Breast-milk iodine concentration declines over the first 6 mo postpartum in iodine-deficient women[1–3]

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ABSTRACT

Background: Little is known about the iodine status of lactating mothers and their infants during the first 6 mo postpartum or, if deficient, the amount of supplemental iodine required to improve status.

Objective: The objective was to determine maternal and infant iodine status and the breast-milk iodine concentration (BMIC) over the first 6 mo of breastfeeding.

Design: A randomized, double-blind, placebo-controlled supplementation trial was conducted in lactating women who received placebo (n = 56), 75 μg I/d (n = 27), or 150 μg I/d (n = 26) after their infants' birth until 24 wk postpartum. Maternal and infant urine samples and breast-milk samples were collected at 1, 2, 4, 8, 12, 16, 20, and 24 wk. Maternal serum thyrotropin and free thyroxine concentrations were measured at 24 wk.

Results: Over 24 wk, the median urinary iodine concentration (UIC) of unsupplemented women and their infants ranged from 20 to 41 μg/L and 34 to 49 μg/L, respectively, which indicated iodine deficiency (ie, UIC $<$ 100 μg/L). Mean maternal UIC was 2.1–2.4 times higher in supplemented than in unsupplemented women ($P < 0.001$) but did not differ significantly between the 2 supplemented groups. BMIC in the placebo group decreased by 40% over 24 wk ($P < 0.001$) and was 1.3 times and 1.7 times higher in women supplemented with 75 μg I/d ($P = 0.030$) and 150 μg I/d ($P < 0.001$), respectively, than in unsupplemented women. Thyrotropin and free thyroxine did not differ significantly between groups.

Conclusion: BMIC decreased in the first 6 mo in these iodine-deficient lactating women; supplementation with 75 or 150 μg I/d increased the BMIC but was insufficient to ensure adequate iodine status in women or their infants. The study was registered with the Australian New Zealand Clinical Trials Registry as ACTRN12605000345684. *Am J Clin Nutr* 2010;92:849–56.

INTRODUCTION

An adequate intake of iodine is particularly important in vulnerable groups, such as pregnant women, lactating women, and infants, who have high requirements for iodine. In infants, iodine deficiency at crucial periods of development may lead to growth retardation, impaired hearing capacity and reduced cognitive function (1, 2). The World Health Organization (WHO) recommends that infants are exclusively breastfed until 6 mo of age (3). Consequently, the iodine intake of the breastfed infant relies solely on the iodine concentration of breast milk, which in turn reflects the mother's iodine status. In countries with a good supply of iodine, the breast-milk iodine concentration (BMIC) typically ranges from 150 to 180 μg/L (4, 5). In iodine-deficient areas, the BMIC often falls to $<$50 μg/L and is unlikely to supply an infant with enough iodine to meet the Recommended Dietary Allowance (RDA) of 110 μg/d (6).

Numerous cross-sectional studies have measured both thyroid hormones and total BMIC in women living in iodine-sufficient and iodine-deficient regions of the world, which have been summarized in 3 reviews on the topic (4, 5, 7). To our knowledge, only 2 longitudinal studies of BMIC have been conducted; this is surprising because the pattern of trace elements in breast milk over the course of lactation has been reported for most other essential nutrients (8, 9). In 1986, Etling et al (10) observed an increase in BMIC (n = 23) in the first month of lactation from 41 μg/L at 2–5 d to 50 μg/L at 6–10 d and to 59 μg/L at 10–32 d. Chierici et al (11) observed a decrease in the BMIC of unsupplemented mothers (n = 10) of 270, 150, and 110 μg/L at 3 d, 4 wk, and 12 wk postpartum, respectively, whereas mothers (n = 10) receiving a multimineral supplement that contained 116 μg potassium iodide had BMICs of 320, 130, and 80 μg/L, respectively. These studies are limited because they were of short duration and did not assess maternal iodine status. Furthermore, in the study by Chierici et al, compliance was not measured in those women taking the supplement.

To date, no longitudinal studies have examined the iodine status of lactating mothers concurrently with their breastfed infants during the first 6 mo postpartum. The RDA for iodine of lactating women is 290 μg/d (6), which is based on the assumption that this intake of breast milk will provide $\approx$114 μg I/d to exclusively breastfed infants. It is unlikely that breastfeeding women living in areas of iodine deficiency could meet the RDA from dietary sources alone. The use of iodine sup-

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[2] Supported by an Otago Research Grant and Laurenson's Fund.

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Received April 4, 2010. Accepted for publication July 1, 2010.

