Iodine Supplementation of Mildly Iodine-Deficient Adults Lowers Thyroglobulin: A Randomized Controlled Trial

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Context: An inverse relationship between thyroglobulin (Tg) and urinary iodine concentration (UIC) has been found in children, potentially making Tg a viable blood marker of iodine status. The application of Tg in adults is unknown.

Objective: The objective of the study was to determine the efficacy of Tg to assess iodine status in adults.

Design: This was a randomized, double-blind, placebo-controlled, clinical trial.

Setting: The study was conducted in Dunedin, New Zealand.

Participants: Mildly iodine deficient adults (n = 112) aged 18–40 years participated in the study.

Intervention: Participants were supplemented with 150 μg of iodine as potassium iodate or placebo daily for 24 weeks. At baseline and 24 weeks, participants provided five casual urine samples for UIC determination; serum TSH and free T_4 (FT4) was also measured. Tg was determined at baseline and 8, 16, and 24 weeks.

Main Outcome Measure: A change in Tg concentration between the iodine-supplemented and placebo groups at 24 weeks.

Results: At baseline, the overall median UIC was 65 μg/L, confirming that participants were mildly iodine deficient (ie, median UIC between 50 and 99 μg/L). The overall median Tg was 16.6 μg/L; TSH and FT4 were within normal reference ranges. At 24 weeks, the median UIC of the placebo and supplemented groups was significantly different, 79 and 168 μg/L, respectively ($P < .001$). Tg in the iodine-supplemented group decreased by 12%, 20%, and 27% compared with the placebo group at 8 ($P = .045$), 16 ($P < .001$), and 24 weeks ($P < .001$); there were no significant changes in TSH and FT4.

Conclusion: Improved iodine status as assessed by UIC was associated with a concomitant decrease in Tg concentration, demonstrating that Tg is a useful biomarker of iodine status in a group of adults. **(*J Clin Endocrinol Metab* 101: 1737–1744, 2016)**

Iodine is a trace element needed by the thyroid gland to produce thyroid hormones (1). Sufficient iodine is required throughout life to ensure normal thyroid function (2). Iodine deficiency remains one of the most common micronutrient deficiencies worldwide, affecting approximately 30% of the world's population (3). New Zealand has a history of iodine deficiency due to its low soil iodine content; 30% of schoolchildren had goiter in the 1930s.

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Abbreviations: CV, coefficient of variation; FFQ, food frequency questionnaire; FT4, free thyroxine; ICCIDD, International Council for the Control of Iodine Deficiency Disorders; Tg, thyroglobulin; TgAb, Tg antibody; TPOAb, thyroid peroxidase antibody; UIC, urinary iodine concentration; UNICEF, United Nations Children's Emergency Fund; WHO, World Health Organization.

The introduction of iodized table salt and the use of iodophors in the dairy industry improved iodine intakes from the 1950s to the 1980s (4). Decreased consumption of salt and the replacement of iodophors with detergent-based sanitizers contributed to the reemergence of mild iodine deficiency in the early 1990s. In 2009 the New Zealand government mandated the use of iodized salt in bread as a strategy to increase dietary iodine. This initiative raised the iodine status of New Zealand schoolchildren (5), but its effect in adults is unclear (6), in part due to the lack of clarity surrounding the most appropriate indicators and cutoff values to use in an adult population.

Because 90% of dietary iodine is excreted in the urine, iodine status is typically assessed by determining the median urinary iodine concentration (UIC) in casual or spot urine samples obtained from a representative group of the population (7). UIC, however, is considered a short-term index of iodine status (ie, days to weeks) because it reflects recent intake, which may not be representative of usual consumption and true iodine status. Furthermore, UIC does not provide information on thyroid function (2). A biomarker that can categorize iodine status and can also measure thyroid function would be highly valuable for assessing iodine status.

