EXPERT REVIEWS

Selenium status in patients with autoimmune and non-autoimmune thyroid diseases from four European countries

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Context: Selenium supplementation has been suggested for Hashimoto thyroiditis and Graves' ophthalmopathy. Objective, Design: Our aim is to measure selenium status (p-Se, p-SePP), urine iodine (UI) levels and urine iodine/creatinine ratio (UI/C) in different thyroid diseases (n = 416) from four European countries and to compare the results between patients with and without thyroid autoimmunity. Results: p-Se and p-SePP showed positive correlation and did not correlate with UI/C. Also, these measurements were higher in patients from Italy in comparison with the other countries. Austria had the lowest UI/C ratios. Selenium deficiency exists in these four European countries. Selenium status was lower in patients with Hashimoto thyroiditis and Graves' disease in comparison with non-autoimmune thyroid disease patients and did not differ between autoimmune patients with or without thyroid peroxidase antibodies. The latter correlated positively with age. Conclusions: Our findings suggest that Se supplementation might have a beneficial effect in autoimmune thyroid patients.

KEYWORDS: Graves' disease • Hashimoto's thyroiditis • non-autoimmune thyroid disease • plasma selenium • plasma selenoprotein P • selenium status • thyroid diseases • urine iodine

In 1817, the Swedish chemist Berzelius discovered selenium (Se). He named it Selene after the Greek goddess of the moon [1]. One hundred and forty years later, Schwarz and Foltz identified Se as essential to animal health, when they discovered that trace amounts protected against liver necrosis in vitamin E-deficient rats [2]. Since then, a significant number of biological functions have been associated with Se [1,2]. Its biochemistry has been a matter of long-standing interest, because it becomes toxic at elevated levels irrespective of its general essentiality [3].

It was found that Se has several biological actions, which in most cases are mediated through the expression of at least 30 selenoproteins coded by 25 selenoprotein genes in humans [4]. Se is essential for optimal endocrine and immune function and moderating the inflammatory response [5,6].

The importance of Se to endocrine systems is highlighted by the fact that many endocrine tissues have evolved mechanisms to maintain relatively high concentrations of Se, even when there is severe dietary deficiency [7]. Dietary Se intake ranges from 7 to 4990 μg/day, with mean values of 40 μg/day in Europe and 93 μg/day (in women) to 134 μg/day (in men) in the USA. Se status, as measured by p-Se or serum Se (s-Se), varies by country and corresponds to intake. Intakes are high in Venezuela, Canada, the USA and Japan, and much lower in Europe, particularly in Eastern Europe. China has areas of both Se deficiency and excess. Intakes in New Zealand, which were formerly low, have improved after increased importation of high Se Australian wheat. Recommendations for Se intake average 60 μg/day for men and 53 μg/day for women [8,9]. Cancer preventive properties of Se have been described upon daily

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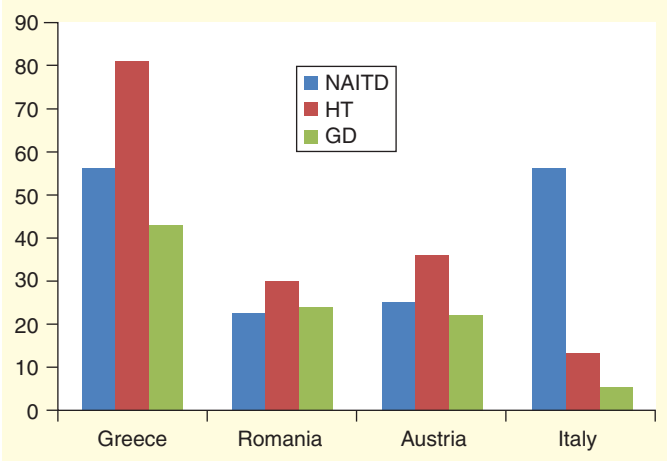

Figure 1. Number of patients with thyroid diseases recruited from different countries.
GD: Graves' disease; HT: Hashimoto thyroiditis; NAITD: Non-autoimmune thyroid disease.

supplementations of 200 μg Se/day, suggesting that a re-appraisal of dietary Se intake should be considered [8].

