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Particulate Air Pollution and the Rate of Hospitalization for Congestive Heart Failure among Medicare Beneficiaries in Pittsburgh, Pennsylvania.

Gregory A. Wellenius[1,2], **Thomas F. Bateson**[2,3], **Murray A. Mittleman**[1,3], and **Joel Schwartz.**[2,3]

1 *Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center.*

2 *Department of Environmental Health, Harvard School of Public Health.*

3 *Department of Epidemiology, Harvard School of Public Health.*

Abstract

We used a case-crossover approach to evaluate the association between ambient air pollution and the rate of hospitalization for congestive heart failure (CHF) among Medicare recipients (age ≥ 65) residing in Allegheny County (Pittsburgh area), PA, during 1987–1999. We also explored effect modification by age, gender, and specific secondary diagnoses. During follow-up, there were 55,019 admissions with a primary diagnosis of CHF. We found that particulate matter with aerodynamic diameter ≤ 10 μm (PM_{10}), carbon monoxide (CO), nitrogen dioxide (NO_2), and sulfur dioxide – but not ozone – were positively and significantly associated with the rate of admission on the same day in single-pollutant models. The strongest associations were observed with CO, NO_2 and PM_{10}. The associations with CO and NO_2 were the most robust in two-pollutant models, remaining statistically significant even after adjusting for other pollutants. Patients with a recent myocardial infarction were at greater risk of particulate-related admission, but there was otherwise no significant effect modification by age, gender, or other secondary diagnoses. These results suggest that short-term elevations in air pollution from traffic-related sources may trigger acute cardiac decompensation of heart failure patients and that those with certain comorbid conditions may be more susceptible to these effects.

Medical Subject Headings

Heart Failure; Congestive; Air Pollution; Disease Susceptibility; Epidemiology

Abbreviations

CHF: Congestive heart failure; PM_{10}: Particulate matter with aerodynamic diameter < 10 μm; $PM_{2.5}$: Particulate matter with aerodynamic diameter < 2.5 μm; ICD-9: *International Classification of Disease, 9th revision*; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; CO: carbon monoxide; O_3: Ozone; NO_2: Nitrogen dioxide; SO_2: Sulfur dioxide; EPA: Environmental Protection Agency; CI: Confidence interval; NMMAPS: National Morbidity, Mortality, and Air Pollution Study

Address for Correspondence: Gregory A. Wellenius, Cardiovascular Epidemiology Research Unit, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Deaconess 306, Boston, MA 02215. Telephone: (617) 632-7680. Fax: (617) 632-7698. E-mail: gwelleni@bidmc.harvard.edu.

Congestive heart failure (CHF) affects approximately five million people in the US (1). Age-adjusted incidence rates do not appear to be increasing (2,3), but the prevalence is expected to increase as the population ages and heart failure mortality continues to decline (4). Hospital discharges for CHF have increased 164 percent over the past two decades from 377,000 in 1979 to 995,000 in 2001 (1). As such, the identification of precipitating factors that lead to acute cardiac decompensation and subsequent hospitalization is of considerable public health interest.

Acute decompensation can be precipitated by pathological, behavioral (5–9) and environmental factors such as extreme temperatures (5), smoking (10) and exposure to carbon monoxide and air particles with aerodynamic diameter ≤ 10 μm (PM_{10}) (11–14). Although a secondary diagnosis of CHF may affect pollution-related hospitalizations for ischemic heart disease (15,16) subgroups of CHF patients more susceptible to environmental triggers have not been identified.

Accordingly, we evaluated the following specific hypotheses: 1) short-term elevations in PM_{10} are associated with an increased rate of cardiac decompensation and subsequent hospitalization for CHF, and 2) the increase in rate is more pronounced in older individuals and those with specific comorbid conditions. We evaluated these hypotheses using the case-crossover study design (17), which is well suited to assessing the effects of transient exposures on the subsequent risk of acute events (18). Although our primary hypotheses relate to particulate matter, we also evaluated the association between ambient measures of other criteria pollutants and the rate of hospitalization for CHF.