Thyroglobulin (Tg) is produced exclusively by the thyroid gland and a small amount is found in the blood (8). Tg is used in endocrinology as a tumor marker in monitoring patients with previous diagnosis of thyroid cancer, but recently attention has turned to its use as a possible biomarker of iodine status (9). Tg is correlated with thyroid volume (10–12), suggesting that Tg is sensitive to thyroid stimulation (13, 14). Observational studies have reported elevated Tg in most iodine-deficient populations (12, 15–17). In children, Tg decreases when iodine status improves, associated with a reduction in thyroid volume (11, 14, 18) and an improvement in cognition (19). Zimmermann et al (20) proposed that a median Tg < 13 μg/L indicates adequate iodine status in school-aged children. There are only two intervention studies that have measured Tg concentration in adults supplemented with iodine; the intervention period of both studies was less than 3 months. One study was conducted in iodine-deficient New Zealand older adults supplemented with too little iodine to improve status (21), whereas the other was conducted in a Spanish population with sufficient iodine status at baseline (22). A randomized, placebo-controlled intervention study in adults that documents an increase in UIC from $<$ 100 to $\geq$ 100 μg/L while simultaneously measuring Tg concentration is needed. The aim of this study was to determine the efficacy of Tg as a biomarker of iodine status in adults.

Participants and Methods

Eligibility and study design

This was a two-armed, randomized, double-blind, placebo-controlled supplementation trial conducted in Dunedin, New Zealand. Participants were randomly allocated to either iodine-supplemented or placebo groups for 24 weeks. Inclusion criteria were as follows: adults aged 18–40 years who would be resident in Dunedin for 24 weeks; self-reported consumption of two servings per day or less of iodine-fortified bread products; a mean UIC $<$ 100 μg/L of five spot urine samples; and negative for thyroid antibodies (ie, thyroid peroxidase antibody [TPOAb] and Tg antibody [TgAb]). Exclusion criteria were as follows: having a known history of thyroid disease; pregnant or planning to become pregnant in the next 24 weeks; breast-feeding; and taking an iodine-containing supplement.

The study was approved by the University of Otago Ethics Committee (reference number 13/059) and registered with the Australian New Zealand Clinical Trials Registry (trial identification number ACTRN12613000789763). The study results are reported in accordance with the Consolidated Standards of Reporting Trials statement (23). All participants provided signed written consent.

Study protocol

Participants were recruited by advertisement displayed around the University of Otago (Dunedin, New Zealand) between July 2013 and July 2014. Interested participants were given a uniform resource locator directing them to an online survey that included questions about age, current health status, frequency of consumption of iodine-rich foods in the previous week, and willingness to comply with the study protocol. Willing participants (n = 178) attended a 30-minute appointment at which height and weight were measured and a 10-mL blood sample collected. The internationally accepted method to assess iodine status is the determination of UIC in morning or spot urine samples; the recommendation does not require fasting samples. Rasmussen et al (24) reported no significant difference in the categorization of iodine status in groups of mildly iodine-deficient adults when using either a fasting or nonfasting urine sample. Furthermore, fasting urine samples are likely to underestimate iodine status in groups of mildly iodine-deficient adults (24). At present, there is no consensus on the use of fasting samples to reduce individual variability in UIC. Participants were provided with instructions and equipment to collect nonfasting urine samples on different days of the week (between 9:00 AM and 12:00 PM) within 1 week. UIC is associated with high intra-individual variation; thus, a single urine sample cannot be used to accurately assess iodine status in an

individual (25). For the purpose of screening for mild iodine deficiency in our cohort, we obtained five spot samples per participant to control for intra-individual variability while minimizing respondent burden. In addition, participants completed an online sociodemographic questionnaire (eg, education, ethnicity, household income, use of dietary supplements, medical conditions, and overall health) that included a 22-item iodine-specific food frequency questionnaire (FFQ) (26). Questions regarding the use of iodized salt were also included.

