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Iodine intakes of 100–300 μg/d do not modify thyroid function and have modest anti-inflammatory effects

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Abstract

Little information is available as to whether doses of iodide similar to those recommended in clinical practice for the prevention of iodine deficiency in pregnant women affect thyroid function. The aim of the present study was to analyse whether doses of iodide can affect thyroid function in adults, and evaluate its effect on plasma markers of oxidative stress, inflammation and acute-phase proteins. A total of thirty healthy volunteers (ten men and twenty women) with normal thyroid function were randomly assigned to three groups (n 10). Each group received a daily dose of 100, 200 or 300 μg of iodide in the form of KI for 6 months. Free tetraiodothyronine (FT4) levels at day 60 of the study were higher in the groups treated with 200 and 300 μg (P=0·01), and correlated with the increase in urinary iodine (r 0·50, P=0·007). This correlation lost its significance after adjustment for the baseline FT4. The baseline urinary iodine and FT4 correlated positively with the baseline glutathione peroxidase. On day 60, urinary iodine correlated with C-reactive protein (r 0·461, P=0·018), and free triiodothyronine correlated with IL-6 (r −0·429, P=0·025). On day 60, the changes produced in urinary iodine correlated significantly with the changes produced in α1-antitrypsin (r 0·475, P=0·014) and ceruloplasmin (r 0·599, P=0·001). The changes in thyroid-stimulating hormone correlated significantly with the changes in α1-antitrypsin (r −0·521, P=0·005) and ceruloplasmin (r −0·459, P=0·016). In conclusion, the administration of an iodide supplement between 100 and 300 μg/d did not modify thyroid function in a population with adequate iodine intake. The results also showed a slight anti-inflammatory and antioxidative action of iodide.

Key words: **Iodine: Thyroid function: Urinary iodine: Antioxidants**

The recommended daily iodine intake has changed over the years[1,2]. The current recommended daily iodine intake is 150 μg/d for adults and 250 μg/d for pregnant and lactating women[2]. Recent studies have shown that even a mild degree of iodine deficiency has repercussions on cognitive function and school performance in clinically euthyroid school-aged children[3,4]. The increasing awareness of the importance of adequate iodine intake during pregnancy[5] has led not just to the recommendation to consume iodised salt, but also to the prescription of iodide to pregnant women, especially in those areas where dietary iodine is deficient, even just moderately. Programmes controlling normal pregnancies in Spanish health centres include the recommendation to prescribe at least 150 μg of iodide/d[6]. However, although some studies have shown the beneficial effect of iodine supplements during pregnancy[7,8], certain doubts exist concerning the systematic administration of iodide[9]. Reasons for this include the most suitable dose and, very particularly, whether certain doses might induce a reduction in free tetraiodothyronine (FT4)[10]. Controlled clinical studies evaluating the thyroid

Abbreviations: α1AT, α1-antitrypsin; Cp, ceruloplasmin; CRP, C-reactive protein; FT4, free tetraiodothyronine; FT3, free triiodothyronine; GSH-Px, glutathione peroxidase; TBARS, thiobarbituric acid-reactive substance; TPO, thyroid peroxidase; TSH, thyroid-stimulating hormone; TV, thyroid volume.

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function response to variable doses of iodine are few and not conclusive[11–16]. Some of the differences in the effect of iodine administration can be related to different baseline iodine intake levels.

Little attention has been paid to extra-thyroid roles of iodine. Iodine has different effects depending on the intake amount and the thyroid status at the time[17]. Iodide excess seems to exert oxidative stress in some target tissues of the thyroid hormones, though the amounts of iodine used in these studies are commonly above the recommended daily allowance[18,19]. However, the role of iodine in mammary and other tissues has also been shown to have an antioxidant function[17,20,21]. Iodide can act as an electron donor in the presence of H_2O_2, peroxidase and some PUFA, decreasing damage by free oxygen radicals[22]. Iodide has been found to effectively scavenge reactive oxygen species in human blood cells[20]. Iodide intake also seems to be related to the activity of the enzymes glutathione peroxidase (GSH-Px), catalase and superoxide dismutase, which act as antioxidants[21,23–25]. Concentrations of iodine as low as 15 μM (achievable in human serum) have the same antioxidant activity as that of ascorbic acid[21]. Iodine is also used by other cells, such as hepatic or immune system cells[26], and seems to have a direct relationship with acute-phase proteins[27].

