Minimal impact of excess iodate intake on thyroid hormones and selenium status in older New Zealanders

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Abstract

Objective: Iodine deficiency has re-emerged in New Zealand, while selenium status has improved. The aim of this study was to investigate the effects of excess iodine intake as iodate on thyroid and selenium status.

Methods: In a randomized, controlled trial with older people (mean±S.D. 73±4.8 years; n=143), two groups received >50 mg iodine as iodate/day for 8 weeks because of supplement formulation error, either with 100 µg selenium (Se+highI), or without (highI). Four other groups received 80 µg iodine as iodate/day with (Se+lowI) or without selenium (lowI), selenium alone (Se+) or placebo. Thyroid hormones, selenium status and urinary iodine concentration (MUIC) were compared at weeks 0, 8, and 4 weeks post-supplementation.

Results: MUIC increased nine and six fold in Se+highI and highI groups, falling to baseline by week 12. Plasma selenium increased in selenium-supplemented groups (P<0.001). The increase in whole blood glutathione peroxidase (WBGPx) in the Se+highI group was smaller than Se+ (P=0.020) and Se+lowI groups (P=0.007). The fall in WBGPX in the highI group was greater than other non-selenium supplemented groups, but differences were not significant. Ten of 43 participants exposed to excess iodate showed elevated TSH (hypothyroidism) at week 8. In all but two, TSH had returned to normal by week 12. In three participants TSH fell to <0.10 mIU/l (hyperthyroidism) at week 8, remaining low at week 12.

Conclusions: Excess iodate induced hypo- or hyperthyroidism in some participants and hyperthyroidism in others. Most abnormalities disappeared after 4 weeks. Excess iodate reduced WBGPx activity and resulted in smaller increases in WBGPx after selenium supplementation.
Introduction

Healthy individuals can tolerate iodine intakes of up to 1mg/day, as the thyroid gland can regulate synthesis and release of thyroid hormones over a wide range of intakes (1). However, such doses may cause hypothyroidism in individuals with damaged thyroid glands because of abnormal down-regulation of iodine transport into the gland. Adverse effects may also occur in individuals with nodular goiter. In populations with chronic iodine deficiency an increase in iodine intake may result in iodine-induced hyperthyroidism (IIH) (thyrotoxicosis), the main complication of iodine prophylaxis in several countries, including New Zealand (2-6). Iodine-induced hypothyroidism may also occur (7).

Chronic excess iodine intake as iodide is associated with an increase in goiter and subclinical hypothyroidism because of inhibition of thyroid hormone synthesis (3, 8). Excess iodine can also trigger an immune response, resulting in autoimmune thyroiditis (1), inflammation of the thyroid, sensitivity reactions or acute toxicity (3, 8). Such effects can occur in persons with normal thyroid glands when exposed to large iodide intakes from dietary supplements, including seaweed extracts, and iodine-containing drugs (8). Effects may reverse when iodine is withdrawn (3). The same high intake of iodine may cause hyperthyroidism in some people and hypothyroidism in others (9). Excess intake of iodine as iodate may have additional toxicological effects (10).

Iodine status in New Zealand has fallen over the past two decades because of reduction in use of iodophor cleaning agents in the dairy industry and in use of iodized table salt, resulting in re-emergence of mild iodine deficiency (11-13). The elderly are particularly vulnerable because they consume fewer servings of dairy products (14). In contrast, selenium status is improving (13), due to higher selenium content of animal foods resulting from supplementation, and to the consumption of high-selenium imported foods. However, our selenium status is still insufficient for maximal activities of the selenoenzyme glutathione.
peroxidase (GPx) (15, 16). Both selenium and iodine are essential for optimal thyroid function (17, 18). Selenium is an essential component of iodothyronine deiodinase enzymes that convert thyroxine (T\textsubscript{4}) to the active hormone triiodothyronine (T\textsubscript{3}). The GPxs are also implicated in protection against oxidative damage to the thyroid gland (18). Interaction between selenium and thyroid metabolism occurs particularly where there is severe deficiency of both iodine and selenium (19), and is also of interest in New Zealanders with marginal selenium status and mild iodine deficiency (15).

