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Association between ambient air pollution and hospitalization caused by atrial fibrillation

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Original Article

Abstract

BACKGROUND: Many studies have shown the worst effects of air pollution on cardiovascular diseases (CVDs). Present study focused on the relationship between atrial fibrillation (AF), as one of the common arrhythmias, and air pollutants in Isfahan, Iran, an industrial city in the Middle East.

METHODS: A case-crossover design was used to explore the associations between air pollution and AF hospitalized patients with ventricular response (VR) > 90 beats per minute (bpm) (fast response) and those with VR ≤ 90 bpm. All patients' records were extracted from their hospital files. Air pollutants data including particulate matter less than 10 µ (PM_{10}), $PM_{2.5}$, carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3) were obtained from the Correlation of Air Pollution with Hospitalization and Mortality of Cardiovascular and Respiratory Diseases (CAPACITY) study. Conditional logistic regression test was used to measure the relationship between pollutants and hospitalization due to AF.

RESULTS: Records of 369 patients, including 173 men (46.9%) who were hospitalized for AF during the study period and had complete data were extracted. Although a positive but not statistically significant relationship was shown between 10-unit increases in all pollutants (except PM_{10}) and the hospitalization due to AF in patients with rapid VR (RVR), the only significant relationship was observed in case of NO_2 [odds ratio (OR) = 1.26, 95% confidence interval (CI) = 1.0-2.1, P = 0.031].

CONCLUSION: This study showed positive significant relationships between NO_2 and the hospitalization due to AF in patients with RVR. NO_2 is a greenhouse gas whose levels are expected to increase due to global environmental changes. Therefore, relevant strategies should be adopted to decrease its levels, especially in industrial cities like Isfahan.

Keywords: Air Pollution, Atrial Fibrillation, Nitrogen Dioxide

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Introduction

Recent studies by the World Health Organization (WHO) have shown that more than 90% of the world's population is exposed to air pollution. Ambient air pollution was responsible for about

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four million deaths, mainly due to cardiovascular diseases (CVDs) in 2017. In addition to an increase in death rate due to CVD, air pollution is associated with increased complications and duration of hospitalization in patients suffering from heart problems. Hypertension (HTN),[1-3] cardiac arrhythmias,[4,5] heart failure (HF) deterioration, and acute ischemic and atherosclerotic cardiovascular complications are among the short-term consequences of air pollution.[6] Exposure to airborne contaminants causes a variety of cardiac arrhythmias, including atrial fibrillation (AF).[7] Independent relationships have been reported between death due to AF and concentrations of contaminants on the day before death.[8] Cardiac autonomic dysfunction caused by air pollution leads to various complications including AF.[9] In addition, air pollution can cause inflammation, oxidative stress, changes in atrial pressure, and ultimately AF.[10]

AF is the most widespread treatable cardiac arrhythmia.[11] It is associated with increased risk of stroke,[12] myocardial infarction (MI),[13] HF,[14] dementia,[15] and chronic kidney disease (CKD).[15] This prevalent arrhythmia doubles the risk of mortality following acute coronary disease and stroke.[16,17] There is an association between the incidence of AF and age, i.e., the prevalence of this arrhythmia varies from 1% in people younger than 60 years to 9% in those over 80 years of age. In Iran, the prevalence of AF in individuals over 70 years of age has been reported as high as 6%.[18] The prevalence of this disorder may even reach 14% in patients with stroke.[19]

The prevalence of AF in Iranians over 50 years of age has been estimated as 3%.[20,21] Considering the prevalence of AF and its potential irreversible complications, identification of its risk factors, determination of risk factor exposure, and planning of risk factor control policies can be a priority in the management of irrelevant diseases. This study investigated the relationship between AF and different air pollutants as part of a study on "The Correlation of Air Pollution with Hospitalization and Mortality of Cardiovascular and Respiratory Diseases (CAPACITY)" conducted in Isfahan, Iran, from March 20, 2010 to March 20, 2012.[22]

Increased ambient air pollution was associated with increased risk of episodes of rapid ventricular response (RVR) and AF, and we analyzed this association using a case–crossover design.

