ehp ENVIRONMENTAL HEALTH PERSPECTIVES

ehponline.org

Case report: Supraventricular Arrhythmia Following Exposure to Concentrated Ambient Air Pollution Particles

Andrew J. Ghio, Maryann Bassett, Tracey Montilla, Eugene H. Chung, Wayne E. Cascio, Martha Sue Carraway

http://dx.doi.org/10.1289/ehp.1103877

Online 6 September 2011

NIEHS
National Institute of Environmental Health Sciences

National Institutes of Health
U.S. Department of Health and Human Services

Case report: Supraventricular Arrhythmia Following Exposure to Concentrated Ambient Air Pollution Particles

Andrew J. Ghio,[1] Maryann Bassett,[1] Tracey Montilla,[1] Eugene H. Chung,[2] Wayne E. Cascio,[1] and Martha Sue Carraway[1]

[1]Environmental Public Health Division, National Health and Environmental Effects Research Laboratory, US Environmental Protection Agency, Chapel Hill, North Carolina and
[2]Division of Cardiology, University of North Carolina, Chapel Hill, North Carolina

Corresponding Author: Andrew Ghio
Campus Box 7315, Human Studies Facility
US EPA, 104 Mason Farm Road
Chapel Hill, NC 27599-7315
Phone: (919) 966-0670
Fax: (919) 966-47-67
E-mail: ghio.andy@epa.gov

Running Title: Arrhythmia after air pollution particles

Disclaimer: This report has been reviewed by the National Health and Environmental Effects Research Laboratory, United States Environmental Protection Agency and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency nor does mention of trade names or commercial products constitute endorsement or recommendation for use. None of the authors has any actual or potential competing financial interests.

Abbreviations: concentrated ambient particles (CAPs), implantable cardioverter defibrillator (ICD), particulate matter (PM); University of North Carolina (UNC)

Key words: Air pollution; arrhythmias; atrial fibrillation; atrial flutter; heart diseases; particulate matter

Abstract

CONTEXT: Exposure to air pollution can result in the onset of arrhythmias.

CASE PRESENTATION: We present a case of a 58 year old woman who volunteered to participate in a controlled exposure to concentrated ambient particles (CAPs). Twenty minutes into the exposure, telemetry revealed new onset of atrial fibrillation. The exposure was discontinued and she reverted to normal sinus rhythm approximately two hours later. No abnormality was evident on the volunteer's laboratory examination or echocardiography which could explain an increased risk for supraventricular arrhythmia.

DISCUSSION: Epidemiologic evidence strongly supports a relationship between exposure to air pollutants and cardiovascular disease, but population-level data are not directly relevant to the clinical presentation of individual cases. To our knowledge, this is the only case report of an individual suffering an episode of atrial fibrillation following exposure to an air pollutant. The resolution of the arrhythmia with termination of the particle exposure further supports a causal relationship between the two.

RELEVANCE TO CLINICAL PRACTICE: Exposure to air pollution including particulate matter may cause supraventricular arrhythmias.

Introduction

Epidemiologic investigation supports a positive relationship between exposure to air pollution and cardiovascular disease (Rich et al. 2006) with the number of deaths from such illness estimated to exceed that for respiratory disease following elevated levels of pollutants (Dockery 2001). Air pollutants have been associated with acute cardiac events including myocardial infarctions and cardiac arrests (Forastiere et al. 2005; Rosenthal et al. 2008; Zanobetti and Schwartz 2005). In addition, air pollution has been associated with the incidence of cardiac arrhythmias (Link and Dockery 2010; Peters et al. 2000; Routledge and Ayres 2005). Studies have demonstrated that discharges by implantable cardioverter defibrillators (ICDs) for ventricular arrhythmias increase with higher levels of black carbon, fine particles, coarse particles, nitric oxide, ozone, NO_2, nitric oxide, carbon monoxide, and SO_2 (Rich et al. 2006; Peters et al. 2000; Metzger et al. 2007; Rich et al. 2005; Santos et al. 2008). Evidence also supports an association between measures of air pollution and the incidence of supraventricular arrhythmias. In one ICD study, there was a statistically significant relationship between the incidence of supraventricular arrhythmias and increased O_3 concentrations in the hour preceding the arrhythmia (Rich et al. 2005). Holter examinations revealed an increased risk of supraventricular arrhythmias in association with 5-day moving averages of $PM_{2.5}$, ozone, and sulfate in non-smoking adults (Sarnat et al. 2006). In yet another holter study, both supraventricular and ventricular arrhythmias were increased in association with PM and NO_2 exposures (in the previous 24 to 72 hours and with 5 day moving averages) among men with coronary artery disease (Berger et al. 2006). These arrhythmias developed within a few hours of increased levels of air pollution (Ljungman et al. 2008).