The thyroid contains more Se per gram of tissue than any other organ [10]. Se, like iodine or iron, is an essential trace element for normal thyroid function and thyroid hormone homeostasis. Beneficial effects of Se supplementation have been reported in several studies for the treatment of Hashimoto's thyroiditis (HT). In such patients, both selenite and selenomethionine were effective at dosages of 200 μg/day [11]. In addition, it has also been reported that Se administration may decrease thyroid receptor antibodies (ABs) in Graves' disease (GD) patients [12]. Mechanisms of action of this treatment remain as unclear as do possible preventive Se effects in thyroid cancer [13].

Recently, supplemental Se intake for over 6 months, as compared with placebo or pentoxifylline, was investigated in patients with mild Graves' disease. It was found that Se significantly improved the ocular involvement and the quality of life in patients with mild Graves' ophthalmopathy (GO). The mechanism of this effect remains unclear [14].

The aim of this multicenter, cross-sectional, prospective study is to determine plasma selenium status and urine iodine levels in patients with autoimmune (GD and HT) and non-autoimmune thyroid diseases from four European countries (Greece, Romania, Austria and Italy) and compare the results. This trial was undertaken by the Union Européenne des Médecins Spécialistes (UEMS) – section of Endocrinology, Diabetes and Metabolism and it may be considered as the first UEMS Endocrinology study.

Table 1. Characteristics of patients with thyroid diseases and controls included in the study.

	Patients (n = 416)	Controls (n = 27)
Age (years)	49.1 ± 14.6	39.0 ± 16.1
Males (%)	14.9	11.1
Country (n)		
Austria	83	2
Greece	180	5
Italy	77	7
Romania	76	13
Disease (n)		
Non-autoimmune thyroid disease	159	Not applicable
Graves's disease	97	
Hashimoto's thyroiditis	160	
p-Selenium levels (μg/l)	86.7 ± 37.1	89.3 ± 28.7
p-Selenoprotein P levels (mg/l)	3.6 ± 1.0	3.7 ± 1.0
Urine iodine levels	22.6 ± 49.4	32.4 ± 59.5
Urine iodine/creatinine ratio	0.3 ± 0.8	0.4 ± 0.8

Patients & methods

Four hundred and sixteen patients were recruited from four European countries (Greece, Thessaloniki [n = 180], Romania, Timisoara [n = 76], Austria, Vienna [n = 83] and Italy, Rome [n = 77]). Italian patients were recruited in almost equal numbers from two different hospitals, that is, Azienda Ospedaliera Sant'Andrea – La Sapienza University of Rome and Hospital Regina Apostolorolum-Albano Laziale, Rome. Of note, Latvia also contributed with 15 patients, which finally, due to the small number, was decided not to be included in the study. Mean age was 49.1 ± 14.6 years and 14.9% were males. They suffered mainly from three thyroid diseases: HT (n = 160), non-autoimmune thyroid disease (NAITD, n = 159) and GD (n = 97) at different phases (Figure 1 & Table 1). Twenty-seven gender-matched healthy controls (11.1% males, mean age 39.0 ± 16.0 years) were also recruited mainly from Greece and Romania.

NAITD patients with or without thyroxine treatment had an enlarged thyroid gland with negative thyroid Abs and all thyroid hormones were normal. The group of HT included newly diagnosed patients before any treatment (26) and patients on LT4 treatment (134). This group also included HT patients after thyroidectomy. The diagnosis of HT was mainly established by positive thyroid Abs and appropriate findings on thyroid ultrasound. Finally, the GD group included novel GD patients before any treatment (in hyperthyroid condition) with or without GO (19) and GD patients on antithyroid drugs with or without GO (78). GD patients after radioactive iodine therapy or thyroidectomy and now on any type of treatment or off treatment were also included in this group.

