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Ambient geothermal hydrogen sulfide exposure and peripheral neuropathy

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ABSTRACT

The mechanism of toxicity of hydrogen sulfide (H_2S) gas is thought mainly to operate through effects on the nervous system. The gas has high acute toxicity, but whether chronic exposure causes effects, including peripheral neuropathy, is yet unclear. The city of Rotorua, New Zealand, sits on an active geothermal field and the population has some of the highest measured ambient H_2S exposures. A previous study in Rotorua provided evidence that H_2S is associated with peripheral neuropathy. Using clinical methods, the present study sought to investigate and possibly confirm this association in the Rotorua population.

The study population comprised 1635 adult residents of Rotorua, aged 18–65. Collected data relevant to the peripheral neuropathy investigation included symptoms, ankle stretch reflex, vibration sensitivity, as measured by the timed-tuning fork test and a Bio-Thesiometer (Bio-Medical Instrument Co., Ohio), and light touch sensitivity measured by monofilaments. An exposure metric, estimating time-weighted H_2S exposure across the last 30 years was used. Principal components analysis was used to combine data across the various indicators of possible peripheral neuropathy. The main data analysis used linear regression to examine associations between the peripheral nerve function indicators and H_2S exposure.

None of the peripheral nerve function indicators were associated with H_2S exposure, providing no evidence that H_2S exposure at levels found in Rotorua is a cause of peripheral neuropathy. The earlier association between H_2S exposure and peripheral neuropathy diagnoses may be attributable to the ecological study design used. The possibility that H_2S exposure misclassification could account for the lack of association found cannot be entirely excluded.

1. Introduction

Hydrogen sulfide (H_2S) is a toxic gas responsible for the second highest number of occupational gas-related deaths, after carbon monoxide (Bronstein et al., 2007). This gas is emitted from a number of natural and industrial sources, including geothermal areas, oil and gas fields and refineries, sewage treatment plants, and confined animal feeding operations (CAFOs or "factory farms") (Lewis and Copley, 2015). It is also endogenously produced in humans and animals by gut bacteria and by the cells of some organs, where it has important physiological functions (Guidotti, 2015). H_2S has a "rotten egg" smell, with a detection threshold of 10 ppb or lower. As the acute exposure concentration increases, the gas becomes an irritant to the eyes and lungs. At concentrations of 150–200 ppm, it can paralyze the olfactory nerves so that it is no longer detectable by smell. Death from respiratory paralysis can occur at around 1000 ppm (U.S. Environmental Protection Agency (EPA), 1978).

The mechanism of acute toxicity of H_2S appears to involve effects on the nervous system, raising the question of whether long-term low-level H_2S exposures may cause chronic neurological damage. Only a few studies have produced data that address this possibility. Of most relevance to the present study was an ecological epidemiology study in New Zealand that found a positive association between the estimated H_2S exposures where people lived and hospital discharge diagnoses for disorders of the peripheral nervous system (ICD-9 codes 350–359) (Bates et al., 2002). For persons categorized as living in "high", "medium" and "low" H_2S exposure areas, the standardized incidence ratios were 2.59 (95% confidence interval: 1.91, 3.44), 1.94 (1.36, 2.67) and 1.76

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(1.48, 2.09), respectively, relative to the rest of New Zealand. A study of chronic environmental H_2S exposure compared H_2S-exposed populations in Odessa, Texas, and Puna, Hawaii with a reference population drawn from unexposed communities in the two states. This study produced an overall odds ratio of 12.7 (7.59–22.00, 95% CI) for self-reported central nervous system symptoms (Legator et al., 2001). However, interpretation of the results is limited by questions about the comparability of the reference communities, co-exposure to other emissions and litigation (Odessa) and an ongoing political controversy (Puna).

There is also some support from animal studies for the possibility of nervous system effects caused by H_2S. Chao et al. (2012) found evidence that H_2S interacted with Na^+ channels in mouse brains, possibly causing neuronal injury (Chao et al., 2012). A month-long exposure of rats to emissions from a gas field with a high content of H_2S was associated with demyelination of central nervous system axons (Solnyshkova, 2003). However, the natural gas emissions also contained hydrocarbons and mercaptans, which are highly associated with central and peripheral neurotoxicity (LoPachin and Gavin, 2015), casting doubt on any causal relationship with H_2S. In a review article, Lewis and Copley (2015), found that most studies that examined the effects of H_2S on the central nervous system involved self-reported H_2S exposure and that few were likely to involve exposure to H_2S alone, making interpretation difficult (Lewis and Copley, 2015).