The aim of the present study was (1) to test the hypothesis that pharmacological doses of iodide, below the tolerable upper intake levels recommended by various scientific bodies[28] and similar to those usually recommended in clinical practice for the prevention of iodine-deficiency in pregnant women, can affect thyroid function in adults without iodine-deficiency disorders, and (2) to evaluate its effect on various different plasma markers of oxidative stress, lipid peroxidation and acute-phase proteins.

Methods

Subjects

The study was undertaken in thirty healthy volunteers (ten men and twenty women), mean age 34·9 (SD 10·5) years, with normal thyroid function, no palpable goitre, non-smokers, no history of any intercurrent process during the 2 weeks before the evaluation and negative anti-thyroid peroxidase (TPO, <50 IU/ml) and anti-thyroglobulin antibodies (<100 IU/ml). The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the Ethics and Research Committees of Carlos Haya University Hospital, Málaga. Written informed consent was obtained from all subjects.

Subjects, who commonly consumed iodised salt as part of their usual daily diet, were randomly assigned to one of three groups (*n* 10). Each group received a daily dose of 100, 200 or 300 μg of iodide in the form of KI. The study lasted 6 months and followed the sequence shown in Table 1. Group 1 (35·3 (SD 11·3) years, three men and seven women) took 100 μg of iodide for 2 months, no iodide during the third month, and from the fourth month to the end of the study took 300 μg of iodide. Group 2 (34·4 (SD 9·9) years, four men and six women) started the study taking 200 μg of iodide in two daily doses of 100 μg of iodide during the first 2 months, took no iodide during the third month, and from the fourth month to the end of the study took 200 μg of iodide in a single daily dose. Group 3 (35·2 (SD 11·5) years, three men and seven women) started the study with 300 μg of iodide for the first 2 months, took no iodide during the third month, and from the fourth month to the end of the study took 100 μg of iodide.

Procedures

Thyroid-stimulating hormone (TSH) and the thyroid hormones FT4, free triiodothyronine (FT3), thyroglobulin and TPO were measured at baseline (baseline) and at the end of the first (day 30), second (day 60), third (day 90), fifth (day 150) and sixth (day 180) months. The 24 h urine was collected for the measurement of iodine excretion at baseline and on days 60, 90, 150 and 180. The baseline intake of iodine was measured indirectly by 24 h urinary iodine excretion. Thyroid volume (TV) was measured by ultrasound at baseline and on days 60, 90 and 150. GSH-Px activity, superoxide dismutase activity, catalase activity, thiobarbituric acid-reactive substances (TBARS, an indicator of lipid peroxidation), high-sensitive C-reactive protein (CRP), IL-6, α1-antitrypsin (α1AT), α1-acid glycoprotein and ceruloplasmin (Cp) were measured at baseline and on day 60.

