Effect of Air Pollution on Exacerbations of Bronchiectasis in Badalona, Spain, 2008–2016

Ignasi Garcia-Olivé^{a–c} Zoran Stojanovic^{a, d} Joaquim Radua^{e–g}
Laura Rodriguez-Pons^{a, d} Carlos Martinez-Rivera^{a–c} Juan Ruiz Manzano^{a–d}

^aDepartment of Pulmonary Medicine, Hospital Universitari Germans Trias i Pujol, Badalona, Spain;
^bCibeRes – Ciber de Enfermedades Respiratorias, Bunyola, Spain; ^cFundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain; ^dDepartment of Medicine, Universitat Autònoma de Barcelona, Bellaterra, Spain; ^eDepartment of Statistics, FIDMAG Research Unit, Sant Boi de Llobregat, Spain;
^fCiberSam – Ciber de Salud Mental, Madrid, Spain; ^gCentre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Keywords

Air pollution · Bronchiectasis · Exacerbation · SO₂ · Sulfur dioxide

Abstract

Introduction: Air pollution has been widely associated with respiratory diseases. Nevertheless, the association between air pollution and exacerbations of bronchiectasis has been less studied. **Objective:** To analyze the effect of air pollution on exacerbations of bronchiectasis. **Methods:** This was a retrospective observational study conducted in Badalona. The number of daily hospital admissions and emergency room visits related to exacerbation of bronchiectasis (ICD-9 code 494.1) between 2008 and 2016 was obtained. We used simple Poisson regressions to test the effects of daily mean temperature, SO₂, NO₂, CO, and PM₁₀ levels on bronchiectasis-related emergencies and hospitalizations on the same day and 1–4 days after. All *p* values were corrected for multiple comparisons. **Results:** SO₂ was significantly associated with an increase in the number of hospitalizations (lags 0, 1, 2, and 3). None of these associations remained significant after correcting for multiple comparisons. The number of emergency

room visits was associated with higher levels of SO₂ (lags 0–4). After correcting for multiple comparisons, the association between emergency room visits and SO₂ levels was statistically significant for lag 0 (*p* = 0.043), lag 1 (*p* = 0.018), and lag 3 (*p* = 0.050). **Conclusions:** The number of emergency room visits for exacerbation of bronchiectasis is associated with higher levels of SO₂.

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Introduction

Bronchiectasis is a chronic respiratory disease defined by abnormal and permanent dilatation of the bronchi [1]. Many of the patients with bronchiectasis have frequent exacerbations [1], which is associated with a decline in lung function [2] and increased mortality [3, 4].

Variant air pollutants have been described, either gaseous pollutants or particulate matter, and humans enter in contact with these air pollutants primarily via inhalation. The association between air pollution and respiratory diseases is well established [5–11]. Air pollution has been associated with a decrease in lung function [6, 7],

Table 1. Characteristics of the 250 subjects and 273 exacerbations (128 hospitalizations and 145 emergency room visits) included in the study

Mean age, years (SD)	74.7 (14.7)
Gender, <i>n</i> (%)	
Male	56 (22.4)
Female	194 (77.6)
Comorbidities, <i>n</i> (%)	
COPD	28 (11.2)
Asthma	36 (14.4)
Mortality, <i>n</i> (%)	12 (4.4)
Sputum, <i>n</i> (%)	
Not available	112/273 (41.0)
Commensal flora	105/273 (38.5)
<i>Pseudomonas aeruginosa</i>	25/273 (9.2)
<i>Haemophilus influenzae</i>	8/273 (2.9)
Non-fermenting Gram-negative bacilli	7/273 (2.6)
Other microorganisms	16/273 (5.9)
COPD, chronic obstructive pulmonary disease.	

exacerbation of preexisting pulmonary diseases [8–10], or even increased mortality [11]. Nevertheless, the association between air pollution and exacerbations of bronchiectasis has been less studied [12–15].

Our objective was to analyze the effect of air pollution on exacerbations of bronchiectasis in Badalona (Barcelona, Spain).

Material and Methods

Location

This was an observational, retrospective study, conducted in a hospital in Badalona, a city of the region of Barcelones (Barcelona, Spain). It is located north of Barcelona, on the coast of the Mediterranean Sea. In 2015, the city had 216,085 inhabitants. Hospital Universitari Germans Trias i Pujol is a tertiary hospital with 600 beds. It is also a referral hospital for a population of 700,000. By 2015, there were 28,000 hospital admissions to this institution.