Fifty people were ineligible (ie, mean UIC of five urines was ≥ 100 μg/L [n = 42] and tested positive for TPOAb or TgAb [n = 8]), and 16 people did not complete either the urine collection or iodine-specific FFQ. The remaining 112 people were block randomized (block size of 20, stratified by sex and treatment) to either a supplement containing 150 μg/d iodine (n = 56) or a placebo (n = 56) using the random number function of Microsoft Excel by one of the researchers (Z.F.M.), who was blinded throughout the intervention. Participants were asked to attend a 30-minute clinic visit at 8 and 16 weeks for the collection of a 6-mL blood sample; baseline measurements were repeated at 24 weeks.

Supplements

Supplements and placebo were identical in appearance and supplied by Blackmore's. The active tablets contained 150 μg iodine as potassium iodate mixed with cellulose, whereas the placebo tablets contained only cellulose. The iodine content (mean ± SD) of iodine (143.4 ± 3.9 μg; n = 10) and placebo tablets (<0.1 μg; n = 10) was measured by Hill Laboratories (27).

Supplements were packed into blister packs (Medico Pak; Douglas Pharmaceuticals) and distributed in three batches to the participants at the baseline and 8- and 16-week visits. Compliance was assessed by counting remaining tablets in returned blister packs. If a pack of supplements had been lost or was not returned, compliance for that month was assigned as zero. If participants took ≥ 80% of the supplements, they were considered as compliant.

Assessment of thyroid function and Tg

Blood samples were left to clot at room temperature then centrifuged at 4000 × *g*/min for 10 minutes at 4°C. Serum was stored at −80°C until analysis. Tg at baseline and 8, 16, and 24 weeks, TSH, and free thyroxine (FT4) at baseline and 24 weeks, and TgAb and TPOAb at baseline were analyzed using an electrochemiluminescene immunoassay on an Elecsys 2010 (Roche Diagnostics New Zealand Ltd). The normal reference ranges for Tg, TSH, and FT4 were as follows: 3–40 μg/L, 0.4–4.0 mU/L, and 9–23 pmol/L, respectively (28). Each assay detection limit was as follows: Tg II, 0.04 μg/L; TSH, 0.005 mU/L; FT4 II, 0.5 pmol/L; TgAb, < 10.0 U/mL, and TPOAb, < 5.0 U/mL. All assays were performed according to the manufacturer protocols in the Department of Human Nutrition, University of Otago.

External quality control samples were included in each batch of analysis to check for accuracy of Tg, TSH, and TgAb. Certified Reference Material (CRM) Community Bureau of Reference-457 (Institute for Reference Materials and Measurements, Geel, Belgium) (expected value 39.8 μg/L) was used for Tg and gave a mean (±SD) concentration of 38.8 ± 1.5 μg/L (coefficient of variation [CV] = 4.0%; n = 24). The third World Health Organization (WHO) International Reference Preparation 81/565 (National Institute for Biological Standards and Control, Hertfordshire, UK) (expected value 1.58 mU/L) was used for TSH and gave a mean of 1.53 ± 0.06 mU/L (CV 4.0%; n = 27). The WHO International Reference Preparation 65/093 Standard (National Institute for Biological Standards and Control) (expected value 11.3 U/mL) was used for TgAb and gave a mean of 11.7 ± 1.1 U/mL (CV 9.4%; n = 10).

The CVs of the pooled serum samples as an internal quality control were as follows: 3.9% at 23.5 μg/L Tg (n = 29); 3.0% at 0.75 mU/L TSH (n = 28); 7.0% at 17.7 pmol/L FT4 (n = 18); 9.5% at 24.6 U/mL TgAb (n = 11); and 9.8% at 5.7 U/mL TPOAb (n = 11), respectively. Two levels of controls for Tg, TSH, and FT4 provided by the manufacturer were run with each batch and had the following CVs: 3.8% and 3.6% at 20.3 and 80.8 μg/L Tg (n = 11), 2.8% and 2.2% at 1.53 and 8.8 mU/L TSH (n = 10), and 3.2% and 3.8% at 16.1 and 41.6 pmol/L FT4 (n = 7), respectively. Samples at each time point from each participant were analyzed in the same batch.

