## □ ORIGINAL ARTICLE □

# Asthma Control and Management Changes in Japan: Questionnaire Survey

Takashi Hasegawa<sup>1</sup>, Toshiyuki Koya<sup>2</sup>, Takuro Sakagami<sup>2</sup>, Shinichi Toyabe<sup>3</sup>, Hiroshi Kagamu<sup>2</sup>, Masaaki Arakawa<sup>2</sup>, Fumitake Gejyo<sup>2</sup>, Ichiei Narita<sup>2</sup>, Eiichi Suzuki<sup>1</sup> and the Niigata Asthma Treatment Study Group

## Abstract

**Background** Despite the advances of asthma management and the accompanying improved asthma control, many problems related to asthma management still remain. The Niigata Asthma Treatment Study Group has been regularly collecting information via surveys since 1998 using a questionnaire, on problems related to asthma management; various studies on asthma management have been reported using data from the questionnaire.

**Methods** The aim of this study was to investigate the changes in asthma control and management for every two-year period using the data from 1998 to 2008; future problems requiring resolution were extracted and discussed.

**Results** The number of cases surveyed each year was about 3,000 (2,593-3,347 cases). The changes in the data from 1998 to 2008, including asthma attacks and symptoms rate, indicated the improvement of asthma control with the spread of medication according to the guidelines; of particular note, there was a 24.1% increase in the usage rate of inhaled corticosteroids during the study period. From 2002 to 2008, however, some asthmatic conditions seemed to show no improvement with regards to asthma control related to the rates of changes in peak flow meter use, leukotriene receptor antagonist use and oral sustained-released theophylline use. Moreover, there was no decrease in the occurrence of emergency episodes related to asthma deaths.

**Conclusion** In the actual clinical setting, asthma control seems to be progressing well with the appropriate changes of medication according to the guidelines, and in part due to inhaled corticosteroid use. However, there were two problems which need to be addressed: 1) no improvement in some asthmatic conditions and 2) the occurrence of emergency episodes related to asthma deaths. In the future, it will be necessary to manage asthma in view of these points.

Key words: asthma, control, inhaled corticosteroid, questionnaire survey

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### Introduction

The widespread use of inhaled corticosteroids (ICS) has resulted in more improved asthma control than achieved before (1, 2), however, the prevalence of asthma and resulting mortality are significantly high (3), leading to an annual loss of 15 million disability-adjusted life-years, as estimated by the World Health Organization (4). The social and economic burden of asthma remains heavy and needs to be immediately addressed (5, 6). Therefore, there is a need for determining the various problems concerned with asthma, includ-

Received for publication September 19, 2011; Accepted for publication November 14, 2011 Correspondence to Dr. Takashi Hasegawa, htaka@med.niigata-u.ac.jp

<sup>&</sup>lt;sup>1</sup>Department of General Medicine, Niigata University Medical and Dental Hospital, Japan, <sup>2</sup>Division of Respiratory Medicine, Niigata University Graduate School of Medical and Dental Sciences, Japan and <sup>3</sup>Department of Patient Safety, Niigata University Medical and Dental Hospital, Japan

Year	All institutes	All institutes	All institutes	Hospitals (be	eds ≥ 200)	Hospitals (b	eds < 200)	Cli	nics
rear	NPQ	NAQ	Recovery rate	NII	NAQ	NII	NAQ	NII	NAQ
1998	6000	3347	55.8	32	1940	35	780	86	627
2000	6100	3069	50.3	32	1900	30	668	47	501
2002	6000	2593	43.2	27	1626	24	602	27	365
2004	6200	2865	46.2	27	1649	16	710	35	506
2006	5460	3066	56.2	27	1613	21	717	67	736
2008	5260	3146	59.8	28	1633	14	782	62	731

 Table 1.
 Numbers of Questionnaires Prepared and Answered and of Institutions Involved

NPQ: number of questionnaires prepared; NAQ: number of questionnaires answered; NII: number of institutions involved.

ing the relationship with chronic obstructive pulmonary disease, the management of aspirin intolerant asthma and cough variant asthma, as a part of asthma management (3, 7). Moreover, the management and the treatment of asthma can greatly differ according to the time and the surrounding environment and, in fact, the guidelines for asthma have been revised several times (3, 7, 8). It is important to obtain exact information about the actual clinical situations concerned with the management and the treatment of asthma to accomplish the best revision of the guidelines.