MATERIALS AND METHODS

Study population

We obtained information on hospital admissions from the Centers for Medicare and Medicaid Services which provides financial reimbursement of inpatient hospital admission costs for most US citizens aged 65 years and over. Cases were defined as persons admitted from the emergency room with a primary discharge diagnosis of CHF (*International Classification of Disease, 9th revision* (ICD-9): 428.0 and 428.1) between January 1, 1987, and November 30, 1999, and residing in Allegheny County (Pittsburgh area), Pennsylvania, as noted in the Medicare claims record. For patients with multiple admissions, we only included those admissions that occurred more than 14 days since the last included admission. Pittsburgh was chosen because it is one of the larger cities for which daily air quality data is available for many years. This study was conducted under an exemption from the Harvard School of Public Health Institutional Review Board.

We obtained daily integrated (24-hr) measures of PM_{10} and hourly measures of ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2) from the Aerometric Information Retrieval System of the US Environmental Protection Agency (EPA). The measurement methods used for determining ambient concentrations of each pollutant have been described elsewhere (19). Measures of PM_{10} were available from 17 monitoring sites, O_3 from 4 sites, CO from 3 sites, SO_2 from 10 sites and NO_2 from 2 monitoring sites. We computed local daily mean concentrations of each pollutant using an algorithm that accounts for monitor-specific means and variances, as previously described (20). We excluded from analysis two days on which PM_{10} levels exceeded 150 $\mu g/m^3$, the current 24-hr EPA standard.

We obtained National Weather Service data on daily mean ambient temperature, barometric pressure, and dew point from the EarthInfo CD-ROM (NCDC Surface Airways; EarthInfo Inc., Boulder, CO), and calculated apparent temperature (an index of human discomfort) as previously described (21–23).

Study design and statistical analysis

We used the case-crossover study design to assess the effect of changes in daily mean concentrations of PM_{10}, SO_2, NO_2, CO, and O_3 on the rate of hospitalization for acute decompensated CHF. Our primary exposure of interest was mean daily PM_{10} concentrations. Exposure during the case period was defined as mean PM_{10} concentration either on the day of admission (lag 0) or 1 to 3 days preceding admission (lags 1 to 3). Control periods were chosen using the time-stratified approach (24,25) such that exposures during the case period were compared to exposures occurring on all other days of the same month (before or after the event day) that fell on the same day of the week as the case period (26).

We performed conditional logistic regression, stratifying on each hospitalization, to obtain estimates of odds ratios and 95 percent confidence intervals (CI) associated with an interquartile range increase in the mean daily level of each pollutant. Effect estimates are reported as percent change in rate of hospitalization. In all analyses, we modeled the mean apparent temperature at lag 0 as a quadratic function and mean apparent temperature at lag 1 and mean barometric pressure at lag 0 as linear functions of continuous variables. We modeled PM_{10}, SO_2, NO_2, CO, and O_3 as linear functions of continuous variables. We first evaluated the effect of PM_{10} separately at lags 0 to 3 days in single-pollutant models. Based on the results of this analysis, we selected a single lag for all subsequent analyses. Pollutants were first considered separately using single-pollutant models and then jointly using two-pollutant models. We assessed the assumption of linearity using standard methods including examining the shape of the dose-effect curve fitted with fractional polynomials and linear splines and found the assumption of linearity over the range of our data to be reasonable.

We examined effect modification by considering categories of age (≥80 vs 65–79 as referent), gender, and the presence of secondary diagnoses of atrial fibrillation (ICD-9: 427.31), other cardiac arrhythmias (427 except 427.31), chronic obstructive pulmonary disease (COPD, 490–496), essential hypertension (401), type II diabetes (250.×0 and 250.×2), acute myocardial infarction (MI) within the past 30 days (410), old MI (412), angina pectoris (413), other forms of ischemic heart disease (411 and 414), and acute respiratory infections (460–466 and 480–487).