Case Definition

The number of daily hospital admissions and emergency room visits due to exacerbation of bronchiectasis was obtained. We considered exacerbation of bronchiectasis to include all those hospitalizations or emergency department visits with a diagnosis of acute exacerbation of bronchiectasis (International Classification of Diseases [ICD]-9 code 494.1, bronchiectasis with acute exacerbation) in the discharge report, between January 2008 and December 2016. Patients with life-threatening hemoptysis or cystic fibrosis (CF) were excluded, as well as those whose postal code did not correspond to the area of Badalona. To avoid counting the same event twice, emergency room visits followed by an immediate hospitalization were not included in the analysis.

Obtaining Environmental Data

Catalonia has a network of monitoring stations operated by the Department of Environment of the Generalitat de Catalunya. The data were obtained from a station in Badalona (<http://dtes.gencat.cat/icqa/>, accessed May 13, 2017). The daily average sulfur dioxide (SO₂), nitrogen dioxide (NO₂), carbon monoxide (CO), and particulate matter with a median aerodynamic diameter of 10 µm or less (PM₁₀) were obtained.

Obtaining Weather Data

Daily mean temperature was obtained from the Catalan Meteorological Agency (<http://www.meteo.cat>, accessed February 13, 2016) from a station in the center of Badalona. Other weather variables, such as relative humidity, were not available and were not included in the analysis.

Statistical Analysis

We used simple Poisson regressions to test the effects of mean temperature, SO₂, NO₂, CO, and PM₁₀ levels on bronchiectasis-related emergencies and hospitalizations on the same day and 1–4 days after. To control for multiple comparisons (there were 5 independent variables × 2 events (emergencies and hospitalizations) × 5 time lags = 50 Poisson regressions), we applied a permutation approach. Specifically, the mean temperature and pollutant levels were randomly permuted 5,000 times in time (e.g., simulating that on February 2, 2010, there were the temperature and pollutant levels of April 13, 2014), and the Poisson regressions were repeated using the permuted data. Finally, we created the null distribution of the maximum *z* value from the maximum *z* value of each permutation. The effect of seasonality was not assessed.

Ethical Aspects

The study protocol was approved by the Ethics Committee on Clinical Research of the Hospital Universitari Germans Trias and Pujol.

Results

Two-hundred and fifty subjects and 273 exacerbations were included in the study. The characteristics of patients included in the study can be seen in Table 1. The description of temperature and atmospheric pollutants is shown in Table 2. The comparison of the mean levels of temperature and atmospheric pollutants in days with or without exacerbations of bronchiectasis can be seen in Table 3. The evolution of exacerbations and air pollutants according to the month of the year can be seen in Figure 1.

Hospitalizations for Bronchiectasis

The results of Poisson regressions for hospitalizations due to exacerbation of bronchiectasis are exposed in Table 4. SO₂ levels were significantly associated with an increase in the number of hospitalizations (lags 0, 1, 2, and 3). None of these associations remained significant after correcting for multiple comparisons.

Table 2. Description of temperature and atmospheric pollutants during the study period (2008–2016)

Variable	Mean (SD)	Maximum	Minimum
Mean temperature, °C	16.7 (5.6)	30.2	2
SO ₂ , µg/m ³	2.6 (1.8)	19.7	1
NO ₂ , µg/m ³	39.8 (15.6)	95	1.4
CO, µg/m ³	0.32 (0.14)	2.78	0.2
PM ₁₀ , µg/m ³	24.0 (9.9)	115.4	2.8

The table shows monthly mean values of the variables analyzed. CO, carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter with a median aerodynamic diameter of 10 µm or less; SO₂, sulfur dioxide.

Table 3. Comparison of mean levels of temperature and atmospheric pollutants in days with or without exacerbations of bronchiectasis

Variable	Exacerbation		<i>p</i> value
	present	absent	
Mean temperature, °C	15.9	16.7	0.061
SO ₂ , µg/m ³	3.1	2.6	0.000
NO ₂ , µg/m ³	39.8	39.2	0.586
CO, µg/m ³	0.32	0.32	0.574
PM ₁₀ , µg/m ³	24.2	22.5	0.121

CO, carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter with a median aerodynamic diameter of 10 µm or less; SO₂, sulfur dioxide.

Fig. 1. Evolution of exacerbations of bronchiectasis and pollutants according to the month of the year. CO, carbon monoxide (µg/m³); ERO, emergency room visits lag 0 (*n*); H0, hospitalizations lag 0 (*n*);

NO₂, nitrogen dioxide (µg/m³); PM₁₀, particulate matter with a median aerodynamic diameter of 10 µm or less (µg/m³); SO₂, sulfur dioxide (µg/m³); T, temperature (°C).

