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ORIGINAL ARTICLE

Clinical Evaluation of Severe Asthma Attacks Requiring Tracheal Intubation and Mechanical Ventilation

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ABSTRACT

Background: Although the number of patients requiring hospitalization due to asthma attacks has decreased over the years, there are many who still require hospitalization for tracheal intubation and mechanical ventilation following a severe asthma attack. Therefore, we evaluated the characteristics of patients with asthma who required tracheal intubation and mechanical ventilation in our hospital.

Methods: We evaluated 20 patients who had severely exacerbated asthma, requiring tracheal intubation and mechanical ventilation. An evaluation was made based on their smoking history, the number of days from the onset of the asthma attack to admission, the level of asthma control, treatments before presenting to our hospital, the frequency of hospital visits, the reason for tracheal intubation and mechanical ventilation, and outcome.

Results: Of the 20 patients with asthma 13 were men and 7 women, with a mean age of 48.7 years. The characteristics of patients who required tracheal intubation and mechanical ventilation were as follows: ① smokers, ② not taking or irregularly taking medication, ③ using inhaled short-acting $\beta_2$agonist (SABA) alone as needed, and ④ not using inhaled corticosteroids (ICS).

Conclusions: Our findings suggest that treatment mainly using ICS, in addition to increased awareness of the dangers of asthma among the patients themselves, are important in preventing severe asthma attacks requiring tracheal intubation and mechanical ventilation.

KEY WORDS

bronchial asthma, mechanical ventilation, SABA, smoking, tracheal intubation

INTRODUCTION

Bronchial asthma is a common chronic inflammatory condition characterized by variable airway narrowing and hyper-responsiveness due to an underlying inflammatory process and bronchial structural change. The clinical manifestations of asthma are daily respiratory symptoms which affect the patient's quality of life. During an asthma attack, these symptoms become more severe and can endanger the patient's life.

The prevalence of asthma in adults was reported to be about 3.2% in Japan.[1] Since the establishment of the Asthma Prevention and Management Japanese Guideline (JGL) in 1993, the number of inpatients with a severe asthma attack has decreased in Japan. However, there are still many who visit emergency wards due to a severe asthma attack. The fatality rate of asthma for every 100,000 population has decreased and was approximately 2.6 in 2004.[1] The widespread use of inhaled corticosteroids (ICS) for long-term asthma management is considered to be an important factor for these improvements although there are still many who require tracheal intubation and mechanical ventilation following a severe asthma attack.

We evaluated the characteristics of 20 patients with asthma who required tracheal intubation and mechanical ventilation in our hospital to determine how this could be prevented.

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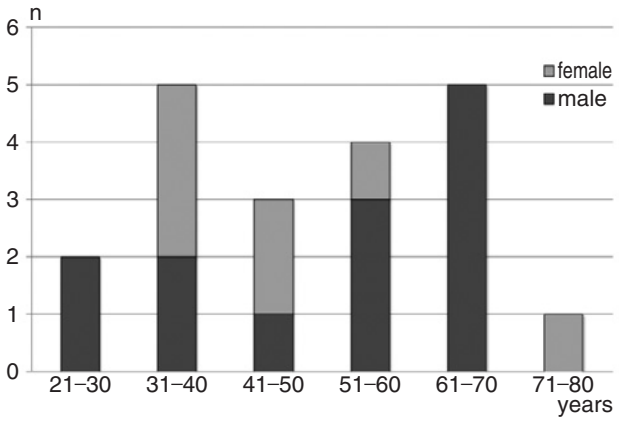

Fig. 1 Age distribution chart ($n = 20$).

