Decline in Asthma Prevalence and Severity in Israel over a 10-Year Period

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Key Words

Asthma · Prevalence · Inhaled corticosteroids · Aeroallergens · Pollution

Abstract

Background: The prevalence of asthma has increased in western countries towards the end of the last century, but recently seems to have stabilized. **Objective:** To evaluate trends in the prevalence and severity of asthma that occurred in Israel over the past decade. **Methods:** The medical records of 17-year-old boys, eligible for national service, between 1999 and 2008 were reviewed. National annual hospitalization and death rates for asthma were extracted. **Results:** Three hundred thousand medical records were reviewed. During the study period, lifetime asthma prevalence decreased from 9.7 to 8.1% ($p = 0.002$). The point prevalence of moderate-to-severe and mild persistent asthma decreased significantly from 0.88 and 3.41% to 0.36 and 2.44%, respectively, during this period. The prevalence of intermittent asthma and asthma in clinical remission for more than 3 years did not change significantly. The annual hospitalization rate for asthma decreased from 13.0 to 7.5 per 10,000 population ($p < 0.0001$), whilst the annual death rate due to asthma decreased between 1999 and 2008 from 2.1 to 1.4

per 100,000 population ($p = 0.003$). **Conclusions:** The prevalence of asthma in Israeli teenage boys decreased significantly over the last decade. In addition, asthma hospitalization and asthma-related death rates in the total population also decreased.

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Introduction

The worldwide prevalence of asthma dramatically increased in the last 30 years of the 20th century [1]. This was also been the case for Israel, where the lifetime prevalence of asthma in 17-year-old boys also increased from 7.9% in 1986 to 9.6% in 1990 [2]. Since 1995 however, the prevalence of asthma and its related morbidity and mortality appears to have plateaued and may even have decreased in some western countries [3–6]. The reasons for the changes in trends of asthma prevalence and severity are probably multiple [3] and may theoretically have involved improved access to appropriate medical care, increasing use of inhaled corticosteroids (ICS) [7], changes in outdoor air pollution levels [8], reduced active and passive exposure to tobacco smoke [9–13], and reduced concentrations of airborne pollen allergens [14–17].

In this study, we evaluated the trends in asthma prevalence and severity in Israel from 1999 to 2008. We therefore studied the rates of asthma in a cohort of 17-year-old boys presenting to recruitment offices for national service during the study period. We also reviewed the Israeli Ministry of Health National Registry of annual hospitalizations and death rates related to asthma during the same period.

Patients and Methods

Subject Cohort

We reviewed the medical records of a cohort of 17-year-old males who underwent a comprehensive medical evaluation for eligibility for national service between 1999 and 2008, with regard to the diagnosis and the severity of asthma. Medical records are based on information obtained from the family physician, medical history obtained from all subjects, including the frequency and severity of asthma symptoms, as well as use of asthma medications and a physical examination. Spirometry, exercise and, where indicated, methacholine challenge tests were performed in all patients with reported or suspected asthma. Exercise and methacholine challenge tests were performed according to the American Thoracic Society Guidelines [18]. The presence and severity of asthma (as defined below) are recorded as a numerical code in a central database. For each month in the study period (10 years, 120 months), we were only allowed to examine the medical records of the first 2,500 recruits. The numerical codes allowed asthma severity to be classified as outlined below.

(1) Asthma in remission: physician-documented history of asthma in the past but no symptoms of asthma and no use of any asthma medication during the last 3 years. Normal physical examination, normal spirometry results (FEV_1 and $FEV_1/FVC > 80\%$), a negative exercise challenge test (defined as a fall of $< 10\%$ in FEV_1 following exercise challenge test) and a negative methacholine challenge ($PC_{20} > 8$ mg/ml).

(2) Intermittent asthma: infrequent asthma symptoms, requiring only intermittent β_2 agonist therapy with normal physical examination, normal spirometry and a negative exercise challenge test.