Assessment of UIC

Aliquots of urine samples were stored at −20°C until analysis. Urine samples were thawed at room temperature and vortexed to dissolve sediment. For each participant, 0.2 mL was removed from each of the five urine samples and pooled; previous analysis in our laboratory found that UIC measured in separate urine samples was highly correlated with UIC measured in a pooled sample (r = 0.98; $P < .001$). UIC of the pooled sample was determined in duplicate using a modified method of Pino et al (29). With each batch of urine samples, a certified external reference standard (Seronorm trace element urine; Sero AS) was used to assess the assay accuracy and an internal pooled urine sample was used to assess internal validity. Analysis of the Seronorm trace element urine (expected value 152 μg/L; range 132–174 μg/L) gave a mean of 142 ± 6 μg/L

(CV 4.0%; n = 47). Analysis of the internal pooled urine gave a mean of 100 ± 4 μg/L (CV 4.2%; n = 47).

Outcome measures

The primary outcome from this study was a difference in Tg concentration between the iodine-supplemented and placebo group between baseline and 24 weeks.

Statistical analysis

A median Tg < 13 μg/L is suggested to indicate adequate iodine status in a population of children (20). Based on a previous study conducted in young adults in New Zealand (19), we predicted that at the end of the intervention the mean Tg concentration of the placebo group would be 18 μg/L and the iodine-supplemented group would be 11 μg/L. With a SD of 12 μg/L, this meant at least 47 participants would be needed in each group to detect a significant difference between groups with 80% power and at a 5% level of significance. Thus, a final sample size of 54 subjects per group (n = 108) was needed given an anticipated dropout rate of 15%.

Analysis was performed using STATA 12.0 (StataCorp). A modified intention-to-treat principle was used that included participants who had missed one or two study visits and excluded participants who had no measurements at 8, 16, and 24 weeks; data from 106 participants was included in the analysis. Descriptive statistics were used to present mean, SD, and median for sociodemographics data. For the UIC, TSH, and FT4, the between-group difference was tested using linear regression analysis controlling for baseline values. The effect of iodine supplementation on Tg was evaluated by a linear mixed model using natural-log-transformed Tg data, with a fixed effect for baseline Tg, fixed factor for treatment and time, and participant identification as a random effect.

Results

Recruitment and sample size

Initial interest in the study was facilitated with the use of an online survey. Of the 2437 people who logged into the survey, 86% (n = 2090) were ineligible primarily because they ate two or more slices of iodine-fortified bread a day. Of the remaining 347 adults, 169 adults declined to participate. There were 178 adults who underwent screening, with 66 excluded resulting in 112 participants; 99 participants completed all study visits. The flow of participants is given in Figure 1.

Compliance with treatment

Of the participants who completed the intervention, 12% in the placebo group and 8% in the iodine-supplemented group were noncompliant.

Participant characteristics and iodine status

The baseline characteristics of the participants are shown in Table 1; the groups were similar in age, body mass index, ethnicity, level of income, education, iodine intake, and use of iodized salt. The main biochemical outcomes at baseline and at 24 weeks are given in Table 2. At baseline, the overall median UIC was 65 μg/L; thus, the participants were categorized as mildly iodine deficient according to WHO/United Nations Children's Emergency Fund (UNICEF)/International Council for the Control of Iodine Deficiency Disorders (ICCIDD) (ie, UIC between 50 and 99 μg/L) (7). The median UIC of the placebo group increased from 64 μg/L at baseline to 79 μg/L at 24 weeks, which still categorized the placebo group as mildly iodine deficient at the end of the intervention. The median UIC of the supplemented group increased from 69 μg/L at baseline to 168 μg/L at 24 weeks, thus categorizing the iodine-supplemented group as having adequate iodine status (ie, UIC between 100 and 299 μg/L) at the end of the intervention (7). Using linear regression, there was a significant treatment effect on UIC at the end of the intervention, with the iodine-supplemented group having a significantly higher UIC than the placebo group ($P < .001$). TSH and FT4 for both groups at baseline and 24 weeks were within the normal reference range and groups were not significantly different from each other at 24 weeks.