Table 1 Patient characteristics

Characteristics	Subjects ($n = 20$)
Male, n (%)	13 (65)
Age (yesrs), mean ± SD	48.7 ± 6.9
Types of asthma, n (%)	
Atopic	9 (45)
Nonatopic	11 (55)
Current smoker, n (%)	14 (70)
(male/female)	(8/6)
History of child asthma, n (%)	9 (45)
Serum IgE (IU/ml), mean ± SD	684 ± 635
Number of days from the asthma attack onset (days), mean ± SD	2.2 ± 0.7
History of tracheal intubation and respirator management, n (%)	1 (5)
Aspirin intolerant asthma, n (%)	0 (0)

METHODS

SUBJECTS

We selected 20 patients with asthma who visited our hospital from January 2001 to December 2005 and required tracheal intubation and mechanical ventilation. All patients had severely exacerbated asthma, as determined by the guidelines set by the Global Initiative for Asthma (GINA) 2002,[2] and required tracheal intubation and mechanical ventilation. We evaluated their smoking history, the number of days from the onset of the asthma attack to admission, the level of asthma control as determined by the GINA 2002 guidelines, treatments given prior to the hospital visit, the frequency of hospital visits, the reason for tracheal intubation and mechanical ventilation, based on the Asthma Prevention and Management Japanese Guideline (JGL) 2003, and their prognosis.

TYPE OF ASTHMA

The type of asthma was determined based on the JGL 2003 classification. A marker of atopic asthma in JGL 2003 suggests the presence of specific IgE antibodies to environmental allergens.

ASTHMA SEVERITY

We evaluated the severity of asthma by interviewing patients, their family or both. The severity of asthma was classified into four categories, intermittent, mild persistent, moderate persistent, and severe persistent in accordance with the classification of control levels based on GINA 2002.

RESULTS

BACKGROUND FEATURES

Of the 20 patients with asthma 13 were men (65%) and 7 women (35%), with an age range of 21–79 years, and mean age of 48.7 years (Fig. 1). The types of asthma were atopic in 9 patients (45%) and nonatopic in 11 patients (55%), and 14 patients (70%) were current smokers. Six of the 7 women were current smokers under the age of 60. Of the 13 male patients, 8 were current smokers of which 5 were under 60. A total of 9 patients had a history of childhood asthma. All patients were admitted to our hospital through the emergency ward. The mean number of days from the onset of the asthma attack to admission was 2.2 days (range, 1–7 days). One patient had a history of tracheal intubation and mechanical ventilation for a severe asthma attack (5%). No patient had aspirin intolerant asthma (Table 1).

The most common cause triggering the asthma attack was infection (Fig. 2).

The reasons for tracheal intubation and mechanical ventilation, in accordance with the JGL2003, were as follows: PaO_2 was less than 50 torr despite maximum oxygen administration (6 patients [30%]); a sudden increase in $PaCO_2$ followed by loss of consciousness (4 patients [20%]); both of the above (5 patients [25%]); extensive ventilatory disturbance or cardiorespiratory arrest (5 patients [25%]) (Fig. 3).

ASTHMA SEVERITY

The severities of asthma before admission due to a near-fatal asthmatic attack were as follows: intermittent (8 patients [40%]); mild persistent (5 patients [25%]); moderate persistent (6 patients [30%]); severe persistent (1 patient [5%]). As for the severity of asthma before presenting, those with mild persistent asthma accounted for over 65% (Fig. 4).

STATUS OF ADHERENCE TO ASTHMA TREATMENT

The status of patient adherence was as follows: no treatment (6 patients [30%]); irregular visits to a clinic (7 patients [35%]); regular visits to a medical institution (7 patients [35%]). Those who did not undergo treatment and visited a clinic irregularly accounted for 65% of the patients (Fig. 5).

The treatments undergone by patients before be-

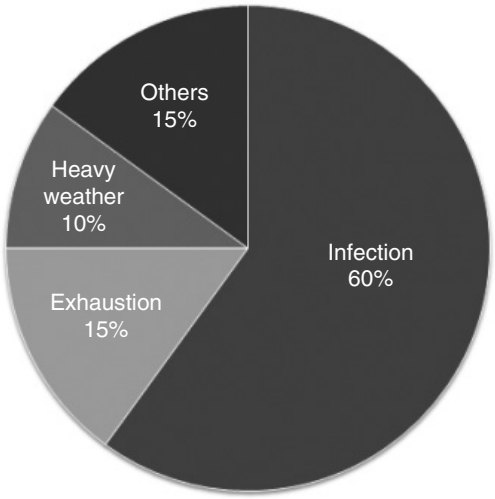

Fig. 2 Causes triggering asthma attacks ($n = 20$).

