Efficacy of daily and weekly multiple micronutrient food-like tablets for the correction of iodine deficiency in Indonesian males aged 6-12 mo[1–5]

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ABSTRACT

Background: Infants are highly vulnerable to iodine deficiency, and little data exist on the effect of multiple micronutrient supplementation on their iodine status.

Objective: We aimed to compare the efficacy of daily and weekly multiple micronutrient food-like tablets (foodLETs) on increasing iodine status among infants.

Design: In a double-blind, placebo-controlled trial, 133 Indonesian males aged 6–12 mo were randomly assigned to 1 of 4 groups: a daily multiple-micronutrient foodLET providing the Recommended Nutrient Intake (RNI)(DMM), a weekly multiple-micronutrient foodLET providing twice the RNI (WMM), a daily 10-mg Fe foodLET (DI), or placebo. Urinary iodine (UI) concentrations were measured at baseline and at 23 wk.

Results: At baseline, the average UI concentration (1.37 μmol/L) was within the normal range, and 30.8% of subjects had iodine deficiency (UI <0.79 μmol/L). At 23 wk, the DMM group had the highest increment in UI; however, after adjustment for initial UI, the changes in UI were not significantly different between the 4 groups ($P = 0.39$). Initial UI correlated inversely with the changes in UI ($P < 0.001$). The DMM group had the greatest reduction and increment in the proportion of iodine-deficient infants and in infants with iodine excess, respectively; however, no significant difference was found in these proportions ($P = 0.13$ and $P = 0.42$) between the 4 groups.

Conclusion: Daily consumption of a multiple-micronutrient foodLET providing the RNI during infancy may be one strategy to improve iodine status.   *Am J Clin Nutr* 2007;85:137–43.

KEY WORDS   Iodine, deficiency, Indonesia, male infants, multiple micronutrient food-like tablet, urinary iodine

INTRODUCTION

Nearly 2 billion people worldwide are considered to be iodine deficient (1). The deleterious effects of iodine deficiency disorders (IDD) on mental and cognitive development in children are well documented. Even mild levels of prenatal iodine deficiency have negative effects on infant development (2). In Indonesia, iodine deficiency is still a major public health nutrition problem, although the national IDD mapping survey reported a substantial reduction in the total goiter rate of schoolchildren from 37.2% in 1980 (3) to 11% in 2003 (4). It is estimated that 16.3% of schoolchildren have low urine iodine (UI) excretion (<0.79 μmol/L) (4, 5), and ≈550 000 Indonesian children are at risk of being born mentally impaired because of iodine deficiency (6). In developing countries such as

Indonesia, infants and children are at a particularly high risk of IDD because of the relatively low iodine content in breastmilk (7) and in many complementary foods, given the relatively high iodine requirements of the growing infant (8).

Although salt iodization is the primary intervention used to eliminate IDD, there are circumstances in which salt iodization programs may not be immediately effective within 1 or 2 y in iodine-deficient areas. The table salt sold in the marketplace very often has a non-uniform iodine content, with many samples having less than the standard level of iodization. Therefore, additional approaches are needed as an alternative to control iodine deficiency in moderate and severe endemic areas. An early trial showed that direct administration of 30 mg monthly or 8 mg biweekly of potassium iodide solution has proven effective in correcting iodine deficiency (9). Consumption of an iron, iodine, and β-carotene-fortified biscuit also resulted in a significant improvement in the iodine status in children in a study conducted in South Africa (10).

The effect of iodine interventions in population groups such as school-aged children and adults has been much explored; however, little is known about the efficacy of supplementation on iodine status in infants. We therefore investigated the efficacy of iodine-containing daily and weekly multiple-micronutrient supplements in improving the iodine status of Indonesian male infants aged 6–12 mo.

SUBJECTS AND METHODS

The present study was part of the multicenter International Research on Infant Supplementation (IRIS) study, conducted in

4 different populations: Indonesia, Peru, South Africa, and Vietnam (11).