Table 4. Results of Poisson regressions for hospitalizations due to exacerbation of bronchiectasis

	exp (β), % ^a	SE	z value	p	corrected p
Lag 0					
T	97.5	0.016	-1.605	0.108	0.999
SO ₂	108.9	0.041	2.061	0.039*	0.936
NO ₂	101.0	0.006	0.190	0.849	1.000
CO	44.7	0.987	-0.816	0.415	1.000
PM ₁₀	98.9	0.014	-0.805	0.421	1.000
Lag 1					
T	97.3	0.016	-1.746	0.081	0.995
SO ₂	110.2	0.040	2.425	0.015*	0.718
NO ₂	100.3	0.006	0.520	0.603	1.000
CO	114.8	0.793	0.174	0.862	1.000
PM ₁₀	97.6	0.018	-1.350	0.177	1.000
Lag 2					
T	96.8	0.016	-2.014	0.044*	0.950
SO ₂	110.0	0.040	2.362	0.018*	0.766
NO ₂	99.7	0.006	-0.497	0.619	1.000
CO	124.3	0.776	0.280	0.779	1.000
PM ₁₀	97.9	0.016	-1.364	0.173	1.000
Lag 3					
T	97.2	0.016	-1.811	0.070	0.990
SO ₂	109.4	0.041	2.221	0.026*	0.859
NO ₂	99.8	0.006	-0.270	0.787	1.000
CO	39.4	0.990	-0.933	0.351	1.000
PM ₁₀	96.5	0.018	-1.976	0.048	0.960
Lag 4					
T	97.1	0.016	-1.872	0.061	0.982
SO ₂	107.3	0.043	1.652	0.099	0.999
NO ₂	100.2	0.006	0.265	0.791	1.000
CO	57.5	0.933	-0.593	0.553	1.000
PM ₁₀	98.0	0.015	-1.311	0.190	1.000

* $p < 0.05$ before correcting for multiple comparisons. ^a The exponential function of the coefficient may be understood on how much the frequency is multiplied per each unit increase in the contaminant or climatic factor. Note that this value substantially depends on the unit of measure (in this case $\mu\text{g}/\text{m}^3$). CO, carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter with a median aerodynamic diameter of 10 μm or less; SO₂, sulfur dioxide; T, temperature.

Table 5. Results of Poisson regressions for emergency room visits due to exacerbation of bronchiectasis

	exp (β), % ^a	SE	z value	p	corrected p
Lag 0					
T	98.1	0.015	-1.281	0.200	1.000
SO ₂	114.5	0.034	4.013	0.000*	0.043**
NO ₂	99.3	0.006	-1.273	0.203	1.000
CO	100.3	1.108	0.003	0.998	1.000
PM ₁₀	97.3	0.015	-1.829	0.067	0.987
Lag 1					
T	98.1	0.015	-1.313	0.189	1.000
SO ₂	115.8	0.032	4.546	0.000*	0.018**
NO ₂	100.3	0.005	0.501	0.617	1.000
CO	18.6	1.466	-1.146	0.252	1.000
PM ₁₀	99.8	0.012	-0.137	0.891	1.000
Lag 2					
T	98.0	0.015	-1.345	0.179	1.000
SO ₂	113.9	0.034	3.826	0.000*	0.057
NO ₂	100.5	0.005	0.922	0.357	1.000
CO	66.6	1.225	-0.332	0.740	1.000
PM ₁₀	99.6	0.013	-0.305	0.760	1.000
Lag 3					
T	97.5	0.015	-1.652	0.098	0.999
SO ₂	114.2	0.034	3.918	0.000*	0.050**
NO ₂	100.2	0.005	0.384	0.701	1.000
CO	139.5	0.987	0.337	0.736	1.000
PM ₁₀	100.2	0.012	0.135	0.893	1.000
Lag 4					
T	97.1	0.015	-1.928	0.054	0.973
SO ₂	111.5	0.036	3.003	0.003*	0.305
NO ₂	100.7	0.005	1.278	0.201	1.000
CO	112.9	1.068	0.114	0.909	1.000
PM ₁₀	101.2	0.011	1.067	0.286	1.000

* $p < 0.05$ before correcting for multiple comparisons. ** $p < 0.05$ after correcting for multiple comparisons. ^a The exponential function of the coefficient may be understood on how much the frequency is multiplied per each unit increase in the contaminant or climatic factor. Note that this value substantially depends on the unit of measure (in this case $\mu\text{g}/\text{m}^3$). CO, carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter with a median aerodynamic diameter of 10 μm or less; SO₂, sulfur dioxide; T, temperature.

Emergency Room Visits

The results of Poisson regressions for emergency room visits due to exacerbation of bronchiectasis are shown in Table 5. The number of emergency room visits was associated with higher levels of SO₂ (lags 0–4). After correcting for multiple comparisons, the association between emergency room visits and SO₂ levels was statistically significant for lag 0 ($p = 0.043$), lag 1 ($p = 0.018$), and lag 3 ($p = 0.050$).