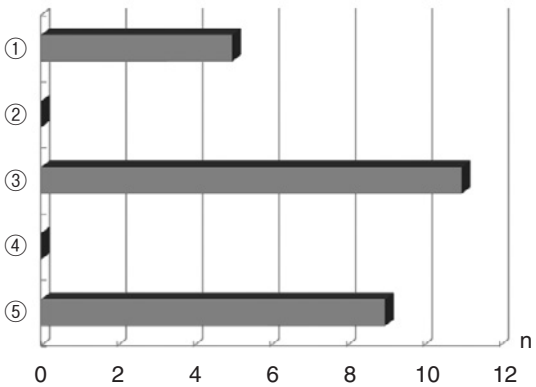

Fig. 3 Reasons for tracheal intubation and respirator management in accordance with the JGL 2003. 1, extensive ventilatory disturbance or cardiorespiratory arrest; 2, clear respiratory muscle fatigue; 3, PaO_2 of less than 50 torr despite maximum oxygen administration; 4, $PaCO_2$ increasing to more than 5 torr for 1 hour; 5, sudden increase in $PaCO_2$ followed by loss of consciousness.

ing admitted to our hospital were as follows: no treatment (6 patients [30%]); using short-acting inhaled β_2 agonists (SABA) alone as needed (7 patients [35%]); continuous use of oral theophylline and use of SABA as needed (5 patients [25%]); continuous use of ICS and leukotriene receptor antagonists (LTRA) (1 patient [5%]); continuous use of ICS, long-acting inhaled β_2 agonists (LABA), oral theophylline, and LTRA (1 patient [5%]) (Fig. 6). Only 2 patients (10%) used ICS continuously.

OUTCOME

Two patients (10%) died despite tracheal intubation, respirator management, and intensive drug therapy. These 2 patients had cardiorespiratory arrest immediately after arrival at the hospital.

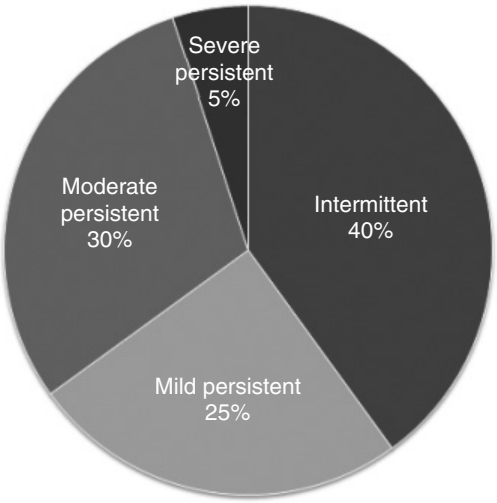

Fig. 4 Asthma severity before a near-fatal attack. The classification of asthma control was determined from the GINA 2002 guidelines ($n = 20$).

DISCUSSION

Patients who required tracheal intubation and mechanical ventilation had the following characteristics: ① smokers, ② not taking or irregularly taking medication, ③ using SABA alone as needed, and ④ not using ICS.

In recent years, the prevalence of asthma has been increasing. On the other hand, the fatality rate of asthma for every 100,000 population has decreased and was approximately 2.6 in 2004.[1] The reasons for the decrease in the fatality rate of asthma are the establishment of the Asthma Prevention and Management Japanese Guidelines in 1993, and the widespread use of inhaled glucocorticosteroids as medication for long-term management. However, more than 3,000 patients still die annually in Japan. According to a report by the Japanese Society of Allergology, the risk factors for asthma death are advanced age, male gender, severe asthma, nonatopic type asthma, and previous hospitalization for a near-fatal asthma attack. Concerning the time and place of death, 28.9% died before arrival, 19.4% died in the emergency room, and 38.6% died during hospitalization.[3] We evaluated the risk factors in the 20 patients who required tracheal intubation and respirator management because of a severe asthma attack in our hospital, as identifying such risk factors may lead to the prevention of a severe asthma attack.

