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Title: Effect of NO2 on inflammatory response in subjects with asthma

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Body: Patients with asthma may be more susceptible to NO2. Our aim was to investigate whether repeated exposure to realistic indoor concentrations of NO2 enhances inflammatory response in the airways of subjects with asthma. Participating were 19 nonsmoking subjects with intermittent asthma and airway hyperresponsiveness during methacholine-challenge. The study had a double-blinded, crossover design. On day 1, the subjects were exposed to either 200 ppb NO2, 600 ppb NO2, or purified air for 30 min, and on day 2, to the same pollutant, for 2 x 30 min. The order of exposure to the two concentrations of NO2 and air-only was randomized and exposures were separated by 2 weeks. Markers of inflammation were measured in sputum daily, 6 hours after the first (on Day 1) and the third exposure (on Day 2) and 48 h after the first exposure (Day 3) and compared to baseline. The effect of NO2 on bronchial responsiveness to methacholine was tested at baseline and on Day 3. Exposure at rest to 200 ppb or 600 ppb of NO2 had no direct effect on respiratory function either during or after the exposure sessions. Compared to baseline, the variation in the percentage of eosinophils in induced sputum after exposure to NO2 was -2% after air, +16% after 200 ppb NO2, and +78% after 600 ppb NO2. The linear association between the variation and the level of exposure was significant (p=0.01). Exposure to NO2 did not cause any change in lung function and no NO2-related effect on responsiveness to methacholine was found. NO2 exposure had a significant and dose-related effect on the eosinophilic inflammatory response of patients. These data suggest that exposure to NO2 might enhance the eosinophilic activity in sputum in subjects with intermittent asthma.