First published online August 11, 2010; doi: 10.3945/ajcn.2010.29630.

plements for lactating women is a simple and cost-effective strategy to increase iodine intakes. In 2006, the American Thyroid Association recommended that breastfeeding women take a supplement containing 150 μg I/d (12). The aims of this study were 2-fold: *1*) to determine the iodine status of unsupplemented lactating women and their infants during the first 24 wk postpartum and *2*) to compare the effect of 2 levels of iodine supplementation on the BMIC and iodine status in mothers and their infants.

SUBJECTS AND METHODS

Subjects and recruitment

A double-blind, placebo-controlled trial with imbalanced randomization (2:1:1) of mothers and their infants was conducted from March 2004 to October 2005 in Dunedin, New Zealand. Pregnant women were recruited in the third trimester of pregnancy by advertisements in a local newspaper and maternity hospital. To be eligible for inclusion in the study, women had to be healthy, have no history of thyroid disease, have had a singleton birth, not be currently taking a dietary supplement containing iodine, be due to deliver their infant between May 2004 and April 2005, and intend to breastfeed for ≥24 wk. The study was approved by the University of Otago Ethics Committee, and all participants provided informed written consent after the study had been fully explained.

Sample size

The primary outcome for this study was the change in BMIC. On the basis of the literature and the iodine status of the New Zealand population (4, 5, 13, 14), it was estimated that, at 1 wk postpartum, the BMIC would be 50 μg/L with an SD of 11 μg/L. To detect a change of 7 μg/L in the BMIC over time in unsupplemented women by using an SD of 11 μg/L, assuming the worst case of no correlation between baseline and follow-up samples, with 90% power and 2-sided alpha = 0.05, 52 mother-child pairs would be needed in the placebo group for the primary aim of the study. Accounting for ≈15% attrition, this meant that 60 mother-child pairs would be required to be recruited into the placebo arm of the study. To assess the effect of iodine supplementation on BMIC and detect a difference of 9 μg/L in BMIC at any point of time between any pair of groups (placebo, 75 μg I/d, and 150 μg I/d), again by using an SD of 11 μg/L with 80% power and a 2-sided alpha = 0.05, 24 mother-child pairs would be needed in each group. Accounting for ≈15% attrition, 30 mother-child pairs each would be required to be recruited into each of the placebo group, 75 μg I/d group, and 150 μg I/d group for the secondary aim of the study.

Randomization

Participants were allocated to intervention groups by using a block randomization process. Randomization was planned and generated by a researcher not directly involved in data collection (ELF) and was performed in blocks of 20. Because randomization was imbalanced (2:1:1) and twice as many women were allocated to the placebo group, the placebo arm was split into 2 groups to maintain blinding. Each block contained 5 allocations each for the 2 placebo groups and the 75 μg I/d and 150 μg I/d groups. Letter codes were used to denote treatment group; both the researchers and participants were blinded to treatment until all data collection and biochemical analyses were completed.

Intervention

At the time of the trial, there were no clear guidelines on recommended levels of iodine supplementation during pregnancy and lactation. Furthermore, dietary recommendations for iodine were being revised by the Australian and New Zealand government, and, in 2002, the Estimated Average Requirement (EAR) and RDA for iodine in lactating women was proposed at 170 and 240 μg/d (13), respectively. A supplement containing 75 or 150 μg/d in addition to an estimated daily intake of 95 μg/d [≈70 μg/d from foods (14) + ≈25 μg/d from iodized salt] would mean that subjects would meet the proposed EAR or RDA. Thus, the trial involved women taking a daily supplement of 75 or 150 μg I/d or a placebo for 24 wk postpartum beginning as soon as possible after delivery of their infant. Every month, each participant received a bottle containing 31 tablets and was asked to take 1 tablet/d. At the end of each month, remaining tablets were returned to the researchers and counted as a measure of compliance. Compliance, expressed as a proportion of the intended tablets consumed, did not differ between the groups with a mean (± SD) of 86 ± 17% for all groups (P = 0.353). The mean (± SD) day that tablets were started by the women was 5 ± 4.2 d postpartum. Tablets were prepared for the purpose of this study by Alaron Products (Port Nelson, New Zealand) and were indistinguishable from each other, with potassium iodate (Merck KGaA, Darmstadt, Germany) as the source of iodine. Tablets complied with the British Pharmacopoeia Standard Disintegration Test. Ten tablets per intervention group were randomly chosen from different bottles and tested for quality control by Hill Laboratories (Hamilton, New Zealand). All placebo tablets contained <0.001 μg I/tablet; the 75-μg and 150-μg tablets contained a mean iodine content (range) of 79 μg I/tablet (73–86 μg I/tablet; n = 10) and 154 μg I/tablet (146–164 μg I/tablet; n = 10), respectively.

