REVIEW ARTICLE

Asthma and Tobacco Smoke

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Introduction

A cigarette is the only consumer product which, when used as directed, kills its consumer. Smoking causes around 4 million deaths annually throughout the world and is associated with respiratory diseases such as emphysema and chronic obstructive pulmonary disease as well as with cardiovascular diseases. At least 12 types of neoplasms are associated with smoking,[1] which doubles the risk of developing cancer during middle age. The risk of delayed intrauterine growth and perinatal fetal morbidity and mortality is known to increase in pregnant women exposed to tobacco smoke. Children, particularly during the first years of life, are the population at greatest risk.

Currently, passive smoking affects between 20% and 80% of the population, depending on the country, and is associated with long- and short-term health risks, principally of ischemic heart disease and lung cancer. Smoking and exposure to environmental tobacco smoke (ETS) constitute the main cause of preventable morbidity and premature disease and death in developed countries.[2]

According to the 2001 Spanish National Health Survey, 34.4% of the general population in Spain smokes, confirming the tendency of smoking to decline over the last 20 years.[3] By age groups, 40.8% of persons between 16 and 24 years smoke, and the rate increases to 52.6% for the 25 to 44 year age group and decreases again to 42.6% for the 45 to 64 year age group. The lowered age of onset of smoking, currently at 13 years in some studies and 11 in others, is a worrying trend.[4]

The impact of smoking on the population has become a growing concern throughout the world over recent decades. Of note is the progressive adoption of smoking by adolescent girls at young ages and at a higher rate than boys,[5] a tendency observed in many countries including Spain. Likewise there are an increasing number of studies that reveal the importance of ETS exposure at work and, for children, both at home and in recreation and entertainment centers.

The consequences of ETS exposure have been under investigation since the adverse health effects of tobacco became known. A report from the Surgeon General of the United States of America in 1971 warned against the risks of tobacco smoke exposure.[2] A US Environmental Protection Agency report in 1993 published evidence of an association between ETS and respiratory health effects in nonsmoking children and adults,[6] and that link has recently been supported by reports from the California Environmental Protection Agency[7] and the Scientific Committee on Tobacco and Health in the United Kingdom.[8]

The World Health Organization published a report in 1999 on child health and exposure to ETS, summarizing the information of a large number of studies.[9] More recently, the European Conference on ETS, held in Berlin, 10 and 11 May, 2001, has become a widely accepted reference for those who must draft solid arguments for making serious changes in workplace environments. ETS has been classified as carcinogenic by the International Agency for Research on Cancer,[4] no level of exposure being considered safe. Exposure to ETS increases the risk of bronchogenic carcinoma and other diseases and is a serious health problem in Europe, where an estimated 1146 deaths from lung cancer related to ETS exposure occur annually.[10]

Asthma is a common complex disease, the pathogenesis of which is affected by exposure to exogenous agents and modified by a series of genetic determinants that regulate key elements in bronchopulmonary function. Risk or trigger factors of asthma include several allergens and nutrients, some infections, neonatal factors, pollution, and smoking.[11,12] Tobacco smoke is thought to encourage inflammation of the airways by activating the inflammatory cells, altering cell functions and subtypes, and encouraging proinflammatory mediator release, neurogenic inflammation, and oxidative stress.[13]

Likewise, several epidemiological studies have signaled the growing number of new asthma cases in recent years.[14,15]

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Manuscript received April 1, 2004. Accepted for publication April 15, 2004.

ETS as a Health Risk

Tobacco smoke is made up of mainstream smoke, which is directly inhaled by the smoker, and sidestream smoke generated by spontaneous combustion of the cigarette. ETS consists of sidestream smoke and the smoke exhaled by the smoker, also called second-hand smoke.

Mainstream and sidestream smoke contain the same toxic substances, with about 4000 components, 60 of which are suspected human carcinogens such as 4-aminobiphenyl, benzene, nickel, and a wide variety of polycyclic aromatic hydrocarbons and N-nitrosamines as well as irritant gases such as ammonia, nitrogen dioxide, sulfur dioxide, and several aldehydes.

Although the chemical composition of mainstream and sidestream smoke is similar, elements are more diluted and lower in quantity in sidestream smoke. On the other hand, sidestream smoke is produced at lower temperatures and has a higher proportion of many carcinogens and toxic substances.

Exposure to tobacco smoke takes place at home, in the workplace, and in public places and transport. The level of exposure depends on the number of smokers present, the quantity of tobacco smoked, the duration of the exposure, and the characteristics of the location.

