Maturitas 90 (2016) 42–48

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Inhaled medication usage in post-menopausal women and lifetime tobacco smoke exposure: The Women's Health Initiative Observational Study

Kenneth M. Piazza[a], Jean Wactawski-Wende[b], Margaret W. DeBon[c], Kathleen M. Hovey[b], Cheryl L. Rivard[a], Danielle M. Smith[a,*], Andrew J. Hyland[a]

[a] Roswell Park Cancer Institute, Department of Health Behavior, Division of Cancer Prevention & Population Sciences, Buffalo, NY 14263, USA
[b] University at Buffalo, Department of Epidemiology and Environmental Health, Buffalo NY, 14214, USA
[c] University of Tennessee Health Science Center, Department of Preventive Medicine, Memphis TN, 38163, USA

ARTICLE INFO

Article history:
Received 18 March 2016
Received in revised form 9 May 2016
Accepted 13 May 2016

Keywords:
Tobacco
Secondhand smoke
Inhaler
Post-menopausal
Asthma
COPD

ABSTRACT

Objective: While active smoking is a causal agent in respiratory disease, the independent role of secondhand smoke (SHS) merits further investigation. We investigated associations between lifetime active smoking and exposure to secondhand smoke – studied independently – and current use of 1 or more inhaled medications as a surrogate for prevalent pulmonary disease in post-menopausal women.
Study design: Information on lifetime active and passive tobacco exposure and inhaled pulmonary medication usage at enrollment was collected from 88,185 postmenopausal women aged 50–79 enrolled in the Women's Health Initiative Observational Study from 1993 to 1998 at 40 centers in the United States. Participants were recruited from localities surrounding the study centers using a variety of methods, including informational mailings and mass media campaigns.
Main outcome measures: Multivariate adjusted regression models were used to estimate odds ratios and 95% CI according to levels of active smoking and SHS exposure, and trends were tested across categories.
Results: Ever active smokers had an overall OR of 1.97 (95% CI 1.58–2.45) for having one or more prescribed inhaled medication compared with never-smoking women not exposed to active or passive smoke. The overall OR for using inhalers for never-smoking women exposed to any SHS compared with the same reference group was 1.33 (95% CI 1.07–1.65). In a quantified analysis of SHS, never-smoking women with the highest levels of lifetime SHS exposure had an estimated risk of inhaled medication usage of 1.74 (95% CI 1.32–2.30).
Conclusions: The risk of requiring one or more prescribed inhaled medications for pulmonary disease was significantly higher in post-menopausal women who ever smoked or who had lifetime exposure to SHS.

1. Introduction

Tobacco remains the number one causative agent in respiratory morbidity and mortality [1]. It is well accepted that tobacco smoke exposure through active smoking is causal in respiratory disease, but the independent role of secondhand smoke (SHS) is still being investigated [2–7]. The most common types of pulmonary disease are asthma, and chronic obstructive pulmonary disease (COPD) with its two main subgroups, emphysema and chronic bronchitis. Asthma has several causes, including a strong genetic component [8], and exposure to SHS has been shown to be related to the frequency and severity of asthma attacks [5]. For COPD, active smoking is the primary cause and smoking cessation is an important means to reduce mortality [9]; however, far fewer well designed studies have examined the independent role of SHS for COPD [10–12]. For example, prior findings from a nested case-control study using data from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort suggest that exposure to SHS at home or work among never smokers increased risk of developing respiratory illness later in life, particularly cancers of the lung and COPD [11]. Another prospective study examining the role passive smoke exposure has on the development of respiratory illnesses later in life showed no association [13]. Results from case-control and cross-sectional studies also suggest that SHS exposure may serve as a risk factor for the development of COPD [10,12], with findings from one such study suggesting increased levels of risk resulting from greater exposure to SHS [10].

* Corresponding author at: Department of Health Behavior, Roswell Park Cancer Institute, Elm & Carlton Streets, Buffalo NY 14263, USA.
E-mail address: danielle.smith@roswellpark.org (D.M. Smith).

http://dx.doi.org/10.1016/j.maturitas.2016.05.008
0378-5122/

A fact important to this project is that the concept of asthma and COPD and other subgroups of pulmonary disease as distinct entities in populations over 50 years of age has been re-evaluated, where each of these airway diseases – characterized by the broad categories as obstructive, inflammatory, fibrotic, or interstitial – may co-exist or give rise to the other; the condition where this occurs is known as overlap syndrome [14]. As the patient with respiratory disease ages, the percentage with overlap syndrome increases; the majority of patients over 50 have some form of overlapping disease [14,15]. Tobacco exposure from active smoking is still considered a risk factor for overlapping disease, but the independent role of lifetime SHS in such combinations of airflow obstructive disease has not been established [16].

In epidemiological studies, precise definitions of outcome diseases are essential to credible results. In pulmonary disease, particularly asthma in older populations, this is challenging for study design [14,15,17,18], even going beyond standard pulmonary function studies to gene cluster analysis [8]. The American Thoracic Society notes 11 different subgroups of pulmonary disease, and the potential overlap [14,16,19]. Precise epidemiologic definition of individual pulmonary diseases using only historical data from many large cohort datasets is often unreliable, not only because data on clinical respiratory function studies, detailed family histories, data about participants' atopy, key covariates and comorbidities are often missing, but because of overlapping disease. For this reason, inhaler usage is often used as a surrogate measure in secondary data analysis of prevalent respiratory disease.

