Environment International 60 (2013) 112–122

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Concentrations of urinary 8-hydroxy-2′-deoxyguanosine and 8-isoprostane in women exposed to woodsmoke in a cookstove intervention study in San Marcos, Peru

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ARTICLE INFO

Article history:
Received 22 January 2013
Accepted 18 August 2013
Available online 14 September 2013

Keywords:
8-OHdG
8-Isoprostane
Cookstove
Household air pollution
Oxidative stress
Peru

ABSTRACT

Nearly half of the world's population is exposed to household air pollution (HAP) due to long hours spent in close proximity to unvented cooking fires. The effect of woodsmoke exposure on oxidative stress was examined by investigating the association between woodsmoke exposure and biomarkers of DNA oxidation (8-hydroxy-2′-deoxyguanosine [8-OHdG]) and lipid peroxidation (8-isoprostane) among control and intervention stove users. HAP exposure assessment was conducted within the framework of a community-randomized controlled trial of 51 communities in San Marcos Province, Cajamarca Region, Peru. The first morning urine voids after 48 h HAP exposure assessment from a subset of 45 control and 39 intervention stove users were analyzed for 8-OHdG and 8-isoprostane. General linear models and correlation analyses were performed. Urinary oxidative stress biomarkers ranged from 11.2 to 2270.0 μg/g creatinine (median: 132.6 μg/g creatinine) for 8-OHdG and from 0.1 to 4.5 μg/g creatinine (median: 0.8 μg/g creatinine) for 8-isoprostane among all study subjects ($n = 84$). After controlling for the effects of traffic in the community and eating food exposed to fire among all subjects, cooking time was weakly, but positively associated with urinary 8-OHdG ($r = 0.29$, $p = 0.01$, $n = 80$). Subjects' real-time personal CO exposures were negatively associated with 8-OHdG, particularly the maximum 30-second CO exposure during the sampling period ($r = -0.32$, $p = 0.001$, $n = 73$). 48 h time integrated personal $PM_{2.5}$ was negatively, but marginally associated with urinary 8-isoprostane ($r = -0.21$, $p = 0.09$, $n = 69$) after controlling for the effect of distance of homes to the road. Urinary 8-isoprostane levels reported in the available literature are comparable to results found in the current study. However there were relatively high levels of urinary 8-OHdG compared to data in the available literature for 8-OHdG excretion. Results suggest a sustained systemic oxidative stress among these Peruvian women chronically exposed to wood smoke.

1. Introduction

The use of solid fuels occurs mostly in the developing world where wood and crop residues are employed by households for cooking and heating (Smith and Mehta, 2003). These fuels are often used in unvented or poorly designed stoves which create high levels of household air pollution (Rehfuess et al., 2006). Biomass combustion in the indoor environment is considered to be probably carcinogenic for humans (IARC, 2010). Although numerous pollutants including carbon monoxide, polycyclic aromatic hydrocarbons, formaldehyde and benzene are produced from biomass combustion, particulate matter (PM) is considered the best indicator of smoke exposure (Naeher et al., 2007; Perez-Padilla et al., 2010).

Mounting evidence points to the mutagenic, genotoxic and cytotoxic properties of biomass smoke, particularly for woodsmoke particulate matter (Danielsen et al., 2009). One toxicological mechanism by which PM has been shown to induce health effects, in in-vitro studies

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http://dx.doi.org/10.1016/j.envint.2013.08.013

involving human cells or cell lines, is through the pathway of oxidative stress (Danielsen et al., 2009). Oxidative stress can cause damage to deoxyribonucleic acid (DNA) through the production of 8-hydroxylated guanine species such as 8-hydroxy-2′-deoxyguanosine (8-OHdG) (Arnett et al., 2005). Another toxicological effect of PM observed in in-vitro studies, specifically of woodsmoke PM, involves the generation of reactive oxygen species (ROS) such as perioxides that can react with the lipids of cell membrane. A common stable product of ROS-induced lipid peroxidation is 8-isoprostaglandin $F_{2\alpha}$ (8-isoprostane) (Danielsen et al., 2009). Hence, both 8-OHdG and 8-isoprostane are known markers of oxidative stress (Barregard et al., 2006; Loft et al., 1992).

8-Isoprostane is a prostaglandin (PG)-F2-like compound belonging to the F2 isoprostane class that is produced in vivo by the free radical-catalyzed peroxidation of arachidonic acid (Montuschi et al., 1999). On the other hand 8-OHdG is an oxidized nucleoside of DNA and it is considered as the most frequently detected and studied DNA lesion (Wu et al., 2004). 8-OHdG is excreted during the repair of DNA damage (Wu et al., 2004). Measurements of these compounds have been performed in biologic fluid, particularly in urine and can provide quantitative indices of oxidative stress (Montuschi et al., 1999). Aside from experimental studies where the effect of woodsmoke on oxidative stress has been studied (Barregard et al., 2006, 2008), the literature is scant on studies of biomass smoke exposure and resulting health effects, particularly regarding women in the developing world who cook with biomass fuels. Given the daily HAP exposure experienced by these women over a lifetime, there is the need to better understand the effect of woodsmoke exposure on oxidative stress in this vulnerable population.