Discussion

In our study, the number of emergency room visits was associated with higher levels of SO₂ (lags 0–4). After correcting for multiple comparisons, the association between emergency room visits and SO₂ levels was statistically significant for lags 0, 1, and 3.

Our findings, suggesting an association between air pollution and exacerbation of bronchiectasis, are in line with previous studies which have reported the effect of ambient air pollution in these patients. Goss et al. [12] described an increase in the odds of having two or more exacerbations in CF patients with an increased annual average exposure to several ambient air pollutants, specifically PM₁₀, PM_{2.5}, and ozone. No clear significant association was found with other pollutants (NO₂, SO₂) in their study, despite the fact that the level of NO₂ in their study is similar to ours (24.8 vs. 24) and the level of SO₂ is lower in our observation (4.9 vs. 2.6). Another study [13] described a significant increase in the risk of having an exacerbation on days with higher air concentrations of NO₂, ozone, and PM₁₀. Nevertheless, in this study, the authors did not investigate the effect of SO₂ on CF exacerbations. Goeminne et al. [14] found that living near a major road was associated with an increased mortality in patients with non-CF bronchiectasis, describing for the first time the impact of traffic-related pollution on patients with non-CF bronchiectasis. More recently, Garcia-Olivé et al. [15] described an increase in hospital admissions for exacerbation of bronchiectasis in those months with higher atmospheric concentrations of SO₂ and lower mean temperature.

SO₂ is a gas that is rapidly oxidized to sulfuric acid in contact with epithelial surfaces in the nasopharynx and lower airways, where it may cause damage [16]. It is a major airborne pollutant in industrialized countries, and the primary outdoor source of SO₂ is the combustion of sulfur-containing fossil fuels (coal and oil). SO₂ exposure has been associated with chronic cough, sputum production [17, 18], bronchoconstriction [19, 20], or irreversible airway obstruction [21] and one study even described the case of a patient who developed severe bronchiectasis after acute sulfur dioxide poisoning [22].

The mechanisms by which SO₂ can damage the lungs have been well studied [23–27]. In chronically exposed animals, it has been seen to cause mucus gland hypersecretion and replacement of ciliated cells by nonciliated cells [23]. Several authors have described dysfunction of mucociliary clearance in animals exposed to SO₂ [24–26]. This functional impairment can be reversible [24] and might occur at concentrations which yield no detectable morphological alterations, such as widening of intercellular spaces [25]. When the barrier function of the airway mucosa and/or the mucociliary function are impaired, the contact of bacteria with the mucosa could be increased and the invasion of inhaled pathogens could be eased [25], thus predisposing to exacerbations. In a study ana-

lyzing the bronchoalveolar fluid of 12 subjects exposed to SO₂, the authors found an increase in lysozyme-positive alveolar macrophages and mild lymphocytosis [16]. Seventy-two hours after exposure, total cell numbers had virtually returned to pre-exposure levels. On the contrary, Li et al. [27] did not find any obvious inflammatory response in rat lungs exposed to SO₂. Given the fact that the key components of the disease are chronic bronchial infection, inflammation, impaired mucociliary clearance, and structural lung damage [1], air pollution could play a role in exacerbations in patients without clear signs of bronchial infection.

Our study has several limitations. First, it is a retrospective study. Secondly, the definition of exacerbation is based on diagnostic codification at the time of discharge; therefore, we cannot exclude the possibility of errors in codification. Third, we considered the first day of the exacerbation to be the day the patient is admitted to the hospital, while certainly the symptoms had begun earlier. And last, although we have not included those patients with a postal code that does not belong to our city, the real time of exposure remains uncertain. Strengths of this paper are its long follow-up period and the fact that we have included ambient temperature in the analysis, which could have acted as a confounder.

In short, we have detected an increase in the number of emergency room visits for exacerbation of bronchiectasis associated with higher levels of SO₂, especially on the same day (lag 0) and the day after (lag 1). Further studies with different geographical locations and larger follow-up improving the exposure assignment are desirable in order to improve our understanding of the effects of ambient air pollution on patients with bronchiectasis.

Disclosure Statement

The authors do not have any financial or personal relationships with people or organizations that could inappropriately influence their work in the present article.

Author Contributions

Study design: I.G.-O., Z.S. Data collection: I.G.-O., Z.S., L.R.-P., C.M.-R. Statistical analysis: J.R. Writing of the manuscript: I.G.-O., Z.S. Critical reading of the manuscript: I.G.-O., Z.S., J.R., L.R.-P., C.M.-R., J.R.M.

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