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Variation of thyroid hormone levels in patients receiving peritoneal dialysis

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Original Article

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Summary:

***Background**: In chronic kidney disease (CKD) there are structural and functional alterations of the thyroid gland, in addition to concomitant situations that modify the metabolism of their hormones. It has been shown that in CKD there are abnormalities that interfere with peripheral hormonal metabolism. **Objectives**: To determine the variation of thyroid hormones levels in patient's receiving peritoneal dialysis (PD) and to identify the prevalent of thyroid disease. **Methods**: Cross-sectional and descriptive study conducted with patients under PD. Age, the cause of the nephropathy, the modality of PD and the time received were taken into account, as well as the serum levels of triiodothyronine (T3), total thyroxine (T4), and thyroid stimulating hormone (TSH). **Results**: 100 patients were studied (63 men and 37 women). The average age was 58.2 years and the average time of PD was 29.2±3.7 months; the main modality of PD was continuous ambulatory. About 3/4th of the respondents had at least one alteration in one thyroid hormone; there were 36 with subclinical hypothyroidism and 7 with primary hypothyroidism (PH). **Conclusions**: The thyroid profile should be used as screening in patients undergoing PD.*

***Keywords:** Chronic kidney disease, Thyroid hormone, peritoneal dialysis, hypothyroidism. Time needed for peritoneal dialysis*

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1.INTRODUCTION

The kidney intervenes in the excretion of iodine and in the metabolism of thyroid hormones. In the chronic kidney disease (CKD), besides structural and functional alterations of the thyroid gland, there are concomitant situations, as malnutrition and increased catabolism, which, by themselves, they modify the metabolism of hormones thyroid. [(1)] On the other hand, in the ERC (End stage renal complications), the decreased iodine excretion produces an increase of plasma values and the same, as well as of its inorganic fraction, giving rise to the Wolff-Chaikoff phenomenon. There are data in uremic patients that suggest a reduction in the incorporation of iodine to thyroid hormones. [(2)] According to the studies found, the plasma concentration of thyroid hormones depends on the duration and intensity of the renal function insufficiency, time and type of dialysis, and techniques of determination. The most common biochemical alteration in CKD is the reduction of triiodothyronine total (T3) and free T3. [(3)]

Less often observed is a decrease in total T4. 4 Low levels of T3 result from a decrease in peripheral conversion from T4 to T3. The concentration of transporting thyroxine binding globulin (TBG) is usually normal, so the decrease in total T4, when it exists, is attributed to the presence of union inhibitors between T4 and TBG. [(4)]

For the same reason, with some techniques, a decrease in free T4 can be observed in cases of total T4 reduction. However, 5-10% of patients with CKD have low levels of free T4 with any of the methods of determination. [(5)]

Serum reversed triiodothyronine concentration (rT3), is the metabolically inactive product that results from the deiodination of the inner ring of T4, is normal in the uremia. The absence of elevation of rT3 in uremia is attributed to an increase in rT3 output from the plasma to the extravascular compartment. [(5,6)]

Frequently, thyrotropin (TSH) levels are normal in uremia 4. Studies of the hypothalamic axis pituitary glands show a blockage or decrease in the response of TSH to the administration of hormone thyrotropin releasing (TRH). In patients under treatment with dialysis, this test may be normal. There may be also an alteration of the circadian rhythm of TSH with a decrease in the afternoon peak and amplitude of the secretory pulses. [(2)]These anomalies persist in patients on hemodialysis (HD) and PD, although differences in levels may occur hormones between the two dialysis techniques. The TBG it tends to decrease in patients with PD[(7).] The existence of concomitant hypothyroidism in the ERC

can be difficult to suspect because the Symptoms are similar to those of the uremic syndrome. Do not However, the elevation of baseline TSH values, an exaggerated response of TSH to HRT and the decrease of the total rT3 will detect the presence of hypothyroidism. [8] An adequate dialysis treatment, a good state of nutrition and the correction of anemia can improve uraemic thyroid dysfunction of unknown clinical meaning. Some trials support that, after kidney transplantation, the normalization of most of the thyroid function indices in patients with CKD. [9] The frequency of thyroid alterations in patients adults with CKD is 5-30% [10,11] and in children it varies from 10 to 55%. [12]

Peritoneal Dialysis

Peritoneal dialysis (PD) is usually associated with low T3 levels and subclinical hypothyroidism. Low T3 levels might be due to inflammation and malnutrition in PD, as there is an association between free T3, CRP, and serum albumin. [13] Subclinical hypothyroidism may be due to a decrease in iodide clearance. Iodide clearance is done mainly by glomerular filtration; thus, in advanced CKD, iodide excretion is diminished with subsequent elevation in plasma inorganic iodide concentration. Such increases in total body inorganic iodide may block thyroid hormone production which may explain the high incidence of subclinical hypothyroidism in CKD patients. The T4 and T3 losses are minor (10% and 1%, resp.) and easily compensated in PD[14].