We have reported previously results of a randomized controlled trial comparing the effects of 12 weeks supplementation with 100 µg/day selenium with or without 80 µg/day iodine or a placebo on selenium, iodine and thyroid status in older New Zealanders (16). An error in iodine supplement formulation resulted in some participants in two further groups receiving supplements containing >50 mg iodine as iodate/day for 8 weeks before the error was discovered and supplementation stopped. This paper reports the effects of 8 weeks of supplementation with excess iodate on selenium status and thyroid function of these two groups in comparison with the results at 8 weeks of the above four groups supplemented with selenium (100µg/day), low iodine (80 µg/day), selenium plus low iodine, or placebo.

**Experimental methods**

**Subjects and recruitment**

A randomized controlled trial was carried out with 143 older male and female residents of Dunedin in the South Island of New Zealand from August to November 2005. Participants were aged (mean±S.D.) 73±4.8 years, non-institutionalized, free from serious medical illness, not using medications for thyroid function or with any known thyroid problems, and not taking supplements containing selenium or iodine. Subjects were recruited via advertisements in newspapers and newsletters, on notice boards in retirement villages, supermarkets,
hospitals and leisure centres; by letters sent to participants in a previous study; and by visits and presentations to various senior citizen organizations. Potential participants were screened by telephone using a brief questionnaire that included questions on age, health and inclusion criteria. All participants gave informed consent, and the Ethics Committee of the University of Otago, Dunedin, New Zealand approved the protocol. The study was registered with the Australian New Zealand Clinical Trials Registry as ACTRN012605000368639

**Study design**

Respondents who met inclusion criteria were mailed information sheets and consent forms, and after consent were randomized into treatment groups. Block randomization with stratification by sex was used to assign participants into one of six treatment groups. The randomization schemes were generated by using the website Randomization.com (http://www.randomization.com). An error in the manufacture of some supplements resulted in very high levels of iodate (>50 mg iodine) in tablets used for two groups. This error was not discovered until 8 weeks after commencement; supplementation was terminated immediately on discovery of the error. The six groups were as follows: 100 µg selenium (Se+) (n=25); 100 µg selenium + 80 µg iodine as iodate (Se+lowI) (n=26); 100 µg selenium + 50 mg iodine as iodate (Se+highI) (n=22); 80 µg iodine (lowI) (n=25); 50 mg iodine (highI) (n=21); placebo (n=24). The focus of this paper is the results for the two groups receiving high iodate (Se+highI; high I). Results of the Se+, Se+lowI, lowI and placebo groups at 0 and 12 week have been analyzed to determine the effects of 12 weeks supplementation with nutritional levels of selenium and iodine on selenium, iodine and thyroid status, and published previously (16). For this paper the raw data at 8 weeks for these four groups have been analyzed for comparison here with the two groups receiving high iodate supplements, whose supplementation was terminated at 8 weeks. There were no statistically significant differences
ANOVA) in baseline measures of selenium, iodine or thyroid hormone status among the six groups (Table 2).

Randomization, recruitment and allocation to groups were all carried out by independent researchers. The participants, those administering the interventions and those assessing the outcomes of the intervention were blinded to treatment assignment.

Participants completed a brief questionnaire on demographics, dietary habits, supplement and medication use, smoking habits, consumption of foods high in selenium or iodine, and self-reported health status. Fasting blood samples were collected at baseline, week 8 and 4 weeks post-supplementation (week 12), and casual morning urine samples at baseline, week 8 and 12. Thyroid hormone status (thyroid-stimulating hormone (TSH), free triiodothyronine (FT₃), free thyroxine (FT₄)), selenium status (plasma selenium (PlSe), whole blood GPx activity (WBGPx)) and median urinary iodine concentrations (MUIC) were determined at baseline, weeks 8 and 12.