Materials and Methods

This case-crossover study was part of the CAPACITY research which evaluated the relationship between hospitalization and death from cardiovascular and respiratory diseases and airborne contaminants during March 20, 2010 to March 20, 2012. Data about all cases of hospitalization and/or death due to cardiovascular and respiratory diseases in Isfahan City during the mentioned period were collected from the hospitals and cemetery of Isfahan. Data on the concentrations of gaseous and non-gaseous pollutants including particulate matter < 10 μ and < 2.5 μ (PM_{10} and $PM_{2.5}$, respectively), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3) were collected from fixed air monitoring stations in the city of Isfahan. The CAPACITY study used two time-series and case-crossover models to assess the relationships between cardiovascular and respiratory diseases and air pollutants.[22]

The present study extracted the names and characteristics of all patients who were diagnosed with AF [I48 in the International Classification of Diseases, 10th revision (ICD-10)] and admitted to Isfahan hospitals during March 20, 2010 to March 20, 2012 from the CAPACITY study. The causes of hospitalization were determined by the hospital physician but were re-examined in this study. The patients' additional information, including symptoms at the time of admission, history of diabetes, and history of HTN, along with ejection fraction (EF) in the echocardiography performed during hospitalization, were extracted from the relevant hospitals. Patients with incomplete data were excluded from the study.

Air pollutant data including PM_{10}, $PM_{2.5}$, CO, SO_2, NO_2, and O_3, as well as weather information, including temperature, humidity, and wind speed were collected from the CAPACITY study (obtained from the Department of Environment, Isfahan Province). This information was collected from six fixed air monitoring stations installed in different areas of Isfahan recording the hourly concentrations of each pollutant. The CAPACITY study collected data on temperature, humidity, and wind speed from Isfahan Weather Forecast Organization and the National Oceanic and Atmospheric Administration (NOAA) National Environmental Satellite, Data, and Information Service (http://www.nesdis.noaa.gov). All data were evaluated in the CAPACITY study and the outliers and missing points were determined. The average daily values of weather pollutants were merged into a single file.

A case-crossover design allowed for investigation of the acute effects of exposure to air pollution. The subject exposure before the time of the event (case period) was compared with the distribution of exposure estimated from separate control periods and the matched sets were analyzed using conditional logistic regression. Thus, each patient served as his or her own control.

Case periods were defined by the time prior to onset of each confirmed arrhythmic event. Daily pollution concentrations and weather conditions were then matched to the case and control time periods for analysis.

The effect of 10-unit increase of air pollutants on hospitalization with heart rate more than 90 beats per minute (bpm) was determined using conditional logistic regression and crude and adjusted odds ratios (ORs) by temperature (˚f), dew point (˚f), and wind speed (mile/h).

The patients were divided in two groups: VR rate > 90 bpm and ≤ 90 bpm. Qualitative variables were expressed as number and percentage and for comparison between them, chi-square test or Fisher's exact test were used. Quantitative variables were expressed as mean ± standard deviation (SD) and compared with independent t-test or Mann-Whitney U test (if normality assumption was not hold). Kolmogorov-Smirnov test (K-S test) was used to determine whether normality assumption existed.

Statistical analysis was conducted using Stata software (version 9, Stata Corporation, College Station, TX, USA). P-value less than 0.050 was considered statistically significant.

Results

A total of 451 patients with AF were hospitalized in seven educational hospitals affiliated to Isfahan University of Medical Sciences, Isfahan City, during the study period. However, only 369 patients, including 173 men (46.9%), had complete data and were entered into the study. The patients' mean age was 66.3 ± 15.9 years. The patients visited the hospital mainly due to chest pain (n = 61, 16.0%), dyspnea (n = 41, 10.7%), dyspnea on exertion (DOE) (n = 81, 21.2%), dizziness (n = 19, 5.0%), and tachycardia (n = 17, 4.5%). The frequency of these complaints did not differ significantly between the two groups. Table 1 shows the history of diseases, symptoms, and results of echocardiography in all patients and the two groups.

