

Recent Trends and Future Issues of Asthma Mortality in Japan

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ABSTRACT

Analysis of data on asthma deaths from the vital statistics throughout Japan and deaths from asthma attacks in six prefectures of Tohoku district provided information on recent trends and insight into possible future issues about asthma deaths in Japan. The vital statistics throughout Japan show a favorable downward trend in the number of asthma deaths in Japan since 1997. In particular, the asthma mortality rate among persons aged 5 to 34 years was less than 0.3 per 100,000 in 2001. In addition, the number of deaths from asthma attacks decreased more rapidly in the Tohoku district and the rate of reduction was correlated with an increase in the sales of inhaled corticosteroids and anti-leukotrienes but not in the sales of inhaled short-acting β -agonists. Moreover, in the 5 year period from 1997 through 2001 it was clear that the number of asthma deaths in persons 75 years and older and those 60 years and older accounted for 61–66% and 86–88%, respectively, of the deaths in persons of all ages. Therefore, the most important future issue about asthma deaths in Japan should be to focus efforts on decreasing the number of asthma deaths in older persons.

KEY WORDS

anti-leukotrienes, asthma death, deaths from asthma attacks, inhaled corticosteroids, inhaled short-acting β -agonists, Tohoku district, vital statistics

INTRODUCTION

Japanese vital statistics supplied by the Department of the Ministry of Health, Labour and Welfare of Japan show a gradual reduction in the number of asthma deaths since the 1950s. During the same periods, however, the number of deaths in the 5- to 34-year-old-age group showed two 'epidemics' that occurred at the same time as similar epidemics in some other countries. It has been suggested that these epidemics occurred in parallel with the increase in the total sales of two different β -adrenergic agonists.^{1,2} There were increased sales for isoprenaline during the first epidemic and for fenoterol during the second epidemic. In addition, the mortality rate in the 5- to 34-year-old group was disproportionately higher in Japan than in the other countries with similar epidemics.³ While the mortality rate decreased significantly during the late 1990s, the case-fatality rate remained greater in Japan than in other countries.⁴

This report summarizes an analysis of data on the annual number of asthma deaths obtained from Japanese vital statistics and the annual number of deaths

due to asthma attacks obtained from a questionnaire survey in the Tohoku district from 1992 to 2001.⁵ This report revealed the following data ; 1) a recent change in asthma deaths in the 5- to 34-year-old-age group of Japan, 2) an association with the annual number of deaths from asthma attacks over the period 1992–2001 and the sales of anti-asthmatic agents in the Tohoku district, and 3) a summary of the characteristics of asthma mortality in Japan.

THE RECENT CHANGE IN ASTHMA DEATHS IN 5- TO 34-YEAR-OLDS IN JAPAN

Among the 5- to 34-year-old age group in Japan, more than 300 persons died due to asthma yearly prior to 1996 ; however, the number declined dramatically in both males and females beginning in 1997, reaching 116 in 2001 (Fig. 1). The asthma mortality rate per 100,000 in persons aged 5 to 34 years was less than 0.3 in 2001, the same level as in advanced countries in Europe and North America.⁴

In the Tohoku district during 1992–2001, the greatest number of asthma deaths in persons younger than 40 years old was among persons 10 to 20 years

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Received 16 April 2004.

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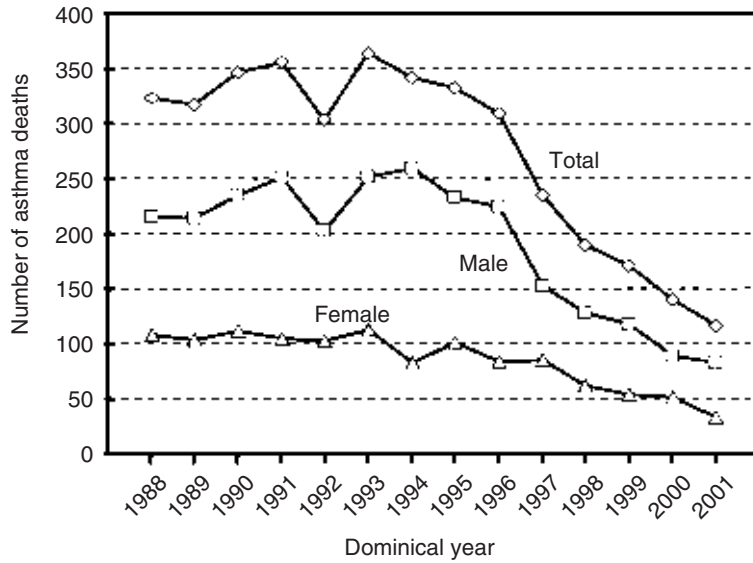