**Treatments**

Tablets, identical in size, shape and colour, were produced by Alaron Products (Port Nelson, New Zealand) in July 2005. We had previously obtained supplements from this company without incident. Iodine tablets contained potassium iodate (KIO₃), and selenium tablets contained L-selenomethionine. Ten tablets were randomly selected from each group and analyzed for iodine and selenium content in September 2005 by Hill Laboratories Ltd (Hamilton, New Zealand) using inductively coupled plasma spectrometry with a detection limit of 0.01 µg Se/tablet and 0.02 µg I/tablet, respectively. Selenium and iodine contents of the tablets are summarized in Table 1. Participants consumed one tablet daily for 8 weeks; they were encouraged to maintain their normal diets and to avoid supplements containing
selenium or iodine for the study duration. Compliance was monitored via completion of a
daily checklist and from the number of tablets returned at study conclusion.

**Sample Collection**

Blood was collected in EDTA vacutainers (Becton Dickinson, Franklin Lakes, NJ) for
separation of whole blood and plasma and additive free vacutainers for serum. Samples were
kept on ice and centrifuged within 3 hours of collection. Aliquots of whole blood, plasma and
serum were stored at -80°C until analysis. Casual morning (between 0730 and 0930) urine
samples were collected in clean, plastic specimen containers and stored at –20°C until
analysis.

**Biochemical analyses**

PlSe concentration was determined in duplicate by graphite furnace Atomic Absorption
Spectroscopy with Zeeman background correction (AA-800, Perkin-Elmer Corp; Norwalk,
Connecticut, USA) by a modification of the method of Jacobson and Lockitch (20). Accuracy
was assessed by analysis of certified reference materials (CRM) with each batch; Seronorm
Reference Serum (batch no. JL4409; Laboratories of SERO AS, Billingstad, Norway), with a
certified selenium concentration of 0.92 (95% CI 0.84, 1.00) µmol Se/l, gave a mean (±S.D.)
concentration of 0.88±0.04 µmol/l (CV 4.9%; n=45). Analysis of Utak Reference Plasma
(batch no. 66816, lot 7081, UTAK Laboratories Inc, Valencia, CA), with a certified selenium
concentration of 1.52 (95% CI 1.14, 1.90) µmol Se/l, gave a mean of 1.39±0.09 µmol/l (CV
6.2%; n=45).

GPx activity was measured in whole blood using RANSEL kits (#RS 505, 506 Randox
Laboratories Ltd, Antrim, UK) and automated on a Cobas Fara autoanalyser (Hoffman-La
Roche, Basle, Switzerland). WBGPx was assayed as a measure of erythrocyte GPx activity,
which has been shown previously by us to constitute 95% of whole blood activity with the
use of this assay method \(^{(21)}\). Because no RANSEL controls were available at the time, pooled
samples of whole blood were analyzed with each batch and gave a mean activity of 45.5±2.8
U/g Hb (CV 6.2%; \(n=196\)).

Urinary iodate concentration (UIC) was determined using the ammonium persulphate
method recommended by the WHO/UNICEF/ICCIDD \(^{(22)}\). Analysis of a CRM, Seronorm
Trace Elements Urine (Lot no. NO2525, Sero AS, Asker, Norway), with a certified iodine
concentration of 141 (95% CI 132, 150) µg I/l gave a mean of 13±8 µg I/l (CV 5.7%; \(n=92\))
µg I/l. Analysis of pooled aliquots of urine with each batch of samples gave a mean of 45±10
µg I/l (CV 4.4%; \(n=43\)). Urines with high iodate concentrations were diluted for analysis as
required.