Patients on thyroxine or antithyroid drugs were euthyroid at the stage of investigation.

Patients with different systemic diseases like diabetes mellitus, heart problems, rheumatic diseases or on any pharmacological treatment were excluded from the study. However, patients with mild forms of systemic diseases who occasionally received or are at the moment on some type of treatment – for example, anti-hypertensive drugs – were included in the study.

Details of recruitment process & blood collection

In each center, patients with thyroid diseases who had an official appointment at the thyroid clinic independently if they were new patients or had a follow-up appointment were asked to participate in the study and after obtaining informed consent full details regarding past and present history of disease, family history, investigation and treatment were recorded. None of the patients was on selenium or iodine dietary supplements or had received such compounds in the last year. After clinical examination, a fasting venous blood sample was taken between 9 and 10 h. Within 1 h of collection, samples were centrifuged and frozen in aliquots at –20°C.

Also, a morning urine sample in a sterile urine container was taken and from this specimen a small portion was sent to the local laboratory for creatinine measurement, while another specimen was kept at –20°C for iodine measurement. Finally, a thyroid ultrasound was performed on all patients on an outpatient basis.

Few normal individuals mainly from the Hospital staff from Greece and Romania were participated in the study acting as controls.

At the end of the recruitment period, which lasted 6–9 months, all specimens were forwarded to Thessaloniki and from there transportation was arranged for plasma specimens to be sent to Berlin for Se status measurements, while urine specimens were forwarded to Vienna for iodine measurements. Both analytical centers and the laboratory staff were blinded with respect to the clinical diagnosis of the patients.

Se status was assessed by quantifying total plasma Se (p-Se) and selenoprotein P (p-SePP) concentrations. p-Se and p-SePP were measured at Charité – Universitätsmedizin Berlin, Institute for Experimental Endocrinology, Berlin, while urine iodine levels were determined at the Institute of Laboratory Medicine at the Medical University of Vienna.

TSH, FT4 and thyroid Abs were measured by radioimmunoassay or immunometric assay or two-site ultra-sensitive ELISA at the local laboratory of each country. Normal ranges for the latter measurements were different in each country and for this reason in the statistical analyses in order to homogenize the results only three categories were used for those measurements: normal, high or low.

P-Se was determined by total reflection x-ray fluorescence analysis using a benchtop total reflection x-ray fluorescence analyzer (S2 Picofox, Bruker Nano GmbH, Berlin, Germany) [15]. For p-SePP measurement, an ELISA assay based on monoclonal Abs was used essentially as described [16]. Validation procedures have been described [17].

No reference intervals for normal SePP values have ever been established; depending on the general average nutritional Se intake, such intervals will likely differ from country to country. A small study in healthy Europeans from the UK claims that mean SePP was 4.99 ± 0.80 μg/ml as determined in 54 healthy men and 65 healthy women displaying a slightly higher Se status than our probands [18].

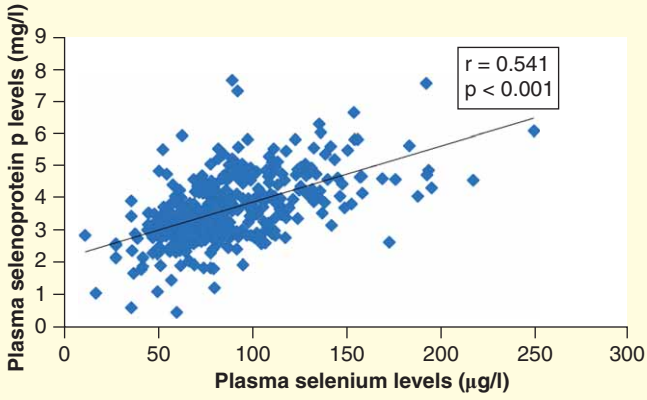

Figure 2. Correlation between plasma selenium and selenoprotein p levels.