In this cross-sectional study, we hypothesize that post-menopausal women who have ever smoked or never-smoking women who have been exposed to SHS have a greater estimated risk of needing one or more inhaled medications that are indicative of prevalent pulmonary disease. Examples of some diseases would be asthma, COPD (chronic bronchitis and emphysema), bronchiolitis, pulmonary fibrosis, and interstitial pneumonitis, among others including overlap diseases.

2. Methods

2.1. Data source—Women's Health Initiative

The Observational Study (OS) of the Women's Health Initiative (WHI) is a cohort of post-menopausal women from 40 centers across the United States. The WHI OS enrolled 93,676 women aged 50–79 from 1993 to 1998. Participants were recruited from localities surrounding the study centers using a variety of methods, including informational mailings and mass media campaigns. Participants were consented and Human Subjects committees at participating centers approved the study. Detailed information on recruitment efforts and baseline characteristics of study participants have been published elsewhere [20,21]. Data used in this analysis was analyzed in 2015, and uses comprehensive questionnaires completed by study participants. The analyzed data was from the enrollment period (1993–1998). Questions throughout the dataset were structured to minimize recall bias and error [21]. A subset of women participated in the WHI OS Measurement Precision Study, which evaluated the reliability of these survey measures. Three months after baseline, participants completed a second set of self-reported questionnaires. Kappa statistics were reported, for active smoking status kappa = 0.94, for passive smoking Kappa were 0.83, 0.73 and 0.63 for years as a child lived with a smoker, years as adult lived with smoker, and years worked with smoker respectively. Additional details on the reliability of survey measures have been published elsewhere [21].

For this study, 88,185 were included who had complete data on smoking status, SHS exposure and data on inhaled pulmonary medication.

2.2. Measurement of tobacco exposure

Data on lifetime active and passive smoking were collected on baseline enrollment questionnaires. Women were initially classified by active smoking status into current, former or never smokers (participants that had not smoked 100 cigarettes in their life). Ever-smokers were defined as answering "yes" to "have you smoked 100 cigarettes in your life?" Other variables considered included age started smoking with the categories <15 years, 15–19 years, 20–24 years, 25–29 years and 30+ years of age; average number of cigarettes per day throughout smoking years was categorized into <5, 5–14, 15–24, and 25+ and pack-years of smoking as <10, 10–<20, 20–<30, 30–<40 and ≥40.

Questions related to exposure to SHS in never-smoking women were categorized as: no exposure to SHS ever, exposure during childhood (<18 years), adult exposure (exposure >18 years) at home and work. Participants who reported any SHS exposure were asked the number of years exposed in each of these three categories, initially predefined as <1, 1–4, 5–9, 10–18 years for childhood exposure; and <1, 1–4, 5–9, 10–19, and 20+ years for adult home and work exposure. Never-smoking women were initially classified by SHS exposure using a dichotomous measure – yes or no for childhood (exposed <18 years of age), yes or no for adult home and work venues (exposed >18 years of age at home, >18 years of age at a workplace). Quantification of SHS exposure was related to the number of years women were exposed in childhood, adult at home and adult at work venues. Using the categories from the questionnaire produced inadequate sample sizes, so new variables for exposure to SHS were created to achieve acceptable power. Considering a priori estimates, frequency of responses and classifications of SHS in other WHI studies [22–24], exposure to SHS was quantified as "no childhood + any adult;" "childhood <10 years + any adult;" "childhood ≥10 years + Adult Home <20 years + Adult Work <10 years;" "childhood ≥10 years, Adult home < 20 years, adult work ≥10 years;" "childhood ≥10 years + adult home ≥20 years + adult work <10 years;" and "childhood ≥10 years + adult home ≥20 years + adult work ≥10 years." This categorization allowed for assessment of the cumulative effect of SHS exposure on inhaled medication usage.

2.3. Covariates

Confounders were selected based on clinical relevance to the outcome under study. Potential confounders used in the multivariate analyses included age at baseline (<60, 60–69, and 70+ years), the average mean body mass index (BMI) for ages 18–50 (<20, 20–<26, 26–<30, and >30), self-reported ethnicity (non-Hispanic Caucasian, African-American, Hispanic, and other), education (<HS grad, HS or some college, and college degree or higher), alcohol use (12 drinks ever in lifetime, yes/no), alcohol intake (Non Drinker, Past drinker, <1 drink/month, <1 drink/week, 1–<7 drinks/week, and 7 or more drinks/week). The covariate of income at baseline was excluded from the final analysis, as income was subject to high levels of item non-response, and models including income did not significantly change results outlining smoking effects on inhaled medication usage. No data were available for atopy and family history of allergy; historical data on comorbidities of respiratory disease, especially of asthma syndromes in older adults (eg. diabetes, GI reflux disease, cataracts, sleep apnea, etc.) [15] were insufficient to include in the final adjusted analysis. See Table 1 for baseline characteristics.