Neonatal Thyroid-Stimulating Hormone Level and Perchlorate in Drinking Water

FENG XIAO LI,[1] DANIEL M. BYRD,[2] GLORIA M. DEYHLE,[3] DAVID E. SESSER,[4] MICHAEL R. SKEELS,[4] STEVEN R. KATKOWSKY,[1] AND STEVEN H. LAMM,[1*]
[1]*Consultants in Epidemiology and Occupational Health, Inc., Washington, DC 20007*
[2]*Consultants in Toxicology, Risk Assessment, and Product Safety, Washington, DC 20024*
[3]*Newborn Screening Program, Nevada State Health Division, Carson City, NV 89710*
[4]*Oregon State Public Health Laboratory, Portland, OR 97201*

ABSTRACT

Background: The effect of perchlorate in drinking water on neonatal blood thyroid-stimulating hormone (thyrotropin; TSH) levels was examined for Las Vegas and Reno, Nevada.

Methods: The neonatal blood TSH levels in Las Vegas (with up to 15 μg/L (ppb) perchlorate in drinking water) and in Reno (with no perchlorate detected in the drinking water) from December 1998 to October 1999 were analyzed and compared. The study samples were from newborns in their first month of life (excluding the first day of life) with birth weights of 2,500–4,500 g. A multivariate analysis of logarithmically transformed TSH levels was used to compare the mean TSH levels between Las Vegas and Reno newborns, with age and sex being controlled as potential confounders.

Results: This study of neonatal TSH levels in the first month of life found no effect from living in the areas with environmental perchlorate exposures of ≤15 μg/L ($P = 0.97$).

Conclusions: This study, which was sensitive enough to detect the effects of age and gender on neonatal blood TSH levels, detected no effect from environmental exposures to perchlorate.

Teratology 62:429–431, 2000.

INTRODUCTION

Perchlorate, an inhibitor of iodine uptake by the thyroid, has been detected in the public drinking water in southern California, southern Nevada, and Arizona at levels of ≤16 μg/L. Published studies in these areas have examined whether chronic maternal exposure to perchlorate has had an adverse effect on the thyroid status of the newborns by measuring the incidence of congenital hypothyroidism (Lamm and Doemland, '99) and the distribution of neonatal thyroxine (T_4) levels (Li et al., '00). This paper completes those studies by comparing the distribution of neonatal thyroid stimulating hormone (thyrotropin; TSH) levels in two Nevada cities—Las Vegas, the largest urban area in Nevada with perchlorate in its drinking water, and Reno, the largest urban area in Nevada without perchlorate in its drinking water.

MATERIALS AND METHODS

Newborns are screened in all states, including Nevada, for metabolic diseases in a mandatory state-run program. This program includes the measurement of neonatal blood T_4 levels as a primary screening procedure for congenital hypothyroidism and the measurement of a thyroid-stimulating hormone (TSH) level on those bloods in the lowest 10th percentile T_4 measurement on a daily basis as a secondary screening procedure. The geometric mean monthly TSH levels have been calculated for newborns from Las Vegas and from Reno and compared on a monthly basis.

The water supply of Las Vegas (Clark County) comes from a bay in Lake Mead that is known to contain perchlorate at levels ranging from nondetect to about 20 ppb (μg/L). Monthly measurements of the perchlorate levels in Las Vegas finished water have been made since July 1997 by the Southern Nevada Water Authority, using an ion chromatography method with a detection level of 4 ppb (μg/L) developed by the California Department of Health Services, Sanitation and Radiation Laboratory in April 1997 (Okamoto et al., '99). The water supply in Reno comes from the high mountains via Lake Tahoe, the Truckee River, and local wells. These sources have no connection to Lake Mead. Tests of these water sources for Reno, using the same laboratory method, detected no perchlorate (Auckly, '99).

The TSH data set was composed of the TSH levels for newborns in Las Vegas and Reno for the period December 1998–October 1999 with a birth weight of 2,500–

Presented at the 13th International Conference of the Organization of Teratology Information Services (OTIS), June 25, 2000, Palm Beach, Florida.

Grant sponsor: Perchlorate Study Group.