Southern Community Laboratories, Dunedin, New Zealand performed analysis of
serum TSH, FT\(_3\), FT\(_4\) and TgAb concentration. TSH was assayed using a 2-site sandwich
chemiluminescent immunoassay with a lower limit of detection of 0.004 mIU/l. Serum FT\(_4\)
and FT\(_3\) were analyzed using a competitive chemiluminescent immunoassay with a lower
limit of detection of 1.3 pmol FT\(_4\)/l and 0.3 pmol FT\(_3\)/l, respectively. Analysis of CRM,
BIORAD Immunoassay Plus material (Irvine CA, USA), with certified concentrations of 0.60
(95% CI 0.48, 0.72) mIU TSH/l, 10.5 (95% CI 8.4, 12.7) pmol FT\(_4\)/l and 3.6 (95% CI 2.9, 4.3) pmol FT\(_3\)/l gave mean concentrations of 0.6±0.03 mIU TSH/l (CV 4%), 9.3±0.7 pmol
FT\(_4\)/l (CV 8.5%) and 3.3±0.14 pmol FT\(_3\)/l (CV 4.2%), respectively. Baseline TgAbs were
measured using an Access 2 analyzer (Beckman Coulter In, Fullerton, CA, USA) by
immunoenzymatic assays with chemiluminescent detection. For clinical assessment, normal
ranges for TSH, FT\(_3\) and FT\(_4\) concentrations given by Southern Community Laboratories
were 0.3-5.0 mIU TSH/l, 2.8-6.8 pmol FT\(_3\)/l and 10-23 pmol FT\(_4\)/l. For all analytical
methods, all samples from each participant were analysed in the same batch.
**Statistical analysis**

All statistical analyses were conducted using PASWStatistics 18 (SPSS Inc, Chicago, USA). Statistical significance was assessed at $P<0.05$. Descriptive statistics (mean±S.D.) are presented for baseline characteristics. Positively skewed data were log transformed and described using median (inter-quartile range, I.Q.R.). Differences among groups of normally distributed variables (baseline PlSe, WBGPx, TSH, FT$_3$, FT$_4$; changes in PlSe and WBGPx) were tested using one-way ANOVA for continuous data, with Bonferroni post-hoc tests for multiple comparisons. Differences between groups of skewed variables (UIC, changes in UIC) were tested using the Kruskal-Wallis test.

**Results**

Baseline MUIC of all participants was 54.5 µg/l (I.Q.R. 67.5; $n=137$); 49% of participants had MUIC <50 µg/l and 82% <100 µg/l, indicating mild to moderate iodine deficiency (Table 2). In participants who received high iodate supplements, and for whom MUIC values were available at 0, 8 and 12 week, MUIC in the Se+highI group ($n=21$) increased from 83 (79) to 7800 (9334) µg/l at 8 weeks, but returned to 62 (52) µg/l by week 12, and in the highI group ($n=17$) from 86 (98) to 4969 (23983) µg/l returning to 93 (131) µg/l by week 12. MUIC in the Se+lowI group increased from 63 (66) to 93 (92) µg/l at week 12, and in the lowI group from 45 (43) to 56 (57) µg/l.

Changes in PlSe concentration and WBGPx activity differed among the six groups ($P<0.0001$) (Figures 1 and 2, respectively). Mean (±S.D.) baseline PlSe was 1.20±0.29 µmol/l ($n=142$) and increased by 0.89, 0.85 and 0.76 µmol/l (72, 77 and 62%) in Se+, Se+lowI and Se+highI groups at 8 weeks, respectively ($P<0.0001$) (Figure 1); these changes were not significantly different among these three groups, but were all greater than those for groups not
supplemented with selenium \((P<0.0001)\), for which there was no change in PlSe. WBGPx increased by 2.8, 3.1 and 1.0 U/g Hb (6.4%, 7.1%, 2.3%) in the Se+, Se+lowI, Se+highI groups, respectively, significantly greater than the non-selenium supplemented groups \((P<0.0001)\) (Figure 2). These changes were significantly different among these three groups \((P=0.05)\). The increase in WBGPx in the Se+highI group (+1.0 U/g Hb) was smaller than the Se+ (+2.8 U/g Hb; \(P=0.020\)) and Se+lowI (+3.1 U/g Hb; \(P=0.007\)) groups in spite of similar selenium intake (100 µg), but the differences were not significant after adjustment for multiple comparisons (Bonferroni). The change in the Se+highI group also was not significantly different from the non-selenium supplemented groups. A fall in WBGPx (-1.10 U/g Hb; -2.6%) in the highI group was greater than that for the lowI and placebo groups (-0.38 U/g Hb; -0.9%), -0.27 U/g Hb; -0.6%), respectively, but differences were not significant.