Blood samples were collected after a 12 h fast. Serum thyroid hormones were analysed in an automated Modular Analytics E170 analyser (Roche Diagnostics GmbH, Mannheim, Germany). TSH, FT3 and FT4 were measured by chemiluminescence (Roche Diagnostics GmbH; reference ranges: TSH >0·20 and <5·00 μIU/ml; FT4 >10·0 and <22·0 pmol/l; FT3 >3·10 and <6·8 pmol/l). Anti-TPO antibodies were measured by a radioimmunometric assay (Biocode S.A., Liege, Belgium). Thyroglubulin was measured by immunoradioanalysis (Tg-S; BRAHMS Diagnostica GmbH, Henningsdorf, Germany). Anti-thyroglobulin antibodies were measured by RIA (BRAHMS Diagnostica GmbH). Iodine concentration in urine samples was measured by the modified Benotti and Benotti technique[29]. TV was measured simultaneously by two investigators by real-time ultrasound using a 7·4 MHz linear transducer[30]. It was measured using the following calculation: TV (ml) = TV of the right lobe (ml) + TV of the left lobe (ml). The volume of each lobe was measured using the following calculation: lobe volume (ml) = long axis (cm) × short axis (cm) × thickness (cm) × 0·520[31]. CRP and IL-6 were analysed by enzyme immunoassay (ELISA) kits (BLK Diagnostics, Barcelona, Spain). GSH-Px, superoxide dismutase and catalase activity were measured in plasma using commercial kits (Cayman Chemical Company, Ann Arbor, MI, USA). α1AT, α1-acid glycoprotein and Cp were measured in plasma using commercial kits (SpinReact, Sant Esteve D'En Bas, Spain). TBARS were determined by spectrophotometry as described previously[32].

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Table 1. Serum levels of thyroid-stimulating hormone (TSH), free tetraiodothyronine (FT4) and free triiodothyronine (FT3) and the FT3:FT4 ratio, thyroid volume and urinary iodine concentration at the different points of the study

(Mean values and standard deviations)

		Baseline (day 0)		Iodide dose administered (μg/d)	Day 30		Day 60		30 d Without treatment	Day 90		Iodide dose administered (μg/d)	Day 150		Day 180		
	Groups	Mean	SD		Mean	SD	Mean	SD		Mean	SD		Mean	SD	Mean	SD	*P**
TSH (μIU/ml)	1	2·05	0·71	100	2·33	0·66	1·79	0·63		1·70	0·60	300	2·8	1·03	1·09	0·42	NS
	2	1·73	0·79	100+100	1·84	0·80	2·28	1·26		1·89	1·31	200	2·03	0·79	1·65	0·49	NS
	3	1·81	1·12	300	1·85	0·94	2·00	1·33		1·36	0·61	100	2·20	1·27	2·03	0·78	NS
P†		NS			NS		NS			NS			NS		NS		
FT4 (pmol/l)	1	14·8	1·8	100	15·4	1·9	14·9	1·4		15·7	1·2	300	16·7	2·7	16·3	1·9	NS
	2	15·4	1·7	100+100	16·0	1·8	15·5	1·5		16·8	1·1	200	15·1	1·7	14·9	0·8	NS
	3	16·4	1·0	300	15·8	1·5	16·8	1·3		16·9	2·3	100	16·7	1·9	15·9	2·2	NS
P†		NS			NS		0·01‡			NS			NS		NS		
FT3 (pmol/l)	1	5·00	0·70	100	5·09	0·75	5·23	0·55		4·91	0·62	300	5·59	0·78	5·5	0·59	NS
	2	5·00	0·62	100+100	5·45	0·35	4·70	0·55		5·39	0·52	200	5·12	0·56	4·5	0·43	NS
	3	5·20	0·50	300	5·04	0·54	5·53	0·53		4·85	0·73	100	5·12	0·58	4·9	0·52	NS
P†		NS			NS		NS			NS			NS		NS		
TG (μg/l)	1	3·89	3·81	100	1·52	2·74	0·84	1·77		6·61	2·38	300	8·31	4·06	6·83	4·54	NS
	2	7·62	4·13	100+100	0·86	2·72	8·81	10·32		8·32	5·14	200	8·02	3·52	5·97	4·83	NS
	3	6·82	9·15	300	1·54	2·96	4·04	6·35		7·82	4·72	100	7·77	4·90	7·44	4·13	NS
P†		NS			NS		NS			NS			NS		NS		
FT3:FT4	1	0·33	0·03	100	0·33	0·03	0·34	0·02		0·31	0·03	300	0·31	0·05	0·31	0·07	NS
	2	0·32	0·03	100+100	0·34	0·05	0·30	0·01		0·31	0·02	200	0·34	0·03	0·34	0·05	NS
	3	0·31	0·04	300	0·32	0·04	0·33	0·04		0·29	0·03	100	0·33	0·04	0·32	0·06	NS
P†		NS			NS		NS			NS			NS		NS		
TV (cm^3)	1	8·8	3·2	100			7·1	2·0		7·5	2·3	300	10·5	3·6			NS
	2	8·6	2·5	100 + 100			7·9	2·9		10·1	2·7	200	11·4	1·8			NS
	3	11·0	4·9	300			7·6	1·2		9·2	2·3	100	7·9	2·3			NS
P†		NS			NS		NS			NS			NS		NS		
Urinary iodine (μg/d)	1	191·6	90·3	100			223·3	91·7		147·1	64·6	300	316·1	90·9	417·7	74·8	NS
	2	140·3	74·6	100+100			230·4	130·9		190·7	91·0	200	207·8	106·8	331·7	100·7	NS
	3	200·6	56·4	300			377·0	179·4		213·4	64·3	100	391·8	127·2	308·6	61·2	NS
P†		NS					0·03			NS			0·01		0·03		

