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Antimony and sleep-related disorders: NHANES 2005–2008

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ABSTRACT

Background: Antimony is used as a flame-retardant in textiles and plastics, in semiconductors, pewter, and as pigments in paints, lacquers, glass and pottery. Subacute or chronic antimony poisoning has been reported to cause sleeplessness. The prevalence of short sleep duration (< 7 h/night) has been reported to be 37.1% in the general US population, and obstructive sleep apnea (OSA) affects 12–28 million US adults. Insufficient sleep and OSA have been linked to the development of several chronic conditions including diabetes, cardiovascular disease, obesity and depression, conditions that pose serious public health threats.

Objective: To investigate whether there is an association between antimony exposure and sleep-related disorders in the US adult population using the National Health and Nutrition Examination Survey (NHANES) 2005–2008.

Methods: We performed multivariate logistic regression to analyze the association of urinary antimony with several sleep disorders, including insufficient sleep and OSA, in adult (ages 20 years and older) participants of NHANES 2005–2008 (n = 2654).

Result: We found that participants with higher urinary antimony levels had higher odds to experience insufficient sleep (≤ 6 h/night) (OR 1.73; 95%CI; 1.04, 2.91) as well as higher odds to have increased sleep onset latency (> 30 min/night). Furthermore, we found that higher urinary antimony levels in participants were associated with OSA (OR 1.57; 95%CI; 1.05, 2.34), sleep problems, and day-time sleepiness.

Conclusion: In this study, we found that urinary antimony was associated with higher odds to have insufficient sleep and OSA. Because of the public health implications of sleep disorders, further studies, especially a prospective cohort study, are warranted to evaluate the association between antimony exposure and sleep-related disorders.

1. Introduction

Antimony is a silvery white metal that is commonly found within the Earth's crust (ATSDR, 1992). Antimony exists in either a trivalent or pentavalent state. Because antimony occurs naturally within the Earth's crust, it is released into the environment through natural processes, including dust, volcanic ash, and forest fire residue. Additionally, exposure to and toxicity from antimony may arise due to occupational exposure, domestic use, or when it is used as a medical therapy (McCallum, 2005; Sundar and Chakravarty, 2010). Antimony is used to treat parasitic diseases including leishmaniasis and schistosomiasis. Furthermore, antimony is used in semiconductors and pewter, as a fire-retardant in textiles and plastics, and as a pigment in paints, lacquers, glass and pottery (McCallum, 2005).

The general US population is exposed to measurable levels of antimony in the environment, primarily through food and, to a lesser extent, from air and drinking water (Navas-Acien et al., 2005). Dermal contact with soil, water, or other substances containing antimony is another means of exposure. The absorption, distribution, and excretion of antimony vary depending on its oxidation state, with urinary excretion appearing to be greater for pentavalent antimony compounds than for trivalent compounds (Elinder and Friberg, 1986). An elimination half-life of approximately 95 h has been estimated after occupational exposures for the trivalent form (Kentner et al., 1995) and 24 h for the pentavalent form (Gebel, 1997). Furthermore, human health effects from antimony at low environmental doses or at biomonitored levels from low environmental exposures are not well known.

Studies have shown that most of the antimony that enters the body concentrates in the liver, lungs, intestines, and spleen (ATSDR, 1992). Exposure to antimony can cause irritation of the nose, throat, skin, and mouth, as well as nausea and loss of sleep (NJDOH, 2004). Chronic inhalation of low levels of antimony can result in lung problems (e.g., pneumoconiosis), heart problems (including increased blood pressure and altered electrocardiograms), and stomach pain, diarrhea, vomiting

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and stomach ulcers (ATSDR, 1992; Cooper and Harrison, 2009, Sundar and Chakravarty, 2010).

The most comprehensive information on health effects following acute and subacute antimony poisoning comes from a self-administered experiment conducted by Mayerhofer (1846). Following ingestion of small doses of tartarized antimony at increasing frequencies, Mayerhofer reported sleep disturbance (1846). Sleeplessness after subacute and chronic antimony poisoning has also been reported (Stemmer, 1976; WHO, 2003); however, there is a deficiency in research surrounding this potential association. Insufficient sleep has been a risk factor to the development of several chronic conditions including diabetes, cardiovascular disease, obesity and depression; these conditions have, in turn, been linked to sleep disorders. and cardiovascular diseases have been associated with antimony exposure (Guo et al., 2016; Nigra et al., 2016) Additionally, genetic factors and other behavioral characteristics, such as alcohol use, smoking, obesity, marital status, and income, can contribute to the development of sleep-related disorders. The National Heart, Lung, and Blood Institute (NHLBI) recommends that adults get 7–8 h of sleep per day (NHLBI, 2011). The prevalence of short sleep duration (< 7 h on weekday or workday nights) has been reported to be 37.1% in the general US population (CDC, 2011). Sleep insufficiency and poor sleep quality can also result from sleep disorders such as chronic insomnia, obstructive sleep apnea (OSA), restless legs syndrome, or narcolepsy (IOM, 2006).