Clinical assessment of the 43 participants in the highI and Se+highI groups exposed to high iodate supplements, showed that 10 had elevated TSH at week 8 (i.e. above normal range of 0.3-5.0 mIU/l), indicating that they had developed an underactive thyroid (hypothyroidism) (Table 3). In all but two, TSH had returned to normal range by week 12. The elevated TSH was accompanied by a fall in FT\(_4\) at week 8, to below the normal range (10-23 pmol/l) in four participants, but which returned to normal at 12 weeks. Thus of the 10 participants with elevated TSH, six had transient subclinical hypothyroidism and four developed transient clinical hypothyroidism. There was a small elevation in FT\(_3\) within the normal range (2.8-6.8 pmol/l) in two participants, but which had returned to baseline concentrations at 12 weeks (Table 3). Two participants (#46, 81) developed evidence of hyperthyroidism, with TSH falling to <0.10 mIU/ml at week 8 and remaining low at 12 weeks, and in a third participant (#97), an already low TSH at baseline fell further at week 8 (Table 3), indicating an underlying thyroid problem exacerbated by excess iodate.
supplementation. The fall in TSH was accompanied by a slightly elevated FT₃ in all
participants and elevated FT₄ outside the normal range in two (participants #46, 97). TgAbs
were elevated in six of the 43 participants exposed to high iodate; two of whom developed
hypothyroidism (#49, 103), one developed hyperthyroidism (#46) and three were unaffected.
All participants exposed to excess iodate intake were asymptomatic. The thyroid
hormone results were referred to an endocrinologist who did not consider that further clinical
evaluation was necessary at that time. Participants were referred to their general practitioners
for further evaluation with respect to the potential toxicity of iodine as iodate.
Mean FT₃ and TSH concentrations differed among the six groups at 8 weeks (ANOVA,
P<0.001, P=0.014, respectively) due entirely to higher mean TSH and FT₃ values for the
highI group and Se+highI (P<0.10) and a higher FT₃ value for the highI group (P<0.05), the
groups that included those participants who developed thyroid dysfunction as a result of high
iodate intake (results not shown). Mean FT₄ concentrations did not change during the study
period.

Discussion
Our results are of particular relevance in assessing potential adverse effects of a prolonged
very high iodine intake, particularly in older people, and in evaluating the upper tolerable
intake limit for iodine. Evidence of iodate-induced hypothyroidism in some participants and
of hyperthyroidism in others was observed. Most of the abnormal thyroid hormone levels had
returned to normal 4 weeks after cessation of high iodate supplementation. We have also
shown a potential adverse effect of excess iodate intake on the selenoenzyme GPx.
Factors affecting the response to excess iodine include route of intake, bioavailability of
iodine, duration of intake and physiological status of the individual including age, sex, body
size, previous iodine intake, thyroid health, and general health (8). For example, older adults
who have lived many years in an iodine-deficient area and those with underlying thyroid disease are more likely to respond adversely to increased iodine intake than are those who live in iodine-sufficient areas or who have normal thyroid glands.

The major factor determining the occurrence of iodine-induced hypothyroidism or hyperthyroidism as a public health problem is the sudden increment of iodine (2), as experienced by our participants. However, the response to excess iodate was variable with some individuals tolerating the large intakes without side effects, whereas some responded adversely. A significant proportion of our participants (25%) who received excess iodate for 8 weeks developed subclinical hypothyroidism as a result of inhibition of synthesis of thyroid hormones, while the remaining participants showed no effect. On the other hand only three participants showed signs of iodate-induced hyperthyroidism, which is most commonly encountered in populations that have had long exposure to iodine deficiency and in older individuals who have long-standing nodular goiter (autonomous thyroid nodules) (3, 8).

