Are Diabetics More Susceptible to the Health Effects of Airborne Particles?

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Convincing evidence now exists that particulate air pollution exacerbates heart and lung disease, leading to increased morbidity and mortality. The populations particularly susceptible to these exposures are still unclear. Recent work on potential mechanisms of action of particulate air pollution point to pathways also influenced by diabetes. We examined whether diabetes modified the effect of airborne particles by looking at the association of PM_{10} with hospital admissions for heart and lung disease in persons with or without diabetes as a comorbidity. In addition we stratified by age within persons with and without diabetes. We used Medicare data for Cook County, Illinois for the years 1988–1994, and found that a 10 $\mu g/m^3$ increase in PM_{10} was associated with a 2.01% (95% CI 1.40–2.62%) increase in admissions for heart disease with diabetes, but only a 0.94% (95% CI 0.61–1.28%) increase in persons without diabetes. Similar effect modification was not seen for lung diseases. When analyzing by age we found twice the PM_{10}-associated risk for heart disease in diabetics than nondiabetics in both age groups. We found for pneumonia admissions that diabetes is an effect modifier in the younger age group, and for COPD in the older age group. We conclude that persons with diabetes are a susceptible population.

Keywords: particles; diabetes; air pollution; heart disease; PM_{10}

Particulate air pollution has been associated with increases in daily deaths and hospital admissions in dozens of studies across the world (1, 2). Recent studies have shown that these associations are not confounded by gaseous copollutants (3–5), seasonal patterns, or weather (5, 6). These results indicate that the associations should be considered as causal. However, it is unclear which populations are particularly susceptible to the adverse effects of particulate matter with aerodynamic diameter < 10 μm (PM_{10}), and this has been identified as a key research need (7).

We previously examined race, sex, and socioeconomic status as modifiers of the effect of air pollution on mortality (8), and found little evidence of substantial modification. Similarly weak patterns were found for hospital admissions (4, 9). In contrast, preexisting chronic obstructive pulmonary disease (COPD) has been reported as an important effect modifier for mortality (10).

In recent studies, exposure to airborne particles has been associated with reduced heart rate variability (11, 12), increased C reactive protein (13) concentrations, and higher peripheral white cell counts (14) and fibrinogen levels (15). Diabetes is a chronic disease characterized by disturbances in all of these cardiovascular risk factors (16–18), and we hypothesized that diabetics might therefore be at increased risk of PM_{10}-associated cardiovascular events. In contrast, although PM_{10} has a larger percentage impact on respiratory hospital admissions (4), it seems less likely that those risks would be modified by diabetes. To test these hypotheses, we used hospital discharge data available from the Health Care Financing Administration and examined admissions for heart and lung disease. These data were then stratified by whether diabetes was present as a comorbidity and analyzed to look at effect modification by concurrent diagnosis of diabetes.

In our previous study on Chicago (9) we did not find that sex, age, and race were modifiers of the effect of PM_{10} on hospital admissions for heart and lung disease, so these factors should not modify the associations that we found for diabetes. However we decided to stratify by diabetes and age, as this was the factor that showed a weak indication of effect modification. This study was approved by the Harvard School of Public Health Institutional Review Board.

METHODS

Health Data

The health data were extracted from the Health Care Financing Administration (MEDICARE) billing records, which provides hospital coverage for all U.S. citizens aged 65 and over. We analyzed data from Cook County, Illinois, between 1988 and 1994. Cook County was chosen because it is the most populous county in the United States with daily PM_{10} monitoring. We computed daily counts of hospital admissions for cardiovascular disease (International Classification of Disease, ICD-9: 390–429), pneumonia (ICD-9: 480–487), and COPD (ICD-9: 490–496, excluding 493). We stratified these counts into admissions with or without a notation of diabetes (ICD-9 250) as a secondary, contributing factor for the admission. We also stratified by age: subjects with and without diabetes were divided into subjects 75 yr and younger and older than 75 yr.

The association between these daily counts and PM_{10} was examined for the years 1988–1994, when daily PM_{10} monitoring data were available in Chicago.