The Niigata Asthma Treatment Study Group has been routinely using a questionnaire since 1998 to assess problems related to asthma management. The surveyed subjects are adult bronchial asthma patients who visited medical institutions in Niigata Prefecture, and the attending physicians of these patients are included in the survey (in the survey design). On the basis of these surveys, we have reported the clinical characteristics of adult bronchial asthma patients (9), elderly bronchial asthma (10), near fatal asthma (11), perimenstrual asthma (12), asthma exacerbation factors (13), the selection of ICS (14), and the relationship between smoking and gender in asthmatics (15). These surveys provide a clear picture of the state of asthma management in Japan. The change in asthma management and control was also one of the most important themes in our previous studies (1, 2), however, the analyzed data for the changes in those reports were data from before the 2002 survey. In this study, we analyzed the biennial survey data from 1988 to 2008, and showed the provided results related to asthma control and management.

#### **Materials and Methods**

Participation in this study was open to all medical institutions in Niigata Prefecture as long as they intended to join the Niigata Asthma Treatment Study Group. This study was performed with the approval of the Ethics Committee at the School of Medicine of Niigata University in Niigata Prefecture, Japan, or at the relevant participating institution, in accordance with the Ethical Principles for Medical Research Involving Human Subjects (Declaration of Helsinki). The numbers and the types of institutions involved each year are shown in Table 1. The numbers of questionnaires prepared, questionnaires answered and the recovery rate are also indi-

cated in Table 1. Table 2 shows the contents of the questionnaire (originally in Japanese). To avoid annual and seasonal influences, the questionnaire used each year was written in a similar way in Japanese and they were handed out over 2 months, from September to October 2008, in principle. Subjects were adult patients (aged 16 and older) with bronchial asthma and who regularly visited the participating institutions for asthma management (typically once or twice a month). As the recruited patients were asked to complete the questionnaire by themselves, the individual patients were expected to be able to understand technical terms such as "attack" or "unconscious" in the questionnaire (Table 2). To evaluate problems as to asthma management and treatment related to normal activity levels, the questionnaires also asked patients about their satisfaction with regard to daily life. The subjects answered by choosing 1 of the 5 options shown in Table 2.

In addition to monitoring the completion of the questionnaire by the patients, physicians were asked to supply details on the patient's current treatment, primary control medication, the type of asthma (atopic or non-atopic) in accordance with the elevation in serum total IgE or detection of a specific IgE for allergens, and the severity of asthma in accordance with the criteria of asthma severity by the Asthma Disease Severity Criteria Reexamination Committee (Miyamoto et al). The definitions of the severity of asthma used are essentially the same as those used by the Global Initiative for Asthma.

The representative results for continuous variables were expressed as arithmetic means and standard deviations. Continuous variables were analyzed using the Kruskal-Wallis test, followed by Scheffe's method for multiple comparisons. Dichotomous variables were analyzed using the chisquare test, followed by Ryan's method for multiple comparisons. The Jonckheere-Terpstra test and Cochran-Armitage test were used to analyze trends across years for continuous variables and dichotomous variables, respectively. For all statistical analyses, a p-value less than 0.05 was considered statistically significant. All analyses were performed using SPSS Statistics 19 (IBM Japan Inc., Tokyo, Japan).