While epidemiologic data strongly support a relationship between exposure to air pollutants and cardiovascular disease, this methodology does not permit a description of the clinical presentation in an individual case. To our knowledge, there has been no case report of cardiovascular disease following exposure to elevated concentrations of any air pollutant.

Case Presentation

A 58 year old, Caucasian female presented to the Environmental Protection Agency's Human Studies Facility in Chapel Hill, North Carolina for participation in a study requiring sequential exposures to filtered air and concentrated ambient particles (CAPs). Protocols and consent forms were approved by the University of North Carolina (UNC) School of Medicine Committee on the Protection of the Rights of Human Subjects and the subject provided informed consent. Two years previously, she had participated in an identical exposure protocol without any complication. At that time, two 24 hour holter examinations obtained during the exposures to filtered air and CAPs demonstrated 29 and 54 episodes of supraventricular ectopy respectively.

On the day of exposure to CAPs, the volunteer had no symptoms. There was a history of osteoarthritis and hypertension treated with an angiotensin-converting enzyme inhibitor and a diuretic (lisinopril 10 mg and hydrochlorothiazide 12.5 mg). Previous surgeries included a hernia repair, a cholecystectomy, and a total left knee arthroplasty. The family history was significant for her father dying at 57 years of age with a myocardial infarction. The volunteer was a lifetime non-smoker. On physical examination, she was 173 cm tall and weighed 104.4 kg (the body mass index was 34.9 and her waist was 45 inches). Her pulse was regular at 66 per minute and her blood pressure was 144/61. The baseline electrocardiogram showed normal sinus

rhythm (Figure 1A). A holter monitor was placed and this demonstrated evidence of increased supraventricular ectopy with 157 ± 34 premature atrial contractions per hour during the 3 hours immediately preceding the exposure to CAPs.

Twenty three minutes into the exposure to CAPs (with a filter weight revealing 112 $\mu g/m^3$ and the particle number being 563912/cc), the telemetry monitor revealed that the subject had non-sustained atrial fibrillation that quickly organized into atrial flutter. She was immediately removed from the exposure chamber. The volunteer reported no symptoms and there was no change in the physical examination. The twelve lead EKG verified that she remained in atrial flutter (Figure 1B). Her serum electrolytes, blood urea nitrogen, creatinine, glucose, and complete blood count were all normal. Creatine kinase and the MB fraction were also normal. During the transfer to the UNC Medical Center (approximately 2 hours following the onset of the arrhythmia), she spontaneously reverted back to a normal sinus rhythm.

The patient was admitted to the hospital overnight for observation and telemetry. The following morning, the EKG documented normal sinus rhythm. Her serum electrolytes, blood urea nitrogen, creatinine, glucose, creatine kinase, and the MB fraction were again normal, and her complete blood count was normal except for a hematocrit of 35.7% (with a lower limit of normal being 36.0%). Resting transthoracic echocardiography demonstrated normal right ventricular contraction with an ejection fraction of 55 to 60%, aortic sclerosis, and diastolic left ventricular dysfunction. The left atrium was considered mildly dilated; all other chambers of the heart were normal in size. She was discharged on no new medication. Approximately 6 weeks later, she underwent electrophysiology study, which did not provoke atrial fibrillation or significant atrial ectopy. The study did indicate a reentrant circuit of the cavotricuspid isthmus which was ablated to prevent potential future episodes of atrial flutter.