(3) Mild persistent asthma: asthma controlled by regular controller medication (ICS or leukotriene antagonists) and/or mildly reduced baseline FEV_1 (70–80% predicted) and/or positive exercise challenge test.

(4) Moderate-to-severe persistent asthma: asthma uncontrolled by regular controller medication and/or reduced baseline lung function with $FEV_1 < 70\%$ despite adequate controller medication and/or severely positive exercise challenge test (defined as a fall of $> 35\%$ in FEV_1).

The criteria for asthma severity classification are similar but not identical to the current GINA classification [19], but were in use at the time the database was created, and did not change during the period of the study (1999–2008).

Asthma-Related Hospital Admissions

Data were obtained from the National Hospital Discharges Database of the Ministry of Health Information Department. The database includes more than 90% of all hospitalizations throughout

the country and collects demographic information, admission and discharge dates at specific hospital sites, as well as all information regarding patient diagnoses. We attributed hospitalization to asthma when the first discharge diagnosis (based on the International Classification of Diseases, Ninth Revision; ICD-9) was listed as the ICD9 code 493.xx. Based on these records, we calculated the total annual asthma-related hospitalization rates for ages 5–74 years and for each decade of life (5–14, 15–24, etc. up to 65–74 years) in both genders, for the years 1999–2008. These rates do not express the risk for a given patient with asthma to be admitted during a given year, but the percentage of all hospitalized patients admitted for an asthma-related diagnosis.

Asthma Death Rate

Data were obtained from the Central Bureau of Statistics of Israel (Registry of Causes of Death). This database is based upon death certificate coding data. For the purposes of this study, death was attributed to asthma when the cause of death on the death certificate was: 'asthma', 'asthma exacerbation' or 'status asthmaticus' (based on the International Classification of Diseases, Tenth Revision; ICD-10). We calculated the total annual asthma death rates for ages 0–74 years and also for each age group (0–44, 45–64 and 65–74 years) during the years 1999–2008. A 3-year moving average of the rates was calculated.

Rate of ICS Sales

Annual sales records of corticosteroid inhalers between 2000 and 2008 were retrieved from one of the four national health maintenance organizations in our country. We recorded the total number of ICS (all inhalers which contain corticosteroids alone or combined with long-acting β -agonist) sold per year, as well as the number of patients purchasing ICS per year.

Statistical Analysis

The prevalence and 95% confidence intervals (CIs) of lifetime asthma, asthma in remission, intermittent asthma, mild persistent and moderate-to-severe asthma, were calculated for each year. A p value < 0.05 was considered significant. Statistical analyses were performed using SPSS version 17.0. CIs were calculated for asthma prevalence and severity. Linear regression analysis was applied to the data analyzing the annual prevalence and severity of asthma in 17-year-old boys, annual hospitalization and death rates for asthma. The independent variable was the year (1999–2008). The square correlation coefficients (R^2 linear) and its significance were calculated for each data set. The Israel Defence Force Medical Corps Review Board gave its approval for this study and it waived the need for informed consent because the anonymity of all participants was respected.

Results

Population Cohort

We reviewed three hundred thousand medical records. Over the 10-year period from 1999 to 2008, the average lifetime prevalence (defined as any diagnosis of asthma at some point in time) for asthma was 8.8%. Among patients in the cohort with lifetime asthma, 22%

Fig. 1. Lifetime asthma prevalence in 17-year-old boys for the years 1999–2008 ($p = 0.002$, R^2 linear = 0.70). Data shown are mean $\pm$ 95% CI.

were in clinical remission during the last 3 years, 37% were classified as having mild intermittent asthma, 36% as having mild persistent asthma and 5% as having moderate-to-severe persistent asthma.