If diabetes modified the effect of particulate matter on the cardiovascular health of persons with underlying heart disease, then the risk of a hospital admission for heart disease might be different in persons with diabetes. If this were true, then the risk ratio of a 10 $\mu g/m^3$ increase of PM_{10} on cardiovascular admissions of persons with concurrent diabetes would be different from the ratio in persons without diabetes.

Weather data for O'Hare Airport were obtained from the EarthInfo CD ROM (EarthInfo CD NCDC Surface Airways, EarthInfo Inc., Boulder, CO), and air pollution data were obtained from the U.S. Environmental Protection Agency's Aerometric Information Retrieval System (AIRS) network (19). The daily values for PM_{10} were computed as the average of 10 monitors, two of which measured PM_{10} almost every day and the others less frequently.

Methods

The associations between hospital admission counts and PM_{10} were investigated with a generalized additive robust Poisson regression model (20). This approach has become the norm in such studies (21–23) and the results for the association between hospital admissions in Chicago and PM_{10} (without stratification by diabetes status) have already been published (4). The generalized additive model uses nonparametric smooth functions to estimate the relation between the outcome and each predictor. This allows us to better model the nonlinear

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TABLE 1. CHICAGO 1986–1994*

	CVD	Pneumonia	COPD
With diabetes	5	0	0
	20	3	1
	42	14	7
Without diabetes	31	3	0
	82	23	7
	138	85	30
By age group			
with diabetes			
⩽ 75	1	0	0
	12	1	1
	26	8	4
75+	0	0	0
	8	2	0.4
	25	9	4
without diabetes			
⩽ 75	10	0	0
	35	8	4
	67	38	15
75+	16	2	0
	47	16	3
	83	54	18

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease.

* Min, mean, and max values of daily admissions for COPD, CVD, and pneumonia by concurrent diagnosis for diabetes and by diabetes and age group.

dependence of daily admissions on weather and season. The covariates we examined were temperature, prior day's temperature, relative humidity, barometric pressure, and day of week.

To control for weather variables and day of the week, we chose the smoothing parameter that minimized the Akaike's Information Criterion (24). To model seasonality we chose the smoothing parameter that minimized the sum of the autocorrelation of the residuals while removing seasonal patterns. Two autoregressive terms (25) were added in the model to eliminate the remaining serial correlation from the residuals. The mean of PM_{10} on the day of the admission and the day before the admission was used as our exposure variable and was treated linearly. Further details have been published previously (4).

We considered effect modification to be indicated when the estimates of PM_{10} in the group with diabetes were outside of the 95% confidence interval of the effect estimate in persons without diabetes.

RESULTS

Table 1 shows the minimum, mean, and maximum values of daily admissions for COPD, cardiovascular disease (CVD), and pneumonia with and without a concurrent diagnosis of diabetes and by diabetes and age group. Admissions for pneumonia and COPD without diabetes were seven to eight times as common as admissions for those causes with diabetes. For heart disease, the ratio was only 4 to 1, reflecting the tighter association of diabetes with heart disease.

TABLE 2. 25, 50, AND 75 PERCENTILE VALUES FOR THE ENVIRONMENTAL VARIABLES IN CHICAGO, 1988–1994

Temperature (°F)	Relative Humidity	Barometric Pressure	PM_{10} ($\mu g/m^3$)
35	62	29.2	23
51	70	29.3	33
67	79	29.4	46

Definition of abbreviation: PM_{10} = particulate matter with aerodynamic diameter < 10 μm.

Table 2 shows the 25, 50, and 75 percentile values for the environmental variables. The mean value for PM_{10} is 33 $\mu g/m^3$.

Table 3 shows the results for the effect of PM_{10} by strata of diabetes and age. The results are expressed as the percentage increase in admissions for a 10$\mu g/m^3$ increment of PM_{10}.

These results show a clear effect modification due to diabetes in persons with CVD. The same effect modification was found when stratifying by age.

We did not find effect modification for COPD and pneumonia due to diabetes in all ages. When we analyzed by age, we found that diabetes is an effect modifier in younger persons with pneumonia, and in older persons for the risk of PM_{10}-induced COPD.