#### Table 2. Questionnaires Administered to Asthmatic Patients during This Study (Original in Japanese)

Age: ye	ars old Gender: male / female
Question 1	When were you first diagnosed as having bronchial asthma? Year: Month: Day:
Question 2	Do you use a peak-flow meter? (Yes/No)
Question 3	Select one answer for each the following questions:
	<ol> <li>How often did you have asthma attacks during the last 12 months? (frequent attacks, seasonal attacks, or few attacks)</li> </ol>
	<ol> <li>How often did you have asthma attacks during the last 2 weeks?</li> <li>(5 - 7/week, 3 - 4/week, 1 - 2/week, or none)</li> </ol>
	<ol> <li>How severe were your asthma attacks during the last 2 weeks? (impossible to move, impossible to lie down, possible to lie down, stridor, dyspnea upon exertion)</li> </ol>
	<ol> <li>Have you ever been hospitalized due to asthma? (yes/no)</li> </ol>
	<ol> <li>Have you ever been taken by ambulance or visited an emergency room due to an attack ? (yes/no)</li> </ol>
	<ul> <li>6) Have you ever been placed on a respirator due to an asthma attack? (yes/no)</li> </ul>
	<ol> <li>Have you ever been unconscious due to an asthma attack? (yes/no)</li> </ol>
	<ol> <li>B) Have you ever had an attack induced by anti-inflammatory drugs including painkillers, antipyretics, or cold medicine (yes/no)</li> </ol>
	9) Have you been absent from work or school due to an asthma attack? (yes/no)
Question 4	Describe your symptoms during the last 2 weeks: 1) in the morning
	(cough, phlegm, chest tightness, stridor, dyspnea, or no symptoms) 2) at night
	(cough, phlegm, chest tightness, stridor, dyspnea, or no symptoms) 3) sleep disturbance
	(sometimes cannot fall asleep due to dyspnea, cannot have a good, sleep due to dyspnea, waking up in the night due to chest tightness, or none)
Question 5	
	Do you feel satisfied with your daily life?
	(very satisfied, fairly satisfied, mediocre, slightly dissatisfied, or dissatisfied)

#### Table 3. Changes in Patient Background

Year	Age (mean ± SD years)	Gender (% female)	Duration (mean ± SD years)	PEFM use (%)
1998	54.4 ± 17.6	49.9	11.5 ± 12.0	30.8
2000	55.8 ± 16.7 **	50.9	15.9 ± 18.4 ***	40.4 **
2002	56.0 ± 16.8 **	53.8	12.7 ± 13.7	39.3 **
2004	56.9 ± 17.3 ***	52.7	13.6 ± 13.4 *** \$	36.1 ** ##
2006	57.5 ± 17.8 *** ### \$\$	56.3 ** ##	13.5 ± 13.3 *** \$	28.4 ## \$\$ ¥¥
2008	57.0 ± 18.0 *** ##	57.5 ** ## ¥¥	14.1 ± 13.9 *** \$\$\$	23.7 ** ## \$\$ ¥¥ ¢

There was a significant variation in the age, the percentage of females, the duration and the rate of PEFM use (p < 0.001) using the Kruskal-Wallis test and the chi-square test. There was a significant increase in the age, the percentage of females and the duration (p < 0.001), and was a significant decrease in the rate of PEFM use (p < 0.001) using the Jonckheere-Terpstra test and the Cochran-Armitage test. \*\*\*: p < 0.001; \*\*: p < 0.01 vs 1998; ###: p < 0.001; ##: p < 0.01 vs 2000; \$\$\$: p < 0.001; \$\$: p < 0.01; \$: p < 0.01 vs 2002; ¥¥: p < 0.01 vs 2004; ¢: p < 0.05 vs 2006 PEFM: peak flow meter.

#### Results

#### Patient backgrounds

The patient backgrounds are given in Table 3. There were significant variations (p<0.001) in the ages, the percentage of females, the duration and the rate of peak flow meter (PEFM) use during the study period. There was a significant increase in the age, the percentage of females and the duration (p<0.001) during the study period. Although there was a significant decrease in the rate of PEFM use (p<0.001) during the study period, the rates of PEFM use in 2000, 2002 and 2004 were significantly higher than that in 1998.

#### Asthma type and severities

The changes of asthma type and severity are shown in Table 4. Although there was a significant variation and decrease (p<0.001) in the rate of atopic asthma during the study period, there was no significant difference between the figures in 1998 and 2008. During the study period, there was a significant variation (p<0.001) in the rates of mild, moderate and severe asthma, and there was a significant increase (p<0.001) in the rate of mild asthma and a significant decrease (p<0.001) in the rate of severe asthma which corresponded with the comparisons between the two arbitrary years with regard to the rates of mild and severe asthma.

