

Evaluation of Thyroid Hormone Profile in Chronic Renal Failure

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Abstract

Original Research Article

Introduction: Kidneys have an important role in the catabolism of thyroid hormones. Deiodination of T4 to T3 takes place mostly in the kidney. Since kidneys are the primary route for iodine elimination, advanced renal disease leads to increased plasma iodide pool because of decrease in renal clearance. Increased incidence of goiter has been reported in chronic renal failure due to defect in thyroid hormone synthesis. **Objective:** To evaluate the thyroid hormone profile including T3, T4, TSH, FT3, FT4 in patients of CRF. **Methods:** In the present study thyroid function test in chronic renal failure attended at NRS Medical College and Hospital. The study was done on 50 patients of chronic renal failure. A group of 20 healthy volunteers was taken as control. All investigations (biochemical and thyroid function tests) were done. **Results:** Results obtained in patients with CRF was compared with those in the control group. Statistical analysis is done using student's unpaired "t" test, p value <0.05 was taken significant. **Conclusion:** While comparing the cases and controls for T₃, T₄, FT₃, FT₄ and TSH values of T₃, FT₃ and T₄ significantly decreased and values of TSH increased and approached to the higher side of the normal limit as creatinine clearance decreased. FT₄ values did not show significant decrease with decreasing GFR. In this study decrease in T₃, T₄, FT₃ and increase in TSH were found as creatinine clearance decreased the exact mechanism of this change with the decreasing renal function still not established. But the possible mechanism may be altered peripheral hormone metabolism, disturbed binding to carrier proteins, and possible reduction in tissue thyroid hormone content and increased iodine store in thyroid gland.

Keywords: Thyroid Hormones, Chronic renal failure (CRF).

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INTRODUCTION

In healthy individuals, T4 is the main thyroid hormone released from the thyroid gland, although T3 is secreted as well. The thyroid hormone circulates attached to plasma proteins. About 70% T4 is bound to Thyroid Binding Globulin (TBG), 20% to transthyretin (also called thyroid binding prealbumin) and 10% to albumin, whereas most T3 is bound to TBG. A small percent of thyroid hormones remain unbound to protein, of which about 0.03% of T4 and approximately 0.3% of T3 arises from peripheral deiodination, with liver and kidney having important role in this transformation. About 35% of T4 is mono-deiodinated to T3 and 15-20% is changed to tetra-iodothyroacetic acid or conjugated and excreted in urine or bile. The

remainder of T4 is deiodinated to 3,3',5' tri-iodo-thyronine (reverse T3 [rT3]) [1, 9].

With changes in thyroxin binding proteins, high or low levels of serum thyroxin occur that is not reflected in corresponding alteration in clinical state. In these situations, free (unbound) thyroxin is more closely correlated with patient's clinical status. Kidneys have an important role in the catabolism of thyroid hormones. Deiodination of T4 to T3 takes place mostly in the kidney. Since kidneys are the primary route for iodine elimination, advanced renal disease leads to increased plasma iodide pool because of decrease in renal clearance. Increased incidence of goiter has been reported in chronic renal failure due to defect in thyroid hormone synthesis [6].

Uremic manifestations are produced as a consequence to retention of certain organic substances which ultimately affect the cell metabolism producing systemic manifestations in form of gastrointestinal, cardiac, neurological, hematological and hormonal aberration. The availability of low serum protein, proteinuria alteration in cationic charge in protein molecule and other mechanism play role in handling of thyroid hormones. Some fraction of these hormones may escape and may be lost in the urine along with urinary protein especially in that form of nephropathy where large amount of proteinuria is present.

AIMS AND OBJECTIVES

To evaluate the thyroid hormone profile including T₃, T₄, TSH, FT₃, FT₄ in patients of CRF.

MATERIALS AND METHODS

In the present study thyroid function test in chronic renal failure attended at NRS Medical College and Hospital. The study was done on 50 patients of chronic renal failure. A group of 20 healthy volunteers was taken as control. All investigations (biochemical and thyroid function tests) were done. Selection of patients and control the study was carried out over the both cases and control attended at NRS Medical College. Criteria for selection of CRF patients was as follows –The patient should be symptomatic for more than 3 months. Biochemically, the patients' blood urea level must be above 40 mg/dl and that of serum creatinine more than 2 mg/dl. GFR as detected

by endogenous creatinine clearance should be less than 50% of normal [3, 4]. The patients in the past had suffered from hypothyroidism or hyperthyroidism were excluded in the study. Criteria for selection of control –Persons who were free from any disease were selected as control. GFR as detected by endogenous creatinine clearance should be more than 80 ml/min. Volunteers who had been suffered from hypo or hyperthyroidism in the past or any chronic illness were excluded. Following selection of both cases and control, were subjected to detailed historical evaluation, detailed clinical examination in which emphasis was given on the examination of endocrinal system. Subsequently each case and control was subjected to different hematological, biochemical, urinary and thyroid function test examination.

