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The Relationship between Perchlorate in Drinking Water and Cord Blood Thyroid Hormones: First Experience from Iran

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ABSTRACT

Background: Considering the controversial information regarding the effects of perchlorate on thyroid function of high risk population as neonates, and given the high prevalence rate of thyroid disorders specially congenital hypothyroidism in our region, this study aims to investigate for the first time in Iran, the relationship between drinking groundwater perchlorate and cord blood thyroid hormones level in an industrial region.

Methods: In this cross-sectional study, drinking groundwater perchlorate level of rural areas of Zarinshahr, Isfahan was measured. Simultaneously, cord blood level of thyroid hormones of neonates born in the studied region was measured. Thyroid function test of neonates in regions with low and high perchlorate level were compared.

Results: In this study, 25 tap water samples were obtained for perchlorate measurement. Level of cord blood thyroid stimulating hormone (TSH), T4 and T3 of 25 neonates were measured. Mean (standard deviation) of perchlorate, TSH, T4 and T3 was 3.59 (5.10) μg/l, 7.81 (4.14) mIU/m, 6.06 (0.85) mg/dl, and 63.46 (17.53) mg/dl, respectively. Mean levels of thyroid function tests were not different in low (<5 μg/l) and high level of drinking ground water perchlorate ($P > 0.05$).

Conclusions: Perchlorate did not appear to be related to thyroid function of neonates in the studied industrial region. It seems that iodine status of the regions, as well as other environmental contaminants and genetic background, could impact on its relation with thyroid function of neonates.

Keywords: Environment, infant, perchlorate, thyroid gland

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INTRODUCTION

Perchlorate ion ($ClO4^-$) is considered as one of the important environmental contaminants with potential harmful effects on human health.[1] It could also impact on aquatic and land animals and indirect effects on human.[2]

Perchlorate has been used industrially as oxidants in aerospace fuels and explosives, road flares, pyrotechnics, and solid rocket propellant.[3] Hypochlorite water disinfection products, fireworks, and certain manufacturing processes are other potential sources of perchlorate.[4] Perchlorate has poor affinity for soils and readily dissolves in water and is highly mobile in groundwater.[5] It is found in a variety of foods including spinach, carrots, milk, and milk products, moreover, food supply has become contaminated by natural water through irrigation.[5]

Human environmental exposure to perchlorate can occur through food or water following industrial contamination or from natural perchlorate.[5]

Perchlorate is an inorganic anion, and it is documented that in the higher dose, it could competitively inhibit iodide uptake through the sodium iodide symporter in the thyroid gland.[6]

Iodine is a key component for the production of thyroid hormone. The hormone has a crucial role for normal brain development, natural growth, as well as other physiological functions. Consequences of thyroid function impairment are so important in some group of population, including neonates and pregnant women.[7,8]

The effects of perchlorate on thyroid function were recently reviewed in several studies and among different age groups.[5,9-12] These findings were not conclusive enough, and it seems that additional studies are needed regarding the association between background exposure to perchlorate and thyroid function in different life periods.[13]

Isfahan is the largest industrial center in Iran with a considerably high number of industries located in cities around Isfahan city like Zarinshahr, which is located in southwest of Isfahan.[14] Studies on chemical quality of ground waters of this region showed that the mean concentration of some contaminants exceeded the standard levels. It is suggested that the main cause of this problem is water wells contamination with high discharge rate of agricultural and industrial wastewater.[15]

Considering the controversial information regarding the effects of perchlorate on thyroid function of high risk populations as neonates, as well as the high prevalence rate of thyroid disorders specially congenital hypothyroidism (CH) in our region,[16] this study aims to investigate the relationship between drinking water perchlorate and cord blood thyroid hormones level in Zarinshahr, Iran.

METHODS

This study was conducted as a cross-sectional investigation in 2012–2013 in Zarinshahr-Isfahan.

During the study, the rural areas of Zarinshahr city with the supply of their drinking water from underground water were selected for water sampling stations. Each rural area (village) usually has one or two wells for drinking water. The main well(s) of each village were selected as water sampling stations.

The study protocol was approved by Environment Research Center and the Ethics Committee of the Isfahan University of Medical Sciences. Written informed consent was obtained from all participants.

To obtain an appropriate sample which would be representative of the region drinking water,10 of the total 15 wells of the region (60% of the wells of the region) were selected for sampling. Selection criterion for the stations was proximity of the wells to industrial areas of the city. Information in this regard was obtained from health care center of the region.