Year	Atopic asthma	Mild asthma	Moderate asthma	Severe asthma
1998	65.6	46.1	38.8	9.5
2000	65.3	42.6 **	44.1 **	9.0
2002	69.4 ** ##	38.7 ** ##	48.1 ** #	9.8
2004	66.0 \$	47.8 ## \$\$	42.7 ** \$\$	6.9 ** # \$\$
2006	62.1 ** \$\$ ¥¥	50.8 ** ## \$\$	39.8 ## \$\$	5.5 ** ## \$\$
2008	64.6 \$\$	50.6 ** # \$\$	38.6 ## \$\$ ¥¥	5.7 ** ## \$\$

#### Table 4. Changes in Type and Disease Severity

There was a significant variation in the rates of atopic asthma and mild, moderate and severe asthma (p < 0.001) using the chi-square test. There was a significant decrease in the rate of atopic asthma, moderate and severe asthma (p < 0.001), and was a significant increase in the rate of mild asthma (p < 0.001) using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01; #: p < 0.05 vs 2000; \$\$: p < 0.01; \$: p < 0.05 vs 2002; \$\$: p < 0.01 vs 2004.

Table 5. Changes in Asthma Attacks

Year	Few attacks 1Y	No attacks 2W	Ambulance use or ER visits	Hospital admissions
1998	31.9	51.9	40.9	47.0
2000	39.2 **	54.3 **	37.4 **	45.7
2002	46.2 ** ##	56.6 **	39.1	43.1 **
2004	44.6 ** ##	55.8 **	36.3 **	41.2 ** ##
2006	46.4 ** ##	63.1 ** ## \$ ¥¥	32.6 ** ## \$\$ ¥	36.7 ** ## \$\$ ¥
2008	44.8 ** ##	64.7 ** ## \$\$ ¥¥	29.1 ** ## \$\$ ¥¥ ¢	33.4 ** ## \$\$ ¥¥ ¢

There was a significant variation in the rate of few attacks (1Y), no attacks (2W), ambulance use or ER visits and hospital admissions (p < 0.001) using the chi-square test. There was a significant increase in the rate of few attacks 1Y and no attacks 2W (p < 0.001), and was a significant decrease in the rate of ambulance use or ER visits and hospital admissions (p < 0.001) using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01 vs 2000; \$\$: p < 0.01; \$: p < 0.05 vs 2002; ¥¥: p < 0.01; ¥: p < 0.05 vs 2004; ¢: p < 0.05 vs 2006; (1Y): during 1 year prior to the questionnaire; (2W): during 2 weeks prior to the questionnaire; ER: emergency room.

Table 6.	Changes	in Emergent	Episodes
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Year	Attacks with unconsciousness	Respirator management	Asthma exacerbation due to NSAIDs
1998	6.8	5.9	8.6
2000	6.8	6.4	8.7
2002	6.9	6.4	8.9
2004	5.5	5.4	6.8
2006	7.1	4.8	6.5 ** ## \$\$
2008	5.9	5.0	6.7 ** ## \$\$

There was a significant variation in the rate of respirator management and asthma exacerbation due to NSAIDs (p < 0.001) using the chisquare test. There was a significant decrease in the rate of respirator management and asthma exacerbation due to NSAIDs (p < 0.001) using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01 vs 2000; \$\$: p < 0.01 vs 2002; NSAIDs: non-steroidal antiinflammatory drugs.

## Attacks during the 1 year prior and the 2 weeks before the questionnaire, ambulance use or emergency room (ER) visits, hospital admissions

During the study period, there were significant variations (p<0.001) in the rate of few attacks during the 1 year prior to the questionnaire, no attacks during the 2 weeks prior to the questionnaire, ambulance use or ER visits and hospital admissions (Table 5). There was a significant increase (p<0.001) in the rate of few attacks during the 1 year prior to the questionnaire and no attacks during the 2 weeks prior to the questionnaire, and a significant decrease (p<0.001) in the rate of ER visits and hospital admissions. There were no significant changes between the two arbitrary years from 2002 to 2008 as to the rate of few attacks during 1 year prior to the questionnaire.