Sample collection

In the final month of pregnancy, mothers collected a casual urine sample as a baseline measure of iodine status. A casual urine sample was collected from both mother and infant and breast milk was collected from the mother at the end of 1, 2, 4, 8, 12, 16, 20, and 24 wk postpartum. All urine and breast-milk samples were collected between 0900 and 1200, except for 5 maternal urine and breast-milk samples (0.6%) and 17 infant urine samples (2.6%). Urine samples were collected from infants by using an adhesive pediatric urine bag (Hollister Inc, Libertyville, IL) or directly into a specimen container. Breast milk (1–10 mL) was expressed by using an electric breast pump (Mini Electric, Medela AG, Switzerland) before the infant was fed, to obtain a foremilk sample. A finger-prick blood sample (1 mL) was collected from the mother at week 24 between 0900 and 1700. Blood samples were separated and serum removed within 1 h of collection. Blood samples were not collected from infants. Urine, breast-milk, and maternal serum samples were frozen at –20°C until analyzed. Reasons why samples were unable to be collected and/or analyzed included illness, the mother was out of

town, and insufficient sample volume. Overall, 5.4% (n = 42), 10.0% (n = 65), 5.8% (n = 39), and 3.4% (n = 3) of samples for maternal urine, infant urine, breast milk, and blood, respectively, were unable to be collected and/or analyzed. A general questionnaire including an iodine-related semiquantitative food-frequency questionnaire was administered in the final month of pregnancy.

Biochemical analyses

The urinary iodine concentration (UIC) was measured in duplicate at the University of Otago by using Method A (by HMM) as recommended by the WHO, United Nations International Children's Emergency Fund (UNICEF), and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) (2). The CV of a standard reference material (Seronorm Trace Elements Urine, Sero As, Norway) was 9.0% (n = 647). All breast-milk samples were transported by air on dry ice from Dunedin to the INSERM Nutritional Epidemiology Unit, Paris, France, for analysis. The BMIC was measured in duplicate (by PV) by using the method of Riley and Gochman with a Technicon AutoAnalyzer (Technicon Instruments Corp, Tarrytown, NY) (15), which has an average recovery of 99% and intra- and interassay CVs of 1.6% (n = 32) and 2.9% (n = 22), respectively. Serum was analyzed for thyrotropin (TSH) concentrations by using a 2-site sandwich chemiluminescent immunoassay and for free thyroxine (fT_4) concentrations by using a competitive chemiluminescent immunoassay (ADVIA Centaur, Bayer AG Diagnostics, Germany) at Southern Community Laboratories (Dunedin, New Zealand) and CVs of internal controls (Immunoassay Plus, Bio-Rad Laboratories, Irvine, CA) were $\leq$10.3%. The normal reference values used were 12.8–20.4 pmol/L for serum fT_4 and 0.4–3.77 mU/L for serum TSH (16).

Statistical analysis

SPSS (version 11.0; SPSS Inc, Chicago, IL) for Macintosh OS X was used for descriptive statistical analysis of unadjusted data. Normally distributed data were expressed as means ($\pm$ SD); nonnormally distributed data were expressed as medians (25th percentile, 75th percentiles). Maternal iodine intakes were calculated as individual mean values of the food-frequency questionnaire, and the participants were subsequently divided into tertiles.

SAS (version 9.1.2; SAS Institute Inc, Cary, NC) was used for inferential statistics. The PROC MIXED command was used for linear mixed model analysis to assess the effect of iodine supplementation during lactation (ie from wk1 to wk 24). Maternal UIC, infant UIC and BMIC values were all log-transformed to stabilize variances between groups and remove skew in the model residuals, therefore, differences between groups are expressed as ratios. Factors included in the maternal UIC and BMIC analyses were: treatment group, time (wk postpartum), antenatal UIC, parity, exposure to an iodine-containing antiseptic during labor, highest level of education, total household income, use of iodized salt, and tertile of iodine intake. For the infant UIC analysis, along with the 9 maternal factors, an additional 3 factors (ie infant birth weight, infant sex, and whether the infant had ever been fed infant formula) were also included. Compliance was examined as a predictor, both as a main effect and as an interaction with treatment group, however, it was found to be nonsignificant in all models and therefore excluded from further analyses. Missing values for continuous variables were assigned the mean value of the data. Missing categorical variables were given the most common value for nominal variables and the median value for ordinal variables. Tukey-Kramer adjustments were used when appropriate for post hoc tests. The level of significance was set at $P < 0.05$ and all tests were 2-sided.