DISCUSSION

PM_{10} has been associated with daily deaths and hospital admissions in numerous studies over the past decade (1, 2, 26, 27). Recently, a comprehensive study of the 90 largest cities in the United States found that no other air pollutant confounded the mortality association, and that no other air pollutant was associated with significantly increased risk (5). A similar result was found for hospital admissions (5). Although the evidence for an effect of airborne particles is overwhelming, to date there are only indications of possible mechanisms.

As noted in the introduction, both diabetes and airborne particles have been associated with decreased heart rate variability (10, 14), increased thrombotic risk factors (12, 15, 16), and increases in systemic markers of inflammation (13). These similarities indicate that particles and diabetes may affect some of the same pathways, and suggested the possibility of a synergistic effect.

We have found a significant interaction for hospital admissions for heart disease, with more than twice the risk in persons with diabetes than in persons without diabetes. The same

TABLE 3. PERCENTAGE INCREASE IN DAILY HOSPITAL ADMISSIONS FOR CVD, COPD, AND PNEUMONIA WITH AND WITHOUT CONCURRENT DIAGNOSIS FOR DIABETES AND AGE GROUPS*

	CVD			Pneumonia			COPD		
	PM_{10}	95% CI		PM_{10}	95% CI		PM_{10}	95% CI	
Chicago									
With diabetes	2.01	1.40	2.62	2.77	1.20	4.37	2.29	−0.76	5.44
Without diabetes	0.94	0.61	1.28	2.20	1.57	2.84	1.50	0.42	2.60
By age group									
With diabetes									
⩽ 75	1.89	1.10	2.86	5.60	3.25	8.01	0.33	−3.54	4.37
75+	2.03	1.10	2.96	1.02	−1.07	3.15	5.07	0.26	10.10
Without diabetes									
⩽ 75	0.69	0.21	1.18	2.38	1.36	3.42	1.38	−0.07	2.86
75+	1.25	0.82	1.68	2.35	1.58	3.13	1.82	0.26	3.40

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; CVD = cardiovascular disease; PM_{10} = particulate matter with aerodynamic diameter < 10 μm.

* Increases are for a 10 $\mu g/m^3$ increase in PM_{10}.

result was found in both age groups. This increase is likely biased downward because of misclassification of some persons with diabetes into our nondiabetic pool. There is no guarantee that all discharge diagnoses for heart disease patients will include a mention of diabetes, although it may be associated with increased payments.

Our finding does not prove that the mechanisms mentioned above play a role in the particle-associated heart disease admissions, but it strengthens the case for that role. It does indicate that persons with diabetes are an important at-risk group. The lack of detailed medical information on subjects was a limitation of this study, and suggests more detailed studies are warranted. We believe the interaction of particle exposure with diabetes deserves more attention, perhaps by some focused panel studies of heart rate variability and air pollution in persons with diabetes. Diabetes is a highly prevalent chronic illness. Data from the Third National Health and Nutrition Examination Survey indicate that 5.1% of the U.S. population older than 20 yr of age have diagnosed diabetes and an additional 2.7% have undiagnosed diabetes (28). Hence the public health implications of this association are important.

Although some have speculated that the population at risk of dying due to particulate air pollution is composed of those who are at the edge of death, and likely to die within a few days in any case, recent studies that investigated that hypothesis have not found that to be the case (29–31). Hence, the susceptible population is not just the critically ill. The finding of enhanced susceptibility in persons with diabetes may partially explain those findings.

Moreover, recent studies have found that subjects with impaired glucose tolerance without type II diabetes also had reduced heart rate variability (15). This suggests the at-risk population may be even larger.

In contrast, we found only weak evidence that diabetes modified the risk of PM_{10}-induced respiratory hospital admissions. Although diabetes modified the risk of PM_{10}-induced COPD admissions in older people and the risk of pneumonia admissions in younger persons, those effects were smaller than for heart disease admissions, as well as inconsistent by age.

There are far fewer admissions for respiratory illness than for heart disease, and it could be that a larger study would have detected a significant association. However, the differences in effect we saw were small as well as having overlapping confidence intervals.

This suggests that the mechanism is more specific for cardiovascular illness and it could depend on age groups. Nevertheless, this certainly deserves further investigation.

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