Patients consisted of many men. In Japan, more men than women have died from asthma in the past 30 years. However, the number of male deaths was slightly lower than that of female deaths in 2002. The result of this study showed there have been more cases of men with near-fatal attacks than women. The

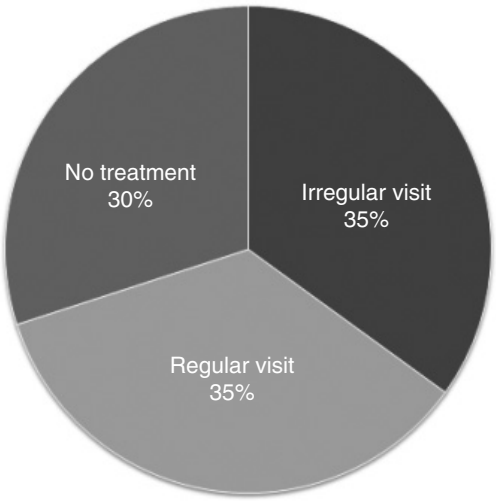

Fig. 5 Frequencies of hospital visits ($n = 20$).

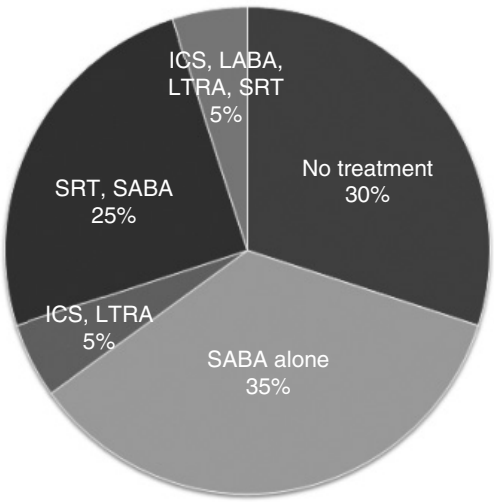

Fig. 6 Treatments undergone by patients before presenting to our hospital ($n = 20$). SRT, slow-release theophylline.

smoking rate is higher in men than in women. The subjects of this study included many smokers, of which there were more men. Most of the men were over 60 years old. Moreover, we believe that men show poor adherence as a result of work and consider this the reason why there are many cases of men having severe attacks.

The reason for this is yet to be clarified. Additional studies will need to be carried out in the future to investigate this issue.

Seventy percent of the patients were smokers. In particular, 6 of the 7 women were current smokers and under the age of 60. Many fatal asthma cases are over the age of 60 in Japan.[1] It is suggested that smoking in women is a risk factor for near-fatal asthma. A recent study has shown that smoking suppresses the efficacy of glucocorticosteroids. Cigarette smoking is responsible for the development and persistence of airway inflammation. In general, patients with asthma are negatively affected by cigarette smoke. Even nonsmoking patients with asthma may have significant exposure to passive smoke.[4]

For example, acute exposure to cigarette smoke triggers bronchoconstriction and symptoms in people with asthma.[5,6] Active cigarette smoking has detrimental effects on asthma morbidity. Compared with nonsmokers with asthma, smokers with asthma have more severe symptoms,[7,8] such as increased number of hospitalization,[9] accelerated decline in lung function,[10,11] and impaired therapeutic responses to inhaled[12,13] and oral corticosteroids.[14]

Particularly high rates of smoking have been noted in adults admitted to emergency departments with acute asthma.[9] It was reported that asthmatic symptoms and bronchial hyperreactivity improved after smoking cessation.[15] Furthermore, it was reported that the response to ICS is attenuated in mild asthma patients who smoke.[16] It was considered that smoking exacerbated asthma in patients.

As for the severity of asthma before the near-fatal attack, most of the patients had intermittent asthma, and those with severe persistent asthma were fewest. These results suggest that a severe asthma attack can occur in any type of patient regardless of the frequency of asthma attack. Regarding the frequency of hospital visits, 65% had received no treatment and visited a hospital only irregularly. Regarding treatment before visiting our hospital, 65% had received no treatment and only used SABA alone as needed.