Data collection and measurements

In Indonesia, the study was conducted in 18 villages of the Central Java Province where infants aged 6–12 mo are deficient in multiple micronutrients (12, 13). Among all subjects, 58.1% were anemic (hemoglobin <110 g/L), 34.5% had plasma ferritin <12 μg/L, 10.4% had plasma zinc <10.7 μmol/L, and 24.3% had plasma retinol <0.7 μmol/L. Detailed results and methodology have been presented in separate publications (12, 13). Briefly, infants aged 6–12 mo were randomly allocated to 1 of 4 groups: a daily multiple micronutrient (DMM) food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI), a weekly multiple micronutrient foodLET providing twice the RNI (WMM), 1 daily 10-mg Fe foodLET (DI), or placebo. The infants met the following criteria: a signed informed consent from a parent, birth weight >2500 g, no congenital defect, no chronic illness, no fever (≥39 °C) at the time of blood collection, and hemoglobin ≥80 g/L. Ethical consideration was based on the guidelines from the Council for International Organizations of Medical Sciences (14). The purpose and procedures of the study were explained to the parents at enrollment, and only parents who gave written informed consent were recruited. The Ethical Committee for Studies on Human Subjects, Faculty of Medicine, University of Indonesia approved the study protocol. A 3-mo supply of WMM foodLETs were given to the placebo group at the end of the study.

The multiple-micronutrient supplement and placebo were produced in the form of foodLETs. Supplements were given as chewable, crushable, or soluble tablets. Roche Laboratories (Nutley, NJ) developed the product, and Hersil (Lima, Peru) produced it. A week's supply of 7 foodLETs was wrapped in identical coded blister packs, and all foodLETs had the same taste, color, and flavor. The micronutrient content of the foodLETs had been formulated according to the daily RNI for infants: 375 μg retinol-equivalents vitamin A (as retinyl acetate), 5 μg vitamin D, 6 mg α-tocopherol equivalents vitamin E (as α-tocopherol), 10 μg vitamin K, 35 mg vitamin C, 0.5 mg vitamin B-1, 0.5 mg vitamin B-2, 0.5 mg vitamin B-6, 0.9 μg vitamin B-12, 6 mg niacin (as niacinamide), 150 μg folate, 10 mg Fe (as ferrous fumarate), 5 mg Zn (as zinc gluconate), 0.6 mg Cu (as cupric gluconate), and 59 μg I (as potassium iodide) (11, 15). WMM foodLETs provided micronutrients once per week in a dose of 2 RNIs. DI foodLETs contained 10 mg ferrous sulfate, whereas the placebo foodLETs contained no micronutrients. The foodLETs were given daily at home for 7 d/wk. Six days were under close supervision of a trained fieldworker, and on day 7 it was given under supervision of the mother. Both investigators and subjects were blinded to the group assignment. The foodLET code as 1, 2, 3, and 4 was broken at the end of the study, before statistical analyses.

During the study, the infants received additional clinical, biochemical, anthropometric, morbidity, health, and dietary assessments. Assessments included UI based on the iodine concentrations in the male infants' urine samples that were collected at baseline and 23 wk after treatment. A total of 133 male infants contributed a single morning urine sample at both time points. At each time point, all urine collections were completed in about 1 wk. Although the study ended at 23 wk, foodLET consumption continued until 25 wk. Urine was collected in a plastic container

which contained ≈1 g thymol. After sample collection, the containers were sealed and identified with labels that had the code of the subject. All urine samples were measured in the IDD laboratory at the University of Diponegoro, Indonesia, which is certified by the International Resource Laboratory for Iodine network (5). The iodine concentration in urine was analyzed on the basis of the Sandell-Kolthoff reaction and was expressed in μmol iodine/L urine (16). The cutoff for mild iodine deficiency was 0.79 μmol/L, for moderate deficiency was 0.40 μmol/L, and for severe deficiency was 0.16 μmol/L (1, 17). The cutoff for excess UI was 2.38 μmol/L (17).

Salt samples from household products were taken and their iodine contents tested semiquantitatively with an iodine test-kit (Indo Farma, Jakarta, Indonesia) once a month during the 23-wk supplementation period. The presence of iodine in a salt sample was measured as 0, <15, 15, 30, or 50 ppm. For the present study, adequately iodized salt was indicated by an iodine content of ≥30 ppm.

The weight and length of the infants were measured monthly. Weight was recorded to the nearest 0.1 kg by using an electronic weighing scale (SECA 770, Hamburg, Germany), whereas length was measured on a length board for infants (SECA 210). The weight and height of the mothers were measured at baseline. Body weight of the mothers was measured to the nearest 0.1 kg by using the electronic weighing scale (SECA 770) and height to the nearest 0.1 cm by using a standing height measurement microtoise.