Table 1. Demographic characteristics of hospital admissions for atrial fibrillation (AF) in Isfahan, Iran, 2010-2012

Variable	All subjects (n = 369)	Subjects with PR ≤ 90 bpm (n = 108, 29.3%)	Subjects with PR > 90 bpm (n = 261, 70.7%)	P
	Total	PR ≤ 90	PR > 90	
Age (year)	66.31 ± 15.88	65.55 ± 15.06	66.56 ± 16.24	0.657**
SBP (mmHg)	130.30 ± 27.78	129.17 ± 29.69	130.58 ± 27.25	0.693**
DBP (mmHg)	78.90 ± 13.42	77.41 ± 13.75	79.43 ± 13.32	0.227†
Number of pulses (bpm)*	117.80 ± 33.05	75.78 ± 51.50	130.91 ± 26.19	< 0.001**
EF value	50.70 ± 15.10	48.69 ± 15.27	51.27 ± 15.06	0.278**
Hb concentration	13.41 ± 2.60	13.16 ± 2.92	13.48 ± 2.53	0.443**
Creatinine (mg/dl)	1.22 ± 0.49	1.20 ± 0.40	1.23 ± 0.51	0.560†
Arterial oxygen saturation	90.71 ± 8.76	88.75 ± 5.12	90.90 ± 9.16	0.221†
History of VHD	87 (23.6)	23 (21.3)	64 (24.5)	0.539*
Medicines received in the hospital				
- Beta blocker	105 (28.5)	27 (25.0)	78 (29.9)	0.596*
- Statin	53 (14.4)	17 (15.7)	36 (13.8)	0.118*
- Warfarin	67 (18.2)	22 (20.4)	45 (17.2)	0.056*
Male gender	173 (46.9)	39 (36.1)	134 (51.3)	0.581*
History of diabetes	86 (23.3)	23 (21.3)	63 (24.1)	0.472*
History of HTN	148 (40.1)	33 (30.5)	115 (44.1)	0.567*
Status (death)	13 (3.5)	2 (1.8)	11 (4.2)	0.529*

Values are presented as mean ± standard deviation (SD) or median [interquartile range (IQR)] for quantitative variables and number and percentage for qualitative variables.
* Chi-square or Fisher's exact test were used where appropriate.
** Two independent samples t-test was used.
† Mann-Whitney U test was used.
PR: Pulse rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; EF: Ejection fraction; Hb: Hemoglobin; Bpm: Beats per minute; VHD: Valvular heart disease; HTN: Hypertension

Table 2. The mean daily concentrations of pollutants in Isfahan, Iran, during the study period (March 20, 2010 to March 20, 2012)

Variable	Mean ± SD	Minimum	Maximum
O_3 (ppb)	29.09 ± 15.18	3.00	101.0
CO (ppm)	3.93 ± 2.46	0.00	16.0
SO_2 (ppb)	41.33 ± 35.04	0.00	147.5
NO_2 (ppb)	40.53 ± 23.11	0.01	128.0
PM_{10} (µg/m^3)	129.86 ± 58.85	36.40	528.3
$PM_{2.5}$ (µg/m^3)	54.14 ± 29.61	8.00	296.1
Temperature (˚f)	55.77 ± 18.58	27.80	92.2
Dew point (˚f)	27.42 ± 9.23	7.30	46.6
Wind speed (mile/h)	4.82 ± 2.52	0.80	15.5

Ppb: Particle per billion; Ppm: Part per million; O_3: Ozone; CO: Monoxide carbon; SO_2: Sulfur dioxide; NO_2: Nitrogen dioxide; PM: Particulate matter; SD: Standard deviation

As seen in table 1, the two groups (VR ≤ 90 and VR > 90 bmp) had no significant differences except in the number of pulses. This difference was expected due to the classification of patients based on pulse rate (PR). Table 2 presents the mean concentrations of pollutants and weather factors during the study period.

Table 3 presents the details of the effect of air pollution on hospitalization due to AF using a crude and adjusted model for temperature (˚f), dew point (%), and wind speed (mile/h).