Fig. 1 Annual number of asthma deaths in the 5- to 34-year-old age group in Japan over the period 1988–2001.

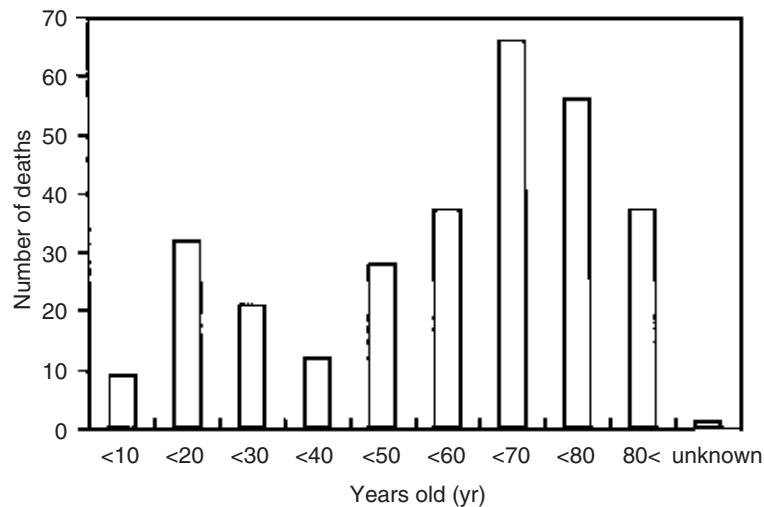


Fig. 2 Ages of patients at the time of death due to an asthma attack in the Tohoku district.

old, and the next greatest number was among those 20 to 30 years old (Fig. 2). Increased risk of asthma death in puberty and adolescence has been previously noted.⁶ In addition, it has been postulated that reduced chemosensitivity to hypoxia and blunted perception of dyspnea may predispose these patients to fatal asthma attacks.⁷ Therefore, young people should be educated more aggressively about asthma severity and risk of death.

ASSOCIATION OF YEARLY DEATHS FROM ASTHMA WITH SALES OF ANTI-ASTHMATIC AGENTS IN THE TOHOKU DISTRICT : 1992–2001

The annual number of deaths from asthma attacks and the corresponding sales of inhaled corticosteroids, anti-leukotrienes, and inhaled short-acting β -agonists (SABA) in the Tohoku district during 1992–2001 are shown in Figure 3. Annual data on the sales of asthma medications were obtained from IMS Japan KK. One of the most interesting trends was that ob-

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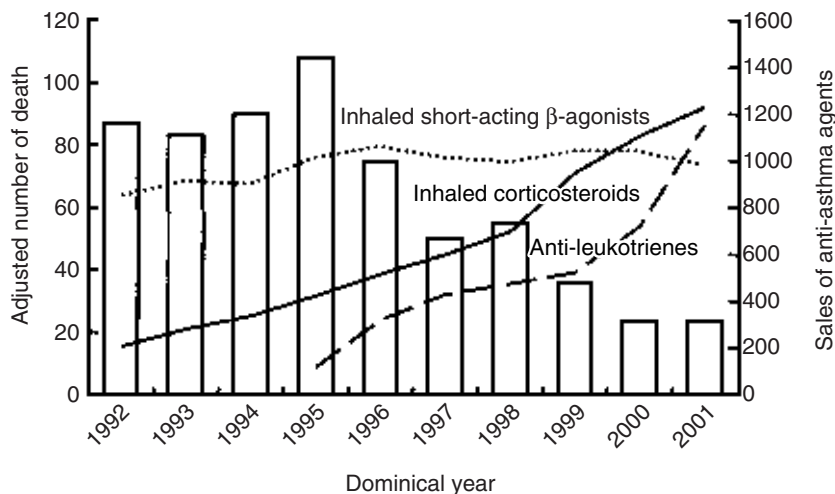