Effect of treatment: primary outcome measure (Tg concentration)

At baseline, the whole cohort had a median Tg of 16.6 μg/L; 8% of the cohort had a Tg concentration > 40 μg/L. At 24 weeks, the proportion of participants with Tg concentration > 40 μg/L in the iodine-supplemented and placebo groups was 1.8% and 8.9%, respectively. At 24 weeks, the median Tg of the iodine-supplemented group had decreased from 19.5 μg/L at baseline to 13.0 μg/L, whereas the median Tg of the placebo group at 24 weeks was similar to baseline (16.2 vs 15.3 μg/L) (Table 3). A linear mixed-model analysis showed that there was a significant time-by-treatment interaction effect on Tg concentration ($P < .05$). Tg in the iodine-supplemented group was 12%, 20%, and 27% lower compared with the placebo group at 8 ($P = .045$), 16 ($P < .001$), and 24 weeks ($P < .001$), respectively (Table 3).

Adverse events

No adverse events were reported in either group.

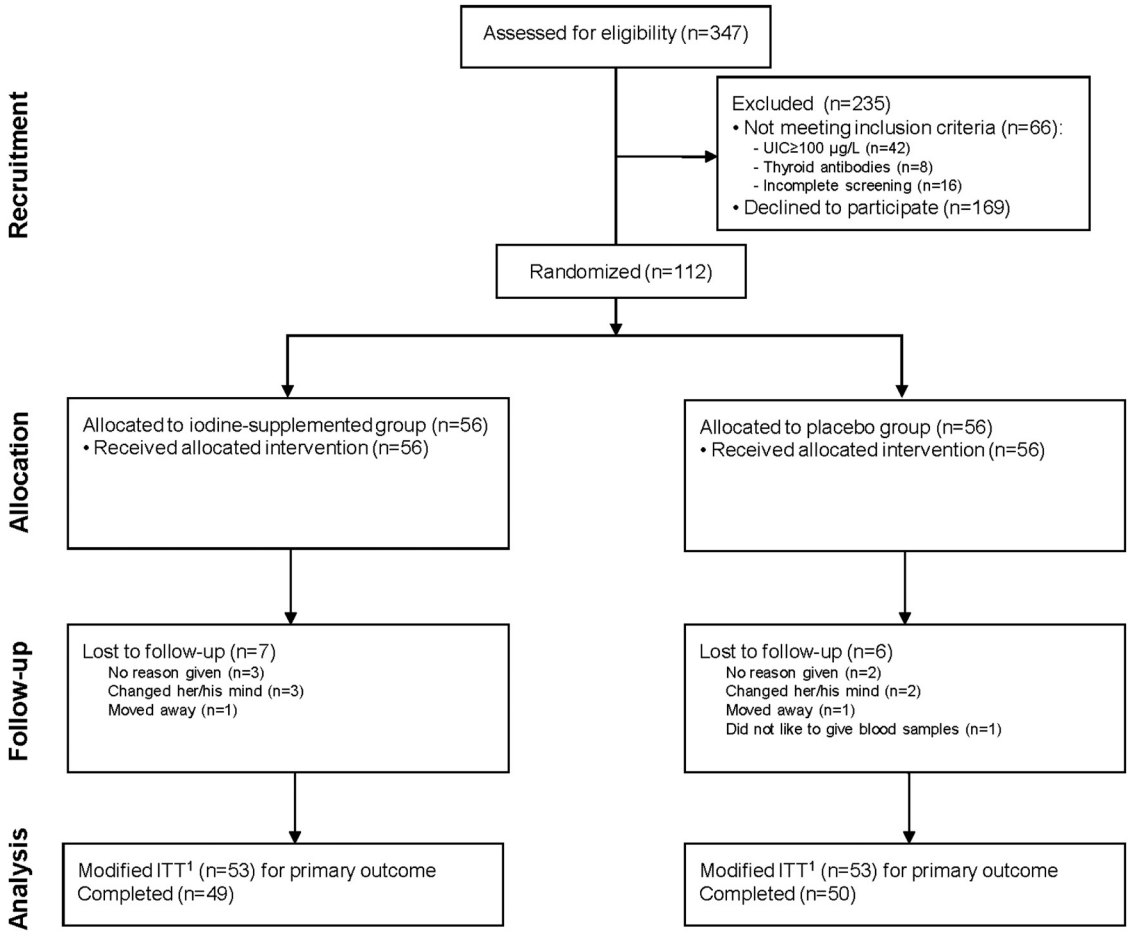

Figure 1. Recruitment, allocation, follow-up, and analysis of participants (adapted from the Consolidated Standards of Reporting Trials statement, 2010). 1, Modified intention to treat (ITT) that included participants who had one or two of the missing follow-up times and excluded participants who had no measurements in the intervention study visits (ie, 8, 16, and 24 wk).

Discussion

To our knowledge, this is the first randomized, double-blind, placebo-controlled intervention study investigating the effect of improving iodine status on Tg concentration in adults. The widespread use of iodized salt in New Zealand and around the world has almost eradicated severe iodine deficiency, and attention has turned to studying the consequences of moderate and mild iodine deficiency (30). There is evidence that mild iodine deficiency can adversely affect cognitive function in children (31) and increase the risk of thyroid cancer in adults (32). A number of indices can be used to assess mild iodine deficiency in children, including thyroid volume, UIC, and Tg, for which exist validated and recommended cutoff values. Although the measurement of thyroid volume indicates long-term iodine status (ie, months to years), it can take 2 years