Urine iodine levels were measured by a fast photometric assay based on the Sandell-Kolthoff reaction as described elsewhere [19]. Concentrations expressed as absolute concentrations (μg/dl) by creatinine were used as an index of iodine intakes. Creatinine levels were measured locally at each country at the initial phase of collection of urine. Creatinine measurement was done by a photometric method.

Ethical approval was obtained from the ethical committee of each hospital.

Statistical analysis

Data analysis was performed with the statistical package SPSS (version 17.0; SPSS Inc., Chicago, IL, USA). Data are reported as mean ± SD. Differences between groups were assessed with one-way analysis of variance with the Holm-Šídák method for multiple comparison testing. Correlations between parameters were assessed with Pearson's correlation. In all cases, a p value < 0.05 was considered significant.

Results

A total of 416 thyroid patients and 27 controls were recruited from 4 European countries. The characteristics of the study population are presented in Table 1.

In patients, p-Se and p-SePP concentrations showed a strong positive correlation (Figure 2) ($r = 0.541$; $p < 0.001$) indicating that the Se status of our patients was below the level needed for full expression of selenoproteins.

p-Se levels in our cohort of patients were 86.7 ± 37.1 μg/l. p-Se levels did not differ between males and females (89.7 ± 29.6 vs 84.6 ± 38.5 μg/l) but correlated positively with age ($r = 0.136$; $p < 0.01$) (Figure 3A).

p-SePP levels were 3.6 ± 1.0 mg/l. p-SePP levels were higher in males than in females (4.0 ± 1.0 vs 3.5 ± 1.0 mg/l, respectively; $p < 0.001$) and correlated positively with age ($r = 0.355$; $p < 0.001$) (Figure 3B).

p-Se, p-SePP, urine iodine levels and urine iodine/creatinine ratios in patients with NAITD (159), HT (160) and GD (97) from the 4 participating countries and their comparisons are presented in Table 2.

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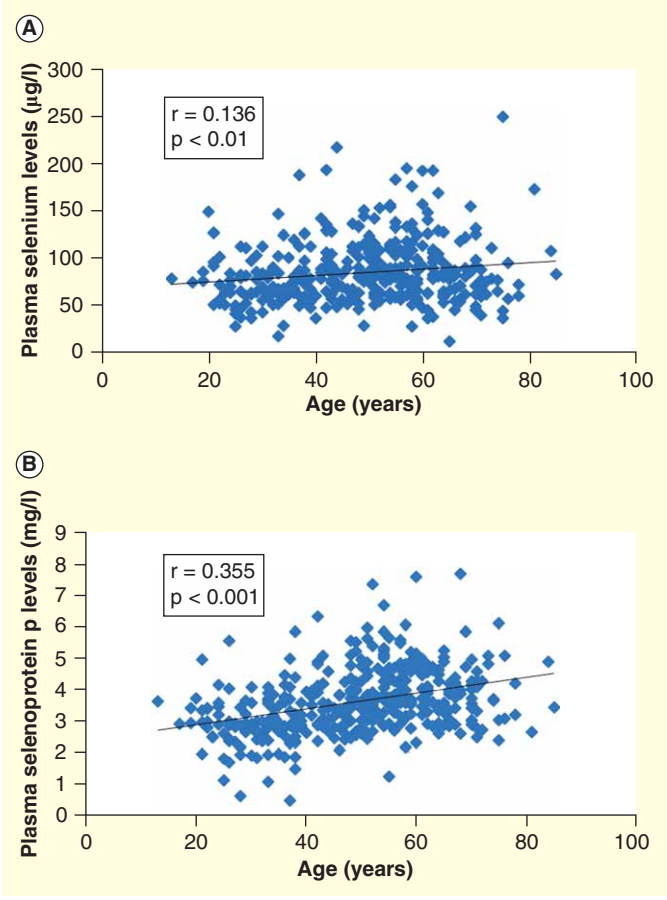