All information was collected with the use of a structured questionnaire and survey methodology (18). Infant feeding practices were checked daily during the 23 wk of supplementation. The mothers were asked whether their infants were being breastfed and given complementary food. This daily dietary intake was converted to a weekly record.

Statistical analysis

Kolmogorov-Smirnov one sample test was used to check the normality of the data. Student's t test was used to determine the differences between the 2 groups for continuous variables. Analysis of variance examined differences among groups for continuous variables and Pearson's chi-square test for discrete variables. A 2-way analysis of variance was used to ascertain the interaction between time and treatment for UI. Changes in UI were analyzed by using analysis of covariance with treatment as a fixed effect and initial UI as a covariate. Generalized estimating equations with treatment × time interaction were used to assess the changes in proportion among the groups. Furthermore, multiple regression was done to identify the main predictor of the change in UI, with initial UI, breastfeeding, complementary food, and household salt intake as independent variables.

Weekly data of the infants' daily feeding practices were expressed as the proportion of infants in categories of dietary intake. Data for salt iodine were expressed as the proportion of households in categories of salt iodization levels (0–30 ppm or ≥30 ppm). To determine whether the proportion of households in the categories of salt iodization changed during the study, differences across all 7 data-collection periods in each treatment group were calculated by using Cochran's Q test.

The data were analyzed by using SPSS version 11.5 (SPSS Inc, Chicago, IL) and STATA version 9.0 (StataCorp, College Station, TX) for WINDOWS, and the anthropometry data were
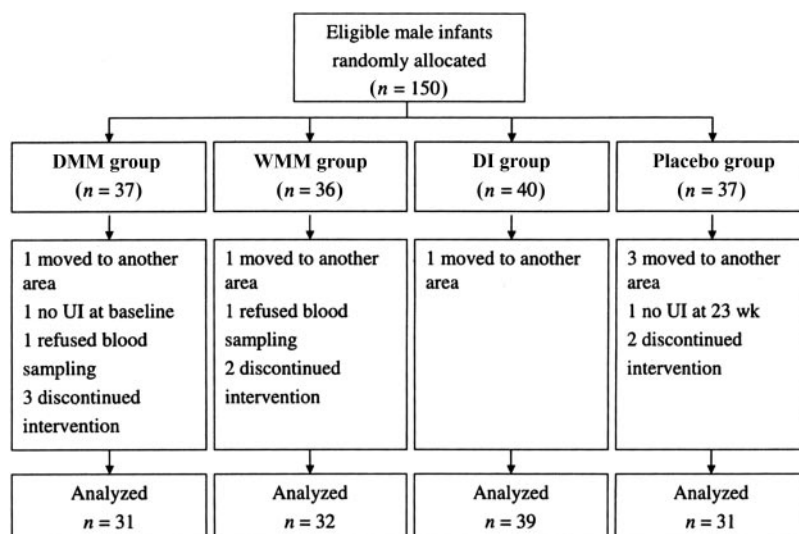
FIGURE 1. Trial profile. UI, urinary iodine; DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10-mg Fe foodLET.

entered into the World Health Organization Anthro 2005 (19). *P* values < 0.05 (two-tailed) were considered to be significant.

RESULTS

Of 150 eligible male infants at baseline, 17 subjects dropped out as follows: 6 from the DMM group, 4 from the WMM group, 1 from the DI group, and 6 from the placebo group (**Figure 1**). The main characteristics of the studied infants did not differ significantly from those of the dropouts. The characteristics of the subjects were not significantly different between the groups at the beginning of the study (**Table 1**). The mean age of the infants was 9 mo, and their nutritional status, in terms of average weight-for-age *z* score, height-for-age *z* score, and weight-for-height *z* score of infants, was within the normal range. Most infants (93.2%) were breastfed at baseline.

At baseline, the average UI was normal (UI >0.79 μmol/L) and was not significantly different ($P = 0.858$) between the groups (**Table 2**). Nearly one-fourth of the infants (24.1%) were mildly iodine deficient (UI <0.79 μmol/L), 6.8% were moderately deficient (<0.40 μmol/L), and none were indicative of being severely iodine deficient (<0.16 μmol/L); the proportion with a UI $\geq$2.38 μmol/L, indicating iodine excess, was 11.3%.