As seen, the only significant relationship was observed between a 10-unit increase in NO_2 and the hospitalization due to AF. However, 10-unit increases in other pollutants, except PM_{10}, had positive but not statistically significant associations with the hospitalization due to AF and RVR (VR > 90 bpm).

Discussion

The direct association between NO_2 concentration and rate of hospitalization due to AF was the only significant relationship in this study. Although increments in other pollutants increased the frequency of hospitalization due to AF, these relationships were not significant. Various studies have investigated the effects of pollutants on the incidence of cardiac arrhythmias, including AF, around the world. A cohort study followed patients with implantable cardioverter-defibrillator (ICD) for three years and found 798 cases of ventricular fibrillation (VF). The incidence of these cases was related with $PM_{2.5}$ and O_3.[5] Another cohort study reported a significant relationship between ventricular arrhythmias and SO_2 concentration. It evaluated 56 patients and a total of 139 VF events and found increased NO_2 24 hours before the incidence of arrhythmia. However, this increase had no significant associations with arrhythmias.[23]

A cohort study extracted electrocardiographic (ECG) changes from the records of patients with ICD and identified significant relationships between the incidence of AF and exposure to PM, CO, and NO_2, especially two hours before AF. Overall, 124 AF events occurred in individuals who had no previous AF records and the incidence of the arrhythmia was strongly associated with the mentioned contaminants, especially NO_2.[24]

Table 3. The effects of a 10-unit increase in pollutants at 24 hours before the onset of atrial fibrillation (AF) in patients with rapid ventricular response (RVR)

Pollutants	Crude			Adjusted*		
	OR	95% CI	P	OR	95% CI	P
$PM_{2.5}$	1.017	0.950-1.089	0.612	1.019	0.951-1.092	0.579
PM_{10}	0.992	0.930-1.059	0.830	0.994	0.931-1.062	0.879
SO_2	1.017	0.849-1.218	0.854	1.014	0.846-1.215	0.878
CO**	1.064	0.864-1.310	0.557	1.062	0.862-1.309	0.570
NO_2	1.260	1.024-1.551	0.029	1.259	1.020-1.553	0.031
O_3	1.082	0.763-1.533	0.657	1.083	0.760-1.544	0.655

* Adjusted for temperature (˚f), dew point(%), and wind speed (mile/h)
** For CO effect, 1-unit increase was conducted
OR: Odds ratio; CI: Confidence interval; PM: Particulate matter; SO_2: Sulfur dioxide; CO: Monoxide carbon; NO_2: Nitrogen dioxide; O_3: Ozone

A two-year time-series study on emergency room (ER) visits in Brazil revealed associations between arrhythmias and air contaminants. The study designed a model based on generalized linear Poisson regression with seasonal adjustment to investigate the relationship between contaminants and the incidence of arrhythmias. The results showed that atrial arrhythmias, including flutter and fibrillation, and other arrhythmias were associated with increases in CO, NO_2, and PM_{10} concentrations within the quartiles.[25]

A 14-year time-series study in Rome, Italy, investigated the relationship between the frequency of patients with AF referring to ER and air pollutants (PM_{10}, $PM_{2.5}$, NO_2) at different time intervals. Models based on two pollutants and adjusted for temperature, humidity, individual characteristics, and consumed drugs were also developed. During the study, nearly 80000 people were admitted to ERs due to AF. The study showed an association between hospitalization due to AF and exposure to PM 24 hours before the incidence of arrhythmia. Hospitalization due to AF had the strongest relationships with PM in men over 75 years of age and with NO_2 in women over 75 years of age. It was also associated with exposure to NO_2, and more strongly with $PM_{2.5}$ 24 hours before the incidence in all ages.[26]

