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Original Article

Nodular Goiter, Low T3 Syndrome and Uremia

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Abstract

Background. There are various changes in the thyroid gland and its function in chronic renal failure. The decrease of excretion of urinary iodine increases serum inorganic iodine level and iodine content of the thyroid, which consequently enlarges the gland, so there is a high incidence of thyroid nodular goiter in uremic patients.
The syndrome of low T3 is characterized by low levels of thyroid hormones, without clinical symptoms of thyroid insufficiency.
In this paper, we describe the thyroid gland structure by ultrasound, the incidence of low T3 syndrome and we investigate their possible relation to the duration of haemodialysis.
Methods. We studied 21 patients under haemodialysis and evaluated the sonographic structure of thyroid, duration of haemodialysis, age, gender, T3, T4, TSH, Free T3, Free T4 levels, and anti-thyroid antibodies.
Results. From the 21 studied patients (13 males, 8 females, mean age 60.14±15.93), 15 (71.43%; 9 males, 6 females), were identified with nodular goiter in contrast to the others 6 (28.57%, 5 males, 1 female).
Conclusions. Due to the high incidence of thyroid nodular goiter in patients undergoing haemodialysis, and frequent finding of sub clinical hypothyroidism, it is necessary to perform sonographic examination and thyroid function laboratory test in these patients.
Incidence of thyroid nodular goiter increases over the time spent on haemodialysis, while incidence of sick thyroid syndrome is high and being not associated with the duration of haemodialysis or the sonographic findings from the thyroid gland.

Keywords: haemodialysis; hypothyroidism; low T3 syndrome; nodular goiter; thyroid ultrasound

Introduction

In chronic renal failure (CRF), there are various changes in the thyroid gland and its function. These changes include lower levels of circulating thyroid hormone, altered peripheral hormone metabolism, decreased binding to carrier proteins, possible reduction in tissue hormone content, and increased iodine storage in the thyroid gland. The decrease of excretion of urinary iodine in CRF increases serum inorganic iodine level and iodine content of the thyroid, which consequently enlarges the gland.

Low T3 syndrome (sick euthyroid syndrome) affects patients in the absence of underlying thyroid disease. It is characterized by low levels of Thyroid Hormones (TH), without clinical symptoms of thyroid insufficiency and appears in patients suffering from various non-thyroid diseases. The syndrome is probably due to the reduction of T4 to T3 transformation from the hepatic system. The liver and the kidneys are responsible for the metabolism, the decomposition and the elimination of thyroid hormones and products of their catabolism. Kidneys take part in the desamination and decarboxylation of the thyroid hormones, the formation of tetraiodinated and triiodinated products of pyruvic and lactic acid, the binding of the thyroid hormones to lactic acid and the formation of metabolites circulating in blood and being eliminated in the bile, fecales and urine.
Patients with the above mentioned hormonal disorders and with several clinical features, which are common in patients with infectious diseases, heart failure and uremia (fatigue, anemia, grappa, edema, constipation, depression), should be suspected for hypothyroidism [1,2,3].
Our purpose was to report the incidence of low T3 syndrome and to investigate its possible association with the duration (years) of haemodialysis. We also used ultrasound to describe thyroid's gland structure and dimensions.

Patients and methods

We studied 21 uremic patients undergoing haemodialysis in our department (13 males, 8 females), mean age 60.14±15.93.
We evaluated the sonographic structure of the thyroid gland (nodular goiter, NG), duration of haemodialysis, age, gender, T3, T4, TSH, Free T3 and Free T4 levels, and anti-thyroid antibodies.

Results

From the 21 studied patients 15 (71.43%, 9 males, 6 females), were identified with nodular goiter in contrast to the others 6 (28.57%, 5 males, 1 female).
During our research only two patients suffering from hypothyroidism were detected (2/21, 9.52 %).
We found that patients with nodular goiter had increased mean duration on haemodialysis 3.45 years, while these without and were on haemodialysis for 1.58 years.
The incidence of sick thyroid syndrome is high (33.3% for both groups) and is not related with the duration of haemodialysis or the sonographic findings from the thyroid (Table 1).

