Health Effects of Real-World Exposure to Diesel Exhaust in Persons with Asthma

BACKGROUND

In the 1990s, results from several epidemiologic and controlled-exposure studies suggested an association between exposure to air pollution from traffic-derived particulate matter (PM) and increases in symptoms of airway diseases, including exacerbations of asthma. Some results also suggested that exhaust from diesel engines, used in a large fraction of vehicles worldwide and particularly in Europe, contributed to these effects. In response to HEI RFA 00-1, Effects of Diesel Exhaust and Other Particles on the Exacerbation of Asthma and Other Allergic Diseases, Dr. Junfeng (Jim) Zhang of the University of Medicine and Dentistry of New Jersey, proposed a study that would investigate how inhaling air with a high concentration of diesel exhaust from vehicular traffic while walking on a street in Central London, United Kingdom, might affect people who had either mild or moderate asthma. Dr. Zhang and his colleagues hypothesized that this exposure would exacerbate asthma symptoms, decrease lung function, and induce lung inflammation and oxidative stress responses. The HEI Research Committee recommended Dr. Zhang’s proposal for funding.

APPROACH

The investigators recruited 60 nonsmoking participants of both sexes between 18 and 55 years old, with mild or moderate asthma. Each subject participated in one 2-hour exposure session by walking along Oxford Street, a busy Central London thoroughfare where vehicles are predominantly diesel-powered, and one 2-hour session walking at a nearby control site, Hyde Park, where there is no traffic.

Before, during, and after each session, the investigators evaluated pulmonary function parameters (forced expiratory volume in the first second [FEV$_1$], forced vital capacity [FVC], and forced expiratory flow during the middle half of the FVC [FEF$_{25-75}$]) and asthma symptoms. At some time points Zhang and colleagues also evaluated bronchial reactivity (PC$_{20}$) and markers of airway inflammation and oxidative stress. These markers included exhaled nitric oxide, the pH of exhaled breath condensate (EBC), blood thiobarbituric acid reactive substances (TBARS), sputum interleukin-8 and myeloperoxidase (MPO). Participants kept a record of asthma symptom scores, peak expiratory flow rate (PEFR), and asthma reliever medication use during the 7 days before and after each session.

Pollutant samplers, placed on a cart that accompanied the participants during sessions, measured concentrations of PM$_{2.5}$ (PM ≤ 2.5 µm in aerodynamic diameter), ultrafine particles (UFP; PM < 100 nm in aerodynamic diameter), elemental carbon (EC), and nitrogen dioxide (NO$_2$).

STATISTICAL METHODS

Zhang and colleagues used two main statistical approaches: comparative analyses between the exposure and control sessions that took advantage of the paired design of the study to compare within-subject responses, and pollutant-specific exposure–response analyses that estimated associations between the concentration of an individual pollutant and a change in a health endpoint from its baseline value. In one set of pollutant-specific exposure–response analyses, each of the four pollutants was used as a single covariate; a second
set of analyses used two of the four pollutants as co-
variates. They analyzed responses for all subjects, and
also analyzed responses separately for participants
with either mild or moderate asthma.

RESULTS

The investigators found that participants were ex-
posed to higher average pollutant concentrations dur-
ing the exposure session than during the control session:
approximately 5-fold higher EC, 4-fold higher NO\textsubscript{2}, 3.5-
fold higher UFP, and 2-fold higher PM\textsubscript{2.5} mass.

FEV\textsubscript{1} and FVC were significantly lower after the
exposure session compared with the control session
(stratified analyses showed that these effects were
dominated by responses in participants with moder-
ate asthma). However, FEF\textsubscript{25–75} and PEFR did not differ
significantly. Also not affected by exposure were asth-
ma symptom scores, asthma medication use, PC\textsubscript{20},
and blood TBARS; some of these responses showed
nonsignificant trends. A significant relative decrease
in EBC pH of 2.0% (correlating with an approximate
half-log change in pH) was noted one hour after the
exposure session; this effect was also dominated by
observations in subjects with moderate asthma. Of
the sputum parameters evaluated, only the neutro-
phil-associated enzyme MPO differed significantly
with a 5-fold increase after the exposure session com-
pared with after the control session.

