

Questionnaire-based Analysis of the Current Status of Adult Bronchial Asthma in Niigata Prefecture — Comparison with the Asthma Guidelines —

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Summary. Objective: Although inhaled steroids are strongly recommended in several guidelines for the management of bronchial asthma, the actual clinical situation requires clarification. This study presents the current status of adult bronchial asthma by questionnaire-based analysis, and suggests an improved method of assessment for asthma management compared with the guideline strategy.

Methodology: Questionnaires were completed by asthmatic patients and their physicians in participating institutions within Niigata Prefecture from September to October 1998. The 3,347 responses were then analyzed.

Results: The rate of peak-flow meter per user was only 30.8%. Attacks that were more than moderate were found in less than 10% of subjects, while asthma related symptoms -- including coughing -- were found in more than 50% of subjects. Emergent events were often existed (unconsciousness attacks; 6.8%, respirator management; 5.9%, aspirin induced attacks; 8.6%, respectively). Although inhaled steroid use reached 62.0%, sustained-release theophylline was used by 76.9% of subjects.

Conclusion: Despite satisfactory results in asthma attack control, there is still room for improvement of the peak-flow meter and inhaled steroid use, as well as for alleviating asthma-related symptoms and preventing death related risk factors. Sustained-release theophylline was positioned as a fundamental medication and requires reevaluation as a long-term controller the same as inhaled steroids.

Key words—questionnaire, guidelines for the management of bronchial asthma, sustained-release theophylline, bronchial asthma.

INTRODUCTION

Bronchial asthma was long characterized by an excess of airway hypersensitivity and reversible contraction of the respiratory tract¹⁾. In recent years, however, the advances that have occurred in the pathophysiological understanding of bronchial asthma have identified the essential aspect of this disease to be inflammation of the bronchi caused by infiltration of a number of different inflammatory cells, including lymphocytes and eosinophils²⁾. Consequently, air flow is limited, asthmatic symptoms are exhibited, hypersensitivity in the bronchial tract is exacerbated and, in addition, chronic airway inflammation brings about an irreversible air-flow limitation (remodeling)³⁾. This new understanding of asthma pathogenesis has changed the management and treatment of bronchial asthma. Some countries, including Japan, are now preparing guidelines for managing bronchial asthma^{4,5)}. These guidelines are designed to focus on the suppression of airway inflammation, with widespread recommendation of anti-inflammatory therapy with inhaled steroids.

Nonetheless, because bronchial asthma is a common disease and one of those respiratory disorders

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Abbreviations—RPs, respiratory physicians; GPs, general physicians in internal medicine; %PEF values, percentage peak-flow values.

most commonly seen in the general clinical scene, the authors believed it important to understand the current status of bronchial asthma in actual clinical situations through an investigation that compared the status with the guidelines. There are still many unknown factors: for instance, how the treatment of asthma uses bronchodilators that have conventionally had a central role in asthma therapy, and how inhaled steroids are to be recommended in the guidelines. Moreover, the actual situation of peak-flow meter use and asthmatic attacks remains unclear. This study attempts to identify the actual state of bronchial asthma in line with the latest understanding of asthma management. To achieve this, a questionnaire-based investigation was conducted among patients with bronchial asthma and their physicians in cooperation with a number of medical institutions in Niigata Prefecture, Japan. The current guidelines show that the goal of asthma therapy includes the prevention of asthmatic symptoms, maintenance of normal pulmonary function and normal activity levels, prevention of asthma exacerbation and the provision of optimal pharmacotherapy without adverse effects. This study proposes a better assessment for asthma management than the guidelines.

MATERIALS AND METHODS

Though a questionnaire, patients with adult bronchial asthma who visited the participating institutions were asked their age, duration and onset age of asthma, as well as the usage status of a peak-flow meter. This was carried out over two months from September to October 1998. At the same time, their physicians answered a questionnaire investigating the severity of asthma and the details of treatment. The investigation involved 156 institutions around Niigata Prefecture, and information was collected on 3,347 cases.

