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Comparisons of combined oxidant capacity and redox-weighted oxidant capacity in their association with increasing levels of FeNO

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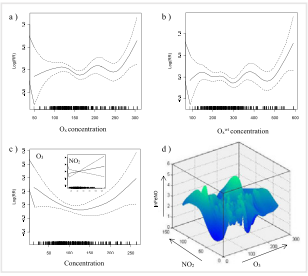
GRAPHICAL ABSTRACT



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ABSTRACT

Background: Some ozone (O_3) and nitrogen dioxides (NO_2) health effects studies use O_x (sum value) as a surrogate. However, little is known about how this related to O_x^{wt} (weighted value).
Objective: We investigated the effects of redox-weighted oxidant capacity (O_x^{wt}) on fractional exhaled nitric oxide (FeNO), a biomarker of airway inflammation, in a set of chronic obstructive pulmonary disease (COPD) patients. We also compare combined oxidant capacity (O_x) and O_x^{wt} in their associations with increasing levels of FeNO.
Methods: We measured FeNO values in 600 participants who have COPD at Shanghai Pulmonary Hospital. O_x was calculated directly by the sum of O_3 and NO_2. The redox-weighted oxidant capacity was calculated by denoting O_x^{wt} as the weighted average of redox potentials. We applied generalized additive models (GAM) to investigate the impacts of O_x and O_x^{wt} on FeNO levels, respectively. We fitted the same models for the influence of O_3 and NO_2 individually and jointly on FeNO levels to compare the result of O_x and O_x^{wt}.
Results: O_x^{wt} were significantly linked with FeNO levels. The impact was robustest in current day after exposure, and were closely linked with the adjustment of $PM_{2.5}$. A 10 $\mu g\,m^{-3}$ increase in average O_x^{wt} concentrations was linked to 0.88 (95% CI: −1.46, 3.28) increase, whereas a 10 $\mu g\,m^{-3}$ increase in average O_x concentration was linked to 0.62 (95% CI: −0.79, 2.07) increase in FeNO. In two-pollutant models, an increase of 10 $\mu g\,m^{-3}$ in average O_3 concentrations with adjustment of NO_2 was associated with 0.57 (95% CI: −1.26, 2.01) increase in FeNO. The impact estimates of O_x and O_x^{wt} were statistically significant among males, non-smoking and elders who age above 65 years old.
Conclusions: This analysis demonstrated that O_x^{wt} is used as a better indicator of atmospheric oxidative capacity as a proxy of O_3 and NO_2 in further epidemiological studies.

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1. Introduction

Ozone (O_3) and Nitrogen dioxide (NO_2) are commonly known as oxidative atmospheric pollutants, which can cause systematic oxidative injuries and airway inflammatory (Huang et al., 2012; Kim et al., 2013; Williams et al., 2014). Published epidemiological literature found the significant associations between single pollutant (NO_2 or O_3) and adverse respiratory effect (Alahmari et al., 2015; Samoli et al., 2006). However, these explanations were problematic because of the inextricably chemical conjunction among O_3, NO and NO_2 (Ghazali et al., 2010). They can mutual interchange in daytime (Munger et al., 1996). The transformation of O_3, NO and NO_2 were described as follows:

$$O_3 + NO = NO_2 + O_2 \quad (1)$$

$$NO_2 + h\nu = NO + O \quad (2)$$

$$O + O_2 = O_3 \quad (3)$$

where $h\nu$ is a photon. Furthermore, O_3 is difficult to quantify the short term association between its daily levels and health effect due to the instability (Clapp and Jenkin, 2001).

Traditional two-pollutant model approach may solve these problems, but it has many statistical problems related to these methods, and seldom simplifies health effect calculation (Williams et al., 2014). From this point of view, it would seem necessary to study the interaction of O_3 and NO_2. The 'combined oxidant capacity' was developed by denoting O_x as sum of NO_2 and O_3, whereas the fact that O_3 has a much stronger oxidation potential than does NO_2 (Chardon et al., 2007; Vanegmond and Kesseboom, 1985; Williams et al., 2014; Yang et al., 2016). Thus, O_3 could possibly be underestimated. And the term 'redox-weighted oxidant capacity' was calculated by denoting O_x^{wt} as the weighted average of redox potentials (Weichenthal et al., 2016). Few studies have explored the use of O_x or O_x^w in investigating the association between adverse health effect and air pollution. Only three studies have considered O_x in associations with daily hospital admission (Chardon et al., 2007), mortality (Williams et al., 2014) and increase levels of FeNO (Yang et al., 2016), respectively. And only one study have explored the influence of O_x^{wt} on emergency room visits individually (Weichenthal et al., 2016). Furthermore, there are deviations in the study area due to regional differences. For example, NO_2 is the main source in many urban areas, so that NO_2 is often closely correlated with particulate matter (PM) such as fine particles ($PM_{2.5}$). And regional differences in the oxidative potential of $PM_{2.5}$ may modify its impact on adverse health effect (Weichenthal et al., 2016). Besides, bias exists due to the difference of approaches, for example, the selection of O_x model or O_x^{wt} model based on oxidative potential or protein nitration. There is not a positive indication to choose O_x or O_x^{wt} as a proxy of NO_2 and O_3 in epidemiological study.