Figure 3. Correlation between plasma selenium (A) and selenoprotein p levels (B) and age.

p-Se and p-SePP levels differed significantly between patients with HT, GD and NAITD. In *post hoc* tests, p-Se and SePP levels were lower in patients with HT and GD than in patients with NAITD (84.6 ± 42.2, 75.1 ± 27.2 and 95.9 ± 34.7 µg/l, respectively; $p < 0.05$ and $p < 0.001$, respectively; and 3.3 ± 0.9, 3.5 ± 0.8 and 4.0 ± 1.0 mg/l, respectively; $p < 0.001$ for both comparisons) (Table 2).

p-Se levels did not differ in GD and HT patients with high levels of thyroid peroxidase (TPO) and thyroid-stimulating hormone receptor Abs in comparison with those with normal levels. On the contrary, p-SePP levels were lower in patients with elevated levels of TPO Abs in comparison with normal levels, but only in HT patients, not in GD. No differences were found in p-SePP concentrations between patients with high and normal levels of thyroid-stimulating hormone receptor and thyroglobulin Abs.

In contrast, p-Se levels were lower in patients with elevated levels of thyroglobulin Abs than in patients with normal levels (64.5 ± 11.1 and 87.1 ± 27.1 µg/l, respectively; $p < 0.05$).

p-Se and p-SePP levels did not correlate with UI/C levels in the total patient population from all countries (n = 416) or when patients with NAITD (n = 159), HT (n = 160) or GD (n = 97) from all countries were analyzed separately.

Moreover, no difference was found between newly diagnosed untreated patients and euthyroid patients on treatment among patients with HT and GD, except p-SePP levels in newly diagnosed GD, which were lower (3.1 ± 0.8 vs 3.8 ± 0.9 mg/l).

Finally, p-Se levels were higher in patients with GO than in patients without GO (80.5 ± 22.9 and 63.3 ± 15.8 µg/l, respectively; $p < 0.005$), while no difference was found in p-SePP (3.5 ± 0.8 and 3.2 ± 0.7 mg/l, respectively; p = not significant).

Regarding p-Se and p-SePP levels in controls, although the number of normal individuals is small and thus without sufficient statistical power, no difference was found when compared with thyroid patients (Table 1).

Discussion

In the present study, we measured p-Se and urinary iodine status in a European cohort of patients with different thyroid diseases and compared the results of patients with autoimmunity and without. In order to assess the Se status, we have determined two meaningful biomarkers from plasma, that is, total p-Se and p-SePP. As expected from European individuals, we observed a linear correlation of both parameters verifying the less-than-optimal Se status of the patients. This is in contrast to healthy subjects residing in Se-rich areas like the USA, for example, where Se and SePP concentrations do not correlate as selenoproteins are fully expressed by a sufficiently high Se intake [20].

p-Se and p-SePP levels were lower in patients with HT and GD in comparison with NAITD patients. However, Se status did not differ between patients with HT and GD, although GD patients had lower levels in comparison with HT patients. Regarding TPO Abs, only p-SePP differed between HT patients with elevated levels compared with those with normal levels, the former having lower levels (Table 3).

Of around 11 trials of Se supplementation in patients with HT, 7 have shown benefit, that is, decreased anti-TPO titer, which indicates that high Se levels in the blood is associated with low TPO levels. Of note, the methodology of many of these studies was flawed and all Se trials were in region of low-medium Se status. Iodine status was not always described. It has to be emphasized that the beneficial effect in some studies and not in others cannot easily be explained on the basis of baseline Se status, baseline anti-TPO titer, stage of disease, form and dose or compound of Se used [21–31].