to reflect the improvement in iodine status after iodine repletion (33). For UIC, the same cutoff values used to categorize iodine status in children are used in adults; however, problems with their application in adults are beginning to emerge, particularly in populations with high urine volumes, which can dilute and lower UIC (6). Of more concern is that UIC is an index of recent iodine status (ie, days to weeks) (25). Another limitation of UIC is that many community laboratories do not have the capacity for analysis. An index of longer-term iodine status that is also a measure of thyroid function and routinely measured in community laboratories is Tg. However, the efficacy of Tg in assessing iodine status in adults is currently unknown.

Ma and Skeaff (34) reviewed the use of Tg to assess iodine status. In children, four of six observational studies reported a median Tg concentration of iodine deficient children of ≥ 13 μg/L, whereas four intervention studies observed a fall in Tg when children's iodine status improved via iodized salt or supplementation. The most comprehensive study was a large cohort of 2512 children from 12 countries from which Zimmermann et al derived the Tg cutoff value < 13 μg/L for children (20). Although Ma and Skeaff (34) cite 12 observational studies in adults, the relationship between median Tg concentration and iodine status (as categorized by UIC) is less consistent than in children, with Tg concentration either < 13 or ≥ 13 μg/L

Table 1. Baseline Characteristics of Participants by Treatment Group

Variable	Iodine (n = 56)	Placebo (n = 56)
Age, y[a]	23.8 ± 3.7	23.6 ± 3.5
Gender, n, %		
Female	44 (79)	43 (77)
BMI, kg/m^{2}[a]	23.8 ± 4.4	24.0 ± 3.4
Ethnicity, n, %[b]		
NZEO	53 (95)	49 (88)
Māori and Pacific Island	3 (5)	7 (13)
Income level, n, %[c]		
<$NZ50 000	49 (88)	47 (84)
≥$NZ50 000	1 (2)	1 (2)
Education level, n, %		
Secondary school qualification	24 (43)	25 (45)
Higher qualification	32 (57)	31 (55)
Median dietary iodine intake, μg/d[d]		
FFQ only	58 (34, 77)	61 (46, 76)
FFQ plus iodized salt	88 (68, 120)	96 (72, 122)
Use of iodized salt, n, %	38 (68)	39 (70)

Abbreviations: BMI, body mass index; NZEO, New Zealand European and Other Ethnicities.