A total of 25 water samples was randomly collected from the selected wells by one of the study investigators. The groundwater samples were taken after flashing water for at least 5–10 min, and sampling was replicated for 3–4 times. The samples were collected in polythene-containing tubes and transferred to Iran Mineral Processing Research Center laboratory for chemical analyzing using standard methods recommended by the American Public Health Association (APHA, 2005).

Simultaneously, other investigator of the study referred to the maternity hospitals of Zarinshahr for cord blood sampling.

Considering the distribution of studied population and uncertainty in the number of individuals who used selected well water, the number of cord blood samples was equal to the water samples and was divided to the number of the selected wells.

Cord blood samples were obtained from neonates whose mothers were residents of the selected regions for at least 5 years, had no medical history of any acute and chronic disease and history of any medication use except than the routine supplements for pregnancy. Personnel of the maternity hospital who perform the routine examinations of mothers confirmed the above-mentioned inclusion criteria for mothers selected for cord blood sampling. Data regarding the residence area and drinking water of selected mothers were recorded by the project team. A trained nurse obtained the cord blood samples (5 ml) immediately after the birth of the infants from a double-clamped segment of the umbilical cord.

Cord blood samples were collected in serum separator tubes and transferred to the hospital laboratory for centrifuging and freezing of the sera. The frozen samples

were transferred under cold chain condition to Pars laboratory, the referral laboratory of Isfahan province for thyroid hormone measurement. Thyroid hormones level of cord blood samples was measured.

The mean level of thyroid hormones (thyroid stimulating hormone [TSH], T4 and T3) was compared in regions with high and low level of perchlorate.

Laboratory measurements

The concentration of $ClO4^-$ ion in groundwater samples was determined by Dionex ICS-1000 from USA.

Umbilical plasma TSH concentration was measured using immunoradiometric assay methods (Iran Kavoshyar Co. Kits-Iran). Umbilical plasma T4 and T3 levels were measured using radioimmunoassay method (Iran Kavoshyar Co. Kits-Iran).

Statistical analysis

Data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA) software. Mean levels of TSH, T4, and T3 in neonates from regions with high and low perchlorate levels were compared using a *t*-test. $P < 0.05$ was considered as statistically significant.

RESULTS

In this study, 25 tap water samples were obtained for perchlorate measurement. Cord blood levels of TSH, T4, and T3 of 25 neonates were measured. Distribution of groundwater perchlorate level in the studied regions is presented.

Mean (standard deviation) of studied variables are presented in Table 1.

In 9 samples (36%) of the regions, the level of groundwater perchlorate was higher than 5 μg/l.

Mean levels of thyroid function tests according to the classification of groundwater perchlorate level are presented in Table 2. Mean levels of TSH, T4, and T3 were not different in regions with high and low level of groundwater perchlorate.

DISCUSSION

In this study, which to the best of our knowledge is the first of its kind in Iran, we did not find significant relationship between water perchlorate and level of cord blood thyroid hormones of neonates born in an industrial area.

Findings of different epidemiological studies are controversial in this field.[9-12] Some studies indicated a significant relationship between water perchlorate and thyroid function tests in neonates,[9,10] whereas others did not.[11,12]

The issue is considered as an important health concern. However, considering the important role of thyroid hormone in neurodevelopmental consequences of young children, any environmental factor that could impair thyroid hormone production should be investigated, especially in regions where the prevalence of CH is more common.[17]

In the current study, the mean levels of thyroid hormones were not significantly different in low and high levels of perchlorate in drinking water. Our results were consistent with two studies in Chile, in which no association was reported between water perchlorate concentration and neonatal thyroid hormones.[11,12]

Some other studies among pregnant women and their neonates have failed to identify any association between mentioned factors.[18,19] A review of the epidemiological literature that evaluated the association between environmental perchlorate exposure and thyroid function concluded that that environmental or occupational exposure to perchlorate could not be a risk for adverse effects on thyroid function.[20]

Some other studies conducted among the potentially susceptible groups demonstrated a significant relationship between perchlorate and thyroid hormone levels. Recently, a study in California identified a strong association between neonatal TSH and maternal drinking water perchlorate exposure during pregnancy.[9] Their study was conducted as a part of the California NBS Program and during the study conducted over 497,000 TSH and 800 per chlorate measurements were performed.[9] Two other studies from California also support the association.[10,21]

Likewise, a study in Arizona, USA showed that in the perchlorate-exposed region, neonatal TSH levels were higher than in unexposed region.[22]

Table 1: Mean (SD) and range of groundwater perchlorate level and thyroid function test of studied neonates in zarinshahr-isfahan