Our findings of low p-Se status in patients with HT compared with patients with NAITD and also low p-SePP levels in patients with elevated TPO Abs are indirectly in line with many of the above reports, which have shown that high Se levels are associated with low TPO levels and would support the explanation of the beneficial effect of Se supplementation in patients suffering from HT.

Regarding GD, in a small study by Kucharzewski *et al.* [32], the authors found that 18 females with GD had lower s-Se than patients with multinodular goiter or thyroid cancer. A recent study from Denmark [33] investigated 97 patients with newly diagnosed GD, 96 patients with newly diagnosed autoimmune overt hypothyroidism and controls. They found a

Table 2. Plasma selenium status, urine iodine levels and urine iodine/creatinine ratios in the total number of patients as well as in patients with non-autoimmune thyroid disease, Hashimoto thyroiditis and Graves' disease from different countries.

	Total (n = 416)	Austria (n = 83)	Greece (n = 180)	Italy (n = 77)	Romania (n = 76)	p-value (overall)
p-Se (μg/l)						
All patients	86.7 ± 37.1 (n = 416)	83.4 ± 28.6 (n = 83)	79.9 ± 40.9 (n = 180)	112.3 ± 34.9 (n = 77)	80.9 ± 25.9 (n = 76)	<0.001
NAITD	95.9 ± 34.7 (n = 159)	93.4 ± 31.2 (n = 25)	82.3 ± 27.8 (n = 56)	116.8 ± 34.2 (n = 56)	80.4 ± 31.0 (n = 22)	<0.001
HT	84.6 ± 42.2 (n = 160)	83.1 ± 31.2 (n = 36)	81.3 ± 50.7 (n = 81)	106.0 ± 41.9 (n = 13)	86.6 ± 23.3 (n = 30)	NS
GD	75.1 ± 27.2 (n = 97)	72.4 ± 14.6 (n = 22)	74.1 ± 34.2 (n = 43)	90.9 ± 19.8 (n = 8)	74.2 ± 23.0 (n = 24)	NS
p-SePP (mg/l)						
All patients	3.6 ± 1.0 (n = 416)	3.5 ± 0.9 (n = 83)	3.3 ± 0.9 (n = 180)	4.4 ± 0.8 (n = 77)	3.7 ± 0.9 (n = 76)	<0.001
NAITD	4.0 ± 1.0 (n = 159)	3.8 ± 1.2 (n = 25)	3.6 ± 0.9 (n = 56)	4.5 ± 0.7 (n = 56)	3.8 ± 1.2 (n = 22)	<0.001
HT	3.3 ± 0.9 (n = 160)	3.3 ± 0.8 (n = 36)	3.1 ± 0.9 (n = 81)	4.1 ± 1.2 (n = 13)	3.7 ± 0.9 (n = 30)	<0.001
GD	3.5 ± 0.8 (n = 97)	3.6 ± 0.6 (n = 22)	3.4 ± 0.9 (n = 43)	4.4 ± 0.8 (n = 8)	3.4 ± 0.8 (n = 24)	<0.05
Urine iodine (μg/dl)						
All patients	22.6 ± 49.4 (n = 416)	8.4 ± 6.9 (n = 83)	21.1 ± 13.6 (n = 180)	45.2 ± 104.4 (n = 77)	19.2 ± 21.5 (n = 76)	<0.001
NAITD	18.0 ± 34.0 (n = 159)	9.2 ± 8.3 (n = 25)	17.8 ± 12.0 (n = 56)	24.2 ± 53.0 (n = 56)	13.4 ± 8.9 (n = 22)	NS
HT	23.9 ± 55.6 (n = 160)	9.3 ± 7.4 (n = 36)	20.8 ± 11.6 (n = 81)	86.7 ± 174.5 (n = 13)	21.6 ± 23.6 (n = 30)	<0.001
GD	27.7 ± 58.5 (n = 97)	5.9 ± 3.4 (n = 22)	25.9 ± 17.8 (n = 43)	126.6 ± 173.9 (n = 8)	21.3 ± 25.9 (n = 24)	<0.001
Urine iodine/ creatinine ratio						
All patients	0.3 ± 0.8 (n = 416)	0.1 ± 0.1 (n = 83)	0.2 ± 0.4 (n = 180)	0.7 ± 1.7 (n = 77)	0.2 ± 0.3 (n = 76)	<0.001
NAITD	0.2 ± 0.5 (n = 159)	0.1 ± 0.1 (n = 25)	0.2 ± 0.2 (n = 56)	0.3 ± 0.9 (n = 56)	0.1 ± 0.1 (n = 22)	NS
HT	0.3 ± 1.0 (n = 160)	0.1 ± 0.1 (n = 36)	0.3 ± 0.5 (n = 81)	1.3 ± 3.0 (n = 13)	0.2 ± 0.2 (n = 30)	<0.001
GD	0.3 ± 0.8 (n = 97)	0.1 ± 0.1 (n = 22)	0.2 ± 0.1 (n = 43)	1.7 ± 2.3 (n = 8)	0.3 ± 0.4 (n = 24)	<0.001