SABAs have been associated with rebound hyperresponsiveness,[17] worsening of severity,[18,19] and increased risk of death.[20] Available evidence suggests that the more recently introduced LABAs do not increase the risk of death,[21] while the use of ICS is associated with a reduction in mortality.[22,23] The results of this study are consistent with those of previous reports. The tendency for increased deaths in patients with prescribed β-agonists alone and fewer deaths in those taking β-agonists with inhaled corticosteroids have been reported.[24]

Moreover, we observed that the daily control of airway inflammation is important. At present, it is considered that ICS is the most important medicine for long-term management of asthma. It was also reported that the numbers of emergency visits and hospitalizations due to asthma have decreased.[25-27] However, there were only 2 patients in our study who used ICS (10%). This emphasizes the importance of ICS for long-term management of asthma. There is evidence showing that early treatment of asthma with ICS may help to prevent chronic airway obstruction.[28] The latter report supports the current asthma treatment strategy advocating the early introduction of ICS. However, little is mentioned concerning this, and therefore, further accumulation of cases is neces-

sary. Cushley[29] and Stableforth[30] stated that sufficient educational guidance, so that the patients themselves can clearly understand the severity of seizures, is necessary to prevent death due to asthma. Therefore, we believe that educating patients about the management and treatment of asthma is important. Understanding the terror of an asthma attack through experience is insufficient. We consider basic pathologic explanation of asthma using simple pamphlets to be effective as it is important to gain knowledge about asthma. Moreover, we consider that self-management is important to make patients think about the management of asthma attacks. We instructed patients to record their symptoms and measure their peak flow everyday (PEF), thus enabling them to take note of the aggravation of symptoms and decrease in PEF. An early visit to a medical institution is also crutial and we strongly advised regular hospital visits to confirm guidance results, as monitoring the progress of these effects is necessary.

Mechanical ventilation can improve poor prognosis of patients with severe asthma, and it is an important means of preventing asthma death. Since tracheal intubation and mechanical ventilation can open the airway and provide effective oxygenation, they can increase the effective alveolar ventilation volume and facilitate breathing. However, tracheal intubation also has risks in addition to the fact that high-pressure ventilation using a mechanical ventilation may promote barotrauma. Therefore, the adaptation of a patient to tracheal intubation and mechanical ventilation must be strictly determined. In this study, 2 out of the 20 patients died (10%), both from cardiorespiratory arrest immediately after their arrival at the hospital. Mechanical ventilation and tracheal intubation are effective means of treating a lethal asthma attack if the adaptation of a patient to these interventions can be determined adequately.

Our findings suggest that treatment using mainly ICS in addition to increased awareness of the dangers of asthma among patients themselves are important in preventing a severe asthma attack requiring tracheal intubation and mechanical ventilation.