Thyroxine-binding globulin (TBG) is lost along with T4 and T3 in the PD; however, TBG levels are normal. Recent studies have demonstrated that subclinical hypothyroidism is associated with an increased risk for cardiovascular disease and can cause mortality in CKD patients. [13]

Subclinical Hypothyroidism

Subclinical hypothyroidism is defined as an elevation in serum TSH concentration (normal range 5–10 μIU/mL) in conjunction with a normal serum free T4 concentration. With the decline in GFR, the prevalence of subclinical hypothyroidism increases consistently. One study showed that approximately 18% of the patients with CKD not requiring dialysis have subclinical primary hypothyroidism. This finding is independently associated with a progressively lower estimated GFR. The prevalence of subclinical primary hypothyroidism increased from 7% to 17.9% in individuals whose GFR has decreased from ≥90 mL/min to 60 mL/min. [15] Some researchers reported that hypothyroidism can be corrected with restriction of dietary iodine in uremic patients on dialysis which decreases the need for

hormone replacement therapy. In one clinical trial, the overall rate of a decline in the estimated GFR was significantly greater in those not treated with thyroid hormones compared to those who were treated with thyroid hormones. [13]

Hyperthyroidism

The prevalence of hyperthyroidism in CKD patients is the same as it is with the general population; thus CKD is not directly associated with hyperthyroidism. However, it is important to understand that aspects of hyperthyroidism can indeed accelerate CKD. These mechanisms are the following: (i) increased renal blood flow seen in hyperthyroidism results in intra glomerular hypertension, leading to increased filtration pressure and consequent hyper filtration. Proteinuria seen in hyperthyroidism is known to cause direct renal injury;

(ii) increased mitochondrial energy metabolism along with downregulation of superoxide dismutase, which occurs in hyperthyroidism, contributes to an increased free radical generation that causes renal injury;

(iii) oxidative stress also contributes to hypertension in hyperthyroidism, which contributes to CKD progression. [13, 14]

2. PATIENTS AND METHODS

A cross sectional descriptive study was conducted at Al-Sader teaching hospital in the period of 1 year duration from the 1st of Jan. 2017 to the end of Dec.2017.

The age of the patients, sex, the cause of the nephropathy, the type and duration of PD was taken into account. The patients age between 20-80 years old.

Exclusion criteria:

1. Patients whose could not be follow up
2. Those who had a diagnosis of already established thyroid disease.
3. The patients who consumed some drug that will alter thyroid function, mainly amiodarone, lithium and corticosteroids.

For the plasma measurement of thyroid hormones the monthly sample taking was used. The determination of the levels of thyroid hormones (T3, T4, and TSH) was done in our hospitals laboratory.

Statistical analysis

After the entering of data in a table devised by the researcher, the analysis was carried out statistic with the SPSS program, version 24. For qualitative variables, we used frequencies and percentages, and for the quantitative variables, we used measures of central tendency (median, media and fashion) and dispersion (standard deviation). For the inferential statistics the tests were used of chi-square test (with a significance of ≤5%).

3.RESULTS

The total number of subjects studied who met the inclusion criteria was 100 patients; 63 (63.0) were male and the rest were female within the average (mean) age was 58.2 ± 11.1 years and the average time for PD was 29.2±3.7 months. Within the causes of nephropathy, the main was secondary to diabetes mellitus and hypertension , followed by hypertension only (both causes contributed for 90.0%). It is worth mentioning that in individuals who had CKD secondary to DM and HT it was not established which of these two diseases was the main trigger of the nephropathy (table 1 & figure 1).

In table 2 the values of thyroid hormones are categorized according to their normal parameters qualitatively (high, normal or low). As for the T3 the most highlight was that 85 (85%) did not present alterations in the values. In T4, 80 (80%) kept in the normal values. The hormone with the greatest alteration was TSH, with 36 (36%) of high figures; no patient (0%) presented a decrease in this parameter.

Referring to dialysis modality (Table 3), the main one was continuous ambulatory peritoneal dialysis (CAPD) (82%), 15% were ambulatory peritoneal dialysis, CAPD/transplant was (2%), and APD/transplant (1%)

Table 1: Age and gender distribution of the studied group (N = 100)

Variable		No.	%
Age (year)	≤40	21	21.0
	41-50	14	14.0
	51-60	23	23.0
	61-70	25	25.0
	≥70	17	17.0
Gender	Male	63	63.0
	Female	37	37.0