In this study, we examined indicators of peripheral neuropathy in a sample of the population of the city of Rotorua, New Zealand, continually exposed to ambient H_2S from vents in the geothermal field on which it is situated. There is considerable H_2S exposure variation across the city and some of the highest exposures occur in the central business district. From an epidemiologic investigation perspective, geothermal sources have the advantage over other ambient H_2S-producing entities of not being known to produce other gases with the potential to confound results. Other geothermal gases are mainly carbon dioxide and water vapor, with small amounts of hydrogen, nitrogen, methane and carbon monoxide (Horwell et al., 2004). Other possible air pollutants in Rotorua, such as vehicle emissions, are not known to cause peripheral neuropathy. Therefore they would not be likely to confound any relationship of peripheral neuropathy with geothermal emissions.

Study results for respiratory, cognitive and ocular outcomes have previously been published (Bates et al., 2013, 2015, 2017; Reed et al., 2014). The purpose of the study component covered by this publication was to investigate whether there is evidence of an association between long term exposure to H_2S and indicators of peripheral neuropathy, after controlling for potential confounding factors.

2. Methods

2.1. Ethics statement

Prior Institutional Review Board approvals were obtained from the University of California, Berkeley, and from the Northern Ethics Committee in New Zealand. All subjects provided written informed consents before their participation.

2.2. Participant recruitment

This has previously been described in some detail (Bates et al., 2013, 2015; Reed et al., 2014). Briefly, a total of 1637 residents of Rotorua, aged 18–65, participated in the study during the period April, 2008, to December, 2010. An estimated 98% of the city's population is included in a centralized patient registry, which was used as the basis for selecting potential participants. The city was initially stratified into three H_2S-exposure level areas (high, medium, low), based on the Rotorua investigation of Horwell et al. (2004), and as previously used Bates et al. (2002). Approximately equal numbers of participants were sought from residents in each of these 3 exposure level areas. This initial stratification was to ensure a good distribution of H_2S exposures, particularly to avoid a preponderance of low-exposure participants. However, since more accurate exposure data were collected during the study, the initial exposure stratification was not used in the data analysis. Participants were invited to the study clinic where a questionnaire was administered and various clinical tests were performed.

Ineligible for participation were persons not resident in Rotorua for at least the last 3 years, persons unable to speak and write English, anyone unable to visit the study clinic due to a disability, and anyone who was blind. Women who reported they were pregnant were also excluded because of the use of mydriatics in another part of the study.

2.3. H_2S exposure estimation

H_2S exposure assessment has been described in detail elsewhere (Bates et al., 2015, 2013; Reed et al., 2014). Briefly, residential, workplace and school location histories were obtained by questionnaire and the locations geocoded. Subjects were also asked the number of hours spent at each location, and lengths of time spent away from Rotorua (vacations or temporary reassignments). Separately, three networks of passive H_2S passive samplers (Radiello, Sigma–Aldrich Co. LLC), were placed in various sites spaced across Rotorua for 2 week periods in 2010 and 2011. Most sampling sites were the same across the collection periods. Concentration surfaces were created for the Rotorua urban area using kriging. From the maps, average ambient H_2S concentrations were assigned to each participant-reported location. An average time-weighted H_2S exposure over the last 30 years was calculated for each participant by applying their time data to estimated concentrations at the geocoded locations. Study participants were categorized into quartiles of this exposure metric.

2.4. Neuropathy measures

Although nerve conduction study is often considered the “gold standard” for diagnosis of neuropathy, we did not utilize this procedure, because it was not feasible to obtain a trained technician to carry out the testing. The test requires technical expertise that was beyond the scope of our field study. Moreover, the discomfort associated with the procedure would likely have discouraged study participation. There is general consensus that an accurate clinical diagnosis of neuropathy can be made with relatively simple screening examinations (England et al., 2005). We chose 5 measures that have been validated as indicators of the possible presence of neuropathy. A single specially trained examiner carried out neuropathy screening for all subjects, to ensure consistency of the data collection. The study neurologist provided the initial training as well as continual data quality monitoring throughout the study.

The 5 neuropathy measures were as follows:

1. A 4-symptom questionnaire asked about balance and pain in the legs and feet, scoring 1 when a symptom was reported present and 0 when it was not. These scores were summed for analysis (0–4). Questions were:
   i. *Do you feel unsteady when you walk?*
   ii. *Do you have constant pain or tenderness in your lower legs or feet?*