RESULTS

Of the 109 women who initially enrolled, 97 (89%) remained in the study until delivery, and 84 (77%) remained in the study until 24 wk postpartum. The flow of participants through the study and the reasons for discontinuations are described in **Figure 1**. There were no significant differences between those participants who withdrew from the study and those who remained with regard to the following factors: treatment group (P = 0.631), maternal education level (P = 0.345), compliance (P = 0.155), household income (P = 0.421), parity (P = 0.292), and maternal medical conditions (P = 0.263).

The maternal and infant characteristics before the intervention are shown in **Table 1**. Maternal median UIC in the final month of pregnancy for all women was 42 μg/L (25th, 75th percentile: 25, 58). At 24 wk postpartum, 69% of infants (n = 54) were currently breastfed and had not received any infant formula, 27% (n = 21) were currently fed both breast milk and infant formula, and 4% (n = 4) were currently fed only infant formula. The estimated mean maternal iodine intakes per day ($\pm$SD) from the food-frequency questionnaire were 41 $\pm$ 8, 61 $\pm$ 4, and 87 $\pm$ 20 μg for the lowest, middle, and highest tertiles, respectively.

For all 3 groups, the maternal median UIC at every time point over the 24 wk postpartum was <100 μg/L (**Table 2**). All 3 groups showed a significant increase in UIC over time between weeks 1 and 24 postpartum, with an increase of 102% (95% CI: 49, 174; $P < 0.001$) in the placebo group, 128% (95% CI: 47, 255; $P < 0.001$) in the 75 μg I/d group, and 88% (95% CI: 24, 184; P = 0.028) in the 150 μg I/d group. In the mixed-model analysis, maternal UIC was significantly different by time ($P < 0.001$) and treatment group ($P < 0.001$) (**Table 3**). Over all time points, the UICs of women in the 75 μg I/d and 150 μg I/d groups were 2.12 (95% CI: 1.61, 2.78; $P < 0.001$) and 2.35 (95% CI: 1.78, 3.09; $P < 0.001$) times higher, respectively, than the UIC of those in the placebo group. However, no significant difference in maternal UIC was found between the 2 iodine-supplemented groups (P = 0.722).

Unadjusted infant median UIC is presented for the 3 groups in Table 2. The median UIC of infants of mothers in the placebo group remained <50 μg/L over the 24 wk postpartum. Infants of mothers in the 75 μg I/d group had a median UIC that ranged from 37 to 58 μg/L, and the median UIC of infants of mothers in the 150 μg I/d group ranged from 46 to 121 μg/L over the 24 wk postpartum. No differences in infant UIC over time were observed between weeks 1 and 24 postpartum in the placebo group (P = 0.638), 75 μg I/d group (P = 0.220), and 150 μg I/d group (P = 0.852). Examination of the factors associated with infant UIC showed that infant UIC was influenced by maternal treatment group (P = 0.006) (Table 3). Infants of women receiving 150 μg I/d had a UIC 1.51 times higher (95% CI: 1.12, 2.05; P = 0.004) than that of those receiving a placebo. No significant

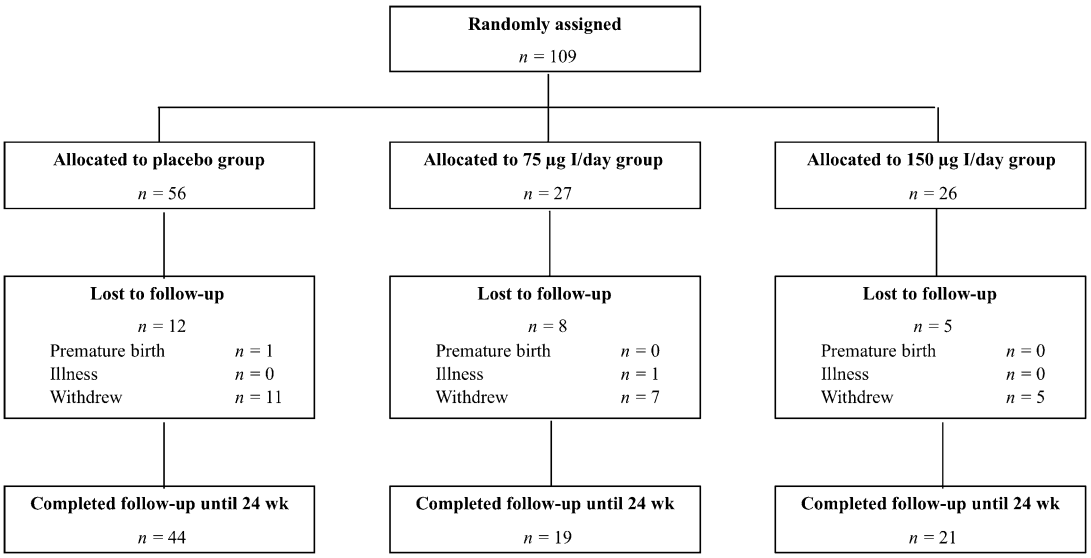

FIGURE 1. Flow diagram of the assignment, losses, and completion of mother-infant pairs until 24 wk postpartum.

difference in infant UIC was found between infants of mothers receiving 75 μg I/d and those receiving a placebo ($P = 0.219$) or 150 μg I/d ($P = 0.429$). When all time points and treatment groups were combined, infant UIC was 13% higher than maternal UIC ($P = 0.037$).