TG, thyroglobulin; TV, thyroid volume.

* *P* value adjusted for baseline FT4.

† Kruskal–Wallis test.

‡ Repeated-measures ANOVA (intersubject factor: group).

Statistical analysis

Data are presented as means and standard deviations. Based on previous results from our group[33], the study was designed to make a comparative analysis with a standard deviation of plasma FT4 of 2·16 pmol/l, a capacity to detect a change (sensitivity) in the FT4 of 2 pmol/l and a detection power of 80 %. For an $\alpha = 0{\cdot}05$, the minimum sample size needed was twenty cases. In the present study, we included thirty cases (ten subjects per group). The hypothesis contrast was done by the Kruskal–Wallis test or repeated-measures ANOVA. The correlation between variables was determined using the Spearman test, designing multiple linear regression models in those cases where it was desired to predict the variance adjusted for other variables, besides the main variable. The variables were evaluated after adjustment for age and sex. In all cases, the level of rejection was $\alpha = 0{\cdot}05$ for two tails. Statistical analysis was performed with SPSS (version 11.5 for Windows; SPSS, Chicago, IL, USA).

Results

Urinary iodine

The baseline level of 24 h urinary iodine excretion was 177·3 (SD 73·7) μg/d (132·6 (SD 51·8) μg/l). Urinary iodine concentrations were significantly higher in those persons who took 200 and 300 μg of iodide than in those who took 100 μg, in both the first part and second part of the study (Table 1).

Thyroid hormones and thyroglobulin

Plasma levels of FT4 at day 60 of the study were significantly higher in the groups treated with 200 and 300 μg of iodide ($P=0{\cdot}01$, Table 1). No significant differences between the groups in the plasma levels of TSH and FT3, the FT3:FT4 ratio, thyroglobulin or TV at any of the various study points (Table 1). TPO were negative and their levels remained unchanged throughout the study.

On day 60, FT4 correlated with the 24 h urinary iodine (Fig. 1(a); r 0·47, $P=0{\cdot}01$; R^2 0·22). However, this correlation lost its significance after adjustment in a multiple regression model for the baseline levels of FT4. The increase in urinary iodine (change in urinary iodine: urinary iodine at day 60 − baseline urinary iodine) correlated significantly with the levels of FT4 on day 60 (r 0·50, $P=0{\cdot}007$) (R^2 0·25) (Fig. 1(b)). However, this correlation lost its significance after inclusion in the model of the baseline levels of FT4. FT4 did not correlate with urinary iodine at any other time during the study. TSH, FT3, thyroglobulin and TV did not correlate with urinary iodine at any time during the study (data not shown).

The baseline levels of each hormone studied (TSH, FT3 and FT4) and thyroglobulin correlated significantly with the levels at the other five points in the study: TSH (Spearman's r 0·55–0·75, $P<0{\cdot}003$); FT4 (Spearman's r 0·50–0·70, $P<0{\cdot}003$); FT3 (Spearman's r 0·40–0·74, $P<0{\cdot}01$); thyroglobulin (Spearman's r 0·62–0·84, $P<0{\cdot}01$).