To investigate the situation surrounding an asthmatic attack, the times and degrees of asthmatic attacks over the two weeks prior to answering the questionnaire were classified based on the information collected in accordance with the adult bronchial asthma severity assessment committee standards of the Japanese Society of Allergology. In brief, a patient with a severe degree of attacks (impossible to move due to dyspnea) or frequent (attacks occurring more than 5 days per week) middle degree attacks (impossible to lie down due to dyspnea) was classified as severe. The middle class indicates middle degree attacks fewer than 4 days per week, with mild attacks (including the ability to lie down with

dyspnea) on more than 3 days per week or wheezing on its own happening more than 5 days per week.

The questionnaires also inquired about asthma related episodes including ambulance use, emergency room visits, hospitalization, anti-inflammatory-agent induced asthma attacks (aspirin induced asthma), unconsciousness asthma attacks and management using a respirator. The subjects were asked to answer "yes" or "no" to the following five questions; 1) Have you ever had a respirator due to an asthma attack; 2) Have you ever been unconscious due to an asthma attack; 3) Have you ever been hospitalized due to asthma; 4) Have you ever been taken by ambulance or visited an emergency room due to an attack; and 5) Have you ever had an attack induced by anti-inflammatory drugs including painkillers, antipyretics, or cold medicine?.

The general profile of cases with asthma was understood as mentioned above. After obtaining and analyzing these results, a comparison was made with the goals in asthma treatment in the guidelines that were published in the USA and Japan for managing and controlling bronchial asthma.

RESULTS

Patient background

The age, age at onset, and duration of the subjects' bronchial asthma were 54.3 ± 17.6 (mean \pm standard deviation), 39.4 ± 25.1 , and 17.6 ± 23.3 years respectively (Fig. 1). There were 1,670 males and 1,673 females, with 4 cases not giving their sex. The physicians in charge graded the severity. The rate of mild cases as a percentage of all cases was 46.1%, moderate cases 38.8%, and severe cases 9.5% (with 5.6% unanswered). Physicians in charge were generally divided into respiratory physicians (RPs) and general physicians in internal medicine (GPs). In cases treated by RPs ($n=2,909$), the grade of severity was mild for 45.6%, moderate for 38.5%, and severe for 10.3%, while the corresponding rates were 49.3%, 40.9%, and 4.1% respectively in cases treated by GPs ($n=438$) (Fig. 2). A significantly higher number of severe cases were found in the former group ($p < 0.0001$). Since a peak-flow meter is strongly recommended in the guidelines for controlling asthma, it was used in 1,032 cases, accounting for only 30.8% (Fig. 3). It was never used in 58.7% of cases, and no answer was given in 10.4% of cases. The rate of peak-flow meter use was 34.1% among RPs, while it was only 9.4% among GPs. Hence the rate of use among GPs was significantly lower than that among RPs ($p < 0.0001$).