Children of nonsmokers have lower concentrations of cotinine in blood and saliva than children of smokers.[16] Exposure of children to ETS is a worldwide problem. In 1996, a national survey carried out in China found that 53.6% of nonsmoking children and adults were exposed to ETS—with exposure defined as being in the presence of tobacco smoke for at least 15 minutes a day for more than 1 day a week.[17] In 1998, nearly half the American children under 5 years were exposed to ETS.[18] In the United Kingdom, 42% of English children and 60% of Scottish children were exposed to ETS caused by parental smoking.[18]

According to several studies carried out in Spain, between 48% and 69% of children and teenagers were exposed to household smoke.[19] A recent study in Granada on a sample of 504 children between the ages of 3 and 6 found that 57.6% lived in houses polluted by tobacco smoke from parents and other relatives.[20]

This data, however, is not available in most countries. According to the World Health Organization, there are some 1000 million adult smokers and at least 700 million children breathe household ETS.[9] To discover the real extent of the problem, though, new studies using biomarkers are needed for the widest possible application in different environments and cultures around the world.[9]

Asthma and ETS

Regarding the consequences of exposure of children and adults to tobacco smoke and the relation of exposure to the onset of asthma or exacerbations of the disease, there have been several studies carried out on children[21] in which no relation has been found between frequency of asthma exacerbations or respiratory infections in children and parental smoking. On the other hand, environmental pollution has been linked to an increase in the prevalence of bronchial hyperresponsiveness, allergic sensitization, and respiratory diseases in general.[22] There are studies on adults that show a direct relation between incidence of chronic bronchitic processes and asthma and exposure to ETS at work and traveling to and from work.[24]

Regarding factors involved in the development of childhood asthma, some viruses, such as the respiratory syncytial virus, have been shown to induce asthma and allergic sensitization, while others appear to have a protective effect.

Exposure of children to ETS basically occurs at home and in play environments. Maternal smoking is the main source of *in utero* and early childhood exposure to tobacco smoke. As children grow up, exposure to maternal smoking decreases and the influence of smoke from other sources, such as ETS in public places, increases. However, exposure to tobacco smoke particularly from maternal smoking is undoubtedly one of the factors that directly influence the development of asthma in children.[22,25]

The effects of maternal smoking during pregnancy are difficult to distinguish from post-natal exposure to ETS given that few parents quit smoking after the birth of their first child. The International Study of Asthma and Allergies in Childhood (ISAAC)[26] examined the relation between parental smoking and childhood asthma and other allergic pathologies. Symptoms of atopy in children of 2 age groups—6 to 7 years and 13 to 14 years—were examined, with the aim of relating the presence or absence of atopic symptoms with the prevalence of smoking in each country. A positive relation was found in the 13- to 14-year age group between smoking women and wheezing episodes within the previous 12 months. However, this same study presented data relating parental smoking and nocturnal wheezing that is difficult to interpret. The 6- to 7-year age group showed an inverse relation between sleep disturbance caused by nocturnal wheezing and parental smoking in the 38 countries that were included in the study. Evidently other risk factors need to be considered that might be responsible for these pathologies.

Although there appears to be evidence of a relation between passive smoking and asthma, the relation between active smoking and asthma is not so well defined. There are contradictory findings, some of which show a relation between smoking and asthma[27-29] and others that do not.[30,31]

The Epidemiological Study on the Genetics and Environment of Asthma, carried out in France, and which included smokers, asthmatics and their families, and healthy individuals, did not find a significant relation between smokers and the risk of asthma onset although there was a strong relation between smoking and asthma severity.[32]

A study carried out in Spain found that the evolution of asthma in smoking asthmatics was more aggressive and severe than in nonsmoking asthmatics but no evidence was found of increased incidence of asthma in smokers.[33] These results were corroborated in other populations.[32]

Similarly, in a prospective study carried out in Australia, no relation was found between asthma and ETS exposure in children,[34] suggesting that there are other factors that influence the onset of asthma and that genetic characteristics moderate susceptibility to environmental factors.[35]

A recent cross-sectional study carried out by Fuertes et al[36] examined the prevalence of asthma, rhinitis, and dermatitis using the ISAAC questionnaire and established that the prevalence of asthma in children between the ages of 6 and 8 in Huesca, Spain, was 5.5%; the prevalence of allergy was 7.29%, and bronchial hyperresponsiveness, 5.3%.[36] No significant relation was found for this same group between asthma and bronchial hyperresponsiveness and sex, gestational age, duration of breastfeeding, gestational smoking, or household pets, or smoking.[37]

Evidence has also been found that relates parental smoking with an increase in the prevalence of asthma and respiratory symptoms in children. Cook and Strachan[38] carried out a meta-analysis of 60 studies to determine the influence of parental smoking on the prevalence of asthma, wheezing, and chronic cough. This study demonstrated an association between parental smoking and childhood asthma (odds ratio [OR]=1.21; 95% confidence interval [CI], 1.17-1.31), wheezing (OR=1.24; 95% CI, 1.27-1.53, and chronic cough (OR=1.4; 95% CI, 1.27-1.53). A dose-dependent relation was also found between parental smoking and the prevalence of asthma, wheezing, and chronic cough. Likewise, while maternal smoking was found to have a greater influence than paternal smoking, the effects of the latter were clearly significant, indicating important postnatal effects.

