

Age-Specific Characteristics of Inpatients with Severe Asthma Exacerbation

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ABSTRACT

Background: The characteristics of inpatients with severe asthma exacerbation remain unclear. It is considered that the characteristics of inpatients with severe asthma vary depending on age. However, these are rarely investigated. The objective of this study is to investigate the differences in characteristics among different age groups. We considered that it is necessary to understand the characteristics of each age group so that we can establish strategies in preventing severe asthma exacerbation.

Methods: All asthma inpatients who were hospitalized between 2004 and 2011 with SpO₂ <90% (in room air), were breathless at rest, and showed increased respiratory rate and pulse rate were examined. We compared the characteristics among the young age group, middle age group, and advanced age group.

Results: The total number of patients was 204. In the young age group, the percentages of patients with irregular visits and non visits to a medical institution were high. This group showed high percentages of smokers and pet owners. The percentage of continuous ICS users in this group was 25.9%. The middle age group had high rates of aspirin-intolerant asthma. The percentage of continuous ICS users in this group was 60.2%. In the advanced age group, the percentages of patients with hypertension/heart disease, diabetes mellitus, and COPD were high. This group showed good treatment adherence. The percentage of continuous ICS users in this group was 77.4%.

Conclusions: The characteristics of inpatients with severe asthma vary depending on age. We need to establish countermeasures for asthma exacerbation according to the characteristics of patients depending on age.

KEY WORDS

acute exacerbation, asthma, asthma attack, asthma death, inhaled corticosteroid

INTRODUCTION

Inhaled corticosteroids (ICS) have become the main drugs in the treatment of asthma, because asthma has been recognized as a chronic inflammatory disorder of the airways. Following this recognition, various asthma guidelines were formulated because a comprehensive treatment strategy was required, resulting in asthma control being improved significantly. It was reported that ICS use could decrease the incidence of asthma related death and the number of pa-

tients with asthma exacerbation.¹⁻³ As a result of the spread of the asthma guidelines and ICS use, it was reported that the incidence of asthma related death and the number of patients with asthma exacerbation significantly decreased in the United States,^{4,5} Canada,⁶ and the United Kingdom.⁷ It was reported that there was a decrease in asthma mortality rate in 20 countries in the 5- to 34-year-old group.⁸ In a survey conducted by the Ministry of Health, Labour and Welfare, the numbers of asthma related deaths and inpatients with asthma exacerbation were found to be

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decreasing in Japan. However, the rate of mortality due to bronchial asthma still remains higher in Japan than in European countries.⁹ In Japan, it was pointed out that the rates of mild type and moderate type asthma associated with death increased, and regarding the circumstances surrounding asthma related deaths, there were many cases of sudden deaths and unstable sudden aggravations.¹⁰ Various factors contribute to asthma related death and near fatal asthma. Asthma-admission-related costs are higher than other medical costs. It was considered that the prevention of asthma related death and near fatal asthma would result in a reduction in medical costs.¹¹ Uncontrolled asthma results in losses for patients, their families, and our society. The precautions against asthma related death and near fatal asthma are very important from various points of view. However, the characteristics of inpatients with severe asthma exacerbation remain unclear. Furthermore, it is considered that the characteristics of inpatients with severe asthma vary depending on age. However, they are rarely investigated. We examined the differences in the characteristics of inpatients with severe asthma exacerbation among different age groups. We considered that it is necessary to understand the characteristics of each age group so that we can establish strategies in preventing severe asthma exacerbation.

METHODS

STUDY POPULATION

We evaluated all asthma inpatients who were hospitalized at Sagami Hospital, one of the core hospitals for allergic diseases located in central Japan, between January 2004 and December 2011. We conducted a complete survey by a retrospective cohort study. The medical records of the patients were reviewed by their allergists or pulmonologists. Patients with severe asthma exacerbation were defined as those who satisfied the objective findings (SpO₂ <90% in room air, breathlessness at rest, an increased respiratory rate of 30 beats/min and a pulse rate >120/min) in accordance with the severity classification of asthma exacerbation based on GINA guidelines.¹² The exclusion criteria included an abnormal shadow in chest X-ray films, a clear heart failure, severe COPD, bronchiectasis, old tuberculosis, interstitial pneumonitis, and chronic eosinophilic pneumonia. This study was approved by the local ethics committee.