All reported *p*-values are based on two-sided tests. A *p*-value of < 0.05 was considered statistically significant. All analyses were performed using SAS V8 (SAS Institute Inc., Carey, NC).

RESULTS

There were 55,019 admissions from the emergency room with a primary discharge diagnosis of CHF among Medicare beneficiaries residing in Allegheny County (Pittsburgh area), PA, between January 1, 1987, and November 30, 1999. Of these cases, 37.4 percent were from patients with only one CHF admission during the observation period and 86.8 percent arose from patients with 5 or fewer admissions. Among patients with more than one admission, the median time between admissions was 154 days. Age on the day of admission ranged from 65–108 years (78.9±7.78, mean±S.D.). Other characteristics of the cases are summarized in table 1. The distribution of average daily concentrations of particulate and gaseous air pollutants are shown in table 2 and pairwise correlations between pollutants are shown in table 3.

PM_{10} and the rate of hospitalization for CHF

Initially, we estimated the effect of PM_{10} separately for lags of 0 to 3 days and found a 3.07 (95 percent CI: 1.59, 4.57; $p < 0.0001$) percent increase in rate associated with an interquartile range increase in PM_{10} on the day of admission (lag 0). Controlling for the effect at lag 0,

PM_{10} levels one to three days before the admission day were not associated with altered rate of hospitalization. Additionally, the use of a 2-day moving average (average of lags 0 and 1) did not materially alter the results. Therefore, in subsequent analyses we only considered PM_{10} levels on the day of admission. Controlling for ambient temperature and barometric pressure rather than apparent temperature also did not materially alter the results. Including only the first observed admission for each patient yielded a qualitatively similar, but less precise effect estimate.

Daily concentrations of other air pollutants were highly correlated with PM_{10} levels (table 3). We used two-pollutant models to evaluate potential confounding by simultaneous exposure to these co-pollutants (table 4). Controlling for either O_3 or SO_2 did not materially alter the estimated effect of PM_{10}. However, in two-pollutant models controlling for either CO or NO_2, the effect of PM_{10} was negligible.

Gaseous co-pollutants and the rate of hospitalization for CHF

In single-pollutant models, daily fluctuations in ambient levels of CO, NO_2, and SO_2− but not O_3− were positively and significantly associated with the rate of hospitalization for CHF on the same day (table 4). In two-pollutant models, the effects of both CO and NO_2 were not materially changed by adjustment for most other measured pollutants, including PM_{10}. Ozone was not significantly associated with the rate of hospitalization for CHF in either single-pollutant or two-pollutant models.

Identification of susceptible subgroups

The effect of PM_{10} was more than three-fold greater in patients with a secondary diagnosis indicating an MI within the past 30 days [9.62 (95 percent CI: 3.14, 16.52) vs 2.80 (1.29, 4.32); $P_{\text{homogeneity}} = 0.042$]. Similarly, the effect of CO was approximately two-fold greater in patients with a recent MI, but this difference in the rate ratios did not reach statistical significance [8.99 (3.34, 14.95) vs 4.36 (3.12, 5.62); $P_{\text{homogeneity}} = 0.12$]. In contrast, the effect of neither PM_{10} nor CO was significantly stronger among patients with a secondary diagnosis for an old MI. The effect of either pollutant did not vary significantly by age, gender, or the presence of any other secondary diagnosis examined.

DISCUSSION

Heart failure patients may remain asymptomatic for extended periods if compensatory mechanisms and/or treatment are sufficient to balance the cardiac dysfunction. Factors that commonly disturb this balance include treatment non-compliance, uncontrolled hypertension, atrial fibrillation, acute respiratory infections, and myocardial ischemia or infarction (5–9). Although short-term increases in ambient particle levels have been associated with cardiovascular morbidity and mortality (27,28) relatively few studies have examined their effect on CHF morbidity. We found that short-term increases in mean daily levels of ambient particles and/or other pollutants may also precipitate acute cardiac decompensation leading to hospitalization, most notably in patients with a recent MI.