## Attacks with unconsciousness, respirator management and asthma exacerbation due to non-steroidal anti-inflammatory drugs (NSAIDs)

The rates of attacks with unconsciousness, respirator management and asthma exacerbation due to NSAIDs are shown in Table 6. There was a significant variation (p<0.001) in the rates of respirator management and asthma exacerbation due to NSAIDs, while there was not a significant variation in the rate of attacks with unconsciousness during the study period. Although there was a significant decrease (p<0.001) in the rate of respirator management during the study period, there were no significant differences between the two arbitrary years. These indicated there was no meaningful improvement in the rate of attacks with unconsciousness or of respirator management during the study period. There was a

Year	Symptom free in the morning	Symptom free at night	No sleep disturbance
1998	41.6	57.2	66.9
2000	45.8 **	60.7	70.6 **
2002	59.2 ** ##	74.2 ** ##	88.2 ** ##
2004	60.2 ** ##	73.5 ** ##	87.5 ** ##
2006	50.0 ** ## \$\$ ¥¥	59.8 \$\$ ¥¥	73.0 ** \$\$ ¥¥
2008	52.3 ** ## \$\$ ¥¥	63.7 **  \$\$ ¥¥ ¢¢	78.0 ** ## \$\$ ¥¥ ¢

 Table 7.
 Changes in Asthma Symptoms

There was a significant variation in the rate of symptom free in the morning, symptom free at night and no sleep disturbance (p < 0.001) using the chi-square test. There was a significant increase in the rate of symptom free in the morning, symptom free at night and no sleep disturbance (p < 0.001) using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01 vs 2000; \$\$: p < 0.01 vs 2002; ¥¥: p < 0.01 vs 2004; ¢¢: p < 0.01; ¢: p < 0.05 vs 2006.

 Table 8.
 Changes in Drug Medication

Year	OCS use	ICS use	LTRA use	OSRT use	Inhaled LABA use	p-TUB use
1998	18.8	62.0	27.2	79.6	-	-
2000	12.3 **	71.4 **	34.1 **	75.7 **	-	-
2002	10.4 **	77.4 ** ##	40.6 ** ##	71.9 ** ##	-	11.3
2004	7.4 ** ## \$\$	79.5 ** ## \$\$	45.9 ** ## \$\$	60.8 ** ## \$	17.2	10.6
2006	7.8 ** ## \$	80.7 ** ## \$\$	42.2 ** ## ¥¥	53.7 ** ## \$\$ ¥	26.4 ¥	11.9
2008	5.2 ** ## \$\$ ¥¥ ¢¢	86.1 ** ## \$\$ ¥¥ ¢	42.8 ** ##	44.5 ** ## \$\$ ¥¥	⊈¢ 37.2¥¢	9.1 \$\$ ¥ ¢¢

There was a significant variation in the rate of OCS use, ICS use, LTRA use, OSRT use, inhaled LABA use and p-TUB use (p < 0.001) using the chi-square test. There was a significant increase in the rate of ICS use, LTRA use, inhaled LABA use and p-TUB use (p < 0.001), and a significant decrease in the rate of OCS use and OSRT use using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01 vs 2000; \$\$: p < 0.01; \$: p < 0.05 vs 2002; ¥¥: p < 0.01; ¥: p < 0.05 vs 2004; ¢¢: p < 0.01; ¢: p < 0.05 vs 2006; OCS: oral corticosteroid; ICS: inhaled corticosteroid; LTRA: leukotriene receptor antagonist; OSRT: oral sustained-released theophylline; LABA: long acting beta agonist; p-TUB: tulobuterol patch.

significant decrease (p<0.001) in the rate of asthma exacerbation due to NSAIDs during the study period, which corresponded with the comparisons between the two arbitrary years.

## Symptom free in the morning and at night during the 2 weeks prior to the questionnaire, no sleep disturbance during the 2 weeks prior to the questionnaire

The rates of symptom free in the morning and at night during the 2 weeks prior to the questionnaire, and no sleep disturbance during the 2 weeks prior to the questionnaire are shown in Table 7. There was a significant variation and increase in the rate of symptom free in the morning and at night and no sleep disturbance (p<0.001) using the chi-square and Cochran-Amitage tests. However, the Ryan test showed that these 3 rates in 2006 or 2008 were significantly lower than those in 2002 or 2004.