OUTCOME VARIABLES

The evaluated clinical backgrounds were as follows: age, gender, type of asthma, smoking history, pet ownership, history of childhood asthma, onset age, complications, trigger of exacerbation, prehospital severity, status of adherence to asthma treatment, and prehospital treatments. Each item was evaluated on the basis of answers given in a questionnaire and to

specific questions asked by the allergists or pulmonologists. Atopic asthma was defined as positivity for specific IgE antibodies to more than two common environmental allergens (e.g. house dust, mites, environmental fungi, pets). Patients not satisfying this definition were considered non atopic. Prehospital severity was classified on the basis of GINA guidelines, subjective symptoms, and treatments within one month prior to asthma exacerbation onset. The severity of asthma was classified into four categories, namely, intermittent, mild persistent, moderate persistent, and severe persistent, in accordance with the classification of the control level based on GINA guidelines. Regarding the status of adherence to asthma treatment, no visit to a medical institution means that the patient had not visited a medical institution for one year prior to admission, and irregular visits to a medical institution means that the patient had visited only at the time of asthma exacerbation in the year prior to admission. The complications were determined on the basis of responses to a questionnaire. The complications were defined as the diseases that had been diagnosed by medical doctors and treated in the present or the past. Patients were diagnosed as having aspirin-intolerant asthma (AIA) when they developed severe symptoms following the challenge test or internal use of NSAID. In addition, we investigated the age-specific (young age, middle age, advanced age) background characteristics of inpatients with severe asthma exacerbation. The specific criterion for young adults was not available. Wijesinghe used the criterion of less than 35 years of age in his study of asthma mortality rate in 20 countries.⁸ Therefore, we used the criterion of less than 35 years old as the definition of young adult asthma.

STATISTICAL ANALYSES

Data are expressed as arithmetic mean and standard deviation (SD). We used the Mann-Whitney U-test, χ^2 test, and Kruskal-Wallis test to determine statistically significant differences. Analyses were conducted with SPSS 11.0 for Windows (SPSS Japan Inc.). $p < 0.05$ was considered statistically significant.

RESULTS

BACKGROUND CHARACTERISTICS OF ALL INPATIENTS

The background characteristics of all inpatients with severe asthma exacerbation are shown in Table 1. The total number of patients with severe asthma exacerbation was 204 (85 men and 119 women, mean age of 50.1 years). Atopic-type asthma accounted for 64.2% of the patients, 39.7% were current smokers, 33.3% were pet owners, 38.2% had mild asthma before hospitalization, 21.6% had moderate persistent asthma, and 40.2% had severe persistent asthma. The most frequent trigger of severe asthma exacerbation was infection. The total percentage of patients with

Table 1 Background characteristics of all inpatients

	2004-2011
Total number of severe asthma exacerbations	204
Gender (male, %)	41.7%
Age (years)	50.1 ± 19.1
Type of asthma (atopy, %)	64.2%
Smoking Current smoker (%)	39.7%
Ex-smoker (%)	19.1%
History of childhood asthma (%)	28.9%
Onset of asthma (years)	31.1 ± 21.0
Pet ownership (%)	33.3%
dog	22.1%
cat	10.3%
rabbit	4.4%
Trigger of exacerbation (%)	
infection	64.2%
heavy weather	13.7%
exhaustion or emotional stress	6.4%
NSAIDs	2.0%
others	2.0%
uncertainty	11.8%
Complications	
hypertension/heart disorder	25.0%
allergic rhinitis	27.0%
atopic dermatitis	17.7%
sinusitis	18.1%
diabetes mellitus	7.8%
aspirin-intolerant asthma (AIA)	19.6%
obesity	13.7%
psychiatric disorder	9.8%
COPD	7.8%
Prehospital severity	
severe persistent type	40.2%
moderate persistent type	21.6%
mild persistent type	20.1%
intermittent type	18.1%
Status of adherence to asthma treatment	
regular visits to a medical institution	55.9%
irregular visits to a medical institution	27.5%
none	16.7%
Prehospital treatments (%)	
oral corticosteroid	17.7%
ICS	54.9%
SABA monotherapy as needed	16.7%
no treatment	27.5%
Days of hospitalization (days)	15.8 ± 13.7

unscheduled visits or non visit was 44.2%. The total percentage of patients without treatment and with short-acting inhaled β_2 agonist (SABA) monotherapy as needed was 44.2%. Regular ICS users accounted for 54.9%.