PM_{10}, CO, NO_2, and SO_2 (but not O_3) were significantly associated with CHF admissions in single-pollutant models--CO, NO_2 and PM_{10} most strongly. Previous studies found similar results for these three pollutants (13,14,29) or for only CO and NO_2, but not PM_{10} (30). In two-pollutant models, associations with CO and NO_2 were the most robust as noted before (12,14,29). However, given the high correlation between ambient measures of PM_{10}, CO and NO_2, two-pollutant modeling is of limited value in disentangling their effects.

Generally, the effect estimates derived from single-pollutant models (Table 5) in the current study are similar to those from previous reports. For example, previous estimates of the increase in CHF morbidity range from 2 to 7 percent (13,14,29,30) for a 1-ppm increase in ambient CO. Previous estimates of the effects of PM_{10} have also been similar (14,30,31) although not always statistically significant. For instance, Schwartz and Morris (12) found a 0.99 (0.37, 1.60) percent higher rate of admissions for CHF associated with a 10 $\mu g/m^3$ increase in 2-day mean PM_{10}. Hoek et al. (32) found that a 10 $\mu g/m^3$ increase in the 7-day mean concentration of PM_{10} was associated with a 0.44 (95 percent CI: −0.51, 1.40) percent increase in the risk of CHF mortality. Two other studies (33,34) reported an association between ambient particles and CHF mortality, but differences in exposure metrics for ambient particles prevent direct comparison to the current study (32–34).

Our effect estimate for PM_{10} from the current study is similar to that of the National Morbidity, Mortality and Air Pollution Study (NMMAPS), a large multi-city study. With a 10 $\mu g/m^3$ increase in same day PM_{10} we found a 1.27 (95 percent CI: 0.66, 1.88) percent increase in risk in CHF hospitalization and NMMAPS found a 0.84 (0.51, 1.18) percent increase in total-CHD hospitalization risk among Medicare beneficiaries 65 and older in Pittsburgh and a 1.02 (0.76, 1.27) percent increase in 14 cities combined (26).

Agent(s) responsible for the observed associations

In studies carried out in single cities, it is not possible to clearly distinguish the effects of multiple pollutants that covary strongly over time. Therefore the effect we are attributing to ambient particles may be mediated at least in part by gaseous co-pollutants.

Three pieces of evidence support ambient particles as the responsible agent. First, ambient measures of gaseous pollutants at a central site are poorly correlated with personal exposure to those pollutants. For example, one study (35) found this true of NO_2. Instead, ambient measures of both NO_2 and CO were strongly and significantly associated with personal measures of exposure to particulate matter with an aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) and even more so with personal exposure to elemental carbon, a surrogate for traffic-related particles. Second, several large multi-city studies have concluded that gaseous co-pollutants do not confound the association between PM_{10} and daily deaths (28,36,37), and it may, in fact, be inappropriate to control for them.. Third, biological plausibility is evidenced by animal toxicological and human panel studies, which suggest that particulate-related decompensation of heart failure patients may be mediated by relative increases in sympathetic nervous system activity (38,39), inappropriate changes in vasomotor tone (40), or triggering or exacerbating myocardial ischemia (41,42). In contrast, CO has been shown to have vasodilatory (43) and antiarrhythmic (44) properties in laboratory animals, both of which would be expected to reduce the risk of acute decompensation.

Most consistent with our data is that elevations in the combination of ambient particles, CO, and NO_2 are responsible for the association. In urban areas, the primary source of CO is motor vehicles emissions, which also contribute significantly to ambient levels of NO_2 and PM_{10}. Thus, motor vehicle emissions may be the responsible exposure. This interpretation is supported by recent epidemiologic studies showing that living in proximity to major roadways is associated with increased rates of cerebrovascular (45), cardiopulmonary (46), and all-cause (47) mortality. Additionally, a study of 14 US cities (48) found that the magnitude of the association between PM_{10} and cardiovascular hospital admissions increased significantly as the proportion of particles from highway vehicles increased. As discussed above, toxicological evidence points to particles as the most likely culprit. However, toxicological studies that examine the cardiovascular effects of traffic-related pollutant mixtures are still needed.

