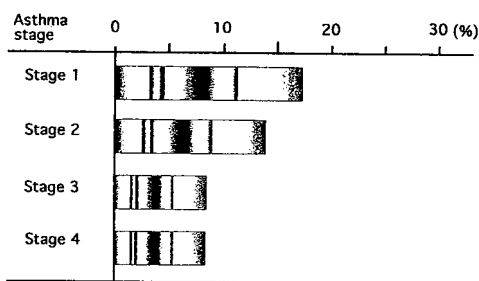


Fig.4. The proportion of the cost of mucolytics against total drugs in each asthma type

the cost of antibiotics in total drugs in each asthma stage was the largest in patient of stage 1, and the proportion tended to increase as the asthma stage went up from 1 to 4 (Fig. 5).

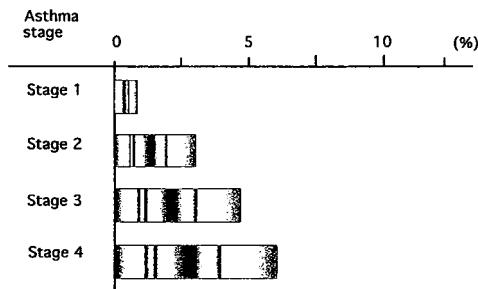


Fig.5. The proportion of the cost of antibiotics against total drugs in each asthma type

## Discussion

Many antiasthmatic drugs such as inhaled sympathomimetics, inhaled corticosteroids and leukotriene C4 receptor antagonists have been developed in recent years. However, the costs of these newly developed drugs are in general considerably high. Particularly, the use of prescribed inhaled sympathomimetics and corticosteroids has been increase with severity of illness<sup>8,9)</sup>. In addition, the number of patients with asthma, particularly, of elderly asthmatics, has been increasing in recent years in Japan. It has been also reported that pharmacotherapy for asthma is underused or inadequate. In particular, treatment with inhaled corticosteroids is insufficient. In contrast, short-term sympathomimetics are excessively prescribed. Only one-third of asthma patients were treated according to asthma guidelines.

A relationship between total costs for asthma treatment and disease severity has been discussed in recent years. The most empirical data, for 1995-1996, clearly showed an increased costs depending upon illness severity<sup>16)</sup>, and other reports have also shown an enormous increase as total costs as asthma severity increases<sup>6-12,15,17)</sup>.

In this study, the costs of drugs used for the treatment of asthma were examined in 32 patients with asthma. The results obtained here demonstrated that the total costs of drugs for asthma increased as disease severity increased from stage 1 to stage 4. Regarding the proportion of the costs of each drug against total drugs in each asthma stage, the proportion of costs of antiallergics and antibiotics increased. In contrast, the proportion of costs of bronchodilators and mucolytics decreased, and the proportion of the costs of corticosteroids did not change, as asthma severity increased from

stage 1 to stage 4. This suggests that the proportion of the costs of antiallergics and antibodies against total drugs was the largest, and the proportion of bronchodilators and mucolytics against total drugs was smallest in patients of stage 4 (severe persistent). The proportion of the costs of each drug used in patients of all stages tended to increase as asthma stage went up from stage 1 to 4. The results reveal that the costs of bronchodilators, corticosteroids, and antiallergics increased as asthma severity became stronger.

