THYROID
Volume 22, Number 11, 2012

DOI: 10.1089/thy.2012.0294

Breastmilk Iodine Concentrations Following Acute Dietary Iodine Intake

Angela M. Leung,[1] Lewis E. Braverman,[1] Xuemei He,[1] Timothy Heeren,[2] and Elizabeth N. Pearce[1]

Background: Breastmilk iodine levels may vary temporally in response to recent changes in dietary iodine intake. We assessed the effect of and time to peak breastmilk iodine levels after potassium iodine ingestion, which has never been studied and is important toward interpretation of studies of breastmilk iodine measurements.

Methods: Sixteen healthy lactating Boston-area women with no known thyroid disease were each given 600 μg oral potassium iodide (KI) (456 μg iodine) after an overnight fast. Iodine was measured in breastmilk and urine at baseline and hourly for 8 hours following iodine intake. All dietary iodine ingested during the study period was also measured.

Results: Mean age of mothers was 30.2 ± 4.1 (SD) years. Median (interquartile range [IQR]) baseline breastmilk and urine iodine levels were 45.5 μg/L (IQR 34.5–169.0) and 67.5 μg/L (IQR 57.5–140.0), respectively. Following 600 μg KI administration, median increase in breastmilk iodine levels above baseline was 280.5 μg/L (IQR 71.5–338.0), and median peak breastmilk iodine concentration was 354 μg/L (IQR 315–495). Median time to peak breastmilk iodine levels following KI administration was 6 hours (IQR 5–7). Dietary iodine sources provided an additional 36–685 μg iodine intake during the 8-hour study.

Conclusions: Following ingestion of 600 μg KI, there is a measurable rise in breastmilk iodine concentrations, with peak levels occurring at 6 hours. These findings strongly suggest that breastmilk iodine concentrations should be interpreted in relation to recent iodine intake.

Introduction

Normal thyroid function, important for fetal and neonatal neurodevelopment (1), depends on sufficient dietary iodine intake. Breastfed infants rely on maternal dietary iodine for their iodine nutrition. As iodine is concentrated into breastmilk at a gradient 20–50% higher than in plasma (2) through increased expression of the sodium iodide symporter in lactating breast cells (3), dietary iodine requirements are higher during lactation. The Institute of Medicine's Recommended Dietary Allowance (RDA) for dietary iodine intake is 290 μg/day for lactating women, compared with 150 μg/day recommended for nonpregnant, nonlactating women (4).

Although there are no normative ranges for breastmilk iodine levels, the recommendations for iodine intake by the U.S. Institute of Medicine are 110 μg/day for infants 0–6 months old, 130 μg/day for infants 7–12 months old, and 90 μg/day for children 1–8 years old (4). However, there are insufficient data to determine iodine turnover in infants, and the recommendations for infants 0–6 and 7–12 months are Adequate Intake (AI) levels, which are based on dietary intake estimates in healthy people, rather than RDA levels. For infants 0–12 months old, AI levels are based on a mean breastmilk iodine concentration of 146 μg/L measured in 37 U.S. women (5) and the assumption that infants ingest an average of 0.78 L/day of breastmilk during 0–6 months of age and 0.60 L/day during 6–12 months of age (4).

A recent review of 14 global studies that have measured breastmilk iodine levels reported a wide range of mean or median concentrations (13–155 μg/L) among women living in areas of varying iodine sufficiency (2), while other reviews have reported breastmilk iodine concentrations ranging from 5.4 to 2170 μg/L (medians) (6) and from 9 to 1267 μg/L (means) (7). Observational data regarding breastmilk iodine levels in lactating women in the United States are extremely limited. We reported that the median breastmilk iodine concentration in 57 Boston-area women was 155 μg/L (8), similar to that of a 1984 study of 37 women (178 μg/L) (5). Although the United States is considered generally iodine-sufficient, the

[1]Section of Endocrinology, Diabetes, and Nutrition, Boston Medical Center, School of Medicine; [2]Department of Biostatistics, School of Public Health; Boston University, Boston, Massachusetts.

median breastmilk iodine levels in our study were far higher than those observed recently by Kirk and colleagues in three studies based mostly in Texas (33.5, 43.0, and 55.2 μg/L) (9–11). The range of breastmilk iodine concentrations in our sample was wide, from 2.7 to 1968 μg/L (8), and some women may have been providing insufficient breastmilk iodine to their infant.