In a large case-crossover study in the United Kingdom (UK), patient registration programs, e.g., the Myocardial Ischaemia National Audit Project (MINAP), were used to extract the data of around 2 million patients admitted to ERs due to CVD during 2003-2008. Data about the mean daily concentrations of CO, PM_{10}, $PM_{2.5}$, SO_2, and NO_2, as well as the maximum 8-hour concentrations of O_3 per day, were extracted from air monitoring stations with minimum distance from each individual patient. The designed model was examined based on different time intervals and up to four days before the event. The strongest relationship was observed between NO_2 levels and hospitalization due to different cardiovascular causes, including AF. In addition, the hospitalization of patients after non-ST-segment elevation MI (NSTEMI) had significant relationships with SO_2 and NO_2 during the four-day period before the incidence. The effects of NO_2 were more profound in subjects over 70 years old and also in women.[27]

NO_2 is produced from diesel fuel and secondary reactions of NO with O_3. It is usually related with other pollutants and can exacerbate their effects. NO_2 per se can cause autonomic system dysfunction and increase the risk of AF.[26,28]

It should be borne in mind that although AF is a major risk factor for stroke and MI, it is often asymptomatic and undetectable. Consequently, the treatment may not be initiated until a complication occurs. Therefore, based on the results of this study, it is preferable to control the risk factors of AF, e.g., airborne contaminants, especially NO_2. Furthermore, in addition to pollutant reduction policies, screening methods to diagnose and treat AF should be adopted in the country. A combination of these measures and control strategies, especially on polluted days, will reduce the hospitalization due to both AF and its complications.

Another important point is the rapid change in the AF process and the development of symptoms, due to which studies on the effects of pollutants on the hospitalization due to AF should consider the few hours before hospitalization as the exposure time.[24] Based on the results of other studies, obtaining reliable results regarding the effects of environmental factors, such as pollutants, on the incidence of AF requires larger research, cohort studies, using large databases such as health information system (HIS) and Iranian electronic health record (SEPAS) in Iran, updating the available databases, and recording patients' full information (e.g., history of hospitalization, diseases, and medication use) and changes in their home and work addresses.

Another finding of this study was that the mean annual concentrations of NO_2, PM_{10}, $PM_{2.5}$, and SO_2 within the study period were almost twice the Iranian and global standards. High levels of pollutants can be attributed to the presence of various industries using fossil fuels, as well as the increased number of vehicles, in particular diesel cars, followed by elevated use of fossil fuels in the city of Isfahan. Moreover, due to sanctions in 2011, Iran could not import gasoline and had to use the gasoline produced in the country which did not have Euro 4 standard according to some sources. It is, hence, critical to pay attention to high levels of pollutants and develop relevant measures to control them.

Another notable result of this study was the high frequency of women hospitalized for AF in Isfahan. Similar to our findings, Habibzadeh et al. studied patients referred to a first-level health center and showed a higher frequency of women among the 463 50-80-year-old patients with AF.[20] In contrast, Schnabel et al. reviewed a 50-year record of patients admitted for AF and reported a higher incidence of this arrhythmia in men.[29] In the Gulf Survey of

Atrial Fibrillation Events (Gulf SAFE) on 2043 patients with AF visiting ERs, men had a higher overall frequency, but the frequency of women was higher in patients with comorbidities and resistant AF.[30] Accordingly, it seems necessary to assess gender distribution of Iranian patients with AF, especially those at a high risk of complications.

Conclusion

The greater frequency of women among patients with AF, higher concentrations of pollutants compared to global standards, and a relatively strong significant relationship between NO_2, as an important pollutant, and the hospitalization due to AF or development of its symptoms were the most important findings of this study. Therefore, relevant strategies should be adopted to identify patients and examine the reasons for the higher rate of hospitalization due to AF in women. It is also essential to develop effective measures to decrease the levels of pollutants (especially NO_2) and precursor pollutants (e.g., O_3). Timely AF control methods should also be used before the development of complications on highly-polluted days. In addition, due to the possibility of quick effects of pollutants on the hospitalization due to AF, further studies are required to design models assessing very short exposure times before the hospitalization due to AF symptoms. Models should also consider combinations of pollutants in order to study the impacts of precursor pollutants on other contaminants.

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Conflict of Interests

Authors have no conflict of interests.

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