TABLE 1
Baseline characteristics of the subjects and their mothers by treatment group[1]

Characteristics	Treatment groups				
	DMM (n = 31)	WMM (n = 32)	DI (n = 39)	Placebo (n = 31)	P[2]
Infant					
Age (mo)	8.9 ± 1.7[3]	8.9 ± 1.8	9.0 ± 1.7	9.3 ± 1.7	0.80
Weight (kg)	8.4 ± 1.2	8.1 ± 1.1	8.2 ± 1.1	8.2 ± 1.1	0.68
Height (cm)	71.5 ± 2.7	69.9 ± 3.5	70.4 ± 2.9	70.2 ± 3.0	0.20
WAZ score	−0.50 ± 1.18	−0.80 ± 1.04	−0.82 ± 1.21	−0.87 ± 1.16	0.59
HAZ score	−0.14 ± 1.15	−0.80 ± 1.18	−0.63 ± 1.08	−0.89 ± 1.31	0.06
WHZ score	−0.54 ± 1.29	−0.43 ± 1.05	−0.61 ± 1.30	−0.48 ± 0.97	0.93
Received fluid after birth besides breastmilk (%)	51.6	59.4	48.7	51.6	0.84
Initiation of breastfeeding after birth (%)					0.14
Immediately	40.0	35.5	56.8	45.2	
1–12 h	30.0	35.5	10.8	12.9	
>12 h	30.0	29.0	32.4	41.9	
Mother					
Age (y)	28.5 ± 6.3	28.9 ± 7.1	28.4 ± 5.2	28.5 ± 5.5	0.66
Weight (kg)	49.0 ± 8.2	47.8 ± 8.7	47.8 ± 6.5	47.5 ± 8.0	0.58
Height (cm)	150.3 ± 5.3	148.2 ± 5.8	151.5 ± 4.7	149.8 ± 6.1	0.69
BMI (kg/m^2)	21.6 ± 2.8	21.7 ± 3.5	20.8 ± 2.6	21.1 ± 3.0	0.74

[1] DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10-mg Fe foodLET; WAZ, weight-for-age *z*; HAZ, height-for-age *z*; WHZ, weight-for-height *z*.
[2] *P* for continuous variables were calculated by ANOVA. *P* for categorical variables were calculated by using Pearson's chi-square.
[3] $\bar{x}$ ± SD (all such values).

TABLE 2
Concentrations of urinary iodine (UI) at baseline and after 23 wk of supplementation in Indonesian male infants aged 6–12 mo[1]

	Treatment groups				
Indicator	DMM	WMM	DI	Placebo	P[2]
Overall UI (μmol/L)[3]					
n	31	32	39	31	
Baseline	1.33 ± 0.86 [1.09][4]	1.42 ± 0.80 [1.35]	1.43 ± 0.86 [1.32]	1.29 ± 0.62 [1.34]	
23 wk	1.79 ± 0.76 [1.87]	1.73 ± 0.72 [1.91]	1.56 ± 0.84 [1.61]	1.58 ± 0.76 [1.47]	
Change	0.47 ± 0.79 [0.38]	0.32 ± 1.00 [0.35]	0.13 ± 0.79 [−0.02]	0.29 ± 0.83 [0.27]	0.39
UI <0.79 μmol/L[3]					
n	10	10	13	8	
Baseline	0.44 ± 0.17 [0.46]	0.53 ± 0.20 [0.56]	0.49 ± 0.13 [0.54]	0.49 ± 0.17 [0.50]	
23 wk	1.45 ± 0.92 [1.01]	1.47 ± 0.75 [1.39]	1.01 ± 0.71 [0.72]	1.28 ± 1.00 [0.94]	
Change	1.02 ± 0.95 [0.59]	0.95 ± 0.76 [0.69]	0.52 ± 0.73 [0.29]	0.78 ± 0.93 [0.34]	0.51
UI ≥0.79 μmol/L					
n	21	22	26	23	
Baseline	1.75 ± 0.71 [1.72]	1.82 ± 0.62 [1.70]	1.90 ± 0.66 [2.13]	1.56 ± 0.46 [1.47]	
23 wk	1.96 ± 0.64 [2.12]	1.85 ± 0.68 [1.95]	1.83 ± 0.77 [1.87]	1.68 ± 0.65 [1.62]	
Change	0.21 ± 0.56 [0.25]	0.03 ± 0.97 [−0.13]	−0.07 ± 0.76 [−0.19]	0.12 ± 0.74 [0.24]	0.74

[1] DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10mg Fe foodLET. No significant differences were observed between the treatment groups at baseline. No significant main effect of treatment was observed.