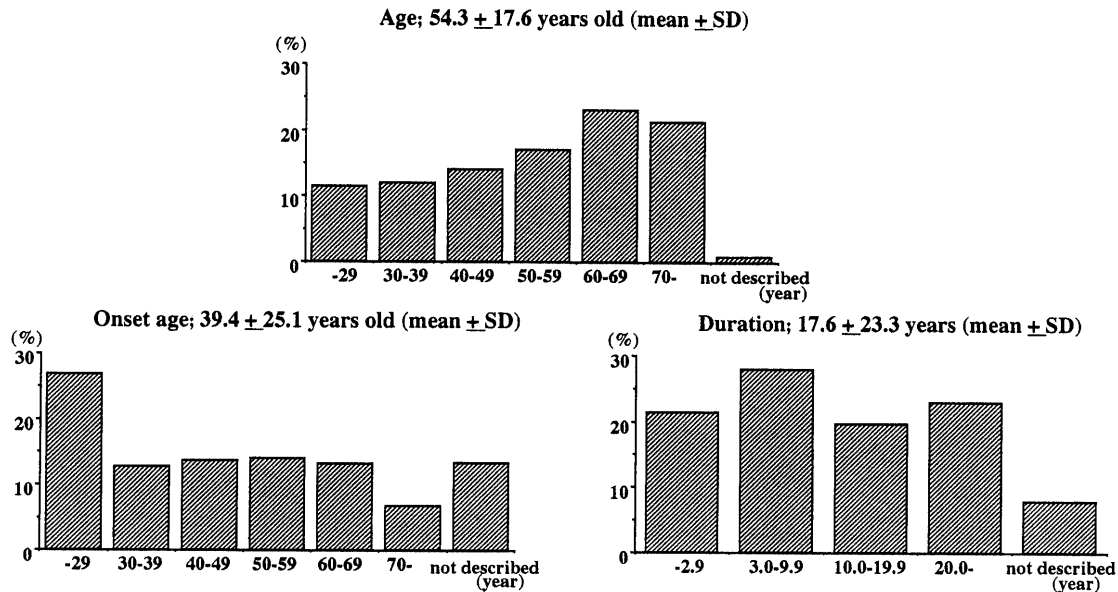


Fig. 1. Age, onset age and duration of the study patients. These were expressed at the time of the questionnaires' performance.

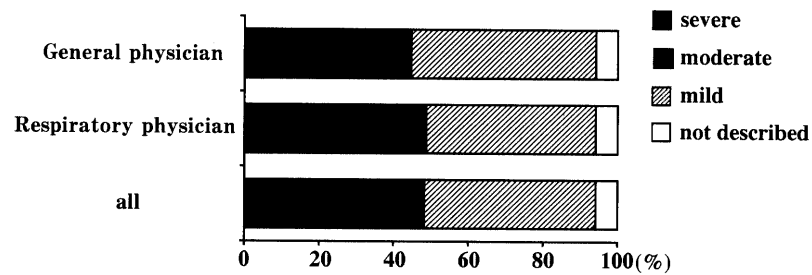


Fig. 2. Severity of patients with asthma. A significant difference in severe patients is seen between two groups, general physicians and pulmonary physicians ($p < 0.0001$).

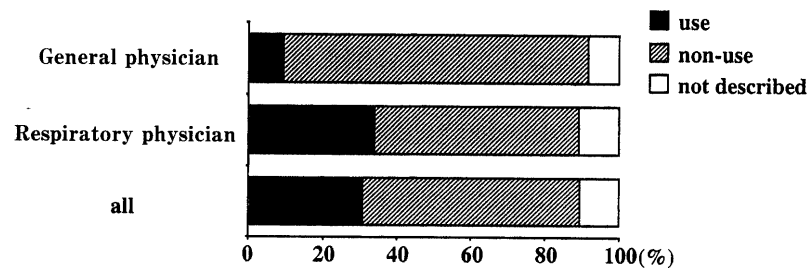


Fig. 3. Rate of peak-flow meter use in asthmatic patients. A significant difference in severe patients was seen between two groups, general physicians and pulmonary physicians ($p < 0.0001$).

Asthma attacks during the 2 weeks prior to answering the questionnaire

The percentage of cases without an attack was 62.6%, and the percentage of mild class was 28.1%, for a total of 90.7%. The percentage of cases with moderate class and severe class were 8.2% and 1.0% (Fig. 4).

In 1,032 cases using a peak-flow meter, the percent-

age peak-flow value was evaluated compared with the predicted values (%PEF values); $76.4 \pm 20.5\%$ ($n=794$) in the morning and $79.7\% \pm 20.1\%$ ($n=777$) at night on average. Fig. 5 showed the distribution of each user's %PEF value, indicating that the %PEF values of less than 80% were observed in about half of the cases: 56.0% in the morning, and 49.2% at night.