The geometric mean BMICs (± 95% CIs) over time for the placebo group and 2 iodine-supplemented groups are presented in **Figure 2**. The geometric mean BMIC of the placebo group ranged from 25 to 43 μg/L during the 24 wk, whereas the BMIC ranged from 29 to 50 μg/L in the 75 μg I/d group and from 44 to 78 μg/L in the 150 μg I/d group. Between weeks 1 and 24, a significant 40% (95% CI: 25, 52%; $P < 0.001$) decrease in BMIC was seen in the placebo group. Decreases in BMIC were seen in both iodine-supplemented groups between weeks 1 and 24, but these decreases were not statistically significant ($P = 0.102$ for 75 μg I/d; $P = 0.320$ for 150 μg I/d). In the mixed-model analysis, the BMIC was significantly influenced by time ($P < 0.001$) and treatment group ($P < 0.001$) (Table 3). The women who consumed 75 μg I/d had a BMIC 1.31 times higher (95% CI: 1.02, 1.67; $P = 0.030$) than that of the women who consumed the placebo, whereas the women who consumed 150 μg I/d had a BMIC 1.69 times higher (95% CI: 1.32, 2.16; $P < 0.001$) than that of women who consumed the placebo. The BMIC of those who consumed 150 μg I/d was not significantly different from that of those who consumed 75 μg I/d ($P = 0.093$).

The mean (± SD) maternal serum fT_4 concentration was 13.4 ±1.6 pmol/L ($n = 75$), and the serum TSH concentration was 1.3 ± 0.5 mU/L ($n = 73$) for all groups combined; both

TABLE 1
Baseline characteristics of mothers and their infants from Dunedin, New Zealand

	Treatment group		
Maternal and infant characteristics	Placebo	75 μg I/d	150 μg I/d
Maternal			
n	56	27	26
Age (y)[1]	32 ± 4	31 ± 6	32 ± 4
White (%)	95	93	88
Nulliparous (%)	36	48	42
Total household income >NZ$50,000 (%)	53	55	39
Tertiary educated (%)	78	65	83
Uses iodized salt (%)	89	82	92
Uses a vitamin-mineral supplement (%)[2]	73	78	92
Urinary iodine concentration (μg/L)[3]	42 (23, 61)	43 (27, 55)	42 (30, 55)
Exposed to iodine-containing antiseptic in labor (%)	48	52	21
Infant			
n	49	23	24
Birth weight (g)[1]	3682 ± 450	3927 ± 547	3554 ± 374
Male (%)	46	52	63

[1] Values are means ± SDs.
[2] Vitamin-mineral supplements not containing iodine.
[3] Values are medians (25th, 75th percentiles). Urine samples were collected in final month of pregnancy.

TABLE 2
Effect of iodine supplementation in the first 24 wk postpartum on maternal and infant urinary iodine concentrations of breastfeeding women and their infants from Dunedin, New Zealand[1]

	Treatment group					
	Placebo		75 μg I/d		150 μg I/d	
Time postpartum	*n*	MUIC	*n*	MUIC	*n*	MUIC
		μg/L		μg/L		μg/L
Maternal[2]						
1 wk	47	20 (14, 31)	20	35 (22, 89)	22	50 (22, 128)
2 wk	48	27 (16, 35)	21	49 (35,92)	22	65 (39, 99)
4 wk	50	24 (16, 37)	22	44 (35, 69)	23	41 (32, 66)
8 wk	45	27 (18, 47)	21	60 (43, 72)	21	62 (35, 85)
12 wk	42	41 (28, 57)	22	48 (35, 83)	19	68 (44, 87)
16 wk	41	40 (28, 56)	18	68 (39, 128)	19	69 (32, 95)
20 wk	43	33 (24, 51)	20	50 (26, 115)	17	67 (61, 97)
24 wk	42	34 (26, 57)	18	78 (50, 126)	19	84 (60, 157)
Infant[3]						
1 wk	42	37 (19, 69)	19	42 (23, 76)	22	65 (39, 105)
2 wk	46	49 (34, 85)	20	58 (39, 71)	22	101 (55, 150)
4 wk	48	41 (20, 64)	20	49 (29, 71)	23	68 (57, 122)
8 wk	44	34 (21, 45)	19	54 (34, 82)	20	54 (45, 106)
12 wk	42	36 (24, 53)	20	46 (22, 94)	20	46 (32, 80)
16 wk	41	39 (25, 63)	18	50 (36, 100)	19	121 (53, 195)
20 wk	41	40 (21, 79)	20	37 (19, 69)	17	70 (44, 120)
24 wk	38	47 (20, 86)	15	50 (22, 60)	16	66 (36, 87)