Sampling of breastmilk for iodine measurements may be affected by physiologic fluctuations of iodine content. Kirk *et al.* recently reported that breastmilk iodine levels were higher in women who used iodized salt compared with women taking an iodine-containing multivitamin (12). In small, observational studies, breastmilk iodine levels have been reported to increase during the first postpartum month (13), decrease during the first 6 postpartum months (14), and vary temporally day-to-day (10). Kirk *et al.* measured levels of breastmilk iodide (which comprises 89–90% of breastmilk iodine; S. Pino, unpublished) in 108 total breastmilk samples provided by 10 U.S. lactating women over a 3-day period (10). Considerable variation of breastmilk iodide levels within and between individuals was found (median, 55.2 μg/L; range, 3.1–334 μg/L; mean ± SD, 87.9 ± 80.9 μg/L), suggesting that variable sampling of breastmilk for iodine measurements relative to the timing of peak concentrations may lead to incorrect conclusions regarding maternal breastmilk iodine sufficiency in population studies. In a small sample of 30 women, we previously reported no significant variation in breastmilk iodine content assessed sequentially during a single feed (8).

Whether breastmilk iodine concentrations and the availability of adequate iodine nutrition to the breastfed infant are affected by the physiologic response to dietary iodine ingestion has not been studied. The present study was done to acutely assess breastmilk iodine concentrations following maternal dietary iodine ingestion among U.S. women.

Methods

Study protocol

The Boston University Medical Campus Institutional Review Board approved the study. Sixteen healthy lactating women from the Boston area with no known thyroid disease, no history of using thyroid hormone, anti-thyroid medications, or amiodarone, and no iodinated radiologic contrast administration within the previous 3 months were recruited and provided informed consent. Information regarding subjects' age, United States Office of Management and Budget race and ethnicity code, medications, multivitamin use, and smoking status was collected. Although an imperfect measure of iodine status, subjects also completed a dietary iodine questionnaire to gather information regarding their estimated iodine intake over the previous 3 days of the study.

Following an overnight fast, each subject was administered 600 μg of potassium iodide (KI) orally (two tablets of Walgreen's Finest Prenatal Multivitamin obtained from a single lot [each listed to contain 75 μg of KI] and two tablets of a Pure Encapsulations KI supplement [each listed to contain 225 μg KI]). The iodine content of each potassium iodine source was measured in duplicate to confirm the listed amount, as labeled content may be different from that of actual measurements (15). From these measurements, each subject was administered ~752 μg of KI (572 μg iodine). Subjects who routinely took an iodine-containing multivitamin or supplement did not do so during the 24 hours prior to ingestion of the KI.

Each subject provided breastmilk and spot urine samples at baseline and hourly for 8 hours following potassium iodine administration. Mothers were encouraged to breastfeed their infants or pump breastmilk as needed. The timing (and for consumed products, amounts) of all breastfeeding, pumping of breastmilk, and ingestion of meals and beverages during the 8-hour study period were recorded relative to the hourly breastmilk and spot urine collections. Duplicate portions of all food and beverages consumed during the study were also measured for their iodine content.

Laboratory measurements

All breastmilk and spot urine samples were stored at −80°C prior to measurement. Iodine levels in the KI-containing multivitamin and supplement and in all ingested food and beverages were measured spectrophotometrically using a Technicon Autoanalyzer (Technicon Instrument, Inc., Tarrytown, NY) by a modification of the method of Benotti *et al.* (16). In cases where the initial two measurements were not within 15% of each other, a third or a fourth measurement was obtained and the average of all measurements was reported.