Variables	Perchlorate (μg/l)	TSH (mIU/m)	T4 (mg/dl)	T3 (mg/dl)
Mean±SD	3.59 (5.10)	7.81 (4.14)	6.06 (0.85)	63.46 (17.53)
Range (minimum-maximum)	0.01-17.70	0.30-11.40	4.50-8.10	33.00±102.00

SD=Standard deviation, TSH=Thyroid stimulating hormone

Table 2: Mean of thyroid function tests according to the classification of groundwater perchlorate level

	Groundwater <5 (μg/l) n=16	Perchlorate ≥5 (μg/l) n=9	P
TSH (mIU/m)	7.75 (1.87)	7.9 (2.70)	0.94
T4 (mg/dl)	6.10 (1.00)	5.98 (0.56)	0.76
T3 (mg/dl)	67.09 (15.71)	57.00 (19.65)	0.17

TSH=Thyroid stimulating hormone

Evidences determined that the adverse effect of perchlorate on thyroid function is more prominent in regions or subjects with iodine deficiency.[23,24] It is well-established that iodine uptake inhibition by perchlorate is significantly dependent on the additive effect of other environmental NIS inhibitors including thiocyanate and nitrate and also iodine intake itself.[25]

A study in California, USA investigated the combined effects of perchlorate, thiocyanate, and iodine on thyroid function in the National Health and Nutrition Examination Survey during 2007–2008. It concluded that concomitant exposure to perchlorate, thiocyanate, and low iodine significantly decreases T4 production.[26]

According to the calculations of De Groef *et al*., possible thyroidal effects resulting from perchlorate exposure from drinking water are accounted for <10% of the exposure.[25]

Though iodine level was not measured in our study population, but Iran is considered an iodine replete area.[27] The level of thiocyanate and nitrate was not measured in our study. It is recommended to determine the role of these potential confounders in this regard.

Another explanation for obtained results is genetic susceptibility of the individuals who were exposed to environmental perchlorate. A review study suggested that chronic environmental exposure to perchlorate could inhibit iodine uptake in subjects genetically susceptible to iodination process impairment and the genetic factors impact on the responses of individuals to perchlorate exposure.[28]

This study had some limitations, including small sample size and the cross-sectional design of the investigation. In mentioned study design, we had no information about the historical ground water perchlorate levels which consequently could limit our ability to determine the temporal relation between perchlorate exposure and thyroid function especially in high-risk population such as pregnant women and neonates. The strength of our study is its novelty in Iran, with relatively high prevalence of CH.

CONCLUSIONS

Perchlorate did not appear to be related to thyroid function of neonates in the industrial area of this study. It seems that iodine status of the region, as well as other environmental contaminants and genetic background, could impact on its relation with thyroid function of neonates. To obtain more conclusive results in this field, further studies with larger sample size and consideration of other environmental factors are needed.

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REFERENCES

1. Srinivasan A, Viraraghavan T. Perchlorate: Health effects and technologies for its removal from water resources. Int J Environ Res Public Health 2009;6:1418-42.
2. Stetson SJ, Wanty RB, Helsel DR, Kalkhoff SJ, Macalady DL. Stability of low levels of perchlorate in drinking water and natural water samples. Anal Chim Acta 2006;567:108-13.
3. Blount BC, Alwis KU, Jain RB, Solomon BL, Morrow JC, Jackson WA. Perchlorate, nitrate, and iodide intake through tap water. Environ Sci Technol 2010;44:9564-70.
4. MA DEP (Massachusetts Department of Environmental Protection). 2005. The Occurrence and Sources of Perchlorate in Massachusetts: Draft Report. Available from: http://www.mass.gov/dep/cleanup/sites/percsour.doc. [Last accessed on 2009 Jan 14].
5. Zewdie T, Smith CM, Hutcheson M, West CR. Basis of the Massachusetts reference dose and drinking water standard for perchlorate. Environ Health Perspect 2010;118:42-8.
6. Tonacchera M, Pinchera A, Dimida A, Ferrarini E, Agretti P, Vitti P, *et al.* Relative potencies and additivity of perchlorate, thiocyanate, nitrate, and iodide on the inhibition of radioactive iodide uptake by the human sodium iodide symporter. Thyroid 2004;14:1012-9.
7. Pesce L, Kopp P. Iodide transport: Implications for health and disease. Int J Pediatr Endocrinol 2014;2014:8.
8. Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR Jr, Lee DH, *et al.* Hormones and endocrine-disrupting chemicals: Low-dose effects and nonmonotonic dose responses. Endocr Rev 2012;33:378-455.
9. Steinmaus C, Miller MD, Smith AH. Perchlorate in drinking water during pregnancy and neonatal thyroid hormone levels in California. J Occup Environ Med 2010;52:1217-524.
10. Buffler PA, Kelsh MA, Lau EC, Edinboro CH, Barnard JC, Rutherford GW, *et al.* Thyroid function and perchlorate in drinking water: An evaluation among California newborns, 1998. Environ Health Perspect 2006;114:798-804.
11. Téllez Téllez R, Michaud Chacón P, Reyes Abarca C, Blount BC, Van Landingham CB, Crump KS, *et al.* Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid 2005;15:963-75.
12. Crump C, Michaud P, Téllez R, Reyes C, Gonzalez G, Montgomery EL, *et al.* Does perchlorate in drinking water affect thyroid function in newborns or school-age children? J Occup Environ Med 2000;42:603-12.
13. Leung AM, Pearce EN, Braverman LE. Environmental perchlorate exposure: Potential adverse thyroid effects. Curr Opin Endocrinol Diabetes Obes 2014;21:372-6.
14. "Census of the Islamic Republic of Iran, 1385 (2006)" (Excel). Islamic Republic of Iran. Archived from the Original on 11 Nov, 2011.
15. Ebrahimi A, Amin MM, Hashemi H, Foladifard R, Vahiddastjerdi M. A survey of groundwater chemical quality in Sajad Zarinshahr. Health Syst Res 2011;6:918-26.
16. Hashemipour M, Ghasemi M, Hovsepian S, Heiydari K, Sajadi A, Hadian R,