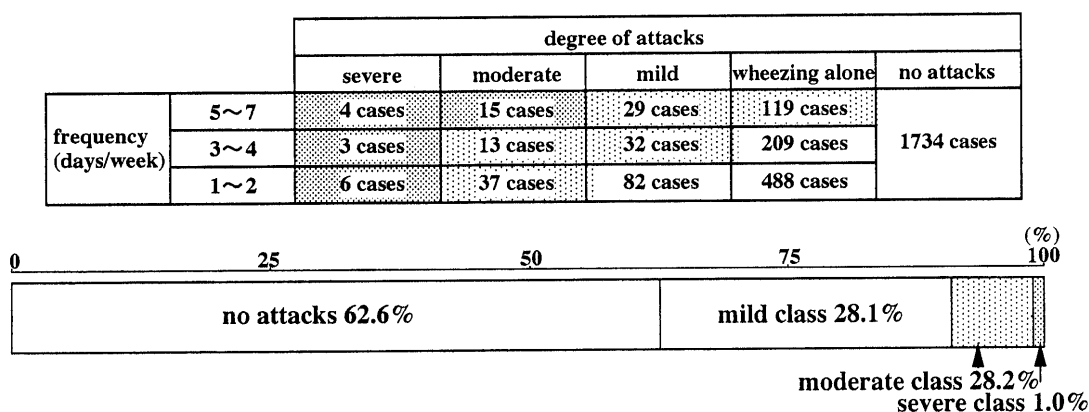


Fig. 4. Frequency and degree of asthma attacks over the two weeks prior to the questionnaires were classified follows: A patient with severe degree attacks (impossible to move due to dyspnea) or frequent (more than 5 days per week) middle degree attacks (impossible to lie down due to dyspnea) is classified as severe class. Middle class means middle degree attacks on fewer than 4 days per week, mild attacks (possible to lie down against dyspnea) on more than 3 days per week or wheezing alone on more than 5 days per week. Patients with mild degree attacks on fewer than 2 days per week or wheezing alone on fewer than 4 days per week were judged to be mild class.

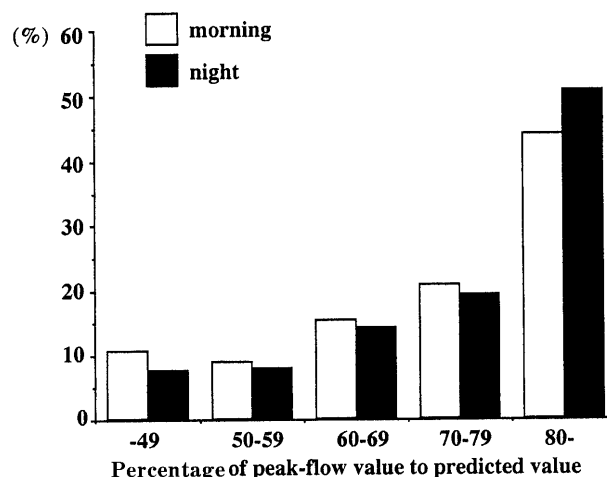


Fig. 5. Distribution of each user's percentage of peak-flow value to the predicted value. The open square shows the rate of peak-flow meter users whose peak-flow value at morning exited at the indicated range (percentage to the predicted value) to all its users, and the closed square at night.

Asthma-related symptoms during the two weeks prior to answering the questionnaire

The guidelines state the importance of eliminating asthma-related symptoms such as coughing and a sense of dyspnea, and enabling satisfactory sleep at nighttime as well as preventing asthmatic attacks. Based on the questionnaire results, the occurrence of a variety of asthma-related symptoms in early morning, night and during sleep, were examined (Fig. 6). Of the respondents, 53.8% answered that they had particular symptoms in the early morning, and 33.5% said they experienced symptoms at night during the two weeks prior to the questionnaire. "sputum" and "coughing" were the most common symptoms. While sleeping, 23.3% of all cases experienced some symptoms, for example, "Waking up in the night due to chest oppression" (15.0%).

Emergent events related to asthma attacks

Another obvious objective of asthma control in the guidelines is to prevent death caused by asthma attacks. Based on the results of the questionnaires, the patients' emergent events were examined, which included ambulance use, visits to the emergency room, and hospitalization (possibly associated with death from asthma), and unconsciousness asthma attacks and management by (often directly leading to death caused by asthma) aspirin induced asthma attacks (known to cause severe attacks and death). Among the respondents, 47.0% had visited or used an emergency room or ambulance, and 40.9% had been hospitalized due to asthma, each rate accounting for about half of the whole. Patients who had lost consciousness due to asthma accounted for 6.8% of the total, while 5.9% had managed using a respirator, and 8.6% had experienced an attack after taking anti-inflammatory drugs (Fig. 7).