[1] All values are medians (25th, 75th percentiles). MUIC, median urinary iodine concentration (ie, <100 μg I/L indicates iodine deficiency; 2, 22).
[2] MUIC increased from week 1 to week 24 in the placebo ($P < 0.001$), 75 μg I/d ($P < 0.001$), and 150 μg I/d ($P = 0.028$) groups.
[3] MUIC did not change from week 1 to week 24 in the placebo ($P = 0.638$), 75 μg I/d ($P = 0.220$), or 150 μg I/d ($P = 0.852$) groups.

mean values were within normal reference ranges. There were no significant differences in serum fT_4 ($P = 0.207$) or TSH ($P = 0.355$) concentrations between the 3 groups.

DISCUSSION

This was the first study to simultaneously assess iodine status, including BMIC, in breastfeeding women and their infants over the first 6 mo of lactation. Our study shows that daily supplementation of iodine deficient lactating women with either 75 or 150 μg I/d was insufficient to adequately improve iodine status, as measured by UIC, in mothers or their infants. Although daily iodine supplementation increased BMIC and prevented the decline of BMIC in these women over the first 6 mo compared with women who received a placebo, the concentration of iodine in breast milk was still well below the cutoff of 100–200 μg/L recommended by the WHO (17) and would be unable to meet the iodine requirements of these young infants. Given that the brain is growing rapidly during this period, the lack of iodine in the diets of these children could permanently affect their neurodevelopment.

The median UIC in these women in the past month of pregnancy was 42 μg/L, 70% lower than the recommended cutoff for pregnant women of 150 μg/L (2). This value is also well below the median UIC reported in pregnant women living in the United States, Switzerland, and China (18–20). New Zealand does have a low soil iodine content, and many locally grown plant and animal foods (excluding seafood) are low in iodine (14). Until recently, recommended strategies to increase iodine intakes, such as the sale of solely iodized table salt and the widespread use of iodized salt in processed foods, have not been implemented. To address iodine deficiency in New Zealand, the mandatory fortification of bread with iodized salt was implemented in 2009; however, it is acknowledged by government authorities that fortification of bread will not increase iodine intakes sufficiently to meet the high iodine requirements of pregnant women. Women living in such an environment who have poor iodine status in pregnancy could consequently enter the postpartum period iodine deficient.

The recommended cutoff for the median UIC in lactating women is 100 μg/L based on the premise that the expression of the sodium iodide symporter (NIS) in the breast during lactation results in dietary iodine being secreted into breast milk rather than into urine (21, 22). In this study, the median UIC of all 3 groups of breastfeeding women at each time point was well below 100 μg/L. As expected, women in the iodine-supplemented groups had higher median UICs than did those taking a placebo (ie, 112% higher in the 75 μg I/d group and 135% higher in the 150 μg I/d group, respectively, than in the placebo group), but the daily consumption of either a 75-μg or 150-μg iodine supplement for 6 mo was unable to increase UIC in both groups to 100 μg/L. However, there was a 31% increase in BMIC in women who consumed 75 μg I/d and a 69% increase in BMIC in women who consumed 150 μg I/d compared with

TABLE 3
Effect of treatment group on maternal and infant urinary iodine concentrations and breast-milk iodine concentrations of breastfeeding mothers and their infants from Dunedin, New Zealand[1]