*Correspondence to: Steven H. Lamm, Consultants in Epidemiology & Occupational Health, Inc., 2428 Wisconsin Avenue NW, Washington, DC 20007. E-mail: steve@ceoh.com

Received 30 June 200; Accepted 25 July 2000

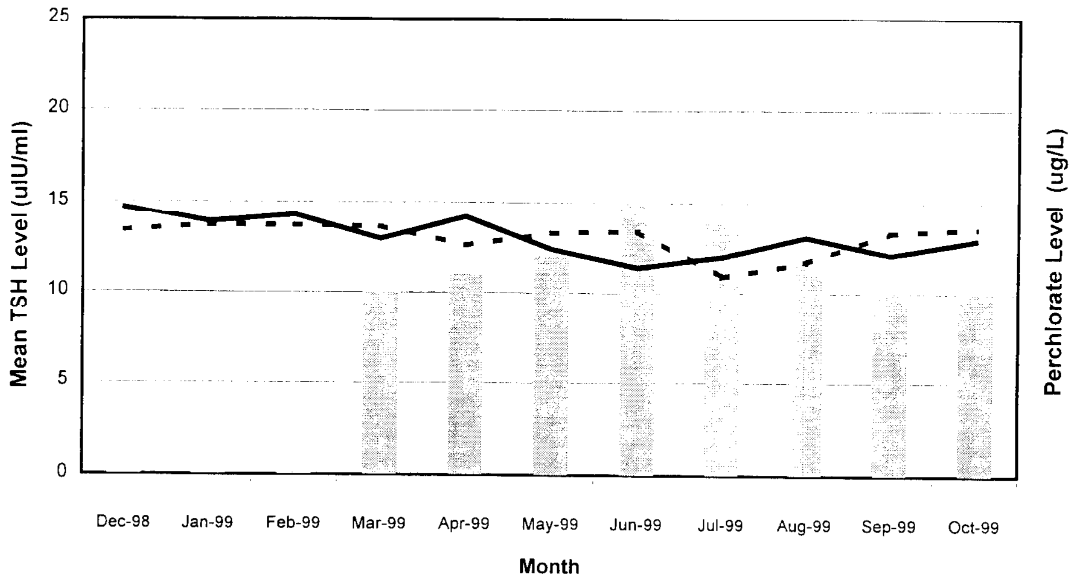

Fig. 1. Temporal presentation of mean monthly neonatal thyroid-stimulating hormone (TSH) level (μIU/ml) in Las Vegas (bold line) and Reno (dashed line) and monthly perchlorate (μg/L) level (columns) in Las Vegas drinking water. Perchlorate level for December, 1998 through February, 1999 was not detectable (detection limit = 4 μg/l).

TABLE 1. Comparison of neonatal thyroid-stimulating hormone levels (μIU/ml) in Las Vegas and Reno—crude and age/sex-specific means*

Variables	Las Vegas (n = 407)	Reno (n = 133)
Overall	11.5 (1.3)[a]	12.5 (1.3)
Age 2–7 days	12.8 (1.3)	12.8 (1.3)
Age 8–30 days	10.2 (1.3)	10.7 (1.2)
Male	11.8 (1.4)	12.9 (1.3)
Female	11.0 (1.3)	11.8 (1.2)

*Analyzed as log-transformed data.
[a]Geometric mean (standard deviation).

TABLE 2. Linear regression analysis of neonatal thyroid-stimulating hormone levels (μIU/ml)* by area, age, and sex

Variables	Coefficient	95% CI	*P*
Las Vegas/Reno**	−0.0004	−0.0241– 0.0233	0.973
Age 8–30/Age 2–7	−0.0934	−0.1143––0.0725	0.000
Female/male	−0.0259	−0.0456––0.0062	0.010

*Analyzed as log-transformed data.
**Reference population of Reno newborn males age 2–7 days had a mean TSH of 13.011 μIU/ml

4,500 g (where T_4 levels are stable) and in their first month of life (excluding first day of life, when TSH levels are unstable). Multiple linear regression analysis was used to compare the mean TSH levels between Las Vegas and Reno, with age (dichotomized for 2–7 days and 8–30 days of life) and sex controlled as potential confounders. The linear regression was performed on the log-transformed TSH level to meet the standard assumption. The perchlorate data set was comprised of the monthly perchlorate measures for the city of Las Vegas for the 11-month period, which ranged from nondetect (i.e. less than 4 ppb) to 15 ppb (μg/L). Graphic analysis is presented to examine for a relationship between the perchlorate data and the TSH data.

RESULTS

A total of 540 newborns were included in the analysis—407 from Las Vegas and 133 from Reno. A total of 316 (58.5%) of the samples were from males, 221 from females, and 3 with sex unspecified; 323 (59.8%) of the blood samples were from newborns aged 2–7 days, and 217 (40.2%) were from newborns aged 8–30 days. Table 1 presents the overall and age/sex specific mean TSH levels for the 11 month period separately for Las Vegas and Reno. The mean TSH levels of the two cities did not differ significantly, whether crude or stratified by age or sex.

Multiple linear regression analysis (Table 2) demonstrated that the TSH level was significantly affected by age at which the sample was taken (higher during ages 2–7 days than at ages 8–30 days) and by sex (higher for males than for females), but not by location (Las Vegas versus Reno) the surrogate variable for the presence of perchlorate in the drinking water. The findings of the effects of age and sex of the newborns on the blood TSH levels are consistent with previous studies (Fisher, '97; Crump et al., '00).