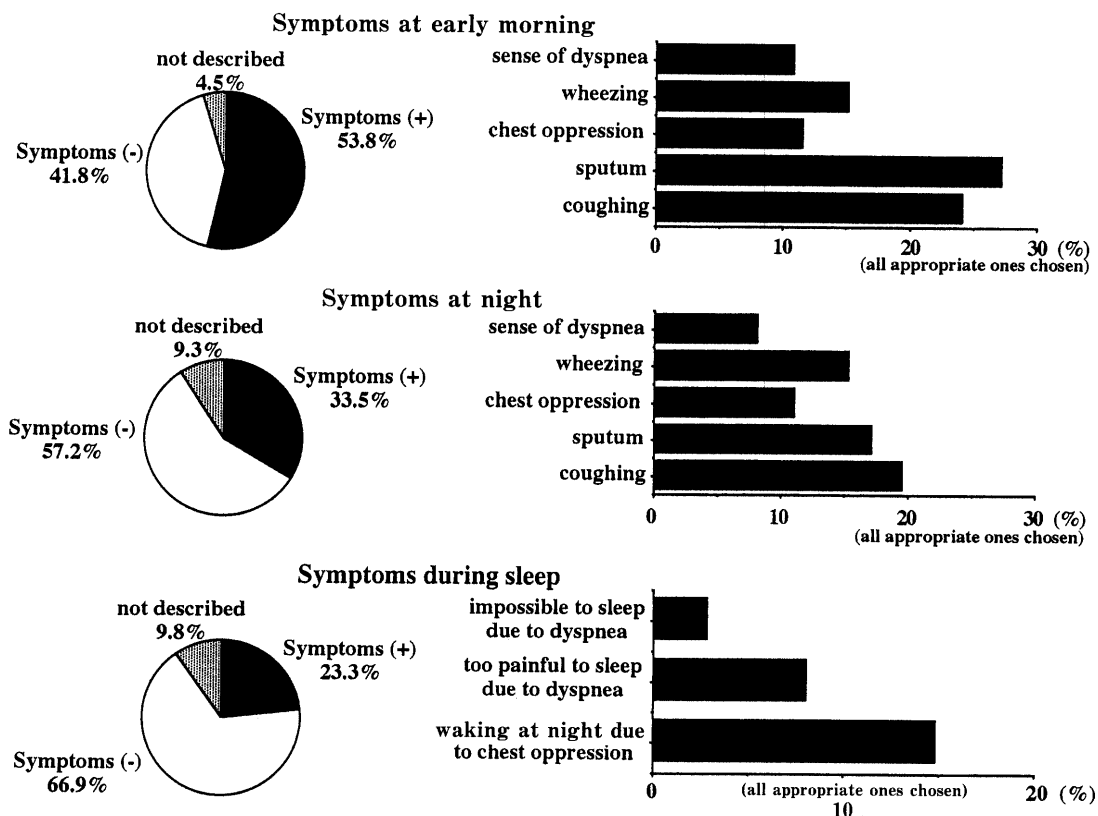


Fig. 6. Asthma-related symptoms. The total percentage of patients who either had or had not experienced symptoms related to asthma two weeks prior to the questionnaire performance is shown on the left of the panel at early morning, night and during sleep. On the right of the panel, the percentage of each symptom's presence is indicated.