If causal, the results of the current study are noteworthy. Among those 65 years and older, the rate of hospitalization with a primary diagnosis of CHF is estimated as 222/10,000 person-years (49). Taking this as the underlying rate of hospitalization in the target population at the median PM_{10} concentration, and assuming that PM_{10} is an adequate marker of the pollution episodes responsible for the observed associations, the daily PM_{10} levels over the median value resulted in a ~1.5 percent excess rate of admission. While this relative increase in rate is small, the absolute increase in hospital admissions may be quite high given that 995,000 hospitalizations for CHF took place in the US in 2001(1).

Identification of susceptible subgroups

Previous studies suggest that patients with CHF are at greater risk of pollution-related hospitalization for ischemic heart disease (15) and acute MI (16), as well as non-accidental mortality (50,51). However, subgroups of CHF patients at increased risk of pollution-related acute decompensation have not been previously identified. We did not confirm for either PM_{10} or CO recent reports that patients with diabetes may be particularly susceptible to the effects of ambient particles (16,52–54), presumably due to increased endothelial dysfunction.

Multiple studies have reported a larger association of ambient pollution with the risk of MI than that observed with all ischemic heart disease admissions (15). The possibility that patients with a history of MI may be at greater risk for pollution-related events was evaluated among Medicare beneficiaries in Cook County, IL (54). The association between PM_{10} and all-cause mortality was more than twice as large in patients with vs. without a history of MI. We found that the association between PM_{10} and the rate of admission for CHF was nearly three-fold greater among patients with a recent MI than those without. A smaller increase in the association, not statistically significant, was observed for CO. Enhanced susceptibility was much less pronounced among patients with an old infarct, suggesting that the remodeling myocardium may be more susceptible to pollution.

Limitations

First, particle concentrations were measured using PM_{10}, whereas $PM_{2.5}$ is the currently regulated measure based on studies suggesting their greater toxicity. Second, the use of ambient PM_{10} levels rather than personal exposure measures, while highly correlated with indoor and personal PM_{10} levels (55), will result in some non-differential misclassification, tending to underestimate risk. Third, admission dates may have differed from the date of symptom onset, resulting in some exposure misclassification and underestimation of the true relative risk. Fourth, disease misclassification is also possible as a result of diagnostic or coding errors, although these errors are likely unrelated to pollution levels. While the direction of the resulting bias is expected to be towards the null, the magnitude is expected to be small.

A strength of the case-crossover design used in this study is that self-matching ensures that within strata, there is no variability in, or confounding by, chronic risk factors for heart disease, whether measured or unmeasured.

Summary and implications

Short-term increases in a combination of particulate air pollution, CO, and NO_2 were associated with acute decompensation and subsequent hospitalization of heart failure patients, especially those with a recent MI. This and other studies suggest that motor vehicle emissions are the responsible exposure. Because of the large number of hospitalizations for CHF, even a modest increase in rate can account for a large number of admissions, which may be preventable.

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TABLE 1

Characteristics of cases of CHF among Medicare beneficiaries in Allegheny County, Pennsylvania, 1987–1999.

	Number of Cases	%
Total	55,019	100
Age ≥ 80	25,713	46.7
Male	22,333	40.6
White	47,674	86.7
Primary Diagnosis:		
428.0*	54,346	98.8
428.1†	673	1.2
Secondary Diagnoses:		
Ischemic Heart Disease	21,232	38.6
Atrial Fibrillation	14,139	25.7
COPD	12,579	22.9
Essential Hypertension	9,182	16.7
Type II Diabetes	7,670	13.9
Other Arrhythmias	6,639	12.1
Acute Respiratory Infections	3,123	5.7
Old Myocardial Infarction	2,212	4.0
Recent Myocardial Infarction	2,024	3.7
Angina Pectoris	1,968	3.6

* ICD-9: Congestive Heart Failure, Unspecified

† ICD-9: Left Heart Failure.