[a] Mean ± SD (all such values),

[b] Due to rounding, the total may not add to 100% exactly.

[c] Not all participants answered this question.

[d] Median (25th and 75th percentiles).

in iodine-deficient adults. As stated earlier, only two intervention studies measured Tg in adults; issues with study protocols mean these studies are unable to evaluate the usefulness of Tg as a biomarker of iodine status in adults.

Our main finding was that supplementation of 150 μg/d iodine for 24 weeks improved iodine status by shifting median UIC from < 100 to ≥ 100 μg/L in the supplemented group; this improvement in UIC was associated with a concomitant decrease in Tg, when compared with the placebo group. Zimmermann et al (20) suggested that a median Tg concentration < 13 μg/L and/or < 3% of the population with Tg concentration > 40 μg/L indicates iodine sufficiency in a group or population of children. However, this cutoff has not been validated in adult populations. In the current study, both the median Tg and proportion of participants with a Tg concentration > 40 μg/L in the iodine-supplemented group decreased from 19.5 μg/L and 7.1% at baseline to 13.0 μg/L and 1.8% at 24 weeks, respectively. Therefore, our results demonstrate that the < 13 μg/L absolute cutoff and the proportion of the population with a Tg concentration > 40 μg/L are valid indices of adequate iodine status (ie, as determined by UIC) in an adult population. Our finding agrees with previous intervention studies conducted in children that found a substantial decrease in Tg concentration when median UIC increased and iodine status was adequate (11, 14, 18, 19). Collectively these studies suggest that Tg can be used an in index of iodine status in both groups of children and adults.

Iodine supplementation and an improvement in iodine status did not alter TSH or FT4 of our participants. Compensatory mechanisms used by the thyroid gland when iodine intakes decreases ensure that adequate amounts of thyroid hormone are produced when iodine deficiency is mild to moderate (1). Consequently, TSH and FT4 in populations with mild iodine deficiency usually fall within the normal reference range (35). Indeed, WHO/UNICEF/ICCIDD do not recommend the use of TSH or FT4 to assess iodine status (7). In contrast, a significant difference was found in Tg between iodine-deficient and iodine-sufficient adults in our study, indicating that Tg is a more sensitive biomarker of iodine status than TSH and FT4, particularly in areas with mild iodine deficiency. Another advantage of Tg is the development of a method in which a drop of blood obtained from a fingerprick is spotted onto filter paper that is left to dry for 24 hours (11). The advantages of a dried blood spot Tg method, particularly in

Table 2. Effect of Treatment on the UIC, TSH, and FT4 Concentration

	Iodine		Placebo		
	n	Value	n	Value	*P* Value[a]
UIC, μg/L					
Baseline	56	69 (45, 90)[b]	56	64 (49, 76)	<.001
24 wk	49	168 (107, 239)	50	79 (53, 112)	
TSH, mU/L					
Baseline	56	1.66 (1.31, 2.37)	56	1.54 (1.18, 2.15)	.532
24 wk	49	1.81 (1.33, 2.17)	50	1.79 (1.27, 2.22)	
FT4, pmol/L					
Baseline	56	16.2 ± 2.3[c]	56	16.7 ± 2.1	.628
24 wk	49	16.0 ± 1.9	50	16.5 ± 2.0	

[a] Between-group difference by multiple linear regression after adjustment for baseline value.

