Use of plasma iodine assay for diagnosing thyroid disorders

P Allain, S Berre, N Krari, P Lainé-Cessac, A Le Bouil, N Barbot, V Rohmer, J C Bigorgne

Abstract

***Aims*—To examine the advantage of systematic plasma iodine assays in establishing the thyroid function of patients with thyroid disorders.**

***Methods*—Iodine was determined by inductively coupled plasma mass spectrometry (ICPMS) in the plasma of 799 patients consulting for possible thyroid disorders, indicated by FT4 and TSH assays.**

***Results*—Plasma iodine was below 40 μg/l in 57 (7%) patients, most of whom had hypothyroidism; 40–80 μg/l in 439 (55%) patients, most of whom had normal thyroid hormone function; 80–250 μg/l in 240 (30%) patients, most of whom had hyperthyroidism; and above 250 μg/l in 63 (8%) patients, almost all of whom had iodine overload caused by iodinated drugs, particularly amiodarone, resulting in euthyroidism (24%), hyperthyroidism (36%), and hypothyroidism (16%). Sixty five (7%) had been treated with amiodarone and 27 (3%) with other iodinated drugs. More than 10% of patients with thyroid disorders therefore had an iodine overload.**

***Conclusions*—The determination of total plasma iodine using the simple, accurate ICPMS technique, should be carried out in patients consulting for thyroid disorders, particularly for the detection of an iodine overload.**

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The concentration of total plasma iodine in healthy subjects is between 40 and 80 μg/l,[1] but plasma iodine assays are not routinely applied and no systematic studies have been made in patients with thyroid disorders. Even in reports on excessive iodine intake from drugs, such as amiodarone, there are generally no data on plasma. The usual practice is to determine iodine in 24 hour urine samples, probably because this is easier than extracting the data from plasma.

Methods

Between June 1989 and December 1990, 799 patients consulting for thyroid disorders underwent plasma iodine assays in addition to the usual investigations such as free thyroxine (FT4) and thyrotropin hormone (TSH) measurements. The data were obtained at the first examination of the patients during the study period, even if many of them had already been examined and treated for thyroid disorders.

The use of inductively coupled plasma mass spectrometry (ICPMS) for plasma iodine assays has been described recently.[1] Briefly, the sample preparation consisted of a 10–fold dilution of 200 μl of plasma with 1800 μl of a diluent containing 1% nitric acid and 25 μg/l of europium, used as an internal standard. The diluted plasmas were nebulised into the torch, and iodine and europium ions were measured at m/z = 127 and 153, respectively, with an ICPMS prototype from Nermag (Argenteuil, France). Mean (SD) plasma iodine concentrations in healthy subjects were 58 (12) μg/l, which agrees with other published data.[1]

FT4 and TSH were measured using commercial kits (Amerlite, Amersham) based on enhanced luminescence immunoassays.

Results

The results are summarised in table 1. The patients were divided into four groups according to their plasma iodine concentrations (<40 μg/l, 40–80 μg/l, 80–250 μg/l and >250 μg/l). Possible exposure to excessive iodine is indicated for patients with a plasma iodine above 80 μg/l.

Among the 799 patients studied, 57 (7%) had a plasma iodine concentration below 40 μg/l, 439 (55%) between 40 and 80 μg/l, 240 (30%) between 80 and 250 μg/l, and 63 (8%) above 250 μg/l.

Group I, mean (SD) plasma iodine concentrations were 27 (10) μg/l: 60% of the patients had hypothyroidism and 22% had normal FT4 and TSH activities. Notably, however, of the 13 patients with normal hormone function and iodine concentrations below 40 μg/l, 10 had iodine concentrations between 32 and 40 μg/l—nearly normal values.

In group II, mean (SD) plasma iodine concentrations were 60 (10) μg/l: 63% had normal hormone function while the others had hyperthyroidism (6%), hypothyroidism (3%), or an unrelated condition with normal TSH and abnormal FT4 values, or vice versa (25%).

In group III, mean (SD) plasma iodine concentrations were 128 (42) μg/l: 60% had hyperthyroidism and 21% had normal thyroid function.

In group IV, the plasma iodine concentrations were above 250 μg/l, the mean value being 1 342 (1 755) μg/l. Thyroid hormone function was normal in about 24%, but 36% had hyperthyroidism and 16% hypothyroidism.