#### Medications

The changes of each medicine used for the asthma control are shown in Table 8. There were significant variations (p< 0.001) in the rates of oral corticosteroid (OCS) use, ICS use, leukotriene receptor antagonist (LTRA) use and oral sustained-released theophylline (OSRT) use over the whole study period, and in the rate of inhaled long-acting beta agonist (LABA) from 2004 and tulobuterol patches (p-TUB) from 2002. There were significant decreases (p<0.001) in the rates of OCS use and OSRT use, which corresponded with the comparisons between the two arbitrary years. There were also significant increases (p<0.001) in the rates of ICS use, inhaled LABA use and p-TUB use, which corresponded with the comparisons between the two arbitrary years. Although there was a significant increase in the rate of LTRA use during the study period, there was a significant decrease (p<0.01) in its use between 2004 and 2006.

#### Satisfaction in daily life

The satisfaction in daily life is shown in Table 9. There were significant variations in the rates of "very satisfied" (p <0.001), "satisfied" (p<0.001), "slightly dissatisfied" (p< 0.001) and "mediocre" (p=0.004). There was a significant increase in the rates of "very satisfied" and "satisfied" (p< 0.001), and a significant decrease in the rate of "slightly dissatisfied" (p<0.001). However, the rate of "very satisfied" for 2006 was significantly decreased (p<0.01) compared with that in 2004.

#### Discussion

The aim of this study was to investigate the changes in asthma control and management using a questionnaire, and to extract various problems that should be resolved with regard to asthma management. In this study, the severity of asthma was based on the criteria of asthma severity as given by the Asthma Disease Severity Criteria Reexamination Committee (Miyamoto et al). Regarding the control of asthma, the patient condition and symptoms during the 2

Year	Very satisfied	Satisfied	Mediocre	Slightly dissatisfied	Dissatisfied
1998	14.8	56.9	15.7	9.1	1.4
2000	13.1	56.6	15.5	10.0	1.9
2002	16.3 ##	54.6	16.6	7.4 ##	1.1
2004	18.6 ** ##	53.5	15.2	7.9	1.0
2006	15.6 ¥¥	54.0	16.9	9.1	1.7
2008	18.4 ** ## ¢¢	57.2	13.2	7.2 ##	1.4

Table 9. Changes in Satisfaction of Daily Life

There was a significant variation in the rate of "very satisfied", "satisfied" and "slightly dissatisfied" (p < 0.001), and "mediocre" (p = 0.004) using the chi-square test. There was a significant increase in the rate of "very satisfied" and "satisfied" (p < 0.001), and a significant decrease in the rate of "slightly dissatisfied" (p < 0.001) using the Cochran-Armitage test. \*\*: p < 0.01 vs 1998; ##: p < 0.01 vs 2000; ¥¥: p < 0.01 vs 2004; ¢¢: p < 0.01 vs 2006.

weeks and the 1 year prior to the questionnaire were evaluated as indicators. The other indicators for asthma control were the emergency episode experiments, including the respirator management, and the satisfaction of daily life.

Amongst the changes of patient background, there were higher patient age, longer disease duration and females more dominant with age (Table 3). These may reflect the aging phenomenon in Japan because the average life span of a woman is longer than that of a man, and the differences between men and women increase year by year in Japan (based on the general condition of the abridged life table in 2009 of Ministry of Health, Labour and Welfare). Apart from this, the important change in the background was the decrease of the PEFM use rate, although the PEFM use for asthma management was strongly recommended in the guideline (3, 7, 8). There were two reasons for this: one was the poor financial reward for asthma management using PEFM for physicians in Japan (less than 300 yen per medical examination), the other being the self-evaluation of asthma control by each patient using the likes of the Asthma Control Test (ACT), becoming more established (16) and spreading in Japan (17, 18).

There was an obvious shift from the severe to mild types in the distribution of disease severity during the study period (Table 4). This showed that asthma control has probably improved with the changes in drug medication, as mentioned below (Table 8). There were the transient decrease in the mild asthma rate in 2000 and 2002 and the increase in the moderate asthma rate in 2000, 2002 and 2004. These were not due to poor control but the inconvenient criteria of asthma severity by the Asthma Disease Severity Criteria Reexamination Committee (Miyamoto et al) in which the patients using more than 400 µg/day ICS were classified as having moderate asthma regardless of how well the asthma was controlled. When we started this survey, this criteria was established and appreciated by our survey, however, we should adopt the criteria for asthma severity of the Japanese Society of Allergology guidelines in conformity with GINA in the future. The stability of the asthma type (Table 4) might indicate the lack of changes in the nature of asthma, while it was reported that there might be some kinds of asthma endotypes (19).