Discussion

The volunteer demonstrated evidence of increased supraventricular ectopy immediately preceding her exposure to CAPs but there was no evidence of atrial arrhythmias. She then suffered the onset of atrial fibrillation within a very short time after exposure to CAPs was initiated. Within 2 to 3 hours after the cessation of exposure, the arrhythmia resolved and she returned to normal sinus rhythm. Atrial fibrillation is the most common supraventricular arrhythmia affecting 1 to 2% of the general population (Falk 2001). This arrhythmia is uncommon before 60 years of age but it afflicts about 10% of the population by 80 years of age.. Risk factors for atrial fibrillation include hypertension (especially uncontrolled), coronary artery disease, heart failure, cerebrovascular disease, diabetes, thyroid conditions, sleep apnea, obesity, a past history of rheumatic heart disease and/or congenital heart defects, pericarditis, sick sinus syndrome, a family history of atrial fibrillation, and echocardiographic abnormalities (Kannel and Benjamin 2008, 2009). In addition, cigarette smoking, alcohol use, caffeine consumption, and stimulant drugs can help trigger atrial fibrillation. Of these defined risk factors, the volunteer had a history of well controlled hypertension and her body mass index was consistent with obesity. Her history of premature atrial contractions may also have increased her risk for atrial fibrillation (Binici et al. 2010). In a similar manner, pre-existing cardiovascular disease, diabetes and impaired glucose tolerance, chronic obstructive pulmonary disease, and current cigarette smoking all increase susceptibility for cardiovascular disease associated with air pollution (Chen et al. 2006; Liao et al. 2009; Mills et al. 2007; Wheeler et al. 2006; Whitsel et al. 2009; Zareba et al. 2009). There was no obvious explanation for her onset of a supraventricular arrhythmia during the exposure. While coincident atrial fibrillation cannot be excluded, the

onset of her arrhythmia was associated with her exposure to ambient air pollution particles. The correlation between the resolution of the arrhythmia and the termination of the CAPs exposure further supports a causal relationship between the two.

Systemic inflammation and underlying oxidative stress may increase the risk of atrial fibrillation (Kumagai et al. 2004). Patients with atrial fibrillation demonstrate evidence of inflammation with elevated levels of inflammatory markers including C reactive protein, interleukin-6, and tumor necrosis factor-α (Chung et al. 2001; Gaudino et al. 2003). There is some evidence that statin treatment may potentially alter the risk for this arrhythmia by modifying oxidative stress (Siu et al. 2003). The specific association between increased arrhythmia induction and air pollution may reflect oxidant generation and inflammation following exposure, consistent with mechanisms involved in the initiation and maintenance of some other forms of atrial fibrillation (Mazzoli-Rocha et al. 2010). The oxidative stress and inflammation associated with the pollutant have been postulated to affect coronary perfusion and consequently enhance the propensity for such arrhythmias through tissue ischemia. However, the rapid onset of the onset of this volunteer's atrial fibrillation following CAPs exposure suggests that the basis for the arrhythmia may be a disruption of the normal cardiac autonomic control rather than a systemic inflammation as the latter would require greater durations of time to develop (Routledge and Ayres 2005). In an animal model, diesel exhaust increased the sensitivity of the heart to triggered arrhythmias via an activation of airway sensory receptors (e.g. TRPA1) (Hazari et al. 2011). It has been suggested that this leads to autonomic imbalance and a predisposition for arrhythmia development. A comparable mechanism has been proposed to explain the cardiac response to ozone and cigarette smoke (Joad et al. 1998; Mutoh et al. 2000).

References

Berger A, Zareba W, Schneider A, Ruckerl R, Ibald-Mulli A, Cyrys J, et al. 2006. Runs of ventricular and supraventricular tachycardia triggered by air pollution in patients with coronary heart disease. J Occup Environ Med 48(11):1149-1158.

Binici Z, Intzilakis T, Nielsen OW, Kober L, Sajadieh A. 2010. Excessive supraventricular ectopic activity and increased risk of atrial fibrillation and stroke. Circulation 121(17):1904-1911.

Chen JC, Stone PH, Verrier RL, Nearing BD, MacCallum G, Kim JY, et al. 2006. Personal coronary risk profiles modify autonomic nervous system responses to air pollution. J Occup Environ Med 48(11):1133-1142.

Chung MK, Martin DO, Sprecher D, Wazni O, Kanderian A, Carnes CA, et al. 2001. C-reactive protein elevation in patients with atrial arrhythmias: inflammatory mechanisms and persistence of atrial fibrillation. Circulation 104(24):2886-2891.

Dockery DW. 2001. Epidemiologic evidence of cardiovascular effects of particulate air pollution. Environ Health Perspect 109 Suppl 4:483-486.