Our observations may reflect age-related changes in thyroid function and increased risk of thyroid insufficiency in the elderly (23), although this was evident in only one of our older individuals (participant #97). Many of our older participants would have been born in the 1930s when iodine-deficiency goiter was prevalent in many parts of New Zealand until adequate iodization of salt was introduced in the early 1940s. From then until the late 1980s was a time of adequate iodine status throughout the country because of high iodine content of dairy products as a result of the use of iodophor cleaning agents in the dairy industry, as well as iodized salt use (12). In the past 10-15 years the use of iodophors has reduced resulting in a decrease in iodine status and a return to mild iodine deficiency from the early 1990s (11-13). Thus our participants may have had varied historical exposure to iodine deficiency depending on their place of residence in New Zealand during their lifetime. Females are more susceptible to the effects of excess iodine intake than are males (8), but this was not evident in
our small sample with six males and four females developing hypothyroidism, and one male
and two females developing hyperthyroidism.

In this study, participants received 50 mg/day of iodine as iodate for 8 weeks, equivalent to
2,800 mg of iodine. Two other studies of effects of high intakes of iodine for prolonged
periods have reported similar transient effects on thyroid status. An increase in serum TSH
and in thyroid volume was observed in 10 male volunteers given 27 mg iodine daily for 4
weeks (total dose 756 mg) (24). Both TSH and thyroid volume had returned to normal within
one month. Similarly, in 33 euthyroid patients given lugol solution (80-100 mg/day) for 15
days (total dose 1200-1500 mg), TSH increased and returned to normal after iodine
withdrawal, but there were no demonstrable changes in serum T_4 or T_3 (25). We cannot
explain why some participants developed thyroid dysfunction while others did not. There is
likely to be a large individual variation response to excess iodate intake, related to factors
outlined above, such as previous exposure to iodine deficiency, nutritional status of the
individual, sex, age, body size, thyroid health, and general health (8). In this respect a major
limitation of the study is that we did not measure TPO-Ab levels of the participants. We
speculate that high TPO-Ab titres were present in those participants who developed
subclinical or clinical hypothyroidism, reflecting an underlying autoimmune thyroid problem.
The presence of TgAbs did not seem to be a contributing factor as only three of those affected
had elevated levels, while another three did not develop thyroid disease.

The upper tolerable limit (UL) of intake for iodine for the USA and Canada was set at
1100 µg/day (26) as is the Australian and New Zealand upper limit (27). This was based on
observations of elevated TSH concentrations after supplemental intakes indicating a lowest-
observed-effect level of 1,700 mg/day. An uncertainty factor of 1.5 was applied to give a no-
observed-adverse-effect level that is the basis for the upper limit of intake. However, this
guideline should be exercised with caution as individuals with chronic iodine deficiency or
with underlying thyroid disease may respond to intakes lower than these (1). In our older population, most abnormalities had returned to normal after only 4 weeks, indicating that long-term adverse effects were unlikely. However, a longer follow-up of these participants would have been desirable. Prolonged exposure to excess iodate at this level, particularly in susceptible individuals, might have more serious adverse consequences affecting their health and well-being. Ocular toxicity has occurred in humans after exposure to doses of 600 to 1,200 mg per individual, and in several animal species oral exposures to high doses of iodate have pointed to corrosive effects in the gastrointestinal tract, hemolysis, nephrotoxicity and hepatic injury (10).

Other nutritional determinants of thyroid function such as selenium, vitamin A and iron may influence the effects of high iodine intakes (1). In particular, several studies have reported an interaction between selenium status and thyroid function (15, 28, 29). Selenium regulates thyroid hormone metabolism through its action as a component of the iodothyronine deiodinases in converting T\(_4\) to T\(_3\). In selenium deficiency, conversion of T\(_4\) to T\(_3\) is impaired \(^{(17, 18)}\). However, the interaction is modest when subjects are not sufficiently iodine and/or selenium deficient (16, 19). Beneficial effects of selenium supplementation on autoimmune thyroiditis have been reported, possibly through the action of GPx in enhancing the immune system and protecting the thyroid gland against oxidant stress (30-32). In a recent randomized controlled trial with patients with autoimmune thyroiditis, physiological doses of selenium improved thyroid structure and reduced autoantibody titre (33). We did not see any protective effect of selenium supplemented with high iodine in comparison with high iodine on the development of thyroid disease in our participants; however, the number of subjects affected adversely by high iodate intake was too small the draw any such conclusions.