Statistical analysis

Sample size determination of 16 individuals was based on detecting an effect size of 0.75, with 80% power at the 0.05 level, for a paired *t*-test comparing change in breastmilk iodine concentrations over time. Breastmilk iodine concentrations are reported as medians and interquartile ranges (IQRs) at the 9 timepoints (baseline, then hourly for 8 hours after iodine ingestion). The Wilcoxon signed rank test was used to assess pairwise unadjusted changes in median breastmilk iodine levels over time, and mixed effects regression models for repeated measures data were used to examine changes in breastmilk iodine levels over the entire study period and to adjust for breastfeeding (measured as a yes/no categorical variable at each of the timepoints; breastmilk volume was not measured or estimated). Time to peak breastmilk iodine levels after ingestion of a known iodine load is described through the median and IQR. Data processing and statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC) and Excel.

Results

Descriptive data for the subjects are shown in Table 1. None of the subjects reported regular use of any iodine-only or kelp supplements. From foodstuffs that subjects consumed, dietary iodine sources provided an additional 36–685 μg of iodine intake beyond the study supplements during the 8-hour study period.

Median (IQR) baseline iodine levels were 45.5 μg/L (IQR 34.5–169.0) in breastmilk and 67.5 μg/L (IQR 57.5–140.0) in urine. Following 600 μg KI oral administration, there was a significant median increase in breastmilk iodine levels (280.5 μg/L; IQR 71.5–338.0) above baseline ($p < 0.01$); the median peak breastmilk iodine concentration was 354 μg/L (IQR 315–495) (Fig. 1). The median time to peak breastmilk iodine levels following KI administration was 6 hours (IQR 5–7) (Fig. 1). When adjusted for breastfeeding during the study period, the

Table 1. Subject Characteristics ($N=16$)

Age, years (mean ± SD)	30.2 ± 4.1
OMB-REC (*n*)	
Caucasian	13
Black	2
Hispanic	1
Cigarette smoker (*n*)	
Yes	1
No	15
Regular multivitamin use (*n*)	
Yes	12
150 μg iodine/serving	2
No iodine	8
Unknown iodine content	2
No	4
Regular salt use (*n*)	
Yes	8
No	8
Salt use in the previous 24 hours (*n*)	
Yes	6
Iodized	1
Noniodized	3
Unknown iodine content	2
No	10

OMB-REC, Office of Management and Budget "Race & Ethnicity" Codes.

increase in breastmilk iodine levels over time, peak breastmilk iodine concentration, and time to peak breastmilk iodine levels were not substantially different from their unadjusted values (data not shown).

Median urinary iodine concentrations (192 μg/L; IQR 132.5–327) remained stable over the study period. Aggregate median breastmilk and urinary iodine concentrations were not significantly correlated ($p=0.39$).

Discussion

This study demonstrates that there is a measurable rise in breastmilk iodine concentrations, with peak levels occurring at 6 hours, following acute oral ingestion of 600 μg KI. These findings provide important data regarding the physiologic variation of breastmilk iodine levels and strongly suggest that breastmilk iodine sampling should be interpreted in relation to recent iodine intake.

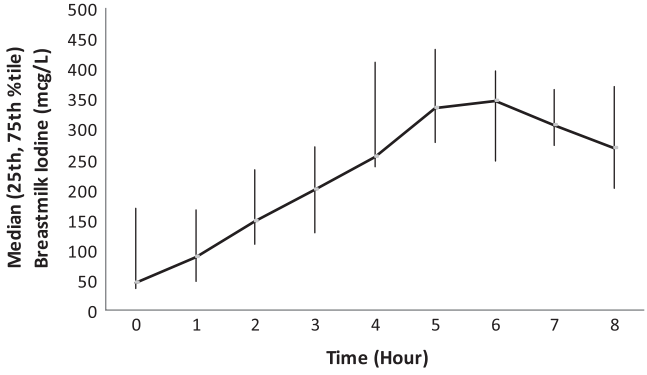

FIG. 1. Hourly median breastmilk iodine concentrations (μg/L) before and following 600 μg acute potassium iodide ingestion.