[2] P for difference between the treatment groups adjusted for initial UI were calculated by using ANCOVA.

[3] Significant time effect, $P < 0.05$ (two-factor ANOVA).

[4] $\bar{x}$ ± SD; median in brackets (all such values).

No significant difference in UI was found between the undernourished [ie, weight-for-age z score <−2 ($P = 0.307$), height-for-age z score <−2 ($P = 0.306$), or weight-for-height z score <−2 ($P = 0.517$)] and the well-nourished infants. Also, no significant differences in UI were observed between normal and anemic ($P = 0.666$), iron-deficient ($P = 0.397$), zinc-deficient ($P = 0.286$), or vitamin A–deficient ($P = 0.245$) infants. After 23 wk of supplementation, the DMM group had the highest increase in UI; however, after adjustment for initial UI, the changes in UI were not significantly different between the 4 groups. The effect of time was significant ($P = 0.006$), but the effect of treatment was not ($P = 0.434$). Additionally, there was no significant time × treatment group interaction ($P = 0.566$). A similar finding was seen in the subjects with UI <0.79 μmol/L—only a significant effect of time ($P = 0.026$) was observed.

The effect of the iodine interventions on the proportion of infants with iodine deficiency and iodine excess is shown in **Figure 2** and **Figure 3**, respectively. At 23 wk, the DMM group had the highest reduction and increment in the percentage of infants with iodine deficiency and of infants with iodine excess, respectively. However, there were no significant differences in these proportions between the 4 groups. A significant effect of time ($P = 0.011$) was found in the iodine-deficient infants, but not in those with iodine excess ($P = 0.051$).

Most mothers (92.5%) reported that they breastfed their infants >4 times/d. About 57.1% of the infants already ate part of an adult's meal as their complementary solid food, and one-third received infant formula for their complementary liquid food (data not shown).

No significant difference in the proportion of households using iodized salt existed between the 4 groups based on the monthly observations, except at baseline (**Table 3**). Additionally, no significant ($P = 0.245$) iodine content of salt × month × treatment group interaction was observed.
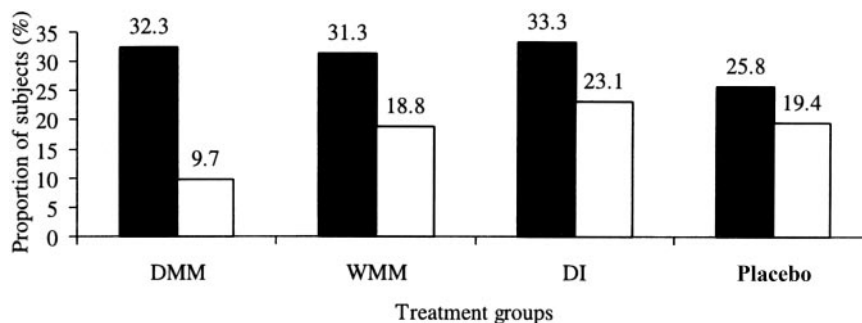

FIGURE 2. Proportion of male infants with a urinary iodine (UI) concentration <0.79 μmol/L at baseline (■) and after 23 wk of supplementation (□) in the 4 treatment groups. DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10-mg Fe foodLET. n = 31, 32, 39, and 31 for the DMM, WMM, DI, and placebo groups, respectively. No significant changes in proportions were observed between the groups, $P = 0.131$ (general estimating equations with treatment × time interaction). A significant time effect was observed ($P = 0.01$); however no significant treatment effect was observed.
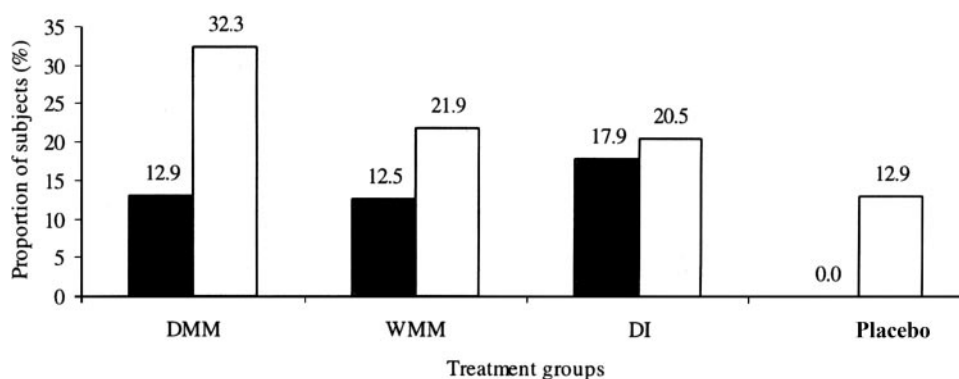
FIGURE 3. Proportion of male infants with a urinary iodine (UI) concentration >2.38 μmol/L at baseline (■) and after 23 wk of supplementation (□) in the 4 treatment groups. DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10-mg Fe foodLET. $n = 31$, 32, 39, and 31 in the DMM, WMM, DI, and placebo groups, respectively. No significant changes in proportions were observed between the groups, $P = 0.415$ (general estimating equations with treatment × time interaction). No significant treatment or time effects were observed.