Falk RH. 2001. Atrial fibrillation. N Engl J Med 344(14):1067-1078.

Forastiere F, Stafoggia M, Picciotto S, Bellander T, D'Ippoliti D, Lanki T, et al. 2005. A case-crossover analysis of out-of-hospital coronary deaths and air pollution in Rome, Italy. Am J Respir Crit Care Med 172(12):1549-1555.

Gaudino M, Andreotti F, Zamparelli R, Di Castelnuovo A, Nasso G, Burzotta F, et al. 2003. The -174G/C interleukin-6 polymorphism influences postoperative interleukin-6 levels and

postoperative atrial fibrillation. Is atrial fibrillation an inflammatory complication? Circulation 108 Suppl 1:II195-199.

Hazari MS, Haykal-Coates N, Winsett DW, Krantz QT, King C, Costa DL, et al. 2011. TRPA1 and Sympathetic Activation Contribute to Increased Risk of Triggered Cardiac Arrhythmias in Hypertensive Rats Exposed to Diesel Exhaust. Environ Health Perspect 119(7):951-7

Joad JP, Kott KS, Bonham AC. 1998. Exposing guinea pigs to ozone for 1 wk enhances responsiveness of rapidly adapting receptors. J Appl Physiol 84(4):1190-1197.

Kannel WB, Benjamin EJ. 2008. Status of the epidemiology of atrial fibrillation. Med Clin North Am 92(1):17-40, ix.

Kannel WB, Benjamin EJ. 2009. Current perceptions of the epidemiology of atrial fibrillation. Cardiol Clin 27(1):13-24, vii.

Kumagai K, Nakashima H, Saku K. 2004. The HMG-CoA reductase inhibitor atorvastatin prevents atrial fibrillation by inhibiting inflammation in a canine sterile pericarditis model. Cardiovasc Res 62(1):105-111.

Ljungman PL, Berglind N, Holmgren C, Gadler F, Edvardsson N, Pershagen G, et al. 2008. Rapid effects of air pollution on ventricular arrhythmias. Eur Heart J 29(23): 2894-2901.
Falk RH. 2001. Atrial fibrillation. N Engl J Med 344(14):1067-1078.

Liao D, Whitsel EA, Duan Y, Lin HM, Quibrera PM, Smith R, et al. 2009. Ambient particulate air pollution and ectopy--the environmental epidemiology of arrhythmogenesis in Women's Health Initiative Study, 1999-2004. J Toxicol Environ Health A 72(1):30-38.

Link MS, Dockery DW. 2010. Air pollution and the triggering of cardiac arrhythmias. Curr Opin Cardiol 25(1):16-22.

Mazzoli-Rocha F, Fernandes S, Einicker-Lamas M, Zin WA. 2010. Roles of oxidative stress in signaling and inflammation induced by particulate matter. Cell Biol Toxicol 26(5):481-498.

Mills NL, Tornqvist H, Gonzalez MC, Vink E, Robinson SD, Soderberg S, et al. 2007. Ischemic and thrombotic effects of dilute diesel-exhaust inhalation in men with coronary heart disease. N Engl J Med 357(11):1075-1082.

Mutoh T, Joad JP, Bonham AC. 2000. Chronic passive cigarette smoke exposure augments bronchopulmonary C-fibre inputs to nucleus tractus solitarii neurones and reflex output in young guinea-pigs. J Physiol 523 Pt 1:223-233.

Peters A, Liu E, Verrier RL, Schwartz J, Gold DR, Mittleman M, et al. 2000. Air pollution and incidence of cardiac arrhythmia. Epidemiology 11(1):11-17.

Rich DQ, Kim MH, Turner JR, Mittleman MA, Schwartz J, Catalano PJ, et al. 2006. Association of ventricular arrhythmias detected by implantable cardioverter defibrillator and ambient air pollutants in the St Louis, Missouri metropolitan area. Occup Environ Med 63(9):591-596.

Rich DQ, Schwartz J, Mittleman MA, Link M, Luttmann-Gibson H, Catalano PJ, et al. 2005. Association of short-term ambient air pollution concentrations and ventricular arrhythmias. Am J Epidemiol 161(12):1123-1132.