Significant differences in *post-hoc* comparisons between patients from different countries with the same thyroid disease.
pSe in NAITD patients: Italy vs Austria: $p < 0.05$, Italy vs Greece and Romania: $p < 0.001$.
p-SePP in NAITD patients: Italy vs Austria and Romania: $p < 0.05$, Italy vs Greece: $p < 0.001$.
pSePP in HT patients: Italy vs Austria: $p < 0.05$, Italy vs Greece $p < 0.005$, Greece vs Romania: $p < 0.05$.
Urine iodine in HT patients: Italy vs Austria and Greece $p < 0.001$, Italy vs Romania: $p < 0.005$.
UI/C in HT patients: Italy vs Austria: $p < 0.001$, Italy vs Greece and Romania: $p < 0.005$.
p-SePP in GD patients: Italy vs Greece: $p < 0.01$, Italy vs Romania: $p < 0.05$.
Urine iodine in GD patients: Italy vs Austria, Greece and Romania: $p < 0.001$.
UI/C in GD patients: Italy vs Austria, Greece and Romania: $p < 0.001$
GD: Graves' disease; HT: Hashimoto thyroiditis; NAITD: Non-autoimmune thyroid disease; NS: Not significant; p-Se: Plasma selenium; p-SePP: p-Selenoprotein P.

significantly lower s-Se in patients with GD compared with controls (89.9 vs 98.8 μg/l, $p < 0.001$). They concluded that patients with newly diagnosed GD had a considerable lower s-Se than the other groups of participants [33]. This finding may relate to the recently reported effect of thyroid hormones on selenoprotein expression, as shown in respective transgenic mouse models [34]. Moreover, they found no difference in s-Se between treated and not treated patients with GD.

Our results confirm and extend the above findings pointing out an effect of thyroid hormones on SePP in humans.

Of interest are our findings that Italy had the highest levels of Se status and UI/C in comparison with the other three countries. In previous reports from different areas of Italy (not from Rome), it was found that control individuals had Se levels within the recommended range of 70–92 ng/ml, similar to most other western (as used to be called) European countries [35]. However, in the recent IMMIDIET study [36] in which healthy Italian, Belgian and British women were analyzed, the authors reported higher Se status (95.6 μg/l) in Italian females, which may explain our results. Of note, in this study Italy had the higher proportion of patients with NAITD (73%) in comparison with the other three countries, which may also explain this difference. It should be mentioned that patients recruited from the two different Italian hospitals had similar results.

We also found that Se status correlated positively with age, which is in line with findings from most similar studies [16,37–39]. Age has also been described to represent an important factor for the sexual dimorphic selenoprotein biosynthesis in experimental mice [40]. Furthermore, an inter-relationship of p-Se with sex hormone secretion has been reported [41]. However, in a recent study from Greece [42], no association was found between s-Se levels and the gender and also they observed a significant decline of Se with age. However, as most of the above studies, as well as this study, are cross-sectional, they generate only hypotheses for further clinical research.

