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Research Article

CHARACTERIZATION OF PATIENTS WITH CHRONIC KIDNEY DISEASE ON HEMODIALYSIS ACCORDING TO THYROID HORMONAL ALTERATIONS

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ABSTRACT

Background: The progression of chronic kidney disease is associated with thyroid dysfunction. The thyroid hormonal disturbances that are associated with chronic kidney disease are subclinical hypothyroidism and euthyroid sick syndrome.

Method: To characterize patients with chronic kidney disease on hemodialysis according to thyroid hormonal alterations.

Results: Retrospective, descriptive study in the Nephrology service of the Hospital Clínico Quirúrgico "Hermanos Ameijeiras" of patients with chronic kidney disease on hemodialysis in the period from November 1 to December 30, 2018. Male sex predominated (50.8%); age 45 years-64 years (42.4%); white skin color (40.7%); time on hemodialysis greater than 5 years (54.2%) and euthyroid sick syndrome (40.7%), followed by subclinical hypothyroidism (30.5%). There were significant differences in the predominant thyroid alterations with the following variables: albumin (p=0.016), hemoglobin (p=0.017), urea (p=0.008) and time on hemodialysis (p=0.007). There was a significant correlation between TSH and time on hemodialysis, urea (r=0.382, r=0.257); between T3 and time on hemodialysis, urea, albumin (r=-0.385, r =-0.413, r=0.493); between T4 and albumin (r=0.381).

Conclusion: The most frequent thyroid hormonal alterations were the euthyroid sick syndrome, followed by subclinical hypothyroidism. Albumin and hemoglobin levels were lower in patients with thyroid disorders. The urea value and time on hemodialysis were higher in patients with thyroid disorders.

Keywords: Hypothalamic-pituitary-thyroid axis; Hypothyroidism; Euthyroid sick syndrome; Chronic kidney disease

INTRODUCTION

Chronic Kidney Disease (CKD) is a global public health problem, which consists of the progressive loss of kidney function over a period of months or years. The progression of CKD is associated with a series of complications, including thyroid dysfunction, dyslipidemia, cardiovascular diseases, among others. CKD is associated with a higher prevalence of thyroid dysfunction. Thyroid dysfunction that is associated with CKD is subclinical hypothyroidism and euthyroid sick syndrome. These 2 disorders have been associated with an increased risk of mortality in hemodialysis patients [1,2].

Euthyroid sick syndrome is characterized by decreased serum Triiodothyronine (T3) and/or Thyroxine (T4) levels, accompanied by increased reverse T3 (rT3) with normal thyroid-stimulating hormone (TSH) levels. Reduced levels of T3 and T4 hormones have been reported in CKD patients, possibly a consequence of chronic nonthyroidal disease, unresolved uremia, and/or protein malnutrition. Low levels of T3 thyroid hormones (low T3 syndrome) of euthyroid sick syndrome is the most common laboratory finding of abnormal thyroid hormone values, followed by subclinical hypothyroidism in patients with CKD [3-6].

T4 is produced only by the thyroid gland, whereas T3, the most biologically active form of thyroid hormone, is produced primarily through local deiodination of T4 by the enzyme T4-deiodinase in other tissues, including the kidney. The kidney contains the D1 isoform of this enzyme, which is less active in uremia. In chronic kidney disease there is decreased activity of deiodinase [6]. In addition, the D3 isoform of liver and skeletal muscle deiodinase, involved in the inactivation of T4 and T3, is induced (D3) is not expressed in these tissues in healthy individuals). Consequently, the levels of T3 decrease markedly and to a lesser extent those of T4. In CKD, physiological compensation for low T3 and T4 levels (with normal TSH levels) causes a reduction in protein catabolism [6].