A strong association was found between household ETS and the incidence of wheezing and asthma in children of up to 6 years of age, but after that the association was weaker,[39] possibly attributable to the degree of exposure to ETS during growth. The long-term prognosis for children with asthma was poorer if their parents smoked.

No consistent relation was found between parental smoking before or after birth and risk of allergic sensitization (positive skin test, immunoglobulin-E concentrations, hay fever, or eczema, excluding asthma) in children, although there was an increased bronchial hyperresponsiveness in children of mothers who smoked.[40]

Lung Function and ETS

To date there have been at least 30 studies relating ETS exposure with altered lung function.[7] Findings indicate three particularly relevant periods of exposure to ETS: *a)* gestation or *in utero* exposure; *b)* the first 2 years of life when breathing rates are faster, there is a greater incidence of infections of the lower airways, and maternal smoking has a greater effect, and *c)* the remaining years of childhood.

Studies carried out in the United States in the 1970s were the first to provide evidence of the effects of passive smoking on lung function in children exposed to ETS.[41] These studies were followed by other longitudinal studies,[42,43] mostly carried out on American children. According to the results of one of these studies, lung function reduction attributable to exposure to ETS from maternal smoking was 28 mL for 1-year-olds, 51 mL for 2-year-olds, and 101 mL for 5-year-olds.[44]

Current testing methods have demonstrated that children of smoking mothers have impaired lung function with reduced forced expiratory volume in one second, and that the worse period of exposure to tobacco smoke is *in utero*.[25,45]

A wide-reaching prospective study in Germany, carried out on 7284 children between 9 and 11 years of age, found that children of parents who smoked at home had lower peak expiratory flows and maximum expiratory flows at 75%, 50%, and 25% of vital capacity than did children with nonsmoking parents. Likewise, both cough and wheezing increased in relation to smoking intensity. The results of the study indicate that passive smoking has a dose-dependent effect on the respiratory system of children.[46]

Both *in utero* exposure to tobacco smoke and passive smoking have an adverse effect on lung function and predispose children to asthma and possibly to bronchial hyperresponsiveness but have scarce or null influence on the development of atopy.[47]

In a systematic review of 40 international studies, only one failed to demonstrate a direct relation between parental smoking and increased respiratory risk in children OR=1.7; (95% CI, 1.6-1.9) if the smoker was the mother and OR=1.3; (95% CI, 1.2-1.4) if the smoker was the father.

The association between these factors persists when results are adjusted for confounding factors and shows a direct association with intensity of exposure in most cases.[9] Parental smoking, then, is an important factor in respiratory diseases in children.

Asthmatic children of smoking mothers have more severe asthma and impaired function than children of nonsmoking mothers and it has been proved that measures aimed at reducing exposure to ETS have resulted in reduced use of medical services for respiratory diseases.[48]

To date, most studies have concentrated on determining the relation between exposure to ETS and childhood asthma and have demonstrated, as we have seen above, that the relation is a close one. Some recent studies have provided evidence on the relation between exposure to ETS and asthma in adults. Exposure to ETS at the workplace, at home, or in both places has been

shown to be related to increased risk of asthma symptoms, days off work, reduced activity, nocturnal symptoms, and asthma exacerbations that need hospital attention.[49,50] In a study carried out in India, asthmatic adults that had never smoked but were exposed to ETS needed bronchodilators (66% compared with 56%; *P*<.01) and intermittent doses of corticosteroids (56% compared with 42%; *P*<.01) more frequently than nonexposed asthmatics.

A case-control study carried out in California using mailed questionnaires found an increased risk of asthma in women exposed to tobacco smoke at home (OR=1.86; 95% CI, 1.1-2.4).[51] The analysis of data from a study carried out in Switzerland on air pollution and respiratory diseases in adults showed that for never-smokers there was an association between self-declared exposure to ETS in the previous 12 months and risk of being diagnosed with asthma (OR=1.39; 95% CI, 1.04-1.86), after controlling for the effect of variables such as age, sex, body mass index, location, atopy, and family history of asthma.[52]

Given that most asthmatic adults also had asthma as children, it is difficult to establish whether exposure to ETS does or does not increase the risk of the onset of asthma in adults. However, 2 cohort studies have found significant associations between both factors. One of the studies, carried out by Greer et al[53] over a 10-year period, concluded that there was a significant association between exposure to ETS and the development of asthma in adults (relative risk, 1.45; 95% CI, 1.21-1.75). The other prospective study showed an increased risk of onset of asthma in women who worked with smokers.[54]

Conclusions

Smoking and the effects of tobacco smoke on active and passive smokers is one of the main problems of public health in developed countries. Parental smoking directly influences the respiratory health of children and predisposes them to asthma, which, when it develops, is more severe.

In adults, the relation is not as clear regarding onset of asthma although there is sufficient evidence to show that the clinical course of the disease is worse in smoking asthmatics than in nonsmoking asthmatics.

We must endorse legislative measures towards controlling smoking in public places and towards avoiding or delaying as much as possible the adoption of this addiction by the young.

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