The UI at baseline was inversely related to the change in UI from 0 to 23 wk of supplementation, whereas frequency of breastfeeding, type and frequency of complementary food, and proportion of households using iodized salt were not significantly associated with the change in UI (**Table 4**).

DISCUSSION

Previous results of the IRIS study on biochemical status either in the pooled data analysis of 4 countries or in Indonesia alone showed a linear dosing effect of the investigated micronutrients. As a result, the use of a DMM supplement during infancy is more efficacious for improving micronutrient status and anemia than is a DI supplement or a WMM supplement (12, 13, 20).

Although DMM foodLETs showed the largest effect on improving UI status compared with other treatment and placebo foodLETs, this could not be substantiated in the present study by statistical tests of interaction. This may be due to an inadequate power to detect a mean difference in UI. Calculations made for

the IRIS as a whole study to get a power of 80% resulted in a sample size of 65 per group (12). In the present study, a sample size of ≈30 per group probably had an inadequate power, especially when using casual UI, which may have high variation. Another possible explanation is that our subjects were not fully free of iodine deficiency, but the average UI concentration was entirely within the normal range throughout our study. The proportion of iodine deficiency in our sample was higher than that of Indonesian school children, ie, 16.3% (4); however, the level of deficiency of most infants (≈24%) was mild and may not have been severe enough to see an effect. A greater benefit through supplementation, as indicated by a relatively higher response in UI, was shown in the iodine-deficient subjects (UI <0.79 μmol/L) than in those with initial normal UI, and linear regression analysis also confirmed the inverse association between initial UI and change in UI over time. However, the average absolute UI concentration at 23 wk was still lower, which may indicate a higher retention of iodine in the thyroid gland of iodine-deficient infants.

TABLE 3
Proportion of households using iodized salt, by month[1]

Treatment groups and iodine content of salt	Month						
	0[2]	1	2	3	4	5	6
DMM							
0 to <30 ppm	64.5	48.4	32.2	38.7	45.2	45.2	35.5
≥30 ppm	35.5	51.6	67.7	61.3	54.8	54.8	64.5
WMM							
0 to <30 ppm	56.3	40.6	46.9	37.5	46.9	53.1	53.1
≥30 ppm	43.8	59.4	53.1	62.5	53.1	46.9	46.9
DI							
0 to <30 ppm	30.8	30.8	33.3	41.0	30.8	51.3	35.9
≥30 ppm	69.2	69.2	66.7	59.0	69.2	48.7	64.1
Placebo							
0 to <30 ppm	48.4	41.9	54.8	48.4	35.5	32.3	35.5
≥30 ppm	51.6	58.1	45.2	51.6	64.5	67.7	64.5

[1] DMM, a daily multiple micronutrient food-like tablet (foodLET) providing the Recommended Nutrient Intake (RNI); WMM, a weekly multiple micronutrient foodLET providing twice the RNI; DI, a daily 10-mg Fe foodLET. There was no significant treatment group × mo × iodine level interaction ($P = 0.245$) and no significant main effect of treatment ($P = 0.095$), month ($P = 0.181$), or iodine content of salt at baseline ($P = 0.054$). No significant difference in each treatment group was observed over 7 mo, $P > 0.1$ (Cochran's Q test).

[2] A significant difference was observed between the treatment groups at baseline, $P < 0.03$ (chi-square test). The percentage of households using adequately iodized salt (≥30 ppm) in the DI group was significantly higher than that of the DMM group.