REFERENCES

1. Ministry of Health and Welfare, Immunology and Allergy Study Group. *[Asthma Prevention and Management Guideline 2003, Japan]*. Tokyo: Kyowa Kikaku, 2004 (in Japanese).
2. Global Initiative for Asthma (GINA). *Global Strategy for Asthma Management and Prevention*, Revised edn. National Heart, Lung and Blood Institute/World Health Organization, 2002.
3. Nakazawa T, Dobashi K. Current asthma deaths among adults in Japan. *Allergol Int* 2004;**53**:205-9.
4. Chaudhuri R, Livingston E, McMahon AD *et al*. Effects of smoking cessation on lung function and airway inflammation in smokers with asthma. *Am J Respir Crit Care Med* 2006;**174**:127-33.
5. Higenbottam TW, Feyeraband C, Clark TJ. Cigarette smoking in asthma. *Chest* 1980;**74**:279-84.
6. Nadel JA, Tierney DF. Effect of a previous deep inspiration on airway resistance in man. *J Appl Physiol* 1961;**16**: 717-9.
7. Siroux V, Pin I, Oryszcyn MP, Le Moual N, Kauffmann F. Relationships of active smoking to asthma and asthma severity in the EGEA study. *Eur Respir J* 2000;**15**:470-7.
8. lthuis M, Sexton M, Prybylski D. Cigarette smoking and asthma symptom severity among adult asthmatics. *J Asthma* 1999;**36**:257-64.
9. Silverman RA, Boudreaux ED, Woodruff PG, Clark S, Camargo CA Jr. Cigarette smoking among asthmatic adults presenting to 64 emergency departments. *Chest* 2003; **123**:1472-9.
10. Apostol G, Jacobs D, Tsai A *et al*. Early life factors contribute to the decrease in lung function between ages 18 and 40. *Am J Respir Crit Care Med* 2002;**166**:166-72.
11. Lange P, Parner J, Vestbo J, Schnohr P, Jensen G. A 15-year follow-up study of ventilatory function in adults with asthma. *N Engl J Med* 1998;**339**:1194-200.
12. Chalmers GW, Macleod KJ, Little SA, Thomson LJ, McSharry CP, Thomson NC. Influence of cigarette smoking on inhaled corticosteroid treatment in mild asthma. *Thorax* 2002;**57**:226-30.
13. Tomlinson JEM, McMahon AD, Chaudhuri R, Thompson JM, Wood SF, Thomson NC. Efficacy of low and high dose inhaled corticosteroid in smokers versus non-smokers with mild asthma. *Thorax* 2005;**60**:282-7.
14. Chaudhuri R, Livingston E, McMahon AD, Thomson L, Borland W, Thomson NC. Cigarette smoking impairs the therapeutic response to oral corticosteroids in chronic asthma. *Am J Respir Crit Care Med* 2003;**168**:1308-11.
15. Thomson NC, Chaudhuri R, Livingston E. Asthma and cigarette smoking. *Eur Respir J* 2004;**24**:822-33.
16. Lazarus SC, Chinchilli VM, Rollings NJ *et al*. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma. *Am J Respir Crit Care Med* 2007;**175**:783-90.
17. Vathenen AS, Knox AJ, Higgins BG, Britton JR, Tattersfield AE. Rebound increase in bronchial responsiveness after treatment with inhaled terbutaline. *Lancet* 1988;**1**: 554-8.
18. Sears MR, Taylor DR, Print CG *et al*. Regular inhaled beta-agonist treatment in bronchial asthma. *Lancet* 1990; **336**:1391-6.
19. Van Schayck CP, Dompeling E, van Herwaarden CL *et al*. Bronchodilator treatment in moderate asthma or chronic bronchitis: continuous or on demand? A randomised controlled study. *BMJ* 1991;**303**:1426-31.
20. Spitzer WO, Suissa S, Ernst P *et al*. The use of beta-agonists and the risk of death and near death from asthma. *N Engl J Med* 1992;**326**:501-6.
21. Meier CR, Jick H. Drug use and pulmonary death rates in increasingly symptomatic asthma patients in the UK. *Thorax* 1997;**52**:612-7.
22. Lanes SF, Garcia Rodriguez LA, Huerta C. Respiratory medications and risk of asthma death. *Thorax* 2002;**57**: 683-6.
23. Suissa S, Hemmelgarn B, Blais L, Ernst P. Bronchodilators and acute cardiac death. *Am J Respir Crit Care Med* 1996;**154**:1598-602.
24. Anderson HR, Ayres JG, Sturdy PM *et al*. Bronchodilator treatment and deaths from asthma: case-control study. *BMJ* 2005;**330**:117-20.
25. Pauwels RA, Pederson S, Busse WW *et al*. Early interven-

tion with budesonide in mild persistent asthma: a double randamised, double-blind trial. *Lancet* 2003;**361**:1071-6.
26. Haahtela T, Jarvinen M, Kava T *et al*. Effects of reducing or discontinuing inhaled budesonide in patients with mild asthma. *N Eng J Med* 1994;**331**:700-5.
27. Williams LK, Pladevall M, Xi H *et al*. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 2004;**114**:1288-93.
28. Selroos O, Pietinalho A, Löfroos AB, Riska H. Effect of early vs late intervention with inhaled corticosteroids in asthma. *Chest* 1995;**108**:1228-34.
29. Cushley MJ, Tattersfield AE. Sudden death in asthma: discussion paper. *J R Soc Med* 1983;**76**:662-6.
30. Stableforth D. Death from asthma. *Thorax* 1983;**38**:801-5.