This is the first study to our knowledge to report an effect of high iodate intake on GPx activity as a measure of selenium status in humans. Selenium supplementation increased GPx
activity, confirming many other intervention studies carried out in New Zealand, which indicate that the baseline selenium status of New Zealanders is insufficient for maximization of GPx activity (12). However, we observed a statistically significant smaller increase in GPx in the Se+highI group than in the other selenium-supplemented groups. In addition, there was a decrease in GPx activity in the highI group that was greater than that for the other two groups not supplemented with selenium. This may partly reflect the smaller but non-significant increase in plasma selenium in the Se+highI group, but this is unlikely to be the only reason. On the other hand, these differences are more likely to be due to higher oxidant stress induced by high iodate intake, resulting in a larger decrease in GPx activity or a smaller increase in response to selenium supplementation because of higher consumption of WBGPx.

Our results agree with those of Xu et al (34) who showed in mice that decreased activities of GPx resulting from excessive iodine intake could be restored through supplementing with selenium. These observations indicate that when high iodate supplements are used to eliminate iodine deficiency, it would appear important to co-administer selenium to ensure adequate selenium intake.

**Declaration of interest**

There are no conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

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References


FIGURE 1. Change in plasma selenium (PlSe) concentrations in participants during 8 weeks supplementation with 100 µg selenium (Se+), selenium plus low (80 µg) iodine (Se+lowI) or high (50 mg) iodine (Se+highI) intakes, low (lowI) or high (highI) iodine intakes or a placebo (Plac). Changes in PlSe concentration differed among the six groups (ANOVA, \( P<0.0001 \)). Changes in selenium-supplemented groups were all greater than changes in groups not supplemented with selenium (\( P<0.0001 \)). Values are mean ±S.E.M.

FIGURE 2. Change in whole blood glutathione peroxidase (WBGPx) activities in participants during 8 weeks supplementation with 100 µg selenium (Se+), selenium plus low (80 µg) iodine (Se+lowI) or high (50 mg) iodine (Se+highI) intakes, low (lowI) or high (highI) iodine intakes or a placebo (Plac). Changes in WBGPx activity differed among the six groups (ANOVA, \( P<0.0001 \)). Values are mean±S.E.M.
Table 1 Iodine and selenium content of tablets\(^a\)

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<thead>
<tr>
<th>Treatment</th>
<th>Selenium content (µg/tablet)</th>
<th>Iodine content (µg/tablet)</th>
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<tr>
<td></td>
<td>Mean(^b) S.D. Median(^b) 1(^{st}) quartile, 2(^{nd}) quartile</td>
<td>Mean(^b) S.D. Median(^b) 1(^{st}) quartile, 2(^{nd}) quartile</td>
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<tr>
<td>Se+</td>
<td>107 15 &lt;0.01</td>
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<tr>
<td>Se+lowI</td>
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<td>Se+highI</td>
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<td>lowI</td>
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<td>placebo</td>
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\(^a\) Analyzed by R. J. Hill Laboratories Ltd (Hamilton, New Zealand) using inductively coupled plasma mass spectrometry.