Figure 1 presents the mean monthly neonatal TSH levels for Las Vegas and for Reno for days 2–7 along with the monthly perchlorate level in Las Vegas drinking water (December 1998–October 1999). There is no evidence of a systematic difference between Las Vegas and Reno, and there is no evidence of covariation between the monthly neonatal TSH levels and the monthly Las Vegas perchlorate levels.

DISCUSSION

Previous analyses found no difference in the incidence of congenital hypothyroidism or in the distribution of neonatal thyroxine (T_4) levels associated with the perchlorate contamination of drinking water in Las Vegas, using Reno as a comparison area. This study has similarly examined for an effect on the neonatal thyrotropin (TSH) levels among newborns with low levels of T_4 hormone and has found none. Multiple linear regression analysis was used to control for confounding effects of the age (in days) and the sex of the newborns on TSH levels. TSH levels in the Nevada neonatal program are only obtained on the 10% of newborns in the lower tail of the daily distribution of neonatal thyroxine (T_4) levels. This analysis is of those neonates who form the "sensitive subpopulation" with respect to elevation of TSH levels. Male infants predominated in this subpopulation in both cities studied.

The boundary conditions of the analytic dataset were established in order to exclude major sources of variability for either neonatal T_4 or neonatal TSH levels so as to increase the sensitivity to detect smaller but significant sources of variability. The Nevada neonatal T_4 dataset (Li Z et al., 2000) shows that the neonatal T_4 level is fairly stable at a birth weight of 2500 grams or greater (slope = 0.5 μIU/100 grams), but that below 2500 grams birth weight the T_4 is markedly dependent upon the birth weight (slope = 5.0 μIU/100 grams). Similarly, the neonatal TSH level is markedly affected by time since birth during the first two days of life because the normal newborn has an immediate neonatal surge in TSH (up to a mean of 86 μIU/ml at 30 minutes, probably due to the release of stored pituitary TSH) and a more chronic TSH hypersecretion that persists throughout the first 24–48 hours of extrauterine life (Fisher DA and Odell WD, '69).

Environmental exposure to perchlorate at up to 15 μg/L showed no effect on neonatal TSH levels for the first month of life. These results are consistent with those seen in newborns in Chile in which no elevation of neonatal TSH was found either in the village with exposure to 5–7 ppb perchlorate or in the village with exposure to 120 ppb perchlorate (Crump et al., '00). This study has sufficient statistical power to have detected the effects of age and gender on the neonatal blood TSH level but detected no effect from environmental exposures to perchlorate. This finding is consistent with those previous studies from Nevada on the prevalence of congenital hypothyroidism (Lamm and Doemland, '99) and on neonatal T_4 levels (Li et al., '00) that found no effect from exposures of up to 15 ppb perchlorate. The recent paper from Arizona (Brechner et al., '00) reported higher TSH levels in a city with 6 ppb perchlorate in the drinking water, results that are inconsistent with the rest of the literature.

ACKNOWLEDGMENTS

This paper was presented at the 13th International Conference of the Organization of Teratology Information Services (OTIS), June 25, 2000, Palm Beach, Florida. The study was funded by the Perchlorate Study Group. We thank Gay Goodman, PhD, DABT for her critical review and comments. We thank Lisa B. Mims for providing the direction and constant support for the completion of this study.

LITERATURE CITED

Auckly C. 1999. Non-detection of perchlorate in source waters for Reno, Nevada. Sierra-Nevada Power Company.

Brechner RJ, Parkhurst GD, Humble WO, Brown MB, Herman WH. 2000. Ammonium perchlorate contamination of Colorado drinking water is associated with abnormal thyroid functions in newborns in Arizona. J Occup Environ Med 42(8):777–782.

Crump C, Michaud P, Tellex R, Reyes C, Gonzalez G, Montgomery EL, Crump KS, Lobo G, Becerra C, Gibbs JP. 2000. Does perchlorate in drinking water affect thyroid function in newborns or school-age children? J Occup Environ Med 42:603–612.

Fisher DA. 1997. Fetal thyroid function: diagnosis and management of fetal thyroid disorders. Clin Obstet Gynecol 40:16–31.

Fisher DA, Odell WD. 1969. Acute release of thyrotropin in newborn. J Clin Invest 48:1670–1677.

Lamm SH, Doemland M. 1999. Has perchlorate in drinking water increased the rate of congenital hypothyroidism? J Occup Environ Med 41:409–411.

Li Z, Li FX, Byrd D, Deyhle GM, Sesser DE, Skeels MR, Lamm SH. 2000. Neonatal thyroxine level and perchlorate in drinking water. J Occup Environ Med 42:200–205.

Okamoto HS, Rishi DK, Steeber WR, Baumann FJ, Perera SK. 1999. Using ion chromatography to detect perchlorate. J Am Water Works Assoc 91:73–84.