Factor	Ratio of means (95% CI)[2]	*P*
Maternal urinary iodine concentration[3,4]		
Overall difference between groups	—	<0.001
75 μg I/d compared with placebo	2.12 (1.61, 2.78)	<0.001
150 μg I/d compared with placebo	2.35 (1.78, 3.09)	<0.001
150 μg I/d compared with 75 μg I/d	1.11 (0.80, 1.53)	0.722
Time-by-treatment interaction	—	0.518
Infant urinary iodine concentration[5,6]		
Overall difference between groups	—	0.006
75 μg I/d compared with placebo	1.17 (0.86, 1.59)	0.219
150 μg I/d compared with placebo	1.51 (1.12, 2.05)	0.004
150 μg I/d compared with 75 μg I/d	1.29 (0.90, 1.86)	0.429
Time-by-treatment interaction	—	0.114
Breast-milk iodine concentration[3,4]		
Overall difference between groups	—	<0.001
75 μg I/d compared with placebo	1.31 (1.02, 1.67)	0.030
150 μg I/d compared with placebo	1.69 (1.32, 2.16)	<0.001
150 μg I/d compared with 75 μg I/d	1.29 (0.97, 1.72)	0.093
Time-by-treatment interaction	—	0.514

[1] Linear mixed models were used to compare treatment groups for overall means for weeks 1–24.
[2] Ratio of means (95% CI) with log-transformed data.
[3] n = 99 (placebo, n = 51; 75 μg I/d, n = 24; 150 μg I/d, n = 24).
[4] Adjusted for treatment group, time (week postpartum), highest level of education, parity, antenatal urinary iodine concentration, total household income, use of iodized salt, tertile of iodine intake, and exposure to iodine-containing antiseptic during labor.
[5] n = 98 (placebo, n = 50; 75 μg I/d, n = 24; 150 μg I/d, n = 24).
[6] Adjusted for treatment group, time (week postpartum), highest level of education, parity, antenatal urinary iodine concentration, total household income, use of iodized salt, tertile of iodine intake, exposure to iodine-containing antiseptic during labor, infant sex, infant birth weight, and whether infant had ever been fed infant formula.

placebo, and a nonsignificant 29% increase in BMIC was seen in women who consumed 150 μg I/d compared with 75 μg I/d. These data support the earlier premise that the extra iodine consumed by supplemented women was being preferentially taken up by the mammary gland and not excreted in the urine.

This study was the first randomized, double-blind, placebo-controlled trial to demonstrate a change in BMIC over 6 mo of lactation. BMIC decreased by 40% in the placebo group over the 24 wk postpartum. Full-term infants need 15 μg I/kg daily to maintain positive iodine balance, which would equate to

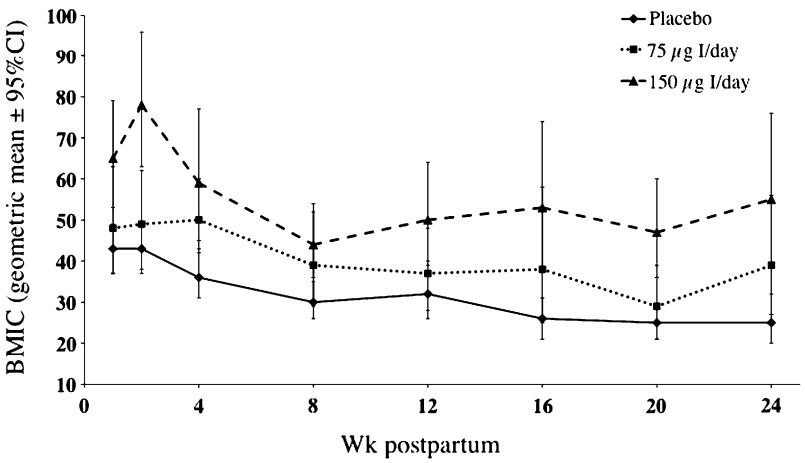

FIGURE 2. The effect of iodine supplementation on breast-milk iodine concentration (BMIC) presented as geometric means (95% CIs) over 24 wk postpartum (placebo, n = 51; 75 μg I/d, n = 24; 150 μg I/d, n = 24). Between weeks 1 and 24, BMIC decreased by 40% ($P < 0.001$) in the placebo group, but no decrease was observed in the 75 μg I/d ($P = 0.102$) or the 150 μg I/d ($P = 0.320$) groups. A mixed-model regression was performed on data from week 1 to week 24 with control for treatment group, time (ie, week postpartum), antenatal urinary iodine concentration, parity, exposure to an iodine-containing antiseptic during labor, highest level of education, total household income, use of iodized salt, and tertile of iodine intake. Compared with women who received a placebo, BMIC was significantly higher in women who took 75 μg I/d ($P = 0.030$) or 150 μg I/d ($P < 0.001$). No significant difference in BMIC was observed between women who took 75 μg I/d or 150 μg I/d ($P = 0.093$). The time-by-treatment interaction was not significant ($P = 0.514$).