Fig. 3 Adjusted number of deaths due to asthma attacks over the period 1992–2001 and sales of anti-asthma agents in the Tohoku district.

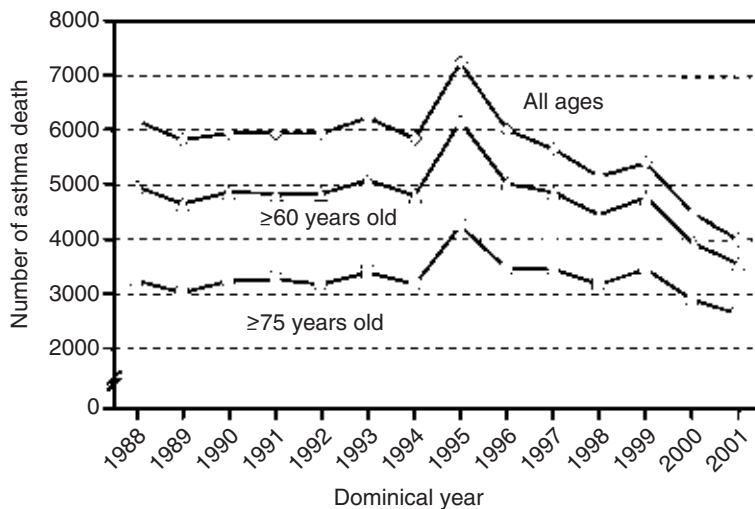


Fig. 4 Annual number of asthma deaths in persons of all ages, ≥ 60 years old, and ≥ 75 years old from 1988 to 2001 in Japan.

served with the anti-leukotriene, pranlukast. In 1995, the number of deaths due to asthma attacks in the Tohoku district was the highest and pranlukast, a CysLT1 receptor antagonist, was first marketed in Japan at this time. The number of deaths decreased substantially beginning in 1997, which coincided with the increased use of pranlukast. In 2001, the sales of anti-leukotrienes increased nearly sixfold and the number of deaths decreased to almost one-fourth compared with that in 1996. While the sales of inhaled corticosteroids increased about threefold from 1992 to 1998 and about twofold from 1998 to 2001, the number of deaths decreased almost one-half from 1992 to 1998 and another one-half from 1998 to 2001. By contrast, the sales of inhaled SABA were almost uniform for these 10 years. Thus, there were no rela-

tionships between the sales of inhaled SABA and the decrease in the number of deaths in the Tohoku district. The sales of other anti-asthmatic agents, such as sustained-release theophylline, long-acting β -agonists, and anti-allergy medications, were irrelevant to the decrease in the number of death due to asthma attacks.

Because the population-based epidemiological study based on an ecological design did not make any direct connection between individual subjects who used specific medications and the absence of fatal asthma attacks, these results must be interpreted with caution. However, the same protective effect of inhaled corticosteroids on asthma mortality has been reported in New Zealand,⁸ Israel,⁹ and Japan,¹⁰ and their prophylactic effect was recently confirmed in a