AGE-SPECIFIC BACKGROUND CHARACTERISTICS

The age-specific background characteristics of inpatients with severe asthma exacerbation are shown in Table 2. In the young age group (15-34 years old; 20 men and 38 women; mean age, 27.2 years), 48.2% had mild asthma before hospitalization. This group showed poor treatment adherence (74.1% were patients with unscheduled visits and non visit, and 25.9% were continuous ICS users) and high percentages of smokers and pet owners.

In the middle age group (35-64 years old; 41 men and 52 women; mean age, 52.1 years), 48.4% had severe asthma before hospitalization. This group had high percentages of patients with AIA. The percentage of continuous ICS users in this group was 60.2%.

In the advanced age group (more than 65 years old; 24 men and 29 women; mean age, 75.9 years), high percentages of patients with of hypertension/heart disease, diabetes mellitus, and COPD were observed. This group showed good treatment adherence (79.3% were patients with scheduled visits, and 77.4% were continuous ICS users).

DISCUSSION

The characteristics and risk factors in inpatients with severe asthma vary depending on age. We investigated the characteristics of patients with severe asthma exacerbation in Japan, and compared the characteristics among different age groups. The young age group had significantly high percentages of smokers and pet owners. Smoking and pet ownership are important asthma exacerbation factors.¹³ All pet owners in the young age group showed an IgE antibody level of more than 0.35 IU/ml for each pet allergen. Cat and dog allergens can be found in virtually all homes, but, not surprisingly, homes with pets contain much higher levels of the allergens than homes without pets. Allergic sensitization to furred pet allergens is quite common, and in some populations, more than 60% of children with asthma are sensitized to cat or dog allergens.¹⁴ In animal-allergen-sensitized asthma patients, animal allergen exposure is directly linked to poor asthma outcomes.^{15,16} Smoking causes inflammation and airway remodeling,¹⁷ makes asthma more difficult to control^{18,19} resulting in more frequent admissions,²⁰ and causes a more rapid decline in lung function.^{21,22} Asthma patients who smoke are poorly responsive to ICS^{23,24} and oral steroids.^{25,26} In the medical care of asthma, we considered that the avoidance of exacerbation factors, such as smoking and pet ownership, is very important. Furthermore, the young age group showed poor treatment adherence and included a small number of continuous ICS users. There were many patients without treatment, and there were patients on SABA monotherapy as needed. Some studies have suggested that young patients are associated with nonad-

Table 2 Age-specific background characteristics of inpatients

	15-34 years old	35-64 years old	More than 65 years old	P-value (Kruskal-Wallis)
Total number of severe asthma exacerbations	58	93	53	—
Gender (male, %)	34.5%	44.1%	45.3%	0.4206
Age (years)	27.2 ± 4.9*	52.1 ± 9.0**	75.9 ± 6.1***	<0.0001
Type of asthma (atopy, %)	82.8%	68.9% **	35.9% ***	<0.0001
Current smoker (%)	62.1%	43.1% **	9.4% ***	<0.0001
Onset of asthma (years)	10.8 ± 10.5*	32.8 ± 16.6**	50.4 ± 16.6***	<0.0001
Pet ownership (%)	55.2%	37.6% **	3.8% ***	<0.0001
Complications				
hypertension/heart disorder	0% *	29.0% **	52.8% ***	<0.0001
allergic rhinitis	53.5% *	15.1%	18.9% ***	<0.0001
atopic dermatitis	27.6%	20.4% **	1.9% ***	0.0012
sinusitis	15.5%	18.3%	20.8%	0.7744
diabetes mellitus	0%	9.7% **	22.6% ***	0.0005
aspirin-intolerant asthma (AIA)	3.5% *	29.0%	20.8%	0.0006
psychiatric disorder	5.2%	15.1%	7.6%	0.1141
COPD	0%	4.3% **	20.1% ***	0.0001
Prehospital severity				
Ratio of moderate/severe type (%)	51.7%	62.4%	71.7%	0.0963
severe persistent type	19.0%	48.4% **	49.1% ***	0.0005
moderate persistent type	32.8% *	14.0%	22.6%	0.0240
mild persistent type	17.2%	20.4%	22.6%	0.7741
intermittent type	31.0%	17.2%	5.7% ***	0.0024
Status of adherence to asthma treatment				
Ratio of irregular visits to a medical institution/none (%)	74.1% *	38.7%	20.1% ***	<0.0001
regular visits to a medical institution	25.9% *	61.2%	79.3% ***	<0.0001
irregular visits to a medical institution	39.7%	26.9%	15.1% ***	0.0152
none	34.5% *	11.8%	5.7% ***	0.0001
Prehospital treatments (%)				
oral corticosteroid	0% *	24.7%	22.6% ***	0.0002
ICS	25.9% *	60.2%	77.4% ***	<0.0001
SABA monotherapy as needed	24.1%	19.4%	3.8% ***	0.0105
no treatment	50.0% *	19.4%	17.0% ***	<0.0001
Days of hospitalization (days)	12.2 ± 8.4	16.1 ± 15.9	19.2 ± 13.6***	0.0084