Lifetime asthma prevalence decreased steadily, from 9.69% (95% CI 9.37–10.01) in 1999 to 8.12% (95% CI 7.81–8.44) in 2008 ($p = 0.002$, $R^2 = 0.70$; fig. 1). The point prevalence of moderate-to-severe persistent asthma decreased from 0.88% (95% CI 0.78–0.98) in 1999 to 0.36% (95% CI 0.29–0.43) in 2008 ($p = 0.006$, $R^2 = 0.62$). This represents a 60% fall in this group. The point prevalence of mild persistent asthma fell from 3.41% (95% CI 3.21–3.60) to 2.44% (95% CI 2.26–2.62; $p = 0.008$, $R^2 = 0.59$), corresponding to a 28% fall. The intermittent asthma point prevalence was 3.57% (95% CI 3.37–3.77) in 1999 and 3.36% (95% CI 3.15–3.57) in 2008 ($p = 0.11$, $R^2 = 0.27$, a fall of 6%). The prevalence of asthma in clinical remission for more than 3 years was 1.84% (95% CI 1.69–1.98) in 1999 and 1.97% (95% CI 1.80–2.13) in 2008 ($p = 0.91$, $R^2 = 0.001$, an increase of 7%; fig. 2).

Hospitalizations for Asthma

The hospitalization rate due to asthma for ages 5–74 years between 1999 and 2008 decreased steadily, from 13.02 to 7.59 per 10,000 population ($p < 0.0001$, $R^2 = 0.90$), a reduction of 42%. There was a significant decrease in the hospitalization rate in all age groups for each decade of life (ages 5–74 years), with a p value range from 0.02 to less than 0.0001, and R^2 range from 0.49 to 0.92 (fig. 3). The decrease was significant in both genders for all age groups. In the age and sex group closest to our

asthma prevalence cohort (15- to 24-year-old males) the annual hospitalization rate for asthma diminished from 5.3 to 3.2 per 10,000 population ($p < 0.0001$, $R^2 = 0.92$), representing a fall of 40%.

Asthma Death Rate

During the last decade the asthma death rate decreased steadily in the total population, from 2.1 to 1.4 per 100,000 population ($p = 0.003$, $R^2 = 0.69$), a reduction of 41%. The decrease in the annual death rate for ages 45–64 years was from 2.70 to 1.30 per 100,000 population ($p = 0.005$, $R^2 = 0.66$), and for ages 65–74 years was from 11.60 to 3.70 per 100,000 population per year ($p = 0.002$, $R^2 = 0.70$) between 1999 and 2008. In younger age groups (0–44 years), initial death rates were very low and remained unchanged throughout the whole period (1–2 per million population; mean 1.9, SD 0.06, $p = 0.41$, $R^2 = 0.08$).

Discussion

In this large population-based study, we found a steady decrease in both the prevalence and severity of asthma for the years 1999–2008. This decrease was more pronounced in the persistent asthma groups as compared to groups with intermittent asthma or asthma in remission. This trend was paralleled by a decrease in annual asthma-related hospitalization rates and mortality rates during the same period.

Our study is in agreement with the data from the International Study of Asthma and Allergies in Children (ISAAC), which concluded that the prevalence of asthma in many western countries appears to have plateaued since the mid-1990s [20]. However, in 2011, the US Department of Health reported that the prevalence and number of individuals with asthma had increased since 2001, despite improvements in outdoor air quality and decreases in cigarette smoking and secondhand smoke exposure [21]. The authors of the US Department of Health report noted that asthma prevalence was greatest in adults from a low socioeconomic background who were mostly uninsured and who could not afford the purchase of antiasthmatic medications. In Israel, all citizens are eligible by law for national medical insurance coverage and medical care, and medications are virtually free of charge. This may explain the difference between the trends found in our study and those in the US reports.

In a previous study, we reported that the asthma-related death rate in Israel for ages 5–34 years during the years 1980–1997 was low and remained unchanged (0.22 per 100,000 population per year) [22]. In the present study,

Fig. 2. Lifetime prevalence of asthma ($\pm 95\%$ CI) of the total study population according to severity between the years 1999 and 2008. **a** Asthma in remission >3 years. **b** Intermittent asthma. **c** Mild persistent asthma. **d** Moderate-to-severe persistent asthma.