Table 1 shows that the patients with plasma iodine concentrations above 250 μg/l

Laboratoire de Pharmacologie, Centre Hospitalier Universitaire, F 49033 Angers Cedex 01 France
P Allain
S Berre
N Krari
P Lainé-Cessac
A Le Bouil
Service d'Endocrinologie
N Barbot
V Rohmer
J C Bigorgne
Correspondence to:
Professor P Allain

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Table 1 Number, age, percentage and percentage of total number (%T) of patients categorised by plasma iodine concentrations

		Group I Iodine <40 Mean (SD) 27 (10)	Group II 40<= iodine <= 80 µg/l Mean (SD) 60 (10)	Group III 80<iodine <= 250 µg/l Mean (SD) 128 (42)	Group IV Iodine>250 µg/l Mean (SD) 1342 (1755)	Total
Patients:	Number	57 (7%T)	439 (55%T)	240 (30%T)	63 (8%T)	799 (100 %T)
	Age (years)	57 (16)	51 (18)	49 (20)	72 (15)	52 (19)
Ratio Men : Women (r)		r = 0·208	r = 0·180	r = 0·176	r = 0·570	r = 0·205
	12 <= FT4 <= 26	13* (22%)	274 (63%)	51 (21%)	15 (24%)	353
0·15 <= TSH <= 4	FT4 < 12	5 (9%)	11 (2%)	2	0	18
	FT4 > 26	0	8	11 (5%)	4 (6%)	23
	12 <= FT4 <= 26	1	58 (13%)	20 (8%)	3 (5%)	82
TSH < 0·15	FT4 < 12	0	2	1	0	3
	FT4 > 26	1	27 (6%)	146 (60%)	23 (36%)	197
	12 <= FT4 <= 26	2	46 (10%)	5	6 (10%)	59
TSH > 4	FT4 < 12	35 (60%)	12 (3%)	3	10 (16%)	60
	FT4 > 26	0	1	1	2 (3%)	4
Exposure to excessive iodine:						
	Not found			206 (86%)	5 (8%)	
	Amiodarone			18 (7%)	47 (75%)	65 (8%T)
	Others			16 (7%)	11 (17%)	27 (3%T)

TSH (mUI/l) and FT4 (pmol/l): (*10 of the 13 patients had plasma iodine concentrations between 32 and 40 µg/l). The normal values for FT4 are 12–26 pmol/l and the normal values for TSH are 0·15–4 mUI/l.

Table 2 Patients (n = 66, 8%T) with euthyroidism (0·15 < TSH < 4 mUI/l and 12 < FT4 < 26 pmol/l) and iodine plasma concentrations above 80 µg/l

	Group III 80 < Iodine <= 250 µg/l		Group IV Iodine > 250 µg/l	
	Mean (SD) 117 (43)		Mean (SD) 1311 (1846)	
Patient numbers	n = 51 (6%T)		n = 15 (2%T)	
Sex	12 men	39 women	6 men	9 women
Age (years)	52 (19)	42 (18)	75 (9)	70 (20)
Exposure to excessive iodine:				
Not found	5	32	1	1
Amiodarone	7	3	4	4
Other drugs	0	4	1	4

Table 3 Patients (n = 169, 21%T) with hyperthyroidism (TSH < 0·15 mUI/l and FT4 > 26 pmol/l) and iodine plasma concentrations above 80 µg/l

	Group III 80 < Iodine <= 250 µg/l		Group IV Iodine > 250 µg/l	
	Mean (SD) 137 (42)		Mean (SD) 882 (671)	
Patient numbers	n = 146 (18%T)		n = 23 (3%T)	
Sex	21 men	125 women	5 men	18 women
Age (years)	51 (21)	48 (20)	74 (11)	68 (18)
Exposure to excessive iodine:				
Not found	15	120	0	2 (1 < 300 µg/l)
Amiodarone	5	1	5	14
Other drugs	1	4	0	2

tended to be older (72 (15) years) than the others (mean age about 50 years). The sex ratio in this group was 0·57 higher than the average of 0·18 for the other groups. In 86% of patients with plasma iodine concentrations between 80 and 250 µg/l, no exposure to excessive iodine was established. The high concentration in these patients was probably directly linked to thyroid hormone activity. In contrast, 92% of patients with plasma iodine concentrations above 250 µg/l (58 out of 63) had been exposed to excessive iodine from iodinated drugs, particularly amiodarone. Overall, 11% of the 799 patients consulting for thyroid disorders had iodine excess due to drug treatment.

Table 2 shows that 66 patients with normal thyroid hormone function had abnormally high plasma iodine concentrations. In the group with plasma iodine concentrations between 80 and 250 µg/l (n = 51), more often than not, exposure to iodinated drugs was not recorded; in the group with values above 250 µg/l (n = 15), iodinated drug use was found in 13 patients.