P* < 0.05; 15-34 years old vs. 35-64 years old.*P* < 0.05; 35-64 years old vs. more than 65 years old.****P* < 0.05; more than 65 years old vs. 15-34 years old.

herence.^{27,28} Continuous ICS use is associated with a decreased numbers of emergency department visits²⁹ and asthma related deaths.^{2,30} Treatment adherence in the young age group was poor. However, 31% of patients in the young age group showed intermittent type asthma, which does not always require continuous treatment. Prehospital severity was classified on the basis of GINA guidelines and subjective symptoms and treatments. Patients with intermittent type asthma are not treated by continuous ICS use. We previously examined patients with intermittent asthma diagnosed on the basis of subjective symptoms. The percentage of patients classified into the mild asthma group by all of the results of the three

tests (FEV1 [% predicted], airway hyperresponsiveness to histamine dihydrochloride, and exhaled nitric oxide level) in patients with young adult asthma was only 20.6%.³¹ We showed that asthma severity classified on the basis of subjective symptoms may be underestimated in young adults. The difference in treatment adherence and asthma severity among the groups may be due to this underestimation. SABA monotherapy is related to rebound airway hyperresponsiveness,¹ worsening of asthma,³² and increased risk of asthma related death.³³ In the young age group, we consider that the strategies that remain to be carried out in asthma management are to decrease the numbers of patients without treatment and with

irregular visits to a medical institution, and to highlight the necessity of long-term management with medicines. The middle age group had high rates of aspirin-intolerant asthma. Furthermore, the middle age group had high rates of severe persistent asthma. Many studies have shown that aspirin intolerance is a risk factor for severe asthma.³⁴ In the middle age group, we consider that the problems remaining in asthma treatments are the correct management of risk factors for severe asthma including aspirin-intolerant asthma. It is necessary for us to identify patients with aspirin-intolerant asthma. The advanced age group had high rates of hypertension/heart disease, diabetes mellitus, and COPD. In patients with acute asthma brought to the emergency department, Tsai *et al.* reported that the number of patients with hypertension or diabetes or COPD was significantly higher among more than 55-year-old patients among than among 18-54.9-year-old patients.³⁵ The advanced age group showed good treatment adherence, but had high rates of severe persistent asthma. It was reported that elderly patients do not adhere to medication guidelines.³⁶ Elderly patients are not used to inhaled medications, and it is difficult for them to correctly use inhaled medications. It is necessary for doctors not only to prescribe medications, but also to confirm the correct use of inhaled medications. Moreover, elderly patients with asthma have various complications, and a high percentage of them succumbed to asthma related deaths.

This study has limitations that should be considered when interpreting the findings. There were many patients who did not visit our hospital before admission. Therefore, we were unable to evaluate their pulmonary function and bronchial hyperresponsiveness before admission. We determined prehospital asthma severity on the basis of only subjective symptoms, because no pulmonary function tests were performed. Moreover, Japanese people are a homogenous race. Therefore, racial differences that are generally considered to be aggravating factors are not considered. However, there are individual differences in socioeconomic background. In this study, we were unable to clarify the patient's socioeconomic background. A prospective large-scale clinical trial considering these limitations is essential in the future.

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