Observational study of the initial management of hypothyroidism in France: the "Orchidée" study

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Introduction

General practitioners or endocrinologists are regularly confronted with hypothyroidism in their daily practice and literature review has shown that 4-10% of the adult population may be affected. The objective of the study was to describe the modalities of the initial management of hypothyroidism in France.

Method

This was a descriptive study on patients with hypothyroidism initiating a treatment with thyroid hormones or having started this treatment within the past 6 months. Patients were then prospectively followed up until first TSH test after initiation of replacement treatment.

The study was proposed to 120 endocrinologists working in private, hospital or both private and hospital settings, and to 500 private practice general practitioners. Physicians were randomly recruited from a representative national sample. All physicians could include up to 5 consecutive patients showing hypothyroidism.

Results

254 GPs out of 500 and 82 endocrinologists out of 120 included at least 1 patient.

The physician distribution was comparable to that of the survey basis used.

• Analyzable population

1284 patients were included in the study from 30 October 2008 to 5 February 2009. Following non-compliance with inclusion criteria, the analysis was performed on 1255 patients, respectively 835 for GPs and 420 for endocrinologists.

• General characteristics of the patients

The proportion of women among the 1 255 patients to be analyzed was 84.4% with 1.6% of pregnant women. Mean patient age was 52.82 ± 16.30 years. The patients included by GPs were older (54 years ± 16.14) than those included by endocrinologists (50 years ± 16.14 p<0.001).

Body mass index was 24.98 ± 4.95 for all subjects.

Associated diseases were high blood pressure (27%), hypercholesterolemia (27.9%), smoking history (22%) and diabetes (6.6%).

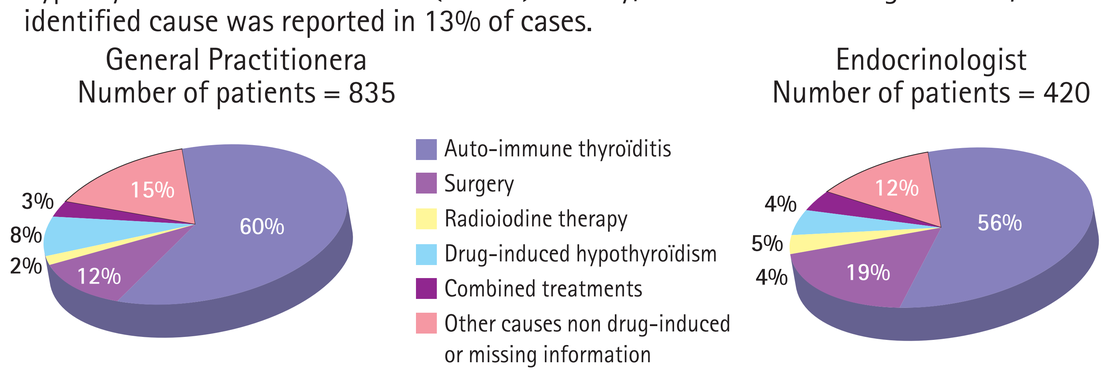
• Circumstances of diagnosis (table 1)

Evidence of clinical signs evoking hypothyroidism was the most frequent circumstance (76.6%). Some differences were observed between GPs and endocrinologists: GPs diagnosis of hypothyroidism was more frequently based on clinical signs and that of endocrinologists on an associated thyroid disease.

Circumstances of hypothyroidism diagnosis	GP N = 835 patients	Endocrinologist N = 420 patients	p
Suspicion of hypothyroidism in view of the clinical and/or biological signs	673 (80.7%)	288 (68.6%)	<0.001
Detection of goiter	157 (18.8%)	40 (9.5%)	<0.001
Patient already known for a thyroid disease whether associated or not:	141 (16.9%)	121 (28.8%)	<0.001
• Thyroid nodule	55 (6.6%)	27 (6.4%)	
• Euthyroid goiter	29 (3.4%)	20 (4.7%)	
• Thyroid cancer	9 (1.0%)	12 (2.8%)	
• Hyperthyroidism	34 (2.8%)	43 (10.2%)	
Other circumstances of diagnosis	45 (5.4%)	52 (12.4%)	<0.001

• Main causes listed

The most common cause of hypothyroidism was autoimmune thyroiditis (59%) followed by the consequences of thyroidectomy. The most frequently reported drug for drug-induced hypothyroidism was Cordarone (14.5%). Finally, another non iatrogenic and/or non identified cause was reported in 13% of cases.



• Clinical signs

Reported clinical signs were by order of frequency: fatigue (89%), weight gain (53.4%), digestive disorders (34.7%), cold intolerance (33.2%), muscular impairment (27.6%), skin changes (24.8%), neurological signs (13.4%), and cardiovascular signs (8.4%).

Table 2: Clinical signs of hypothyroidism

	N = 1255
Fatigue	89.0%
Weight gain	53.4%
Digestive disorders	34.7%
Cold intolerance	33.2%
Muscular impairment	27.6%
Skin changes	24.8%
Neurological signs	13.4%
Cardiovascular signs	8.4%

• Additional biological and morphological examinations of the thyroid

TSH measurement and thyroid ultrasonography were the basic exploratory examinations. Scintigraphy was less frequently conducted, especially by endocrinologists.

TSH was assayed prior to the prescription of hormone replacement therapy in 92% of cases (test not performed after thyroidectomy). Median TSH was 8.51 mIU/L, showing that more than half of the patients probably had a subclinical hypothyroidism. Free T4 levels were still assayed in more than 50% of cases, which might correspond to this subclinical hypothyroidism setting.