### References

1. Underwood DC, Osborn RR, Newsholme SJ, Torphy TJ, Hay DWP : Persistent airway eosinophilia after leukotriene (LT) D<sub>4</sub> administration in the guinea pig. Modulation by the LTB<sub>4</sub> receptor antagonist, Franklast, or an interleukine-5 monoclonal antibody. *Am J Respir Crit Care Med* 154 : 850–857, 1996.
2. Silberstein DS, David JR : The regulation of human eosinophil function by cytokines. *Immunology Today* 166 : 129–144, 1987.
3. Mitsunobu F, Mifune T, Hosaki Y, et al. : Enhanced production of leukotrienes by peripheral leukocytes and specific IgE antibodies in patients with chronic obstructive pulmonary disease. *J Allergy Clin Immunol* 107 : 492–498, 2001.
4. Palmer RM, Stepney RJ, Higgs GA, Eakins KE : Chemokinetic activities of arachidonic and lipoxygenase products on leukocytes of different species. *Prostaglandins* 20 : 411–418, 1980.
5. Fujimura M, Xiu Q, Tsujiura M, et al. : Role of leukotriene B<sub>4</sub> in bronchial hyperresponsiveness induced by interleukin-8. *Eur Respir J* 11 : 306–311, 1998.
6. Mitsunobu F, Mifune T, Hosaki Y, et al. : Enhanced peripheral leukocyte leukotriene production and bronchial hyperresponsiveness in asthmatics. *Eur Respir J* 16 : 504–508, 2000.
7. Mitsunobu F, Mifune T, Hosaki Y, et al. : IgE-mediated and age-related bronchial hyperresponsiveness in patients with asthma. Relationship to family history of the disease. *Age and aging* 29 : 215–220, 2000.
8. Weiss KB, Gergen PJ, Hodgson JA : An economic evaluation of asthma in the United State. *N Engl J Med* 326 : 862–866, 1992.
9. Weiss KB, Sullivan SD, Lyttle CS : Trends in the cost of illness for asthma in the United State, 1985-1994. *J Allergy Clin Immunol* 106 : 493–499, 2000.
10. Smith DH, Malone DC, Lawson KA, Okamoto LT, Battista C, Sanders WB : A national estimate of the economic costs of asthma. *Am J Respir Crit Care Med* 156 : 787–793, 1997.
11. Serra-Batlles J, Plaza V, Movejon E, Comella A, Bruges J : Costs of asthma according to the degree of severity. *Eur Respir J* 12 : 1322–1326, 1998.
12. Godard P, Chanez P, Siraudin L, Nicoloyannis N, Duru G : Costs of asthma are correlated with severity ; a 1-yr prospective study. *Eur Respir J* 19 : 61–67, 2002.
13. Barnes DJ, Jonsson B, Klim JB : The costs of asthma. *Eur Respir J* 4 : 636–642, 1996.
14. Schramm B, Ehlken B, Smala A, Quednau K, Berger K, Nowak D : Cost of illness of atopic asthma and seasonal rhinitis in Germany. : 1-yr retrospective study. *Eur Respir J* 21 : 116–122, 2003.
15. National Institutes of Health. Expert Panel 2 : Guidelines for diagnosis and management of asthma. NIH publication number 97–4051. Bethesda : NIH/National Heart, lung and Blood Institute 1997.

16. Schhulenburg JM, Greiner W, Moolitor S, Kielhorn A: Costs of asthma therapy according to level of severity. *Med Clin* 91: 670-676, 1996.

17. Szucs TD, Anderhub H, Rutishauer M: The economic burden of asthma: direct and indirect costs in Switzerland. *Eur Respir J* 13: 281-286, 1999.

#### 気管支喘息に対する年間薬剤費の重症度別検討

谷崎勝朗, 光延文裕, 保崎泰弘, 芦田耕三, 濱田全紀<sup>1)</sup>, 岩垣尚史, 藤井 誠, 高田真吾

岡山大学医学部・歯学部附属病院三朝医療センター内科, <sup>1)</sup>リハビリテーション科

気管支喘息32例を対象に, 治療のために要した年間薬剤費を, 国際ガイドラインの重症度分類(stage 1-4)により検討した。1. 年間の総薬剤費はstage 4の症例で最も高く(平均¥284,370),

一方, stage 1(平均¥74,670)で最も低い値を示した。2. 個々の薬剤費の検討では, 抗アレルギー薬, 気管支拡張薬などの薬剤費が高く, 次で副腎皮質ホルモン(主として吸入薬), 去痰薬の順であった。3. 気管支拡張薬, 副腎皮質ホルモン, 抗アレルギー薬などの薬剤費は, いずれもstage 4で最も高い値を示した。

気管支喘息に対する薬剤費は, 疾患が重症になるにつれて高くなる傾向を示した。また, その主たる薬剤は気管支拡張薬, 抗アレルギー薬, 吸入用副腎皮質ホルモンなどであった。