Thyroid volume

Thyroid ultrasound was normal in all study subjects, and no thyroid nodules were detected. TV did not correlate significantly with TSH, FT4, FT3 or thyroglobulin at any study point (data not shown). It also did not change throughout the study.

Oxidative stress and inflammation variables

The enzyme activity of the markers of oxidative stress and plasma concentration of the markers of inflammation and acute-phase proteins were studied at baseline (day 0) and on day 60 (time at which the FT4 levels were significantly higher). There were no significant differences between the three groups in the plasma activity of GSH-Px, superoxide dismutase and catalase or in the plasma levels of CRP, TBARS, IL-6, α1AT, α1-acid glycoprotein and Cp, either at baseline or on day 60 (data not shown). Also, no significant differences were found between the two study points (Table 2).

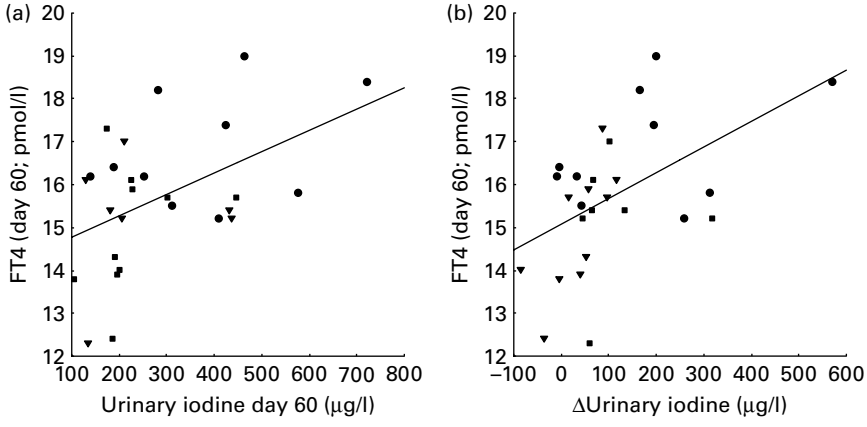

Fig. 1. Association found on study day 60 (a) between free tetraiodothyronine (FT4) and urinary iodine (r 0·47, $P=0{\cdot}01$) and (b) between FT4 and change in urinary iodine (urinary iodine on day 60 − baseline urinary iodine) (r 0·50, $P=0{\cdot}007$). Group 1: 100 μg of iodide/d (▼). Group 2: 100 + 100 μg of iodide/d (■). Group 3: 300 μg of iodide/d (●). Δ, Day 60 − day 0.

Table 2. Oxidative stress and inflammation variables in the subjects at baseline and on day 60 (Mean values and standard deviations)

	Baseline		Day 60		
	Mean	SD	Mean	SD	*P*
GSH-Px (nmol/min per ml)	169·5	21·1	165·1	20·9	0·428
SOD (nmol/min per ml)	2·8	1·1	2·6	1·0	0·253
CAT (nmol/min per ml)	30·5	15·5	27·3	12·6	0·657
TBARS (μg/ml)	19·1	5·5	20·0	4·3	0·127
CRP (μg/ml)	1·10	1·00	0·93	0·77	0·325
IL-6 (pg/ml)	1·55	0·72	1·94	1·19	0·098
α1AT (mg/l)	961	183	956	178	0·943
α1AGP (mg/l)	559	107	587	96	0·108
Cp (mg/l)	362	90	365	78	0·394

GSH-Px, glutathione peroxidase activity; SOD, superoxide dismutase activity; CAT, catalase activity; TBARS, thiobarbituric acid-reactive substances; CRP, high-sensitive C-reactive protein; α1AT, α1-antitrypsin; α1AGP, α1-acid glycoprotein; Cp, ceruloplasmin.

Baseline GSH-Px correlated significantly with baseline urinary iodine concentration (r 0·355, P=0·075) and FT4 (r 0·443, P=0·021). Baseline α1AT and Cp correlated significantly with baseline FT3 (r 0·511, P=0·006 and r 0·419, P=0·029, respectively). There were no significant correlations between any of the other variables studied (data not shown).