Adequate iodine intake is particularly important for exclusively breastfed infants, in whom breastmilk is the sole source of iodine nutrition during a critical period of growth and development. Iodine deficiency affects over 241 million school-aged children (nearly 30%) and is the leading cause of preventable mental retardation worldwide (17). Insufficient maternal iodine during pregnancy and the immediate postpartum period results in neurological and psychological deficits in children (18). The IQ levels of children living in severely iodine-deficient areas are lower than those living in iodine-sufficient areas and are improved with iodine supplementation (19).

Assessment of goiter rates can be used as a measure of population iodine sufficiency (20). One small study demonstrated that thyroid gland volumes of breastfed infants were smaller compared with infants fed iodine-unsupplemented formula for 3 months (21). Another measure of population iodine sufficiency is adequate median urinary iodine concentrations (requiring a minimum of 125 individuals) (22) ≥100 μg/L in infants <2 years old and in nonpregnant adults (23). Urinary iodine concentration thresholds have been identified for populations, but not for individuals, given significant day-to-day variation of iodine intake (24). Although U.S. dietary iodine has been considered adequate since the 1920s, there are very limited data regarding median urinary iodine concentrations of infants in the United States. We reported that in 57 Boston-area partially or exclusively breastfed infants (mean age, 1.6 months), median urinary concentration was 197.5 μg/L (range 40–785 μg/L) (25).

According to data from the National Health and Nutrition Examination Survey (NHANES), the median urinary iodine concentration in U.S. adults decreased by over 50% from the early 1970s to the early 1990s (26). Of particular concern is the fact that the prevalence of urinary iodine values <50 μg/L among women of childbearing age increased by almost 4-fold, from 4% to 15%, during this period. In the most recent NHANES survey (2005–2008), although the median urinary iodine concentration of pregnant women was 125 μg/L, 35.3% had urinary iodine levels <100 μg/L (27). Thus, while the overall U.S. adult population remains iodine sufficient, a subset of pregnant and lactating women may have inadequate dietary iodine intake.

Sources of iodine in the U.S. diet have been difficult to identify because there are a wide variety of potential sources, there is a wide amount of variation in the iodine content of some common foods, and food iodine content is not listed on packaging. For this reason, a public health approach to iodine supplementation in the United States has been advocated. The American Thyroid Association has recommended that women in North America receive dietary supplements containing 150 μg iodine daily during conception planning, pregnancy, and lactation and that all prenatal vitamins contain 150 μg of iodine (28). These recommendations have not yet been adopted. Only 20.3% of pregnant and 14.5% of lactating women in the United States take a supplement containing iodine, according to NHANES data (29). Currently, 114 of 223 (51%) brands of prescription and nonprescription prenatal multivitamins marketed in the United States list iodine as a constituent, and many of those that do contain iodine do not contain the labeled amount, especially when kelp is the iodine source (15).

The results of our study are important in the evaluation of excessive iodine consumption by the breastfed infant.

Guidelines from the World Health Organization recommend a maximum iodine intake of 180 μg/day for infants <2 years old (30). The U.S. Institute of Medicine has not established recommendations for infants 0–12 months, but recommends a tolerable upper limit of 200 μg iodine daily for children 1–3 years old (4). In one Korean study of 50 women and their breastfed infants, breastmilk iodine levels were generally elevated and ranged from 198 to 8484 μg/L (thought to be secondary to the increased consumption of seaweed soup by many Korean women during the postpartum period) (31), which was associated with cases of neonatal subclinical hypothyroidism (32). Finally, as the United States is considered generally iodine sufficient, the timecourse to peak breastmilk iodine levels of the women in the present study may not be applicable to individuals living in regions of inadequate iodine nutrition, in whom iodine reserves may be diminished.

