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Controlled Chamber Studies Showed Protective Effect of Nonsteroidal Antiinflammatory Drugs against Ozone Exposure: The Stage Was Set for Broader Epidemiologic Investigation

To the Editor:

I read with interest the recent article by Gao and colleagues (1) titled, “Nonsteroidal Antiinflammatory Drugs Modify the Effect of Short-Term Air Pollution on Lung Function,” which examined the role of nonsteroidal antiinflammatory drugs (NSAIDs) in particulate matter (PM)-induced changes in lung function in the Normative Aging Study cohort. In the DISCUSSION section, the authors state, “To the best of our knowledge, this is the first study on the subclinical preventive effects of NSAIDs against the adverse effects of air pollution on lung function.” I respectfully submit to the authors that, with regard to examining the potential role that NSAIDs play in modifying respiratory effects of air pollution exposure, that stage had already been set, albeit not using epidemiologic studies, but rather using controlled human chamber exposure studies. For example, Alexis and colleagues (2) examined the pretreatment effect of the NSAID indomethacin in both individuals with asthma and healthy individuals exposed for 2 hours to 400-ppb ozone (not PM). That study reported that indomethacin significantly attenuated ozone-induced decreases in FVC and FEV₁ in healthy subjects but not subjects with asthma; furthermore, there was a marked attenuation of ozone-induced decrements in forced expiratory flow (FEF) at 75% of the FVC and FEF at 60% of the FVC based on partial flow volume curves in subjects with asthma but not in healthy subjects. Alexis and colleagues concluded that cyclooxygenase metabolites of the arachidonic acid pathway, such as prostaglandin F_{2α}, contribute to restrictive changes in healthy individuals and obstructive small airway changes in individuals with asthma. Other studies by Schelegle and colleagues (3), Eschenbacher and colleagues (4), Ying and colleagues (5), and Hazucha and colleagues (6) also used indomethacin (or similar NSAIDs), not only to implicate the involvement of cyclooxygenase metabolites as a potential mechanism of response in air pollution (ozone)-induced spirometric responses but also to demonstrate NSAIDs’ mitigating effect on lung function decrement after ozone exposure. In particular, Hazucha and colleagues (6) showed that the NSAID ibuprofen blunted the ozone-induced decrease in FEV₁ (7% vs. 17%) and caused a concomitant inhibition of increases in respiratory tract prostaglandin E₂ and thromboxane B₂ concentrations.

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The study by Gao and colleagues, together with previous controlled chamber studies with ozone, expands the potential beneficial role of NSAIDs as protectors against both gaseous and PM-induced health effects, the latter involving fine PM (PM_{2.5}) and black carbon, at ambient concentrations. The strengths of the study by Gao and colleagues lie in its use of a large epidemiologic data set (3,220 medical visits of 1,078 white participants between 1995 and 2012 with available data of lung function, PM exposures, and NSAID use), strong statistical modeling (time-varying linear mixed-effects regression with random participant-specific intercepts), and the inclusion of nongaseous air pollutants PM_{2.5} (μg/m³) and black carbon (μg/m³). ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

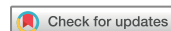
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Reply to Alexis

From the Authors:

We appreciate the valuable opinion shared by Dr. Neil E. Alexis on our article on the modifying effect by nonsteroidal antiinflammatory

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