et al. Prevalence of permanent congenital hypothyroidism in Isfahan-Iran. Int J Prev Med 2013;4:1365-70.
17. Kooistra L, Crawford S, van Baar AL, Brouwers EP, Pop VJ. Neonatal effects of maternal hypothyroxinemia during early pregnancy. Pediatrics 2006;117:161-7.
18. Pearce EN, Spencer CA, Mestman JH, Lee RH, Bergoglio LM, Mereshian P, *et al.* Effect of environmental perchlorate on thyroid function in pregnant women from Córdoba, Argentina, and Los Angeles, California. Endocr Pract 2011;17:412-7.
19. Pearce EN, Alexiou M, Koukkou E, Braverman LE, He X, Ilias I, *et al.* Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women from Greece. Clin Endocrinol (Oxf) 2012;77:471-4.
20. Tarone RE, Lipworth L, McLaughlin JK. The epidemiology of environmental perchlorate exposure and thyroid function: A comprehensive review. J Occup Environ Med 2010;52:653-60.
21. Kelsh MA, Buffler PA, Daaboul JJ, Rutherford GW, Lau EC, Barnard JC, *et al.* Primary congenital hypothyroidism, newborn thyroid function, and environmental perchlorate exposure among residents of a Southern California community. J Occup Environ Med 2003;45:1116-27.
22. Brechner RJ, Parkhurst GD, Humble WO, Brown MB, Herman WH. Ammonium perchlorate contamination of Colorado River drinking water is associated with abnormal thyroid function in newborns in Arizona. J Occup Environ Med 2000;42:777-82.
23. Leung AM, Pearce EN, Braverman LE. Perchlorate, iodine and the thyroid. Best Pract Res Clin Endocrinol Metab 2010;24:133-41.
24. Valentín-Blasini L, Blount BC, Otero-Santos S, Cao Y, Bernbaum JC, Rogan WJ. Perchlorate exposure and dose estimates in infants. Environ Sci Technol 2011;45:4127-32.
25. De Groef B, Decallonne BR, Van der Geyten S, Darras VM, Bouillon R. Perchlorate versus other environmental sodium/iodide symporter inhibitors: Potential thyroid-related health effects. Eur J Endocrinol 2006;155:17-25.
26. Steinmaus C, Miller MD, Cushing L, Blount BC, Smith AH. Combined effects of perchlorate, thiocyanate, and iodine on thyroid function in the National Health and Nutrition Examination Survey 2007-08. Environ Res 2013;123:17-24.
27. Azizi F, Sheikholeslam R, Hedayati M, Mirmiran P, Malekafzali H, Kimiagar M, *et al.* Sustainable control of iodinedeficiency in Iran: Beneficial results of the implementation of the mandatory law on salt iodization. J Endocrinol Invest 2002;25:409-13.
28. Scinicariello F, Murray HE, Smith L, Wilbur S, Fowler BA. Genetic factors that might lead to different responses in individuals exposed to perchlorate. Environ Health Perspect 2005;113:1479-84.

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