Table 3 shows that 169 patients (21% of the total) had hyperthyroidism and plasma iodine concentrations above 80 µg/l. Most of the patients with plasma iodine concentrations between 80 and 250 µg/l were women with no established exposure to excessive iodine, the high iodine concentrations probably resulting from Graves' disease. In patients with plasma iodine values above 250 µg/l, excessive exposure to iodinated drugs, particularly amiodarone, was almost always found. Two women for whom no excessive iodine intake was established had plasma iodine concentrations of 270 and 290 µg/l—values compatible with Graves' disease.

Table 4 shows that 13 patients (less than 2% of the total) had hypothyroidism and plasma iodine concentrations above 80 µg/l. Twelve had received iodinated drugs, usually amiodarone.

Discussion

We have taken into account three biochemical variables of thyroid disorders: plasma iodine, FT4, and TSH values. The main advantages of ICPMS in plasma iodine assays are that it is a direct method, requiring only a simple dilution, and that it permits simultane-

Table 4 Patients (n = 13, <2%T) with hypothyroidism (TSH > 4 mUl/l and FT4 < 12 pmol/l) and iodine plasma concentrations above 80 µmg/l

	Group III 80 < Iodine < 250 µg/l		*Group IV Iodine > 250 µg/l*	
	(Mean (SD) 144 (47)		*Mean (SD) 1638 (1161)*	
Patient numbers	n = 3 (<0·4%T)		n = 10 (<1·5%T)	
Sex	0 men	3 women	3 men	7 women
Age (years)		40 (13)	75 (5)	74 (17)
Exposure to excessive iodine:				
Not found	0	1	0	0
Amiodarone	0	0	2	6
Other drugs	0	2	1	1

ous determination of iodine and bromine. The technique determines total iodine—that is, iodide and iodine incorporated into thyroid hormones and into iodinated drugs. A thyroxine concentration of 80 µg/l, a normal value, corresponds to 52 µg/l of iodine.

The plasma iodine concentrations used as criteria for categorising the patients into four groups are only tentative. They are not entirely satisfactory, particularly when the results are close to normal values. Thus 22% of the patients with plasma iodine concentrations below 40 µg/l had normal thyroid hormone function, but in fact most of them had concentrations between 32 and 40 µg/l—that is, close to normal. Plasma iodine concentrations above 80 µg/l and even above 250 µg/l are compatible with hormonal euthyroidism, but values between 80 and 250 µg/l are strongly suggestive of hyperthyroidism, and values above 250 µg/l are almost always found in patients treated with iodinated drugs.

When plasma iodine concentrations are higher than 250 µg/l, there is no simple relation between iodine concentration and hormone function. Indeed, the mean plasma iodine concentration in patients with hyperthyroidism was 882 (671) µg/l, whereas it was 1311 (1864) mg/l and 1636 (1161) mg/l, respectively, in patients with hormonal euthyroidism and hypothyroidism. Thus very high plasma iodine concentrations do not always attend hyperthyroidism.

The drug most often implicated in iodine overload is amiodarone: 8% of the 799 patients were taking or had taken this drug. It has been reported that during treatment the amiodarone concentration may reach 3 mg/l,[2] which corresponds to 1125 µg/l of iodine because amiodarone contains 37% iodine. Moreover, iodide is progressively released from the amiodarone molecule stored in tissues.[3] The plasma half-life of amiodarone itself is about 25 days.[4 5]

Soon after it was introduced into Europe some 20 years ago, it was recognised that amiodarone may induce hyperthyroidism and sometimes hypothyroidism.[6-9] Several authors[10 14] have recently shown that the prevalence of thyroid disorders in patients treated with amiodarone may be as high as 20%.

Iodine overload from amiodarone is easily suspected and found in patients, often men, treated with this drug for cardiac disorders, but iodine overload from other drugs is difficult to assess because of the large number of iodinated drugs in use. Moreover, the presence of iodine is not always indicated on the packaging. In some cases amiodarone may not be suspected because thyroid disorders could develop even after treatment has been stopped.

In our study 11% of the patients consulting for thyroid disorders had been exposed to excessive iodine from drugs. Thus systematic determination of plasma iodine is clearly important. Indeed, whenever a plasma iodine concentration is above 250 µg/l, the probability that an iodinated drug has been used is very high.

In conclusion, when plasma iodine concentrations are below 40 µg/l, hypothyroidism is highly likely, when they are between 80 and 250 µg/l, hyperthyroidism, particularly Graves' disease, is probable, and when they are above 250 µg/l iodine overload is almost certainly indicated.

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