Fig. 3. Annual hospitalization rates for asthma (per 10,000 population) between the ages of 5 and 74 years, presented by age group, between 1999 and 2008.

we found a further decrease in asthma-related death rates in the younger age groups (0–44 years) during the last decade (from 0.2 to 0.1 per 100,000 per year, between 1999 and 2008). A reduction of more than 50% in the asthma death rate was found in all groups of ages from 0 to 74 years. The decrease in asthma hospitalization rate and mortality found in our study has also been observed in other countries. In Singapore, asthma deaths declined between 1994 and 2002, as did the hospital admission rates, while a rising trend for sales of ICS was observed [23]. In the UK and in the USA, mortality rates have steadily decreased since the mid-1990s [3–6], although the admission rates for asthma among adults have remained stable.

Active and passive smoking are known to be risk factors for asthma [24]. An important positive environmental change experienced in Israel has been a decrease in the prevalence of cigarette smokers [25]. In 1980, the prevalence of smokers in Israel was 46% in men and 31% in women, while by 2009 these figures had decreased to 28 and 16%, respectively. There is also a much greater public awareness of cigarette smoke-related morbidities. Legislation prohibiting smoking in public areas was enacted in 1983 [26] and amended in 2001 so that owners of businesses are held accountable for smoking on premises under their responsibility. Furthermore, in the past few years, the Israeli Cancer Association has run a successful campaign to encourage the public to stand up to smokers for their rights to smoke-free air (the ‘Don’t Be Shy’ commercials) [27]. All these factors have led to reduced active and passive cigarette smoke exposure in the general population over the last decade. We speculate that the reduction in tobacco exposure has contributed to the reduction in asthma prevalence, as well as asthma morbidity and mortality rates.

There is now convincing evidence that ICS markedly decrease both asthma hospitalization and death rates [7, 28]. During the study years, there was a steady increase in the rate of sales of ICS in one of the four national health maintenance organizations (online suppl. fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000368613). Both the number of patients who purchased ICS and the number of ICS inhalers purchased per patient increased significantly. Although a limitation of these data is the fact that ICS sales do not necessarily mean that the patient actually took the medication, we speculate that an increase in the regular use of ICS may explain the reduction of asthma morbidity and mortality.

Air pollution from traffic is known to play a role in causing asthma and be a risk factor for asthma exacerba-

tions [8]. Despite the ever increasing number of motor vehicles in Israel, we found that the ambient air concentration of NO_x, NO₂ and SO₂ at the collecting sites decreased over the study period (online suppl. table 1). We wonder if the improvement in the quality of the ambient air may have played a role in the concurrent decrease in asthma-related morbidity and mortality. Grass pollen counts are significantly associated with asthma morbidity [29, 30]. The significant decrease in the annual grass pollen load detected during the study period (online suppl. fig. 2) may have played a role in the reduced asthma severity observed during the same period.

The strengths of our investigation include the large size of this serial cross-sectional study. The diagnosis and assessment of the severity of asthma in our survey are very reliable and based on comprehensive medical evaluation and bronchial challenges, rather than the questionnaire-based assessment of asthma status generally used for epidemiological studies. However, a limitation of this observational study was that specific segments of the population were not included in the prevalence evaluation, in particular females and selected population subgroups that are not routinely recruited for national service. As in all epidemiological association studies, we cannot rule out the possibility that the observed reduction in asthma prevalence may have been due, at least in part, to other factors not evaluated in this study, such as, for instance, exposure to indoor allergens, climate changes, radiation exposure or the use of other controller medications such as montelukast (which was introduced in 1999), as well as the influence of other environmental factors, for example exposure to microorganisms such as RSV [31].

Conclusions

We found that both the prevalence and severity of asthma in a large cohort of Israeli teenage boys significantly decreased over the last decade, as well as the asthma-related hospitalization and death rates in the general population. We speculate that ongoing efforts to reduce environmental pollution and exposure to tobacco, coupled with improved use of asthma control medications, could impact favorably on asthma prevalence and severity.

Financial Disclosure and Conflicts of Interest

All coauthors disclose that they do not have any conflict of interest.

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