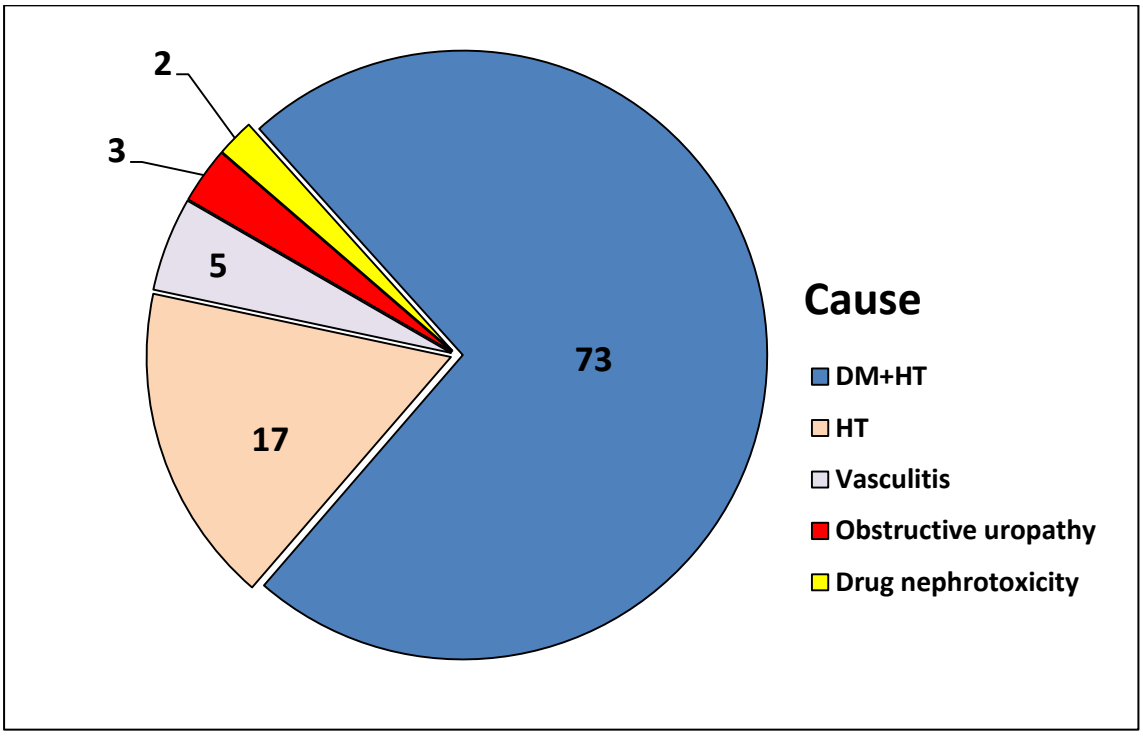

Figure1. Distribution of causes of nephropathy among the studied group (N=100)

Table 2. Categorization and frequency distribution of thyroid hormone levels of the studied groups (N = 100)

Level	T3	T4	TSH
Normal	85 (85%)	80 (80.0%)	64 (64.0%)
Low	1(1.0%)	6 (6.0%)	0 (0.0%)
High	14 (14.0%)	14 (14.0%)	36 (36.0%)
Total	100 (100.0%)	100 (100.0%)	100 (100.0%)

Table 3. Types of dialysis modality of the studied group (N = 100)

Modality	No.	%
CAPD	82	82.0
APD	15	15.0
APD/transplant	1	1.0
CAPD/transplant	2	2.0
Total	100	100.0

4. DISCUSSION

It is important to assess thyroid changes for identifying, treat and assess the disease, considering that there are multiple publications that support the need to treat entities such as subclinical hypothyroidism. [16-18]. Only a specific diagnosis was established of thyroid disease in 43% of cases (36%) corresponded to subclinical hypothyroidism, and 7% to hyperthyroidim. These figures are greater than the incidence of hypothyroidism in Rammana M, et al, study when (2% of women mature and 0.1-0.2% of men), as well as subclinical was represent (4.3%) in the former study.[19]

However, the biochemical results found here are very similar to those referred by Wha, et al.[3], Mainly in the non-variation of the levels of T4 with respect to the other hormones. As

for the causes of nephropathy, it's worth it mention that, between the two main ones (DM and HT and HT), there were no patients who only suffered DM, because in the long run they developed HAS, either as concomitant disease or due to angioesclerotic effect kidney as a result of DM. Instead, yes there were patients who only had HAS. [20]

Furthermore, it had been mentioned that thyroid hormones have to be quantified in patients with CKD before and after the time needed to PD and rule out whether the CKD itself is not the cause of thyroid disease, as it indicated by the results of Silva et al. [21], who found a decrease in serum levels of thyroid hormones in pediatric patients with ERC without time needed to PD . On the other hand, the possibility of taking serial measurements of thyroid hormones in patients undergoing dialysis is needed, that is, pre and post, following the line that marked by Melillo, et al., in their essay they found serum variations of thyroid hormones before and after the hemodialysis. [7] Wha, et al. point out that the excess of blood iodide caused by decreased renal excretion contributes to the high frequency of hypothyroidism in the ERC, causing the blockade of the so-called phenomenon of Wolff-Chaikoff. [3]

5.CONCLUSION

The main cause of PD was secondary to diabetes mellitus and hypertension followed by hypertension only, both causes contributed for 90.0% of cases. The thyroid profile should be used as screening in patients undergoing PD. The main mode of dialysis was continuous ambulatory peritoneal dialysis (CAPD) contributed for (82%), peritoneal dialysis 15% while CAPD/transplant was for 2%, and APD/transplant used in1%. However, the thyroid profile should be used as screening in patients undergoing PD and further studies are highly suggested for further assessment and clinical evaluation.

Ethical Issues: Approved by local ethical committee of medical researches. Data were collected in accordance with WMA declaration of Helsinki, 2013

The conflict of interest: there is no conflict of interest by the authors

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