\(^b\) Ten tablets (n=10) were randomly selected from each group.
<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>PlSe</th>
<th>WBGPx</th>
<th>MUIC</th>
<th>TSH</th>
<th>FT(_4)</th>
<th>FT(_3)</th>
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<td>µmol/l</td>
<td>U/g Hb</td>
<td>µg/l</td>
<td>mIU/l</td>
<td>pmol/l</td>
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<td>All subjects</td>
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<td>1.21±0.29</td>
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<td>55 (68) (^1)</td>
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<td>43.8±12.3</td>
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<td>22</td>
<td>1.22±0.21</td>
<td>43.6±6.0</td>
<td>87 (78)</td>
<td>2.7±1.1</td>
<td>14.0±2.8</td>
<td>4.91±0.50</td>
</tr>
<tr>
<td>Se-lowI</td>
<td>25</td>
<td>1.22±0.36</td>
<td>43.2±9.1</td>
<td>45 (43)</td>
<td>2.5±1.5</td>
<td>13.9±2.2</td>
<td>4.91±0.51</td>
</tr>
<tr>
<td>Se-highI</td>
<td>21</td>
<td>1.20±0.16</td>
<td>41.1±8.6</td>
<td>85 (84)</td>
<td>3.0±1.7</td>
<td>13.8±1.8</td>
<td>5.13±0.39</td>
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<tr>
<td>placebo</td>
<td>24</td>
<td>1.23±0.29</td>
<td>43.6±9.1</td>
<td>53 (52)</td>
<td>2.5±1.1</td>
<td>14.3±2.9</td>
<td>4.73±0.78</td>
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</table>

PlSe, plasma selenium; WBGPx, whole blood glutathione peroxidase; MUIC, median urinary iodine concentration; TSH, thyroid stimulating hormone; FT\(_4\), free thyroxine, FT\(_3\), free triiodothyronine.

Results expressed as means (±S.D.) or \(^1\)median (I.Q.R.)

There were no significant differences in baseline measures of selenium, iodine or thyroid hormones among the six groups (ANOVA; \(P>0.05\)).
<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Treatment</th>
<th>TSH&lt;sup&gt;a&lt;/sup&gt; (mIU/l)</th>
<th>FT&lt;sub&gt;4&lt;/sub&gt;&lt;sup&gt;b&lt;/sup&gt; (pmol/l)</th>
<th>FT&lt;sub&gt;3&lt;/sub&gt;&lt;sup&gt;c&lt;/sup&gt; (pmol/l)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week 0</td>
<td>Week 8</td>
<td>Week 12</td>
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<tr>
<td>Hypothyroidism</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>M</td>
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<td>2.2</td>
<td>6.9</td>
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<tr>
<td>97</td>
<td>M</td>
<td>highI</td>
<td>0.35</td>
<td>0.05</td>
<td>0.05</td>
</tr>
</tbody>
</table>

TSH, thyroid stimulating hormone; FT<sub>4</sub>, free thyroxine, FT<sub>3</sub>, free triiodothyronine; nm, not measured.

For clinical assessment, normal ranges of thyroid hormone concentrations given by Southern Community Laboratories were: <sup>a</sup>TSH, 0.3-5.0 mIU TSH/l; <sup>b</sup>FT<sub>4</sub>, 0-23 pmol FT<sub>4</sub>/l; <sup>c</sup>FT<sub>3</sub>, 2.8-6.8 pmol FT<sub>3</sub>/l
FIGURE 1. Change in plasma selenium (PlSe) concentrations in participants during 8 weeks supplementation with 100 µg selenium (Se+), selenium plus low (80 µg) iodine (Se+lowI) or high (50 mg) iodine (Se+highI) intakes, low (lowI) or high (highI) iodine intakes or a placebo (Plac). Changes in PlSe concentration differed among the six groups (ANOVA, P<0.0001). Changes in selenium-supplemented groups were all greater than changes in groups not supplemented with selenium (P<0.0001). Values are mean ±S.E.M.

254x190mm (72 x 72 DPI)
FIGURE 2. Change in whole blood glutathione peroxidase (WBGPx) activities in participants during 8 weeks supplementation with 100 µg selenium (Se+), selenium plus low (80 µg) iodine (Se+lowI) or high (50 mg) iodine (Se+highI) intakes, low (lowI) or high (highI) iodine intakes or a placebo (Plac). Changes in WBGPx activity differed among the six groups (ANOVA, P<0.0001). Values are mean±S.E.M.