We report that there is a measurable rise in breastmilk iodine concentrations following an acute dietary iodine load, with peak levels occurring at 6 hours. These findings strongly suggest that breastmilk iodine concentrations should be interpreted in relation to recent iodine intake. The results of the present study are not intended to alter clinical or breastfeeding practices, but are expected to broaden the understanding of when breastmilk should be appropriately sampled relative to dietary iodine ingestion.

Acknowledgments

This work was supported by NIH/NICHD 1 K23 HD068552 01 and the Boston University Clinical & Translational Science Institute (1UL1RR025771).

Disclosure Statement

The authors declare that no competing financial interests exist.

References

1. Younes-Rapozo V, Berendonk J, Savignon T, Manhaes AC, Barradas PC 2006 Thyroid hormone deficiency changes the distribution of oligodendrocyte/myelin markers during oligodendroglial differentiation *in vitro*. Int J Dev Neurosci **24:**445–453.
2. Azizi F, Smyth P 2009 Breastfeeding and maternal and infant iodine nutrition. Clin Endocrinol (Oxf) **70:**803–809.
3. Tazebay UH, Wapnir IL, Levy O, Dohan O, Zuckier LS, Zhao QH, Deng HF, Amenta PS, Fineberg S, Pestell RG, Carrasco N 2000 The mammary gland iodide transporter is expressed during lactation and in breast cancer. Nat Med **6:**871–878.
4. Food and Nutrition Board, Institute of Medicine 2006 Dietary Reference Intakes. National Academy Press, Washington, DC.
5. Gushurst CA, Mueller JA, Green JA, Sedor F 1984 Breast milk iodide: reassessment in the 1980s. Pediatrics **73:**354–357.
6. Dorea JG 2002 Iodine nutrition and breast feeding. J Trace Elem Med Biol **16:**207–220.
7. Semba RD, Delange F 2001 Iodine in human milk: perspectives for infant health. Nutr Rev **59:**269–278.
8. Pearce EN, Leung AM, Blount BC, Bazrafshan HR, He X, Pino S, Valentin-Blasini L, Braverman LE 2007 Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab **92:**1673–1677.
9. Kirk AB, Martinelango PK, Tian K, Dutta A, Smith EE, Dasgupta PK 2005 Perchlorate and iodide in dairy and breast milk. Environ Sci Technol **39:**2011–2017.
10. Kirk AB, Dyke JV, Martin CF, Dasgupta PK 2007 Temporal patterns in perchlorate, thiocyanate, and iodide excretion in human milk. Environ Health Perspect **115:**182–186.
11. Dasgupta PK, Kirk AB, Dyke JV, Ohira S 2008 Intake of iodine and perchlorate and excretion in human milk. Environ Sci Technol **42:**8115–8121.
12. Kirk AB, Kroll M, Dyke JV, Ohira SI, Dias RA, Dasgupta PK 2012 Perchlorate, iodine supplements, iodized salt and breast milk iodine content. Sci Total Environ **420:**73–78.
13. Etling N, Padovani E, Fouque F, Tato L 1986 First-month variations in total iodine content of human breast milks. Early Hum Dev **13:**81–85.
14. Mulrine HM, Skeaff SA, Ferguson EL, Gray AR, Valeix P 2010 Breast-milk iodine concentration declines over the first 6 mo postpartum in iodine-deficient women. Am J Clin Nutr **92:**849–856.
15. Leung AM, Pearce EN, Braverman LE 2009 Iodine content of prenatal multivitamins in the United States. N Engl J Med **360:**939–940.
16. Benotti J, Benotti N, Pino S, Gardyna H 1965 Determination of total iodine in urine, stool, diets, and tissue. Clin Chem **11:**932–936.
17. International Council for the Control of Iodine Deficiency Disorders (ICCIDD). Available at www.iccidd.org (accessed August 29, 2012).
18. Cao XY, Jiang XM, Dou ZH, Rakeman MA, Zhang ML, O'Donnell K, Ma T, Amette K, DeLong N, DeLong GR 1994 Timing of vulnerability of the brain to iodine deficiency in endemic cretinism. N Engl J Me**d 331:**1739–1744.
19. Qian M, Wang D, Watkins WE, Gebski V, Yan YQ, Li M, Chen ZP 2005 The effects of iodine on intelligence in children: a meta-analysis of studies conducted in China. Asia Pac J Clin Nutr **14:**32–42.
20. Zimmermann MB, Jooste PL, Pandav CS 2008 Iodine-deficiency disorders. Lancet **372:**1251–1262.
21. Bohles H, Aschenbrenner M, Roth M, von Loewenich V, Ball F, Usadel KH 1993 Development of thyroid gland volume during the first 3 months of life in breast-fed versus iodine-supplemented and iodine-free formula-fed infants. Clin Invest **71:**13–20.
22. Andersen S, Karmisholt J, Pedersen KM, Laurberg P 2008 Reliability of studies of iodine intake and recommendations for number of samples in groups and in individuals. Br J Nutr **99:**813–818.
23. Hetzel BS 2012 The development of a global program for the elimination of brain damage due to iodine deficiency. Asia Pac J Clin Nutr **21:**164–170.
24. Konig F, Andersson M, Hotz K, Aeberli I, Zimmermann MB 2011 Ten repeat collections for urinary iodine from spot samples or 24-hour samples are needed to reliably estimate individual iodine status in women. J Nutr **141:**2049–2054.
25. Leung AM, Braverman LE, He X, Schuller KE, Roussilhes A, Jahreis K, Pearce EN 2012 Environmental perchlorate and thiocyanate exposures and infant serum thyroid function. Thyroid **22:**938–943.
26. Hollowell JG, Staehling NW, Hannon WH, Flanders DW, Gunter EW, Maberly GF, Braverman LE, Pino S, Miller DT, Garbe PL, DeLozier DM, Jackson RJ 1998 Iodine nutrition in the United States. Trends and public health implications:

Iodine excretion data from National Health and Nutrition Examination Surveys I and III (1971–1974 and 1988–1994). J Clin Endocrinol Metab **83:**3401–3408.
27. Caldwell KL, Makhmudov A, Ely E, Jones RL, Wang RY 2011 Iodine Status of the U.S. Population, National Health and Nutrition Examination Survey, 2005–2006 and 2007–2008. Thyroid **21:**419–427.
28. Becker DV, Braverman LE, Delange F, Dunn JT, Franklyn JA, Hollowell JG, Lamm SH, Mitchell ML, Pearce E, Robbins J, Rovet JF 2006 Iodine supplementation for pregnancy and lactation—United States and Canada: recommendations of the American Thyroid Association. Thyroid **16:**949–951.
29. Gregory CO, Serdula MK, Sullivan KM 2009 Use of supplements with and without iodine in women of childbearing age in the United States. Thyroid **19:**1019–1020.
30. WHO Secretariat, Andersson M, de Benoist B, Delange F, Zupan J 2007 Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr **10:**1606–1611.
31. Rhee SS, Braverman LE, Pino S, He X, Pearce EN 2011 High iodine content of Korean seaweed soup: a health risk for lactating women and their infants? Thyroid **21:**927–928.
32. Chung HR, Shin CH, Yang SW, Choi CW, Kim BI 2009 Subclinical hypothyroidism in Korean preterm infants associated with high levels of iodine in breast milk. J Clin Endocrinol Metab **94:**4444–4447.

Address correspondence to:
Angela M. Leung, M.Sc., M.D.
Section of Endocrinology, Diabetes, and Nutrition
Boston Medical Center
Boston University School of Medicine
Boston, MA 02118

E-mail: angela.leung@bmc.org