TABLE 2

Distribution of average daily concentrations of air pollutants in Allegheny County, Pennsylvania, 1987–1999.

	% days missing	Mean	SD	Percentile				
				5%	25%	50%	75%	95%
PM_{10} ($\mu g/m^3$)	0.78	31.06	20.10	8.89	16.31	25.69	40.39	70.49
CO (ppm)	0.23	1.03	0.53	0.42	0.68	0.91	1.23	2.04
NO_2 (ppb)	0.93	26.48	8.02	15.10	20.61	25.70	31.30	41.02
O_3 (ppb)	2.90	24.30	12.23	7.01	14.60	23.15	31.96	46.37
SO_2 (ppb)	0.02	14.78	9.88	3.98	7.70	12.24	18.98	33.93
Temperature (°C)	0	11.09	9.88	−5.36	3.03	11.74	19.83	25.00
Apparent Temperature (°C)*	0	10.32	10.97	−6.12	0.80	9.79	19.92	27.56

*Defined as a person's perceived air temperature using the formula $AT = -2.653 + (0.994 \times Ta) + (0.0153 \times Td^2)$, where AT is apparent temperature, Ta is air temperature in degrees Celsius and Td is dew point temperature in degrees Celsius.

TABLE 3

Pearson pairwise correlation coefficients among air pollutants.

	CO	NO_2	O_3	SO_2
PM_{10}	0.57	0.64	0.29	0.51
CO	1	0.70	−0.25	0.54
NO_2		1	−0.04	0.52
O_3			1	−0.19
SO_2				1

TABLE 4

Percent increase (95% CI) in rate of admission for CHF associated with an interquartile range increase in pollutant levels in single-pollutant and two-pollutant models*.

Pollutant (IQR)	Single-Pollutant	Adjusted for PM_{10}	Adjusted for CO	Adjusted for NO_2	Adjusted for O_3	Adjusted for SO_2
PM_{10} (24 μg/m^3)	3.07 (1.59, 4.57)	--	−1.10 (−3.02, 0.86)	0.52 (−1.46, 2.53)	2.80 (1.29, 4.33)	2.18 (0.37, 4.02)
CO (0.55 ppm)	4.55 (3.33, 5.79)	5.18 (3.49, 6.89)	--	4.84 (3.06, 6.66)	4.35 (3.08, 5.64)	4.51 (3.15, 5.90)
NO_2 (11 ppb)	4.22 (2.61, 5.85)	4.05 (1.83, 6.31)	−0.37 (−2.59, 1.89)	--	3.73 (2.10, 5.39)	3.79 (1.93, 5.67)
O_3 (17 ppb)	−1.60 (−3.77, 0.61)	−1.96 (--4.14, 0.27)	0.13 (−2.12, 2.44)	−1.19 (−3.38, 1.06)	--	−1.41 (−3.58, 0.81)
SO_2 (11 ppb)	2.36 (1.05, 3.69)	1.35 (−0.27, 2.99)	0.10 (−1.35, 1.57)	0.68 (−0.82, 2.21)	2.02 (0.68, 3.37)	--

* In models controlling for barometric pressure and apparent temperature. Symbols: --, not applicable.

TABLE 5

Summary of effect estimates from single-pollutant models expressed for standard increments in each pollutant.

Pollutant	Increment	Increase in rate (%)	95% CI (%)
PM_{10}	10 $\mu g/m^3$	1.27	(0.66, 1.88)
CO	1 ppm	8.43	(6.14, 10.77)
NO_2	10 ppb	3.83	(2.37, 5.30)
O_3	10 ppb	−0.95	(−2.23, 0.36)
SO_2	10 ppb	2.14	(0.95, 3.35)

* In models controlling for barometric pressure and apparent temperature.