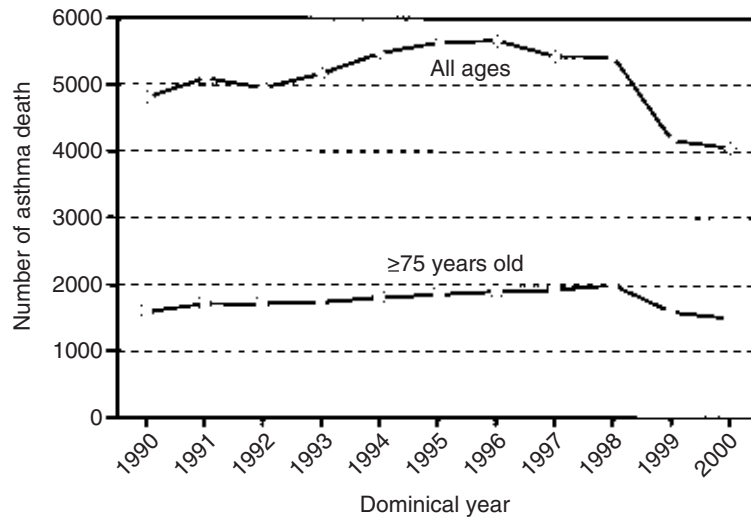


Fig. 5 Annual number of asthma deaths in persons of all ages and ≥ 75 years old from 1990 to 2000 in the United States. Data were obtained from <http://wonder.cdc.gov/mortSQL.html>

case-control study.¹¹ On the other hand, our finding that an increase in the sales of anti-leukotrienes was related to a decrease in the number of deaths due to asthma attacks supports Suissa's finding¹⁰ that the sharpest decrease in asthma mortality among 5- to 34-year-olds followed the introduction of pranlukast. The anti-inflammatory effect of inhaled corticosteroids and the prophylactic effect of anti-leukotrienes on asthma exacerbations¹² together appeared to decrease the number of deaths from asthma in the Tohoku district.

Although the two epidemics in asthma mortality have been reported to parallel the increase in the total sales of β -adrenergic agonists, we found no relationships between the sales of inhaled SABA and the number of deaths due to asthma attacks in the Tohoku district. One of the most practical and useful ways by which a clinician can identify high-risk asthmatic patients is to find those requesting repeat prescriptions of two or more β -adrenergic receptor agonist inhalers per month.¹³ Therefore, our finding suggests that appropriate use of inhaled SABA does not appear to be associated with deaths due to asthma attacks.

CHARACTERISTICS IN ASTHMA MORTALITY OF JAPAN

Data on the number of asthma deaths in the total population, in persons ≥ 60 years old, and in those ≥ 75 years old from 1988 to 2001 in Japan (Fig. 4) show that deaths in persons ≥ 75 years old account for $>50\%$ of all asthma deaths, particularly during the period from 1997 to 2001, when it accounted for 61–66%. In addition, deaths among those ≥ 60 years old accounted for $>80\%$ of all asthma deaths, particularly

from 1997 to 2001, when it accounted for 86–88%. In France the presence of asthma has been reported to increase the mortality rate in those >65 years old,¹⁴ and the recent increase of asthma deaths in the United States has been reported to be due to the increase in the population of women >65 years old.¹⁵ However, analysis of these numbers was undertaken by obtaining data from the Internet on the number of asthma deaths in the United States.¹⁶ In the United States, as shown in Figure 5, the number of asthma deaths among all ages was about 90–100% of the number in Japan in each calendar year, and the number of deaths in those ≥ 75 years old accounts for approximately one-third of all asthma deaths. Because the U.S. population is about twice the Japanese population, on the basis of this population ratio, the number of asthma deaths in Japan was twice that in the United States among all ages and four times that in persons ≥ 75 years old.

CONCLUSION

While the total number of deaths due to asthma in Japan has declined over the last decade, there is still a higher mortality rate among Japan's adolescents and elderly. Given the prevalence of asthma mortality in these two groups, improvements in the diagnosis, treatment, and management of asthma in general and in particular, in the older population is crucial for order to decreasing the total number of asthma deaths in Japan. Specifically, we should take the following steps: 1) establish more precise asthma diagnoses in general, and especially in older persons, with particular care to exclude COPD¹⁷ and aspiration pneumonia; 2) use anti-inflammatory therapy more widely, and particularly among older persons with asthma;

3) make an aerosol formulation of corticosteroids available for older persons ; and 4) develop management tools specifically for older patients that do not require significant physical effort such as pulmonary function tests.

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