TABLE 4
Factors associated with change in urinary iodine (UI) concentrations of male infants aged 6–12 mo[1]

Variable	β coefficient	P	R^2
Change in UI, 0–23 wk (μmol/L)			0.35
UI at baseline (μmol/L)	−0.59	$< 0.001^2$	
Frequency of breastfeeding[3]	0.05	0.55	
Type of solid complementary food[4]	0.05	0.48	
Frequency of solid complementary food[5]	0.01	0.91	
Type of liquid complementary food[6]	0.11	0.25	
Frequency of liquid complementary food[7]	0.06	0.59	
Household iodized salt intake[8]	0.11	0.14	

[1] $n = 133$.
[2] Significantly associated with change in UI, $P < 0.001$ (linear regression).
[3] Frequency of breastfeeding (0 = never or stopped, 1 = 1–3 times, 2 = ≥4 times).
[4] Type of solid complementary food (0 = nothing, 1 = porridge, 2 = mashed fruit, 3 = processed baby food, 4 = part of adult meal, rice, or other).
[5] Frequency of solid complementary food (0 = never, 1 = once, 2 = twice, 3 = 3 times, 4 = ≥4 times).
[6] Type of liquid complementary food (0 = nothing, 1 = cow milk, 2 = infant formula, 3 = water or tea, 4 = fruit juice).
[7] Frequency of liquid complementary food (0 = never, 1 = 1–3 times, 2 = ≥4 times).
[8] Household iodized salt intake (0 = 0 to <30 ppm, 1 = ≥30 ppm).

At baseline, UI concentrations had a wide range (0.17–3.25 μmol/L), showing the variation in iodine intake and urinary volume of the infants. Of the infants, 30.8% were iodine deficient, 57.9% were iodine sufficient, and 11.3% had excess iodine. At follow-up, the proportion of iodine deficiency was reduced to <10%; however, the number of infants with iodine excess more than doubled in the DMM group. This finding is consistent with another study that showed the proportion of children with iodine excess increased twice with a 25% increase in iodine concentration in iodized table salt (21). Although iodine supplementation should be implemented to prevent and treat IDD, excessive levels should be avoided. It has been reported that the incidence of hyperthyroidism increases among persons with chronic, severe iodine deficiency who suddenly increase their iodine intake. But results from a study conducted in China show that iodine supplementation in regions in which iodine deficiency is mild (not severe) would not increase the incidence of overt hyperthyroidism (22).

To our knowledge, this is the first study showing that the iodine status of infants can be improved by giving oral iodine supplementation to infants. This finding is supported by a previous study showing that oral iodine supplementation in infants can reduce mortality. However, data on biochemical indicators of iodine and thyroid status were not available (23).

No significant effect of supplementation on UI was observed in infants given WMM foodLETs. This reflects the lower iodine supplementation dose when calculated on a weekly basis and the randomized collection of urine (1–7 d) after receiving the iodine-containing foodLET. This finding is consistent with another study conducted in Zimbabwean schoolchildren that detected no significant differences in overall change in UI across 5 groups (8.7 mg I biweekly, 29.7 mg I monthly, 148.2 mg I every 3 mo, 382 mg I every 6 mo, and 993 mg I yearly) with intermittent potassium iodide supplementation; UI concentrations generally remained low in all groups after 6 mo of supplementation (9).

The increase in UI in the iodine-unsupplemented groups (DI and placebo) observed at 23 wk may be explained by breastfeeding and complementary food patterns in the infants. Because more than one-half of the infants ate part of an adult's meal by 23 wk, it seems possible that some infants may have been exposed to iodized salt. However, our study did not show that these factors had a significant association with the changes in UI. At the time of the study, ≈90% of the salt samples collected monthly from the subjects contained iodine, but, on average, only 61% of the salt samples were adequately iodized, which was lower than that observed in an Indonesian national survey (24), where the estimated number was 73% in 2003.

We acknowledge several limitations of the present study. First, the use of additional outcome indicators besides UI may be more helpful in showing the effect of intervention. As shown in a previous study (9), other indicators, notably thyroid volume and thyroglobulin, were more useful than was UI and indicated a significant dose-related response. Another study described that although European children were iodine sufficient at the time of measurement as indicated by UI, their higher thyroid volume may have reflected mild-to-moderate iodine deficiency (25). Second, the present study did not assess the iodine content of breastmilk and complementary food, which potentially provided subjects with additional sources of iodine. Although daily multiple micronutrient supplementation may be beneficial in improving iodine status in infant populations, its effects on a broader range of infant functional outcomes need to be further assessed.

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