In one-pollutant exposure–response analyses,
UFP and NO\textsubscript{2} were associated with changes in the
most endpoints, EC with fewer, and PM\textsubscript{2.5} with fewer still. In two-pollutant models, several associations
between the measured pollutants and changes in
endpoints lost significance after the investigators
controlled for other pollutants. Some associations,
however, were unaffected by the inclusion of a second
pollutant. Associations of UFP with endpoints were
not affected by adjusting for other pollutants, except
NO\textsubscript{2}. Adjusting for NO\textsubscript{2} generally appeared to reduce
associations with the other pollutants.

SUMMARY AND CONCLUSIONS

The study by Zhang and colleagues, with an in-
novative approach, has provided interesting new find-
ings. The effects with the most potential clinical sig-
nificance were the relative decreases in FEV\textsubscript{1} (3.0%–
4.1%) and FVC (3.1%–3.7%) during and several hours
after the exposure ended. The magnitude of these
decrements in lung function may be clinically rele-
vant for patients with severe or uncontrolled asthma,
whose lung capacity is severely diminished compared
with healthy people.

Based on the statistically significant changes in
one marker each of airway inflammation (MPO) and
of airway acidification (EBC pH), and in conjunction
with sputum findings of marginal statistical signifi-
cance, results of this study suggest that the exposure
session was associated with a mild increase in inflam-
matory response in the airways that was mediated by
neutrophils.

Asthma symptoms and the use of asthma reliever
medication increased only marginally after the expo-
sure session. Thus, whereas exposure to a diesel-traf-
ic–enriched environment may have produced chang-
es in pulmonary function and inflammatory end-
points, the lack of significant changes in symptoms
or the use of asthma reliever medication suggests that
this single exposure did not affect the clinical status of
asthmatic participants.

Analyses with stratification by the severity of
asthma showed that changes in FEV\textsubscript{1}, FVC, and EBC
pH were significant only in subjects with moderate
asthma. Because the majority of subjects with moder-
ate asthma were taking corticosteroids, it is possible
that corticosteroid use may have blunted responses in
this group. Though the background severity of asthma
may be an important factor affecting responses to die-
sel traffic exposure, further work is needed to confirm
or disprove this hypothesis.

Exploratory one- and two-pollutant analyses to
identify associations between specific components
of the pollutant mix and changes in endpoints found
that UFP and NO\textsubscript{2} were associated with the most end-
points, EC with fewer, and PM\textsubscript{2.5} with fewer still. All
these pollutants are constituents of traffic emissions
and EC is frequently used as a marker of diesel emis-
sions, but none is absolutely specific to diesel. Thus,
because the pollutants measured are not specific to
diesel emissions, the results are only suggestive of the
effects of DE on the endpoints measured.

Explanations for the effects observed, other than
exposure to DE, also need to be borne in mind. One
is that participants were almost certainly concurrently
exposed to air pollutants not associated with
diesel-powered engines, such as pollutants derived
from tailpipe emissions of gasoline-powered cars on streets that cross Oxford Street, as well as particles not derived from tailpipe emissions — such as those generated by tire and brake wear and roadway dust produced by all vehicles. In addition, concentrations of several traffic-associated pollutants (including CO, organic carbon compounds, and particles in the coarse size range) were not measured in the current study and may be associated with the endpoints evaluated. Furthermore, the exposure and control sites differed in other, unmeasured characteristics, particularly in noise levels and the amount of stress experienced by the subjects.

Although the findings of the current study indicate that lung function is slightly decreased and some markers of airway inflammation are increased in people with asthma who are exposed to ambient urban air in a roadside environment dominated by diesel vehicles, the study does not provide direct evidence that DE itself causes these effects. Additional studies would be needed to address that question, and to identify specific components of DE that might be responsible for any observed health effects. A final consideration is that since the study was completed, more stringent emissions and fuel standards have been implemented and new engine technologies introduced in both the United States and Europe. As older vehicles are replaced in the fleet, decreases in most traffic-related pollutant concentrations can be anticipated. The health impact of these changes will need to be assessed; this study may serve as a baseline analysis for future studies on the effects of such changes.

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PREFACE: HEI’s Research on Particles and the Exacerbation of Allergy and Asthma

INVESTIGATORS’ REPORT  by Zhang et al.

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