[b] Median (25th and 75th percentiles) (all such values).

[c] Mean ± SD (all such values).

Table 3. Effect of Treatment and Time on Tg Concentration.

Time, wk	Iodine		Placebo		Ratio (95% CI)[b,c]	*P* Value[b]
	n	Value[a]	n	Value[a]		
0 (baseline)	56	19.5 (11.1, 26.1)	56	15.3 (11.0, 23.7)	–	–
8	53	14.1 (10.3, 22.9)	52	16.2 (10.5, 24.7)	0.88 (0.78, 0.98)	.045
16	51	14.7 (10.1, 20.8)	49	16.5 (10.5, 24.6)	0.80 (0.71, 0.91)	<.001
24	49	13.0 (9.4, 19.7)	50	16.2 (10.7, 23.4)	0.73 (0.64, 0.82)	<.001

[a] Median (25th and 75th percentiles) (all such values).

[b] A linear mixed model was used to compare the ratio of geometric means of the iodine and placebo groups at 8, 16, and 24 weeks, controlling for baseline Tg concentration.

[c] Ratio of geometric means with log-transformed data.

the field, are numerous compared with the collection, storage, and shipping of urine samples.

Study strengths and weaknesses

This study had a number of strengths. The study design was a randomized, double-blind, placebo-controlled trial, which is of high quality. We vigorously screened potential participants using an online survey followed by collection of five spot urine samples to ensure that participants were mildly iodine deficient at baseline. UIC has high intra-individual variability and the measurement of multiple repeated urine samples can be used to minimize this variability (2, 36). We tested participants for thyroid antibodies at baseline and excluded those with thyroid abnormality because thyroid antibodies can confound the measurement of Tg (37). We used Tg CRM Community Bureau of Reference-457 to standardize our data as recommended by Zimmermann et al (20); this will facilitate comparisons with future studies in this area. Another strength was that our supplementation period was 24 weeks. Although a short duration of only 2 weeks has been found to shift median UIC from mildly deficient to sufficient, Tg may take a longer time course to stabilize (38). We found that 24 weeks was needed to observe a fall in Tg to 13 μg/L. It remains a matter of speculation whether Tg would continue to drop if the duration of the intervention extended beyond 24 weeks. The current study was not designed or powered to examine gender differences between the two groups ($\leq$13 males in each group); however, gender disparity is a common finding in thyroid conditions. Another limitation with regard to generalizability may be that participants were aged 18–40 years, and it is untested as to whether the findings are applicable to older age groups. Further studies with older adults (ie, 40–65 years) and sufficient numbers of both males and females are needed.

Conclusion

In conclusion, iodine supplementation of 150 μg/d iodine of mildly iodine deficient adults for 24 weeks improved iodine status and was associated with a concomitant decrease in Tg concentration. Adequate iodine status in this group of adults was associated with a median Tg concentration of 13 μg/L, in agreement with findings in children. Our study is the first to demonstrate the usefulness of Tg as a biomarker of iodine status in an adult New Zealand population.

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The authors' responsibilities were as follows: S. A. S was the principal investigator, secured the funding and obtained ethics; Z. F. M., B. J. V, P. J. M. and S. A. S. designed the study; Z. F. M. developed the questionnaires, recruited the subjects, distributed the supplements, collected and analyzed the blood and urine samples, entered data, and conducted some statistical analysis; linear mixed modeling was undertaken by C. M. C.; Z. F. M. wrote the first draft of the manuscript and S. A. S edited the manuscript. All authors provided input on all versions of the manuscript.

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Preliminary baseline data of this work were presented at the Postgraduate Nutrition Conference (Dunedin, New Zealand) as an oral presentation and the New Zealand Nutrition Society Conference (Queenstown, New Zealand) as a poster abstract. Complete data of this work were also presented at the 12th Asian Congress of Nutrition (Yokohama, Japan) as an oral presentation.

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