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USING BIOMONITORING TO ASSESS HUMAN EXPOSURE TO PERCHLORATE

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ABSTRACT: Perchlorate is commonly found in the environment and can impair thyroid function at pharmacological doses. Because of the potential for widespread human exposure to this biologically active chemical, we developed an IC-MS/MS method for quantifying perchlorate and other anions relevant to perchlorate toxicity (iodide, nitrate, thiocyanate) in human matrices. By measuring these environmental toxicants and iodide in human matrices we can better assess exposure and the potential for adverse health effects.

We applied this method in a nationally representative population of 2,820 U.S. residents, ages 6 years and older, during 2001 and 2002 as part of the National Health and Nutrition Examination Survey (NHANES) and found detectable levels of perchlorate (>0.05 µg/L) in all 2,820 urine samples tested, indicating widespread human exposure to perchlorate. Urinary perchlorate levels were distributed in a log normal fashion with a median of 3.6 µg/L (3.38 µg/g creatinine) and a 95th percentile of 14 µg/L (12.7 µg/g creatinine). We estimated total daily perchlorate dose for each adult (ages 20 years and older), based on urinary perchlorate, urinary creatinine concentration, and physiological parameters predictive of creatinine excretion rate. The 95th percentile of the distribution of estimated daily perchlorate doses in the adult population was 0.234 µg/kg-day [CI 0.202 – 0.268 µg/kg-day] and is below the EPA reference dose (0.7 µg/kg-day), a dose estimated to be without appreciable risk of adverse effects during a lifetime of exposure.

Individual biomarker data can be directly compared with individual thyroid function data to better evaluate potential linkage between exposure and health. We evaluated the relationship between urinary levels of perchlorate and serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T4) in 2299 men and women as part of NHANES 2001 - 2002. Multiple regression models included covariates known or likely to be associated with T4 or TSH levels: age, race/ethnicity, body mass index, estrogen use, menopausal status, pregnancy status, premenarche status, serum C-reactive protein, serum albumin, serum cotinine, hours of fasting, urinary thiocyanate, urinary nitrate, and selected medication groups. Perchlorate was not a significant predictor of T4 or TSH levels in men. For women overall, perchlorate was a significant predictor of both T4 and TSH. Women were further categorized based on a urinary iodine cut-point of 100 µg/L and analyzed separately. For women with urinary iodine < 100 µg/L, perchlorate was a significant negative predictor of T4 ($p < 0.0001$) and a positive predictor of TSH ($p = 0.001$). For women with urinary iodine $\geq$ 100 µg/L, perchlorate was a significant positive predictor of TSH ($p = 0.025$), but not T4 ($p = 0.550$).

These regression analyses predict effects that are clinically small to moderate for women with urinary iodine < 100 µg/L. For example, increasing perchlorate exposure from the minimum to the 50th percentile perchlorate level results in a predicted decrease in thyroxine of 1.06 µg/dL and a predicted increase in serum TSH of 1.24 IU/L. These effects of perchlorate on T4 and TSH are coherent in direction and independent of other variables known to affect thyroid function, but are at perchlorate exposure levels unanticipated based on previous studies.

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