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Table 1. Incidence of thyroid nodular goiter in patients under haemodialysis, the incidence of low T3 syndrome and their possible relation to the duration of haemodialysis

NG	Patients	%	M/F	Duration of Haemodialysis	Free T3 levels	%
With	15/21	71.43	9/6	3.45 years	5/15	33.33
Without	6/21	28.57	5/2	1.58 years	2/6	33.33
NG = Nodular Goiter, **M** = Males, **F** = Females						

Discussion

The thyroid hormones bound to TBG are not filtered by the kidneys. The TBG levels are normal in most diseases, while the diminished binding of TBG to T4 can be caused due to the presence of an inhibitor of the bounding of T4 to TBG. As known from the literature, 80% of the T3 derives from the peripheral deiodination of T4, a reaction catalyzed by the 5-monodeiodinase enzyme in organs such as the liver and kidneys. This enzyme is reduced in patients with severe malnutrition and some chronic non-thyroid diseases. Many mechanisms of suppressing this enzyme's action were reported, like it is the impact of interleukines and TNF (tumor necrosis factor), which are known to increase during infections and in dialysis patients [4,5]. Renal failure influences the biosynthesis and the elimination of hormones.

In end-stage renal disease (ESRD), the iodine clearance is nullified as well as the glomerular filtration. The iodine levels in plasma are increased resulting to a diminished iodine uptake by the thyroid gland. This can possibly block the production of thyroid hormones (Wolf-Chaikoff phenomenon), which explains the increased incidence of hypothyroidism (and goiter) in patients with renal failure (5% vs. 0.6% in common population)[6].

It has also been reported [7] that uraemia affects thyroid function at multiple levels:

a) There is a blunted TSH response to TRH, suggesting pituitary dysfunction or hypersensitivity to hormonal feedback.

b) There may be an intrathyroidal defect in hormonogenesis, hormonal secretion, or both, as evidenced by high incidence of goiter, increased thyroidal iodine content, and, in some patients, low serum TT4 not accountable for by depressed TBG capacity. The subnormal TT4 response to exogenous TSH administration reported by Ramirez *et al*. [8] lends support to this possibility.

c) Abnormal peripheral metabolism is characterized by a profound impairment of T4 to T3 conversion in extrathyroidal tissues, which results in a selective and marked reduction in serum TT3 concentration.

It is interesting that reverse T3 is not increased in uremic patients as it usually happens in other patients with severe but no thyroid diseases presenting the syndrome. While the TBG levels are normal in patients with uremia (except patients with nephrotic syndrome), various non-eliminated substances suppress the protein synthesis. It is proven that urea, creatinine, indoles and phenols have a similar role [9].

Haemodialysis does not improve the endocrine disorders, but it affects them further due to the administration of various drugs (heparin, b-blokers and salicylate), the frequent infections (immune deficiency) and the frequent cardiovascular diseases. We should not forget the temporary increase of T4 noticed during the session of haemodialysis because of the action of heparin in the binding of TBG to T4 [10,11,12]. It seems that only the successful kidney transplantation leads to a rapid restore of all the parameters of thyroid gland function [13,14,15].

CC Lin *et al*, had also demonstrate that uremic patients have higher prevalence of thyroid dysfunction, which include reduced serum concentration of total T3, total T4, and free T4, and increased serum level of TSH [16]. Hypothyroidism is also observed more frequently in uremic patients than in the control group (5.4% vs. 0.7%, $p < 0.05$).

Sim Kutlay *et al*, in their study [17], observed that the presence of goiter demonstrable by ultrasonography has been found in 32.2% of the uremic patients and in 23.5% of the controls and its prevalence increases with age ($P = 0.01$). In 32 (36.8%) of the patients and 29 (17.1%) of the controls at least one thyroid nodule was found in ultrasonography. Between patients with or without a nodular goiter the authors could not observe any difference for the duration of dialysis and serum levels of TSH, FT4, FT3, calcium, and albumin. In ESRD patients the prevalence of nodular goiter was found higher for females (47.5% vs. 27.7%, $P = 0.045$) and increases with age ($P = 0.04$). Though incidence of hyperthyroidism is found to be similar for the two groups (1.14% in ESRD patients vs. 1.10% in controls), hypothyroidism is observed in 3.4% of ESRD patients but only 0.6% of controls. This high incidence of hypothyroidism and nodular goiter in ESRD patients shows that screening for thyroid dysfunction and goiter, using appropriate laboratory tests and ultrasonography, should be considered in a regular evaluation of each ESRD patient.

Also, Chih-Ching Lin *et al*, in an other study [16] with 145 uremic patients on haemodialysis, showed that age, sex of female and anion gap (AG) were the only three parameters that would increase the prevalence of goiter in these patients [18].

Conclusions

Because of the high incidence of nodular goiter in uremic patients, and the frequent finding of sub clinical hypothyroidism (with symptoms common to uremia: fatigue, anemia, dry skin, edema, constipation, depression), screening of thyroid function and goiter detection with ultrasound should be considered in evaluation of end-stage renal disease patients.

Conflict of interest statement. None declared.

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