While large parts of the main indicators for asthma con-

trol were various conditions during the 2 weeks prior to the questionnaire, including the rates of no attacks (Table 5), symptom free in the morning and at night, and no sleep disturbance (Table 7) in this study as mentioned above, all these indicators showed satisfactory and significant changes for the excellent improvement of asthma control during the study period. The other markers for asthma control, the long-term control and/or severe attacks control, were the rates of few attacks during the 1 year period prior to the questionnaire, ambulance use or ER visits, hospital admissions (Table 5), attacks with unconsciousness, respirator management and asthma exacerbation due to NSAIDs (Table 6). In almost all of these markers, there were also significant changes during the study period, indicating an excellent improvement of asthma control, including prevention from aspirin intolerant asthma. The questionnaire of satisfaction of daily life (Table 9) was added in attempt to indicate the quality of life (QOL) of the patient, which was an important target for asthma control (20, 21), although the validity was not evaluated compared with the published QOL questionnaire. The change of the satisfaction of daily life in this study might indicate an improvement of asthma control in the patients (Table 9).

The changes of medication as a controller are summarized in Table 8. It was thought that the decreased rate of OCS use was not a cause but a result of the improvement of asthma control. The changes in the rates of ICS, LTRA and inhaled LABA use reflected good compliance to the strategy of asthma management in various guidelines (3, 7, 8). Since ICS was recommended as the first choice and basic medicine for asthma control, the increased rate of ICS use (24.1%) during the study period was an extremely good value. Although it was reported that the additional effect of LTRA alone on ICS therapy was similar to that of inhaled LABA (22, 23), the increased rate of LTRA was smaller than that of inhaled LABA (24). The reason for this remains unclear, but the higher cost of LTRA compared with inhaled LABA in the actual clinical setting in Japan might contribute to this difference. Note that there was no increase in LTRA use from 2004 to 2008. OSRT was introduced as a potent additional medicine, the same as LTRA and inhaled LABA (25-27), however, the rate of OSRT use decreased during the study period, in particular there was a 27.4% decrease from 2002 to 2008. More frequent adverse effects and lower evidence grade as an additional effect of OSRT on ICS therapy might have influenced this decreasing rate, although the reason was unclear.

Among the various changes during the study period mentioned above, there are two important problems to address here: from 2002 to 2008, there was no increase in the rate of few attacks during the 1-year period prior to the questionnaire. This lack of change was likely to be equal to the changes of the PEFM use rate (Table 3), the LTRA use rate and the OSRT use rate (Table 8) with regard to the "noincreased use rate". This might indicate that further examination for the effect of PEFM, LTRA and OSRT use on the long-term control will be necessary. Regarding the symptom control from 2002 to 2006 (Table 7), including symptom free in the morning and at night and no sleep disturbance, OSRT, LTRA and PEFM use might play important roles. Another problem was the lack of improvement in the rate of attacks with unconsciousness and respirator management. As the patients were required to answer as to their experience of these episodes, it might be difficult to detect a significant change every two years in these rates. However, there was a significant decrease in the rates of asthma exacerbation due to NSAIDs, which was also just an experiment, and the absolute values of the rate of attacks with unconsciousness and respirator management were almost the same as those for asthma exacerbation due to NSAIDs. It was thought that these two rates were not likely to decrease and this may explain the higher rate of asthma deaths in Japan compared with those of developed countries such as the US (7). It is necessary to investigate the relationship between asthma management during emergency episodes and asthma deaths.

In summary, we attempted to determine the changes in asthma control and management in actual clinical settings through giving a questionnaire every two years. The changes of various indexes indicating asthma control showed that the asthma control might be heading on a good course. These changes seemed to be equal to the appropriate changes of medication according to the guidelines, partly due to ICS, however, there were two problems that should be improved as a part of the changes. These were related to the necessity of PEFM, LTRA and OSRT and with asthma deaths. In view of these points, it is necessary to perform better management of asthma in the future.

#### The authors state that they have no Conflict of Interest (COI).

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