Previous literature has reported that FeNO is recognized as a non-invasive biomarker of COPD and could be useful for assessing the respiratory effects of short term air pollution exposures (Kim et al., 2016). The generation of NO relates to many factors, including oxidative stress level and the rate of absorption by antioxidant molecules (Barnes et al., 2010). It has been previously reported that common oxidative pollutants are associated with significant increases in FeNO levels, such as O_3 and NO_2 (Berhane et al., 2011; Olin et al., 2001). To best our knowledge, few study compared the effect of O_x and O_x^{wt} on FeNO level.

In the present paper, we compared the effects of O_x and O_x^{wt} on respiratory inflammation in 600 participants who have COPD in Shanghai, China. Respiratory inflammation was assessed by FeNO, which is used in previous studies (Bowler and Crapo, 2002). We also compare the O_x and O_x^{wt} associations with O_3 and NO_2 evaluated from two-pollutant models.

2. Material and methods

2.1. Study design

The data on hospitalized patients were extracted from the Shanghai Lung Hospital (SLH) electronic medical administration records, and we obtained exhaled nitric oxide levels (FeNO) and some essential information between 2014 and 2015. The essential information provided personal characteristics such as age, gender, smoking, career, permanent residence and length of stay. We selected 600 patients excluded those who were not COPD from 2986 admission of persons, including male of 507 and female of 93. COPD data were selected base on the code in *International Classification of Diseases, 10th revision (ICD-10)* for all patients, COPD (ICD-10: J44, J44.1, J44.9). The study scheme was identified by the SLH and Ethics Committee of Fudan University.

Physical examinations were conducted by trained doctors at the SLH. FeNO level were measured following the ATS recommended procedures [American Thoracic society/European Respiratory Society (ATS/ERS) 2005] (ATS/ERS, 2005) for each hospital admissions of persons by a NIOX MINO® airway inflammation monitor (Aerocrine AB, Solna, Sweden) (Malerba et al., 2016). The time of measurement procedure was 0–2 days after finished the hospital formalities. Doctors performed an animation demonstration to patients until fully grasp, before executing a standard measurement at least 10 s at 50 mL s^{-1}. In order to avoid the inaccurate FeNO results, beverages, foods, smoking and intense exercised were not allowed for at least 1 h before the FeNO measurements (Guo et al., 2018).

2.2. Environmental data

Daily ambient air pollutants data in Shanghai, including $PM_{2.5}$, ozone (O_3), and nitrogen dioxide (NO_2), were collected from Shanghai Environmental Monitoring Center (SEMC) database. We denoted O_x as the sum of NO_2 and O_3 concentrations. We also denoted O_x^{wt} as the weighted average because the O_3 is a stronger oxidant potential than NO_2 (Matalon et al., 2009). The details are described as follows:

$$O_x = O_3 + NO_2 \quad (4)$$

$$O_x^{wt} = (1.07volts(V) \times NO_2 + 2.075volts(V) \times O_3)/3.145 \quad (5)$$

Daily concentrations of each pollutant was averaged by the available monitoring outcomes of 9 fixed-site stations (Putuo, Yangpu, Luwan, Jin'an, Hongkou, Xuhui, Pudong, Chuansha, Zhangjiang) in Shanghai. Detailed descriptions of air pollutants collection and measurement have been reported previously study (Xu et al., 2017). Briefly, the monitoring outcomes could show the general background of urban air pollution level and corresponding exposure of hospital admissions of persons. In order to allow adjustment for the influence of weather on hospitalized patients, meteorological data (relative humidity and daily mean temperature) were collected from the Fudan super meteorological station (near SLH). The station located on the rooftop (20 m above the ground) of teaching building No.4 at Fudan University campus (121.50° E, 31.30° N), nearly 150 m south of SLH.