Because of the ubiquitous exposure to antimony in the general population, the public health consequences of sleep disorders, and the potential but largely unexplored relationship between the two, the objective of this study was to investigate the potential association between antimony exposure with sleep duration, sleep onset latency time, and sleep-related disorders in the adult population using the National Health and Nutrition Examination Survey (NHANES) 2005–2008. We hypothesize that population level exposures to antimony are associated with sleep related disorders.

2. Methods

2.1. Study population

NHANES is a cross-sectional, nationally representative survey of the non-institutionalized civilian population of the United States conducted by the National Center for Health Statistics (NCHS), CDC (NCHS, 2008a). Beginning in 1999, the survey has been conducted continuously and released in 2-year cycles. The NHANES 2005–2006 and 2007–2008 are the only cycles where a complete questionnaire about sleep habit and disorders were performed, so that several outcomes could be defined. For our study we merged the publicly available files for NHANES cycles 2005–2006 and 2007–2008 using the NCHS recommendations (NCHS, 2008b). The survey employs a multistage stratified probability sample based on selected counties, blocks, households, and persons within households.

NCHS-trained professionals conducted interviews in participants' homes. Extensive physical examinations, including blood and urinary collection, were conducted at mobile exam centers (MECs). CDC's National Center for Environmental Health (NCEH), Division of Laboratory Sciences (DLS), coordinates the National Biomonitoring Program (NBP) which offers an assessment of nutritional status and the exposure of the US population to environmental chemicals and toxic substances. In the 2005–2006 and 2007–2008 data sets, urinary concentrations of antimony were measured in a randomly selected one-third subsample.

All procedures were approved by the NCHS Research Ethics Review Board (Continuation of Protocol #2005–2006 http://www.cdc.gov/nchs/nhanes/irba98.htm), and all participants provided written informed consent. The unweighted response rate for adult participants 20 years of age and older for NHANES 2005–2006 and NHANES 2007–2008 were 70.4% and 70.6%, respectively (NCHS, 2006; NCHS, 2008c) (Of the participants who answered questions for the sleep questionnaire, we included only those participants who had measurements for urinary antimony (n = 3328). Pregnant (n = 102) and breast-feeding (n = 27) women were excluded from our analyses. Additionally, participants with missing information on *a priori* covariates adjusted for in the multivariate analyses, for example education (n = 1), body mass index (n = 55), income (n = 221), serum cotinine (174), were excluded from our analysis for a final, total sample size of 2.654 participants.

2.2. Outcome

We investigated the following self-reported prevalent outcomes that are related to sleep disorders: sleep duration, sleep-onset latency, OSA, sleep problems, and day-time sleepiness. These outcomes were defined in the following ways:

- Sleep duration: categorized as insufficient (≤6 h/night), normal (7–8 h/night), or excessive (≥9 h/night) (National Sleep Foundation, 2009; Plantinga et al., 2012).
- Sleep-onset latency: categorized as normal (6–30 min/night), prolonged (> 30 min/night), or short (≤5 min/night) which may be indicative of having a sleep disorder (Dement and Vaughn, 2009; Plantinga et al., 2012).
- Obstructive sleep apnea (OSA): characterized according to Healthy People 2020 (Healthy People, 2020, 2014) and was defined as any of the following: doctor diagnosed sleep apnea; or snoring 3 or more nights per week; or snorting, gasping or stopping breathing 3 or more nights per week; or (feeling excessively sleepy during the day 16–30 times per month despite sleeping around 7 or more hours per night on weekdays or work nights).
- Sleep problems: considered frequent if self-reported "often" or more (≥5 times/month) (Plantinga et al., 2012) in response to any of the following questions from the NHANES sleep questionnaire: "Have you ever told a doctor or other health professional that you have trouble sleeping?"; "In the past month, how often did you have trouble falling asleep?"; "In the past month, how often did you wake up during the night and had trouble getting back to sleep?"; or, "In the past month, how often did you wake up too early in the morning and were unable to get back to sleep?". (Plantinga et al., 2012)
- Day sleepiness: considered frequent if self-reported "often" or more (≥5 times/month) (Plantinga et al., 2012) in response to any of the following questions from the NHANES sleep questionnaire: "In the past month, how often did you feel unrested during the day, no matter how many hours of sleep you have had?" or "In the past month, how often did you feel excessively or overly sleepy during the day?".

2.3. Urinary biomarkers

Spot urine samples were collected from study participants and stored at −20 °C; they were then analyzed by NCEH/DLS. Urinary antimony was measured by inductively coupled plasma-mass spectrometry using a multi-element analytical technique. The interassay coefficient of variation range from 3.1% to 5.6%. Details of detection and measurement of the urinary compounds are described in the NHANES laboratory method (NCHS, 2007).

Urinary antimony was categorized by a weighted quartile distribution based on the distribution of urinary antimony levels among the study population, resulting in approximately the same number of participants within each quartile. Due to their association with antimony exposures (McCallum, 2005), urinary lead and urinary arsenic were entered into the models as natural log- transformed variables. The limits of detection (LODs) for urinary antimony was 0.03 μg/L. Urinary concentrations of antimony below the LOD were assigned the LOD divided by the square root of 2, as recommended by NHANES (NCHS, 2007). There were 22.6% participants with urinary antimony below the