Drug medication

Those drugs being currently used were examined based on the questionnaire results from their physi-

cians (Table 1). Sustained-release theophylline was very frequently used, found in 76.9% of all cases, inhaled beta2 stimulators were used in 46.7% of cases (continuously in 5.4%, temporarily in 39.7%), and oral

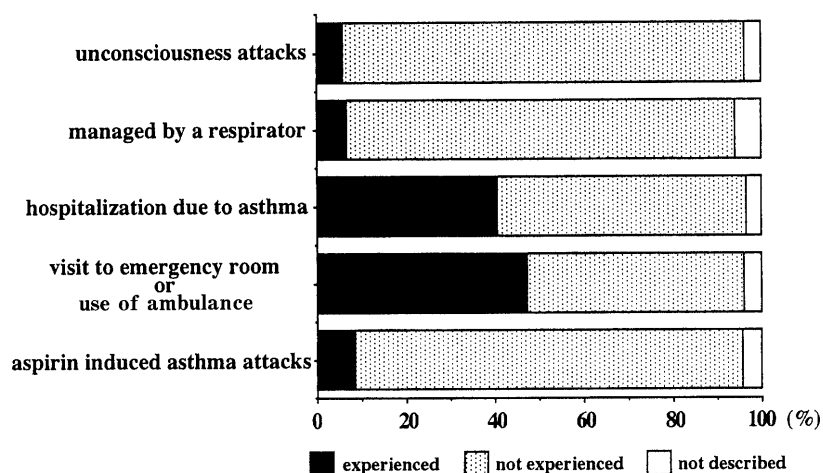


Fig. 7. Emergent events related to asthma attacks. The patients were asked to answer “yes” or “no” to the following five questions: 1) Have you ever had a respirator due to an asthma attack; 2) Have you ever been unconscious due to an asthma attack; 3) Have you ever been hospitalized due to asthma; 4) Have you ever been taken by ambulance car or visited an emergency room due to an attack? and 5) Have you ever had an attack induced by anti-inflammatory drugs including painkillers, antipyretics, or cold medicine? Each frequency in visit to an emergency room or use of an ambulance, hospitalization due to asthma, consciousness due to asthma attacks and management by a respirator was indicated.

Table 1. Summary of drug used

Drug used	Percentage (number)			p value
	All (3347)	Respiratory physician (2909)	General physician (438)	
Sustained-release theophylline	76.9% (2665)	80.3% (2336)	75.1% (329)	p = 0.1992
Inhaled beta2 stimulator	46.6% (1564)	46.3% (1346)	49.1% (215)	p = 0.2706
continuously	5.4% (182)	5.2% (151)	7.1% (31)	p = 0.1045
on demand	39.7% (1329)	40.3% (1173)	35.6% (156)	p = 0.0605
Oral beta2 stimulator	33.6% (1126)	33.2% (966)	36.5% (160)	p = 0.1701
continuously	29.5% (987)	29.8% (867)	27.4% (120)	p = 0.3031
on demand	2.5% (84)	2.2% (65)	4.3% (19)	p = 0.0087
Oral steroid	18.8% (630)	19.3% (560)	16.1% (70)	p = 0.1028
Inhaled steroid	62.0% (2076)	64.5% (1877)	45.4% (199)	p < 0.0001
Anti-allergic	48.8% (1634)	48.6% (1413)	50.5% (221)	p = 0.4623
Anti-histaminergic	3.4% (115)	2.8% (82)	7.5% (33)	p < 0.0001

Table 1 shows the summary of the drug used to control asthmatic patients that were examined based on the questionnaire results with physicians in charge. Comparison was performed between the two groups, by a respiratory physician and by general physicians.

Table 2A. Status of inhaled steroid use (beclomethasone)

Mean \pm SD	621.7 \pm 365.7 μ g/day
Amount of dose (μ g/day)	Percent of users (number of users)
-399	18.3% (376)
400-599	27.2% (564)
600-799	12.5% (260)
800-999	24.1% (501)
1000-1199	0.8% (18)
1200-	11.5% (239)
not described	5.7% (118)

B. Status of inhaled steroid use (calculated as prednisolone)

Mean \pm SD	7.1 \pm 4.9 mg/day
Amount of dose (mg/day)	Percent of users (number of users)
-4.9	16.0% (101)
5.0-9.9	48.4% (304)
10-	26.7% (168)
not described	9.0% (57)

Table 2 shows the dose of inhaled steroid (A) and oral steroids (B). The doses of oral steroids were calculated as prednisolone.

beta2 stimulators were used in 33.6% of cases (continuously in 29.5%, temporarily in 2.5%). Inhaled steroids and oral steroids were used in 62.0% and 18.8% cases, respectively. The rate of use of anti-allergics was 48.8%, and that of antihistamines was 3.4%. RPs used significantly more inhaled steroids and less antihistamine than GPs ($p < 0.0001$).