a BMIC of 100 to 200 μg/L (23, 24). The median BMICs of women in the placebo group ranged from 24 to 43 μg/L. This finding is supported by other studies that also found BMIC to be significantly lower later in the postpartum period (11, 25–27); however, these studies were limited in terms of sample size, duration (ie, <3 mo) and study design. In our study, the effect of iodine supplementation on BMIC was rapid and already established in week 1, with higher median BMICs seen in women who consumed either 75 or 150 μg I/d; however, values remained below 100 μg/L (33–57 and 43–70 μg/L, respectively). The low BMICs found in all 3 groups of women in this study would be unlikely to provide infants with enough iodine to meet the RDA of 110 μg/d. Because BMIC appears to decrease over the postpartum period, BMIC needs to be much higher during early lactation to be able to provide sufficient iodine at 6 mo of age. Furthermore, usual weaning foods (ie, predominantly cereals, fruit, and vegetables) given to infants in New Zealand are typically poor sources of dietary iodine, which means that breast milk needs to supply sufficient iodine to infants while the infant is consuming less breast milk and iodine-poor complementary foods.

These low BMICs are confirmed by the low median UICs of the infants, particularly those infants whose mothers were receiving a placebo, which were consistently <50 μg/L during their first 24 wk of life. Delange (2) suggests that a median UIC in neonates of 180 to 225 μg/L would equate to an iodine intake of ≈90 μg I/d (28, 29). Although the UICs of infants whose mothers received 150 μg I/d were higher than those who received a placebo, they were not different from the 75 μg I/d group. This study showed that 75 or 150 μg I/d was unable to raise BMIC sufficiently to increase infant UIC to adequate levels. Obviously, a higher level of iodine supplementation is necessary in lactating women exposed to this degree of iodine deficiency.

Despite the low median UIC of the women in this study, maternal serum fT_4 and TSH concentrations were within recommended reference ranges at the end of the intervention. The normal concentration of thyroid hormones seen in these women may explain why there were no apparent physical consequences of iodine deficiency, ie, the infants had a healthy average birth weight and apparently normal development and the mothers were not visibly goitrous. However, increasing evidence indicates that mild iodine deficiency and/or subclinical hypothyroidism can have adverse effects. For example, subclincal hypothyroidism has been correlated with depressive symptoms in the elderly (30) and iodine supplementation of mildly iodine-deficient schoolchildren improved cognition even though there were no detectable changes in thyroid hormone concentrations (31). We did not collect information on any functional or long-term clinical outcomes of iodine deficiency, nor did we obtain data on thyroid hormones in these women's infants. A lack of iodine in the diets of breastfeeding women might contribute to an overall sense of fatigue and lack of energy and could exacerbate postnatal depression, if present. In infants, the functional consequences of iodine deficiency include impaired motor and cognitive development (32).

The strengths of the current study were its randomized, double-blind, placebo-controlled design and the high rate of breastfeeding in the study population—96% of infants at 24 wk postpartum were still receiving breast milk. The main limitation of the study was the small sample sizes in the iodine-supplemented groups, which when combined with the high variability in UIC and BMIC resulted in wider CIs than anticipated; nonetheless, significant differences were found. The decline in BMIC over the 24-wk postpartum period may be unique to women with suboptimal iodine status and should be confirmed in a longitudinal study of breastfeeding women with adequate iodine status. Finally, although it would have been of interest to have followed the infants at 18 or 24 mo to determine whether there were any differences in psychomotor development between the children of supplemented and unsupplemented mothers, more subjects would be needed for sufficient power to detect such differences.

In summary, this study found that the iodine status of these lactating women and their breastfed infants was poor in the 6 mo after birth. While increasing maternal UIC, infant UIC, and BMIC, an additional 75 or 150 μg I/d in the postpartum period did not improve maternal and infant iodine status sufficiently to ensure that either these women or their infants had adequate status. It is clear from this study that women living in regions where iodine deficiency exists, who exclusively breastfeed their infants, need to take a supplement containing >150 μg I/d, which supports the WHO/UNICEF recommendation that such women take 250 μg I/d (33). In regions with better iodine status, such as the United States, it is suggested that a similar study be conducted to determine the efficacy of a supplement containing 150 μg I/d during the first 6 mo of breastfeeding.

We thank the women and their infants who participated in this study and acknowledge Kate Spenceley for assistance with the collection of the breast-milk and blood samples.

The authors' responsibilities were as follows—HMM: developed the questionnaires, distributed the supplements, wrote the first draft of the manuscript, and participated in the collection, analyses, and interpretation of the data; SAS and ELF: designed and supervised the study, secured funding, and assisted with interpretation of the data; ARG: conducted the statistical analysis; PV: assisted with interpretation of the data and analyzed the breast-milk samples; and SAS: edited the manuscript. All authors provided input on versions of the manuscript. None of the authors had any conflicts of interest.

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