Iodine status has not been measured in most studies, with the exception of the Italian study in which the majority of patients had a urine iodine excretion ≥100 μg/24 h and a modest reduction in TPO Abs at 12 months [29]. No significant interactions have been observed between s-Se concentrations and iodine status in humans [43]. This study supports this notion.

In contrast to our expectations, p-SePP levels were also similar in GD patients with GO in comparison with those without GO, while p-Se was elevated. However, as Se values do not directly

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Table 3. Plasma selenium status in patients with elevated levels of thyroid peroxidase antibodies and in patients with normal levels of thyroid peroxidase antibodies.

	Patients with HT and elevated levels of TPO Abs	Patients with HT and normal levels of TPO Abs	p-value
p-Se (μg/l)	85.3 ± 33.1	156.1 ± 46.0	NS
p-SePP (mg/l)	3.5 ± 0.9	4.9 ± 0.6	<0.001
	Patients with GD and elevated levels of TPO Abs	**Patients with GD and normal levels of TPO Abs**	**p-value**
p-Se (μg/l)	75.9 ± 23.9	77.8 ± 25.2	NS
p-SePP (mg/l)	3.4 ± 0.8	3.9 ± 0.9	NS

Abs: Antibodies; GD: Graves' disease; HT: Hashimoto thyroiditis; NS: Not significant; p-Se: Plasma selenium; p-SePP: p-Selenoprotein P; TPO: Thyroid peroxidase.

reflect tissue concentrations [33], normal blood Se status values do not exclude in our patients low retrobulbar Se concentrations. Most importantly, the number of patients with GO in our study is too small to draw firm conclusions on this important issue.

It would have been of interest to measure Se metabolites in the urine, measurements which might had been provided useful information, for example, increased excretion of Se in the HT and GD patients. Although that was at our original goals, unfortunately, for reasons over our will, we failed to materialize it.

Conclusion

In this cross-sectional, prospective, European study concerning thyroid patients, a linear correlation of p-Se and p-SePP was found indicating the less than optimal Se status in this cohort of patients. Patients with GD and HT had significantly lower Se status compared with NAITD patients. Italy had the highest levels of Se, SePP, UI and UI/C among the participating countries. Se status correlated positively with age, while no association was found between Se status and UI/C. Inconclusive results were demonstrated between GD patients with and without GO.

The lower levels of Se status in HT and GD patients suggest that Se supplementation may be useful in these patients. However, meaningful clinical outcomes should be demonstrated before Se supplementation can be routinely suggested in patients with thyroid autoimmunity.

Expert commentary & five-year view

In this study it was found that p-Se and p-SePP showed positive correlation and did not correlate with UI/S. Also, these measurements were higher in patients from Italy in comparison with other countries. The message from these results is that Se deficiency exists in these four European countries, although Italy is in a better status. In five years time and after increasing Se consumption these countries should be sufficient in Se.

Se status was lower in patients with AITD in comparison with NAITD patients. These findings suggest that Se supplementation might have a beneficial effect on AITD patients and this is expected to be confirmed in five years time after administration of sufficient amount of Se.

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Financial & competing interests disclosure

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Key issues

- Plasma selenium and selenoprotein P concentrations are correlated well, which means that the area from which these patients are coming from is selenium deficient.
- Another interesting finding is that selenium status does not correlate with urine iodine.
- However, selenium status was lower in patients with Hashimoto thyroiditis and Graves' disease than in patients with non-autoimmune thyroid disease.
- The latter finding may explain why selenium supplementation has a beneficial effect in patients with Hashimoto thyroiditis and Graves' ophthalmopathy, which has been reported so far.

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•• of considerable interest

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