The daily inhalation dose taken by inhaled steroid users was $621.7 \pm 365.7 \mu$ g, calculated in terms of beclomethasone on average. A daily dose from 400 to 599 μ g was employed in 27.2% of cases, exceeding the percentages for other doses, followed by a dose from 800 to 999 μ g used in 24.1% of cases (Table 2A). The internally used mean daily dose of oral steroids was 7.1 ± 4.9 mg, calculated in terms of prednisolone. More patients used such drugs internally at daily doses of 5.0 to 9.9 mg (48.4%). In 26.7% of the cases, the drugs were taken in doses of 10 mg or more a day (Table 2B).

DISCUSSION

In this questionnaire-based investigation, information was obtained on 2,909 cases treated by RPs and 438 cases treated by GPs. This means that a majority of the patients were from specialist institutions and that

the results of this study might indicate the status managed by specialists more than by general practitioners.

Information on age, age at onset and duration cannot serve as accurate epidemiological data since it is impossible to assume the population of cases with adult bronchial asthma in the questionnaires. Nonetheless, this would probably be a useful basis for similar future epidemiological studies. This investigation found that the prevalence rate of the peak-flow meter was only about 30%, indicating that this instrument is not widely used in Niigata Prefecture, Japan, although the guidelines strongly recommend it. The advantage of using a peak-flow meter for patients was probably not recognized for both its cost and complexity, although the questionnaire did not address this. With their feature of daily enabling the evaluation of objective respiratory function, peak-flow meters should be more widely introduced in the future.

The situation of the asthma attacks at the time that the questionnaires were answered was queried in order to understand the current status of asthma control. The percentage of mild class attacks was 28.1%, and no attacks were found in 62.6% of all cases, as shown in Fig. 4, although it was conducted during a so-called "seasonal turning point," Septem-

ber and October. In the guidelines, the prevention of asthma attacks is one of the important targets for managing patients with asthma. This means that the control of asthma attacks in Niigata Prefecture should be judged as comparatively favorable, even though the situation of the treatments given to each patient were not considered, especially that concerning the use of steroids. In assessing peak-flow values, the average %PEF values were nearly 80%; 76.4% in the morning and 79.7% at night, indicating that many patients were well managed in order to maintain the normal pulmonary function recommended in the guidelines.

However, about half of all cases exhibited %PEF values of less than 80%, while %PEF values of less than 70% were observed in 35.6% and 27.8% of the cases in the morning and at night, respectively, which shows that some patients were obviously under-controlled. As for nighttime and early morning symptoms and those during sleep certain symptoms related to asthma occurred in a considerable number of cases, and sleep disturbance was found in more than 20% of the patients (Fig. 6). These indicated that unsatisfactory factors disappeared when the complete management of asthma is considered. As for symptoms observed in the early morning and night, it should be noted that a higher incidence was recognized for coughing, sputum and other symptoms that are comparatively commonly seen in respiratory diseases, rather than symptoms comparatively peculiar to asthma, such as wheezing.

As for preventing death from asthma, the questionnaires found that 5-7% of the patients had episodes related to near-fatal asthma including unconsciousness and management by a respirator, as shown in Fig. 7. Also, 40-50% of the patients had the anamnesis of intermediate to severe attacks requiring treatment at a medical institution. These studies are certainly interesting, even though a comparative study has not been conducted. With respect to aspirin induced asthma, this study presumes that patients acknowledge themselves as suffering from this disease. The percentage of patients who have experienced aspirin induced asthma among all asthmatic patients is generally held to be 10% or more, although the ratio varies somewhat depending on the reporter⁶⁾. It is thus risky to decide on the use of non-steroid anti-phlogistics in patients with asthma only based on medical examinations through an interview.