On day 60, urinary iodine concentration correlated with CRP (r −0·461, P=0·018), α1AT (r 0·406, P=0·039) and TBARS (r −0·414, P=0·060). FT3 correlated with IL-6 (r −0·429, P=0·025). No significant correlations were found between any of the other variables studied (data not shown).

Changes in TSH, FT4 and urinary iodine concentration correlated significantly with different variables of oxidative stress and inflammation (Table 3). No significant correlations were found between any of the other variables studied (data not shown).

Discussion

The main findings of the present study were as follows: (1) the administration of iodide at doses of 100, 200 or 300 μg/d over 6 months in adults with a normal thyroid function and an optimum iodine supply (mean urinary iodine concentrations of 100–199 μg/l)[2] did not significantly change thyroid function or thyroglobulin levels, (2) TV was unaltered and anti-TPO antibodies were negative throughout the study and (3) the urinary iodine and thyroid hormones were associated with oxidative stress and inflammation variables.

Understanding the clinical response to the administration of iodine is of great clinical importance. The question posed is not new, but interventional studies performed in areas with adequate iodine intake are still lacking. Nevertheless, the effect of iodine supplementation is paradoxical. The administration of high doses of iodide/d in persons with a normal thyroid function induces slight, but significant changes in thyroid function, characterised by a reduction in total FT4, an increase in TSH and an exaggerated TSH response to a thyrotropin-releasing hormone stimulation test[12–15,34,35]. Gardner *et al.*[35] treated thirty healthy men with doses of 500, 1500 or 4500 μg of iodide/d. Baseline urinary iodine concentration was above 250 μg/d. A significant reduction was seen in the serum FT4 concentration in the groups treated with 1500 and 4500 μg of iodide/d, but not in the group treated with 500 μg of iodide/d.

On the other hand, Kahaly *et al.*[16] found an increase in the levels of total FT4, a reduction in thyroglobulin and a

Table 3. Changes* in thyroid-stimulating hormone (ΔTSH), free tetraiodothyronine (ΔFT4) and urinary iodine concentration (ΔUI) between day 0 and day 60 with change in different variables of oxidative stress and inflammation (Correlation coefficients and *P* values)

	ΔTSH		ΔFT4		ΔUI	
	r	*P*	*r*	*P*	*r*	*P*
CRP (day 60)		NS	−0·504	0·007		NS
SOD (day 60)	0·413	0·032		NS		NS
α1AT (day 60)		NS		NS	0·475	0·014
Cp (day 60)		NS		NS	0·599	0·001
ΔCRP		NS	−0·501	0·013		NS
Δα1AT	−0·521	0·005		NS		NS
ΔCp	−0·459	0·016		NS		NS

CRP, C-reactive protein; SOD, superoxide dismutase activity; α1AT, α1-antitrypsin; Cp, ceruloplasmin.
*Δ = day 60 − day 0.

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reduction in TV in sixty-one persons with diffuse euthyroid goitre, with a baseline urinary iodine excretion level of 30 μg/d, who were treated for 12 months with 200 μg of iodide/d. In the present study, the consumption of three doses of 100, 200 and 300 μg of iodide/d barely modified thyroid function. Neither FT4 nor FT3 varied significantly throughout the study, according to a repeated-measures ANOVA. The difference compared with the study by Kahaly concerns the baseline iodine intake levels of the populations. Most studies that found a reduction in FT4 levels have been done with higher doses of iodine than those in the present study. The study by Kahaly *et al.*[16], with 200 μg of iodide/d, found an increase in FT4 and an increase in TPO, which returned to baseline after cessation of the treatment. This increase in autoimmune activity, though, was not detected in the present study. Autoimmune thyroiditis is more prevalent in areas of iodine deficiency in which iodine prophylaxis programmes have been started[36–39].