Rosenthal FS, Carney JP, Olinger ML. 2008. Out-of-hospital cardiac arrest and airborne fine particulate matter: a case-crossover analysis of emergency medical services data in Indianapolis, Indiana. Environ Health Perspect 116(5):631-636.

Routledge HC, Ayres JG. 2005. Air pollution and the heart. Occup Med (Lond) 55(6): 439-447.
Metzger KB, Klein M, Flanders WD, Peel JL, Mulholland JA, Langberg JJ, et al. 2007. Ambient air pollution and cardiac arrhythmias in patients with implantable defibrillators. Epidemiology 18(5):585-592.

Santos UP, Terra-Filho M, Lin CA, Pereira LA, Vieira TC, Saldiva PH, et al. 2008. Cardiac arrhythmia emergency room visits and environmental air pollution in Sao Paulo, Brazil. J Epidemiol Community Health 62(3):267-272.

Sarnat SE, Suh HH, Coull BA, Schwartz J, Stone PH, Gold DR. 2006. Ambient particulate air pollution and cardiac arrhythmia in a panel of older adults in Steubenville, Ohio. Occup Environ Med 63(10):700-706.

Siu CW, Lau CP, Tse HF. 2003. Prevention of atrial fibrillation recurrence by statin therapy in patients with lone atrial fibrillation after successful cardioversion. Am J Cardiol 92(11):1343-1345.

Wheeler A, Zanobetti A, Gold DR, Schwartz J, Stone P, Suh HH. 2006. The relationship between ambient air pollution and heart rate variability differs for individuals with heart and pulmonary disease. Environ Health Perspect 114(4):560-566.

Whitsel EA, Quibrera PM, Christ SL, Liao D, Prineas RJ, Anderson GL, et al. 2009. Heart rate variability, ambient particulate matter air pollution, and glucose homeostasis: the environmental epidemiology of arrhythmogenesis in the women's health initiative. Am J Epidemiol 169(6):693-703.

Zanobetti A, Schwartz J. 2005. The effect of particulate air pollution on emergency admissions for myocardial infarction: a multicity case-crossover analysis. Environ Health Perspect 113(8):978-982.

Zareba W, Couderc JP, Oberdorster G, Chalupa D, Cox C, Huang LS, et al. 2009. ECG parameters and exposure to carbon ultrafine particles in young healthy subjects. Inhal Toxicol 21(3):223-233.

Figure legend

Figure 1. The volunteer's electrocardiogram (12 lead and rhythm strip) before (A) and immediately following (B) exposure to concentrated ambient particles. The electrocardiogram before the exposure (A) reveals a regular sinus rhythm with defined P waves (arrows) while that following the exposure (B) is irregular with "flutter" waves (arrows).

Figure 1

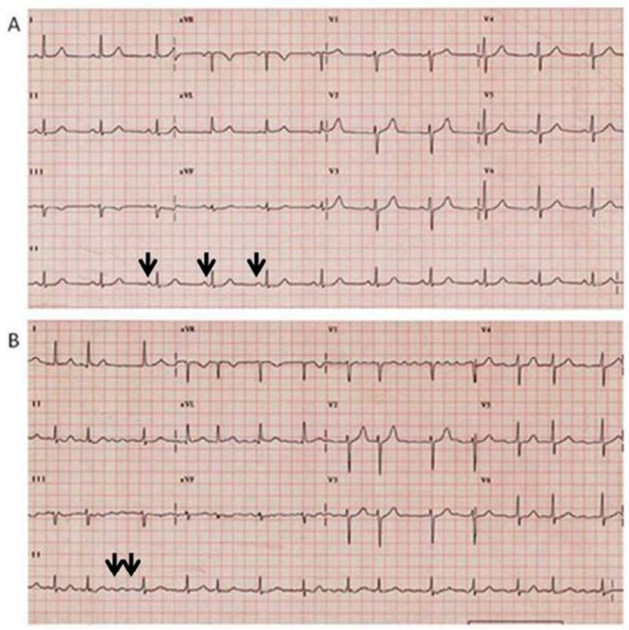

Figure 1. The volunteer's electrocardiogram (12 lead and rhythm strip) before (A) and immediately following (B) exposure to concentrated ambient particles. The electrocardiogram before the exposure (A) reveals a regular sinus rhythm with defined P waves (arrows) while that following the exposure (B) is irregular with "flutter" waves (arrows).
76x57mm (300 x 300 DPI)