METHODS

The TSH response to TRH is delayed due to decreased clearance and increased half-life of TSH [6]. Studies have associated higher TSH levels with greater EPO resistance, indicating that the TSH level should be among the parameters measured when EPO resistance is observed. TSH is the most reliable indicator of thyroid function. These determine whether the abnormality originates in the center of the thyroid gland or in the periphery of the pituitary gland. According to the diagnostic criteria of the laboratory of the "Hermanos Ameijeiras" Clinical Surgical Hospital, the normal values of TSH are from 0.3 mIU/L to 3.5 mIU/L and T4 from 50 nmol/L to 150 nmol/L. In subclinical hypothyroidism, TSH levels are higher than 3.5 mIU/L and T4 levels are within the range considered for normal patients [6-13].

In a study conducted at a tertiary care hospital in northern India with 1,863 CKD patients, patients with clinical and subclinical hypothyroidism were found to have lower levels of serum albumin, serum calcium, and hemoglobin, as well as higher levels of parathyroid hormone. One study reported a higher prevalence of patients with thyroid hormonal alterations for a longer time on HD. Large cross-sectional studies have shown a higher prevalence of hypothyroidism with increasing decline in renal function.

Due to the above, it was decided to carry out this investigation to characterize patients with chronic kidney disease on hemodialysis according to thyroid hormonal alterations..

OPERATIVE TECHNIQUE

A retrospective, descriptive study was carried out in the Nephrology service of the "Hermanos Ameijeiras" Clinical Surgical Hospital of patients with chronic kidney disease on hemodialysis in the period from November 1 to December 30, 2018.

Patients underwent conventional hemodialysis with 4008 S monitors from the Fresenius brand, 3 times a week with a duration of 4 hours per session. The prescribed blood flow was between 200 ml/min-300 ml/min and the dialysate flow of 500 mL/min. The patients used erythropoietin 4000 IU, 3 times a week.

The universe of the study consisted of all patients with chronic kidney disease on hemodialysis at the "Hermanos Ameijeiras" Clinical Surgical Hospital. The following selection criteria were taken into account in the study:

Inclusion criteria: Patients diagnosed with stage 5 chronic kidney disease of any etiology

Exclusion criteria:

- Patients in shock of any etiology.
- Patients with data of sepsis.
- Patients taking drugs that can cause hypothyroidism.
- Patients with mental disabilities.
- Patients with incomplete information in data collection.

It was made up of 59 patients with stage 5 chronic kidney disease on hemodialysis at the "Hermanos Ameijeiras" Clinical Surgical Hospital in the established period of time and according to the eligibility criteria outlined above.

Operationalization of the variables

The data from the medical records were collected at the time established for the study. These were the sources from which the primary information in the investigation was obtained. Medical records were evaluated in order to meet the inclusion and exclusion criteria. The information recorded in the databases of the hemodialysis section was also taken into account.

Information processing

The information obtained was taken to a database using the Microsoft Excel application and processed with the statistical program SPSS version.

Statistic analysis

A descriptive statistical analysis was carried out where the qualitative variables will be summarized with absolute numbers and percentages and the quantitative variables with the mean and its Standard Deviation (SD). The Spearman test was used to measure the relationship between two quantitative variables and the Kruskal-Wallis test to correlate three or more independent variables. A value of $p< 0.05$ was accepted as statistically significant.

RESULTS

In relation to age, the predominance of the participants in the study was between 45 years-64 years with 42.4%, followed by the group over 65 years with 30.5%. Patients in the 45-64 age group presented a predominance of the euthyroid sick syndrome (54.2%). Subclinical hypothyroidism predominated in those over 65 years of age (38.9%) (Table 1).

Table 1: Descriptive statistics of clinical, hematological and biochemical parameters according to predominant thyroid disorders.