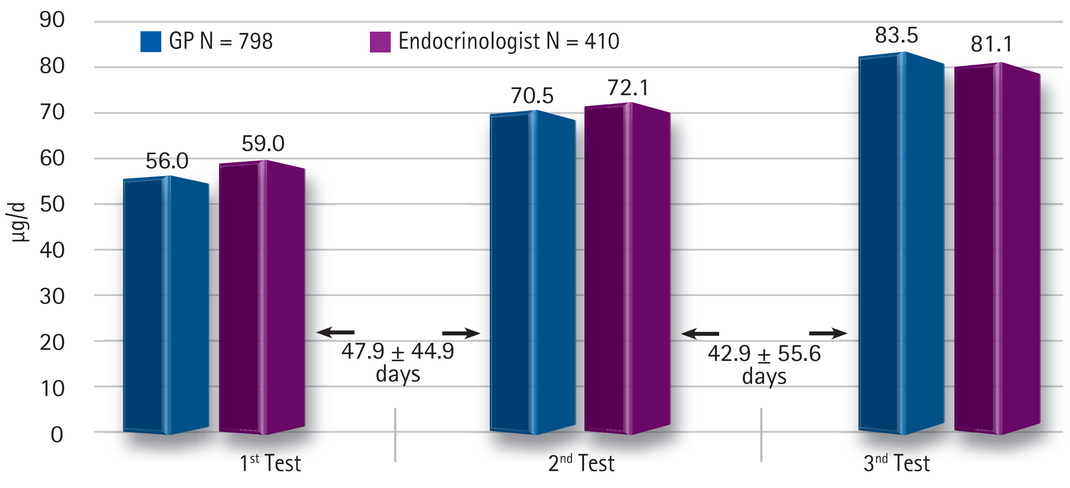
Table 3: TSH test

	GP N = 835	Endocrinologist N = 420	p
TSH mIU/L – Standard (0.4 – 4)	780 (94.8%)	356 (86.4%)	
• Mean (SD)	24.63 (114.28)	20.15 (39.31)	
• Median	8.63	8.1	
Free T4 (pmol/L)	426 (51.4%)	252 (60.9%)	0.0017
• Mean (SD)	9.60 (9.85)	9.30 (6.92)	
• Median	8.95	9.03	
Antithyroperoxydase antibodies	468 (59.4%)	289 (71.6%)	<0.001
• Positive	316 (67.6%)	210 (72.6%)	
Antithyroglobulin antibodies	415 (54.0%)	190 (49.2%)	0.1692
• Positive	247 (59.5%)	122 (64.2%)	
Morphological examinations	652 (78.1%)	304 (72.4%)	0.0252
• Thyroid ultrasonography	641	295	0.2001
• Thyroid scintigraphy	151	29	<0.001

• Treatment

Thyroxin (Lévothyrox®) was the most frequently prescribed drug (98.3% of patients).

Figure 2: Mean daily dose of thyroxin and time interval between 2 titrations



The average starting dose was 57 µg/d (0.84 µg/kg) with for half of the patients a prescribed dose lower than 50 µg/d, escalated to 71 µg/d for the 2nd titration and then to 83 µg/d for the 3rd titration. The duration between each titration was about 6 weeks, with a median of 1 month.

The prescription of thyroid hormones was associated with counseling in 46.9% of patients.

• Biological monitoring

A control of TSH levels was reported in 94.4% of patients, generally 2 to 3 months after treatment initiation. The first assay showed a clear improvement of hypothyroidism, as the mean result decreased from 23.2 mIU/L before treatment initiation to 6.8 mIU/L after treatment initiation.

Free T4 levels were assayed in more than half of the patients with a mean result of 9.49 pmol/L before treatment to 12.38 pmol/L two months and half after treatment.

Table 4: Assay of TSH and free T4 levels after treatment

	N = 1208
TSH test performed after treatment initiation (mIU/L)	1140 (94.4%)
Mean	6.83 (43.66)
Median	3.0
Free T4 test performed after treatment initiation (pmol/L)	602 (49.8%)
Mean	12.38 (10.98)
Median	12.77

Conclusion

This was the first study performed in France on the modalities of the initial management of hypothyroidism. This study enabled to collect the data of 1255 patients, mainly women with an average age of 50 to 55 years.

There were two emergent causes, the most common cause being autoimmune thyroiditis (more than half of cases), then the causes following a suppressive treatment (25% of cases), mainly thyroidectomy (14.5%), showing its significant importance in France. Only 8.5% of cases are were etiologically classified.

Diagnosis was based on TSH levels. Free T4 was still widely assayed and ultrasonography though not systematically recommended is plebiscited by physicians who include it in their diagnostic investigations. During follow-up visits, TSH was the reference test but free T4 was still assayed in more than half of cases.

This assessment included also the determination of antithyroid antibodies, mainly anti-TPO but also perhaps too widely anti-Tg.

Thyroxin (Lévothyrox®) was prescribed in more than 90% of cases.

The initial starting dose and the dose escalations comply with the recommendations. However, the mean interval between each dose escalation seems relatively long (6 weeks), compared to the recommendations (about 1 to 4 weeks) and in view of the low cardiovascular risk factors described in the treated population.

These data may constitute a concrete basis for the development of medical practices and also the evolution of management recommendations.

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