STATEMENT

Synopsis of Research Report 141

HEALTH EFFECTS INSTITUTE

Air Pollution Effects on Ventricular Repolarization

BACKGROUND

Epidemiologic studies have described an association between increases in cardiovascular morbidity and mortality and increases in ambient particulate matter (PM) concentrations, especially in susceptible populations such as the elderly and persons with pulmonary or cardiovascular disease. However, the biological mechanisms by which PM and other air pollutants may affect cardiovascular events are not well understood. Several studies have shown that air pollution may be associated with cardiac outcomes such as arrhythmias, suggesting that air pollutants may affect autonomic control of the heart.

Heart rate variability (HRV) is an electrophysiologic parameter that can be derived from an electrocardiogram (ECG). Low HRV is a marker of poor cardiac autonomic control and is associated with a higher risk of myocardial infarction and sudden cardiac death. Several cohort and panel studies have shown that increases in ambient PM concentrations are associated with decreased HRV, although it remains unclear how decreased HRV contributes to cardiac arrhythmia. Thus, the evaluation of additional ECG parameters, such as ventricular repolarization — the process of electrical recovery of the heart cells after contraction of the ventricles — is warranted.

Robert Lux of the University of Utah and Arden Pope of Brigham Young University proposed to study the association between air pollution and ventricular repolarization, using a novel approach developed by Dr. Lux to analyze ECG data previously collected by Dr. Pope. HEI funded the study because it considered the proposed evaluation of repolarization using novel electrophysiologic parameters to be an interesting approach to studying possible mechanisms underlying PM effects on cardiovascular morbidity and mortality.

APPROACH

Drs. Lux and Pope hypothesized that high levels of ambient PM might affect ventricular repolarization independent of heart rate and that such changes could lead to an increased risk of arrhythmia in elderly persons, who may be more susceptible to the effects of air pollution. They used the ECG data obtained previously in a study of elderly participants conducted by Dr. Pope, which had shown an association between ambient concentrations of particulate matter less than 2.5 µm in diameter ($PM_{2.5}$) and decreased HRV. In the current study, the investigators analyzed novel repolarization parameters in ECGs obtained from 61 participants. For each person, the ECG parameters were compared between days of high and low $PM_{2.5}$ concentrations. If there were more than 2 recordings for a participant, the ECG obtained on the day with the lowest $PM_{2.5}$ concentration served as the control.

Dr. Lux used custom software to calculate a root mean square (RMS) ECG, which captures the magnitude of the ECG wave forms. He then determined RMS ECG repolarization parameters such as RMS RT interval, RMS width of the T wave, and RMS QT interval, as well as their heart rate-corrected forms. Data were averaged over 30-minute periods ("epochs") and presented as a 24-hour time series. Two statistical approaches were used to evaluate differences between parameters on days with low versus high $PM_{2.5}$ concentrations: a nonparametric Kolmogorov-Smirnov test

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Robert L. Lux at the Division of Cardiology, University of Utah School of Medicine, Salt Lake City, Utah, and Dr. C. Arden Pope III at the Department of Economics, College of Family, Home, and Social Sciences, Brigham Young University, Provo, Utah. The complete report, *Air Pollution Effects on Ventricular Repolarization*, can be obtained from HEI or our Web site (see next page). **LUX 141**

and within-subject regression modeling. Fifty-two participants were included in the Kolmogorov-Smirnov analysis; 61 participants were included in the regression modeling.

RESULTS AND INTERPRETATIONS

This study broadly confirmed previous findings that increased concentrations of $PM_{2.5}$ were associated with decreased HRV. However, the novel approach to measuring ventricular repolarization did not find much evidence for an association between repolarization and $PM_{2.5}$ concentration using the Kolmogorov-Smirnov analysis, although some suggestive patterns were observed (e.g., a decrease in RT interval and an increase in T-wave width), which were of borderline significance when fixed-effects modeling was used. No significant changes were observed in the QT interval or its rate-corrected form, which is widely used in clinical settings and is associated with increased risk for arrhythmias.

As discussed by the investigators, there are several possible reasons for the lack of strong evidence for an association between $PM_{2.5}$ and ventricular repolarization in this study, one of which is that the study may have had insufficient statistical power to find subtle effects among large daily variations within and between participants. In addition, although state of the art, the method used in this study was developed based on 12-lead ECGs; however, in this study, only 2 leads were used in the ECG recordings, which may have affected the quality of the data. Further, as discussed by the investigators, the original study population was not controlled for diet, medication use, or activity patterns. Those factors are known to affect cardiac physiology and may contribute to considerable variation among participants.

The Health Review Committee considered the overall strategy in this study for statistical analysis — specifically, reducing the ECG data to 30-minute epoch summaries and subsequent analysis using regression methods — to be a good one. The regression modeling results are more robust than the Kolmogorov-Smirnov analysis and should be considered the primary statistical approach because they control for factors other than pollution that could affect ECG parameters, such as differences in participant characteristics and meteorologic measures. In contrast, results of Kolmogorov-Smirnov analysis on epoch data pooled across participants do not control for those factors and should be interpreted cautiously.

The Committee agreed with the investigators that the regression results do not provide clear support for an effect of air pollution on repolarization. However, the presence of significant associations of air pollution with some repolarization parameters suggests that repolarization should not be dismissed as a possible mechanism involved in the association between air pollution and cardiac effects. Further studies controlling for other sources of variability are needed to provide a more definitive answer.

HEALTH EFFECTS INSTITUTE

101 Federal Street, Suite 500
Boston, MA 02110, USA
+1-617-488-2300 phone
+1-617-488-2335 fax

pubs@healtheffects.org
www.healtheffects.org

Recycled Paper