	18-24 años	25-44 años	45-64 años	≥ 65 años	Total
Síndrome del enfermo eutiroideo	2 (8,3)	3 (12,5)	13 (54,2)	6 (25,0)	24 (100)
Hipotiroidismo subclínico	0 (0)	6 (33,3)	5 (27,8)	7 (38,9)	18 (100)
Hipotiroidismo clínico	0 (0)	0 (0)	1 (50)	1 (50)	2 (100)
Hipertiroidismo subclínico	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)
Sin alteraciones hormonales tiroideas	1 (7,1)	4 (28,6)	5 (35,7)	4 (28,6)	14 (100)

DISCUSSION

The main objective of this work was to characterize patients with chronic kidney disease on hemodialysis according to thyroid hormone changes. In our study we obtained a frequency of 40.7% participants with euthyroid sick syndrome, and 30.5% with subclinical hypothyroidism, these thyroid hormonal alterations being the most frequent. The least frequent were clinical hypothyroidism (3.4%) and subclinical hyperthyroidism (1.7%). 23.7% of patients did not present any thyroid hormonal alterations. Mosharruf Hossain et al, in their work, found 45% of patients with euthyroid sick syndrome, the most frequent finding being disorders of thyroid hormone values, similar to our research. Another report found a high prevalence of euthyroid sick syndrome with 52.4% of patients. Therefore, the most frequent thyroid disorder in general in chronic kidney disease is the euthyroid sick syndrome according to the different works. In the case of hypothyroidism, different studies have found a higher prevalence of subclinical hypothyroidism compared to the clinical form.

In addition, this paper explains that a prevalence similar to that reported internationally on thyroid dysfunction was observed, especially in the subclinical form and regardless of the type of dialysis.In addition, in these patients thyroid hormonal alterations are more frequent due to the chronic metabolic acidosis that these patients experience. There are also studies linking metabolic acidosis with a significant decrease in serum T3 levels, as well as a corresponding increase in serum TSH levels. Thyroid hormonal changes according to age. In our study, patients in the age group of 45 years-64 years were the ones who most presented the euthyroid sick syndrome. In subclinical hypothyroidism, those over 65 years of age predomi-

-nated.. In a reviewed work, subclinical hypothyroidism had a frequency of 20% with predominance in patients between 45 years-59 years of age, with 16 (52%) female patients and 15 (48%) male patients. Another report determined that the prevalence of subclinical hypothyroidism increased with increasing age, with 46.2% being older than 40 years. We obtained from our research results that thyroid hormonal alterations in hemodialysis patients are more frequent for a longer time with this renal replacement therapy, coinciding with the literature and different international studies. One report found that patients with subclinical hypothyroidism represented 60.9% of patients who had been on hemodialysis for more than 5 years. In addition, there are works that relate the euthyroid sick syndrome with a longer time on hemodialysis, being similar to our study, they even give a prognostic value of morbidity to the patient.

In our work, patients with thyroid hormonal abnormalities presented lower albumin and hemoglobin values, similar to other reports and the literature. In addition, thyroid disorders were related to higher urea levels and time on hemodialysis, these results being statistically significant ($p<0.05$). A correlation of TSH levels with urea levels was found in the study carried out with our patients. The higher the TSH level, the higher the urea levels. In the case of T3, a direct relationship with albumin was obtained, as T3 decreased, albumin decreased. T3 in our work was inversely associated with urea and HD time, the higher the urea levels and HD time, the lower the T3 levels. Similar to our work, there are studies that have found a direct correlation between TSH and urea. In addition, they have found inverse relationships between T3 and urea and direct relationships between T3 and albumin.

In uremia, ineffective clearance of abnormal serum components, inflammatory cytokines, iodide excretion, and increased nitrogen conservation have been clinically shown to affect normal thyroid hormone metabolism and physiology. Some dialysis factors such as systemic acidosis, malnutrition, dialysis time, endothelial damage markers, and inflammation are also associated with low T3 levels. Inflammatory cytokines such as tumor necrosis factor alpha and Interleukin 1 (IL-1) inhibit the expression of 5-deiodinase type 1, which is responsible for the peripheral conversion of T4 to T3.

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