History

Name, age, sex, religion, height and weight of each cases and control were noted. Particular attention was given to the mode of onset, duration of illness, previous episodes of similar symptoms present or past history of glomerulonephritis, pyelonephritis, diabetes, hypertension, hypo and hyperthyroid disease thyroiditis, cerebrovascular disease, diarrhea or colonic disorders, tuberculosis, chronic urinary obstruction (enlarged prostate, stricture urethra etc). The family members and near relatives of each case and control were questioned regarding history of diabetes, hypertension, tuberculosis etc. Details of treatment history were also taken, including intake of analgesic if any with duration of intake.

OBSERVATION

Thyroid Function tests in chronic renal failure in patients and control subjects (Mean ± SD)

GROUP	CONTROL	PATIENTS
N	20	50
T ₃ (ng/ml)	1.23±0.197	0.72±0.203*
T ₄ (µg/dl)	8.51±0.88	5.04±0.86*
FT ₃ (pg/ml)	3.718±0.562	2.86±0.50*
FT ₄ (ng/dl)	1.30±0.28	1.05±0.23*
TSH(µU/L)	3.077±0.583	4.785±0.353*

*p<0.05

The above table shows that in CRF patients overall T₃, T₄, FT₃ and FT₄ values are significantly reduced (p<0.05) while TSH values are significantly increased (p<0.05) in comparison to the controls.

DISCUSSION AND CONCLUSION

Thyroid hormone functions are known to be altered in chronic renal failure. For the present work, "Evaluation of thyroid hormone profile in chronic renal failure" a total of 50 patients and 20 controls were selected. The selected patients were subgrouped according to their GFR based on creatinine clearance i.e.

<5% of GFR, 5-20% of GFR and >20-50% of GFR [2].

In the present study five parameters of thyroid hormone profile namely T₃, T₄, FT₃, FT₄ and TSH were estimated. 58% of cases had T₃ value less than 0.7 ng/ml i.e. below normal and rest of the cases 42% were found to have T₃

value in the normal range. T₃ values showed significant decrease with decreasing GFR. 48% of cases had T₄ value less than 5 µg/dl and 54% had normal value. T₄ values in subgroups showed significant decrease in GFR compared to the control. In all the cases TSH value were within the normal range but approaching to the higher upper limit. TSH values changed significantly with the reducing GFR compared to the control. However, TSH values did not significantly change with the reducing GFR in the subgroups. In the present study 6% of FT₃ value <1.4 pg/ml which below the normal range. Although FT₃ value in 94% cases were within normal range, the values were more towards the lower limit. FT₃ values showed significant decrease with decreasing GFR. FT₄ values were decreased in severe and moderate CRF groups and had significant difference with that of the control group. FT₄ values in mild CRF group did not show significant difference with that of the control group. Moreover FT₄ values did not show significant decrease with decreasing GFRs similar to the finding of other authors [9]. While comparing the cases and controls for T₃, T₄, FT₃, FT₄ and TSH values of T₃, FT₃ and T₄ significantly decreased and values of TSH increased and approached to the higher side of the normal limit as creatinine clearance decreased. FT₄ values did not show significant decrease with decreasing GFR. According to Lim V.S. [6] chronic renal failure affects thyroid function in multiple ways which include low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone contents and increased iodine store in thyroid gland [6, 7].

In this study decrease in T₃, T₄, FT₃ and increase in TSH were found as creatinine clearance decreased the exact mechanism of this change with the decreasing renal function still not established. But the possible mechanism may be altered peripheral hormone metabolism, disturbed binding to carrier proteins, and possible reduction in tissue thyroid hormone content and increased iodine store in thyroid gland [5]. Thyroid hormone receptor binding to DNA and T₃-dependent transcriptional activation are inhibited by uremic toxins may be a possible mechanism [10]. Low free plasma triiodothyronine (FT₃) is associated with inflammation and cardiovascular damage in patients with end-stage renal disease (ESRD)[11]. The change in thyroid hormones profile i.e. decrease in T₃, FT₃ and T₄ and increase in TSH values as severity of CRF increases, may have diagnostic and prognostic

tool for the management of end stage renal disease[9]. This high incidence of subclinical hypothyroidism in ESRD patients shows that screening for thyroid dysfunction using appropriate laboratory tests, should be considered in evaluation of every ESRD patient. 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 [8]. However, a lot of work has to be done to establish the exact correlation between the hormone level and deteriorating renal function.

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