The present study differs from others in a few aspects. The study participants did not have goitre, and were euthyroid, and the intake of iodine was within current recommended daily allowance (as measured by the mean urinary iodine concentration). The other studies cited, however, were done with very high doses of iodine and in populations with a very high or a very low intake of iodine. The only study that found an increase in FT4 was done in a sample of persons selected for the presence of goitre, treated with 200 μg/d and with a low iodine intake[16].

However, although some studies have shown the beneficial effect of iodine supplements during pregnancy[7,8], certain doubts exist concerning the systematic administration of iodide. When the thyroid gland is subjected to a sudden large iodine load, biosynthesis of T4 and T3 decreases. This self-regulatory mechanism, known as the Wolff–Chaikoff effect, temporarily protects against the production of excess thyroid hormone[10]. This effect could be a limiting factor for the administration of these iodine supplements. This is very important, since adequate levels of FT4 are essential in order to avoid iodine deficiency disorders related to normothyroid hypothyroxinaemia associated with iodine deficiency[40]. However, our data suggest that the activity of the thyroid was unaltered with these iodine intake levels.

The production of thyroid hormones requires the transformation from iodide to iodine in the thyroids. Both GSH-Px and H_2O_2 are involved in this reaction. The results of the present study show a correlation between a greater plasma activity of GSH-Px and higher urinary iodine and FT4 levels, though only at baseline. These data coincide with those of earlier studies showing greater plasma activity of GSH-Px in a group of subjects who received an iodine brine drinking cure[24]. Another study has also shown that plasma GSH-Px and FT4 were elevated in non-goitrous control children compared with highly iodine-deficient goitrous children[23]. The absence of any change in the levels of TBARS also coincides with other studies[18]. The negative correlation found after 2 months of treatment with KI between the levels of TBARS and urinary iodine may indicate the presence of a slight antioxidative action of iodide. This antioxidant effect of iodine may explain the therapeutic effects of seaweed baths or iodine-rich solutions known as thalassotherapy, used historically to treat different diseases[21].

Scarce attention has been given to the role of iodine in other biological processes. Immune cells are other targets of iodine. Although the levels of CRP and IL-6 remained unchanged with the different iodide doses given, the negative correlations found between CRP and FT4 and urinary iodine, as well as between FT3 and IL-6, suggest the presence of an interrelationship between iodide, the production of thyroid hormones and the inflammation status, as measured by CRP and IL-6. The anti-inflammatory activity of certain iodised products has already been described[41]. It seems reasonable to assume that the anti-inflammatory effect of iodide is based on its radical scavenging, with small contributions from other components in other stages of the inflammatory cascade[41].

Iodide also has an effect in hepatic tissue[18]. This tissue is where acute-phase proteins, such as α1AT and Cp, are mainly generated. In the present study, the levels of α1AT and Cp were significantly associated with those of FT3, TSH and urinary iodine. This association was also found in an earlier study[27]. However, we are unable to show the mechanism of the influence of iodine on the synthesis of acute-phase proteins.

In conclusion, the results of the present study show that, in a population with an adequate intake of iodine, the administration of an iodide supplement between 100 and 300 μg/d (in the form of KI) does not modify thyroid function or induce an increase in autoimmune activity. Iodine levels seem to have certain effects on the antioxidative ability of plasma. The results also show the association between iodine intake, as measured by urinary iodine, and certain inflammation markers and acute-phase proteins. However, the results do not enable us to show the exact mechanism of the influence of iodine or thyroid hormone on oxidative stress, inflammation and acute-phase proteins. *In vitro* studies would be needed to determine whether iodine or thyroid hormones are directly responsible for the observed changes. Although pregnant women currently comprise an important group in iodisation programmes, the results of the present study cannot be directly extrapolated to them. The consequences of the antioxidant and anti-inflammatory effect of iodine on pregnant women remain to be studied.

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selection of patients and coordination of the study. J. L.-O. and M. P. measured TV by real-time ultrasound. M. J. G. analysed the thyroid hormones. All authors helped to write the manuscript and have read and approved the final manuscript.

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