Drugs for bronchial asthma are generally divided into medications for quick relief and those for long-term control. Additionally, the same drug may be included in both types, as with oral steroids. The majority of the drugs used (Table 1) in this study

were drugs for long-term control medications, apart from temporarily inhaled beta2 stimulators. The rate of use was 62.0% for inhaled steroids, which are recommended for use as a chief remedy in the guidelines; this type of drug is fairly prevalent. The investigation results, however, showed that its rate of use was generally lower than sustained-release theophylline, and it was still lower among GPs (45.4%). This data indicates that recent achievements in the elucidation of the pathology of bronchial asthma have not been widely recognized yet, although the questionnaires were sent out before fluticasone (the high-titer inhaled steroid) was launched and the use of inhaled steroids may now be different. This requires further investigation.

It is considered that the status of the use of oral steroids should indicate the rate of so-called steroid-dependent asthma. This investigation found that 14% of all cases internally used 5 mg/day or more, calculated in terms of prednisolone, each day (75.1% of cases with steroid-dependent asthma), and that the mean amount used was 7.1 mg/day (Table 2B). It will be interesting to see how the obtained values will be affected by the prevalence of fluticasone and the leukotriene antagonist that has been shown to effectively reduce doses of high-titer inhaled steroids and oral steroids⁷⁾.

The results of this investigation can be chiefly characterized by the fact that sustained-release theophylline was used in 80% of all cases. This indicates that sustained-release theophylline is considered a basic drug for long-term control in Niigata Prefecture. This is likely a phenomenon that is very peculiar to Japan, given that this drug is hardly used elsewhere, especially in North America⁸⁾. Sustained-release theophylline was probably not chosen at a high frequency overall based only on the expectations that it will act as a bronchodilator based on the old recognition of asthma, given that the drug was more favored by RPs than by GPs. In fact, it has recently been reported that theophylline has an additional efficacy: suppressing cytokines and being anti-inflammatory⁹⁾, and having superior clinical effects with the addition of sustained-release theophylline on inhaled steroids to a doubling dose of inhaled steroid¹⁰⁾. It is thus believed that the position of sustained-release theophylline as a drug for long-term control will possibly be re-evaluated in the near future.

Anti-allergics include conventional basic anti-allergics with antihistaminic effects, acid anti-allergics without antihistaminic effects, leukotriene antagonists, anti-thromboxane, and IgE generation suppressers, although these are not recognized as

long-term control medication in the USA guidelines except for leukotriene antagonists. This questionnaire did not ask participants to discriminate among these drugs, so a detailed investigation of anti-allergics is not possible. Nevertheless, anti-allergics were very frequently used in 48.8% of the cases, which is one of the most noticeable differences compared with Western countries. In addition, interestingly, there was no difference in the rate of use of such drugs between RPs and GPs. The precise situation of the anti-allergic drugs use and changes in the rate of use of such drugs requires examination in the future.

In summary, adult bronchial asthma was investigated in Niigata Prefecture, and the results of a questionnaire-based study were compared with the targets for asthma treatment in the guidelines for controlling adult bronchial asthma. Despite some satisfactory results, there was found to be further room for improvement from the viewpoint of encouraging a greater use of the peak-flow meter as a means of evaluating normal respiratory functions and maintaining normal pulmonary functions, alleviating symptoms at night and in the morning, ensuring satisfactory nocturnal sleep, and preventing death from asthma. Examination of the status of use of drugs found that the rate of use of inhaled steroids was problematic, sustained-release theophylline and anti-allergics were heavily used, and sustained-release theophylline in particular was positioned as a fundamental drug for long-term control medications, being superior to inhaled steroids in a practical sense. In spite of this, it will be necessary to carry out further investigations in the future, widely acknowledging the recognition of the new pathology of bronchial asthma and anticipating impending changes in the situation surrounding adult bronchial asthma in Niigata Prefecture.

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