In this study, we examined the concentrations of oxidative stress biomarkers of women exposed to woodsmoke. Study subjects from San Marcos, Cajarmarca Region, Peru, used wood as fuel for cooking and high PM levels have been measured among this population (Hartinger et al., 2013). Based on earlier studies among this population which did not reveal statistically significant differences in $PM_{2.5}$ and CO measurements (Commodore et al., 2013; Hartinger et al., 2013), the primary focus of this study was to assess the association of urinary oxidative stress with biomass smoke exposure among control and intervention stove users as a combined population. Therefore this study examined the use of biomarkers in investigating oxidative stress, which plays a role in many diseases and in natural aging.

The aims of this study were (1) to determine whether increased exposure to biomass cookstove smoke was associated with increased urinary levels of 8-OHdG and 8-isoprostane among control and intervention subjects and (2) to investigate the factors that are associated with urinary 8-OHdG and 8-isoprostane concentrations among study subjects. We assessed woodsmoke exposure with personal and kitchen measurements of particulate matter and carbon monoxide. Woodsmoke exposure was also assessed with urinary hydroxylated polycyclic aromatic hydrocarbons (hydroxy-PAH), metabolites of PAHs generated through incomplete combustion (Li et al., 2012).

2. Material and methods

2.1. Study design and study homes

From June to August 2009, a cross sectional study was conducted within the framework of a community based randomized control trial (c-RCT) by the Instituto de Investigación Nutricional (IIN) and the Swiss Tropical and Public Health Institute (Commodore et al., 2013; Hartinger et al., 2013). The aim of the parent study was to evaluate an integrated home-based environmental intervention package (IHIP) against childhood diarrhea and respiratory infections (Hartinger et al., 2011). The May–August period in the study region is characterized by dry conditions and cold nights with temperatures ranging from 7 °C to 25 °C (Hartinger et al., 2013). HAP exposure assessment occurred during this season, with no follow up during the rainy season. The altitude in the region ranges between 2200 and 3900 m above sea level. Mean altitudes ± SD for intervention and control households are 2684 ± 284 and 2727 ± 438 m above sea level, respectively.

For this cross-sectional study, control and intervention households were from participating households in the parent c-RCT (n = 250 and 253 for intervention and control homes, respectively). The c-RCT involved 51 community clusters in which households used solid fuels for cooking in the Province of San Marcos, Cajamarca Region, Peru (Hartinger et al., 2011, 2012). The intervention was randomized at the community level, with the 51 community clusters allocated into control and intervention groups by using covariate-based constrained randomization (Hartinger et al., 2013). Field workers for the c-RCT visited all study homes during this 3 month period; however subjects' availability, willingness to participate, availability of air sampling equipment as well as time and budget constraints limited the total sample size of the present study.

Prior to the start of the c-RCT, a pilot study was conducted, where several potential stove designs were tested, and subjects were consulted on cooking habits and preferences to provide a user-friendly stove design which met their household and cooking needs (Hartinger et al., 2012). The final stove model, for the c-RCT was called the OPTIMA-improved stove (hereafter OPTIMA stove). Kitchen performance tests of the OPTIMA stoves revealed a 15% reduction in daily fuel and energy use and a 16% reduction in fuel and energy use per capita compared with the traditional open fire stoves, although there was no statistically significant difference in these reductions (Hartinger et al., 2011, 2012). The OPTIMA stove was built with red burnt bricks plastered with a mixture of mud, straw and donkey manure (Hartinger et al., 2012). It has three pot holes for cooking, a closed combustion chamber, metal chimney with a regulatory valve, a hood, and metal rods for support.

OPTIMA stoves were installed between October 2008 and January 2009 in 250 households (hereafter intervention households). There were no emissions tests or HAP exposure assessment prior to installation of the intervention stoves. The current study reports the only exposure assessment conducted for these stoves 6 to 8 months after installation (median 7.4 IQR = 6.6–8.1 months) (Hartinger et al., 2013). OPTIMA stoves were later stratified (after exposure assessment had occurred) into two categories based on their levels of functionality (FL). FL-I stoves were in good running conditions at the time of the assessment (plastered stove and no visible leaks when in use) and FL-II stoves were in need of repairs (re-plastering, filling small cracks, cleaning the chimney, chimney valve replacement). Field workers, during monthly visits, instructed OPTIMA stove users in the correct use of the stoves including cleaning and removal of ashes and wood residues. Although surveillance occurred in all study homes, stove repair and maintenance were not addressed during home visits until after air quality monitoring had occurred. Households with OPTIMA-improved stoves were re-visited 9 months (median 9.3 IQR = 9.0–9.7 months) after installation and repaired as needed by the original stove builders (Hartinger et al., 2013).

Control households in the c-RCT used a diversity of stove types (Hartinger et al., 2011). As such control households in this study had a wide range of stove types including (1) chimney stoves whose raw materials were provided by nongovernmental organizations (hereafter referred to as NGO), (2) chimney stoves built by the households themselves (hereafter referred to as self-improved by household), and (3) non-vented stoves with pot holes for cooking including the common three stone open fire stove (hereafter referred to as traditional). At the time of sampling, control households had stoves which had been in use between 4 months to over 10 years. Lastly, households were classified according to the primary stove in use and it is possible that some chimney stoves were used together with traditional stoves in some households, particularly for cooking animal feed or other meals which required substantial cooking times.