Association Between Chronic Renal Failure and Thyroid Hormone

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Abstract

The levels of serum urea , creatinine ,total thyroxin (TT4) , Tri-iodothyronine (TT3) , free T4 (fT4) , freeT3 (fT3) and Thyrotropin (TSH) were measured in the serum of 80 Patients with varying grades of chronic renal failure (CRF) ; and 40 healthy individuals . They were divided into 3 groups as : Group 1 Containing 40 healthy individuals as Control group; Group 2 containing 40 Patients on Conservative management ; and Group 3 Containing 40 Patients on Regular haemodialysis therapy.

Groups 2 and 3 showed significant increased in urea and creatinine compared with control group (P< 0.001) and significant decreased in TT4(P < 0.01) , TT3(P < 0.001) , fT4(P < 0.01) and fT3(P< 0.001) , whereas TSH values were not significantly altered .

Conclusions: Uremia is accompanied with endocrine disorders , due to impaired degradation of hormones , because of failed kidney functions and to the interference of the uremic environment with extra renal degradation or synthesis and secretion of certain hormones .

The aim of the study was to investigate the association between chronic renal failure and thyroid function.

Key words: chronic renal failure , thyroid hormones

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الخلاصة

تم دراسة مستويات كل من اليوريا والكرياتينين والثايروكسين الكلي TT4 والثايروكسين الحرfT4 وثلاثي ايوديد الثايروكسين الكلي TT3 وثلاثي ايوديد الثايروكسين الحر fT3 وهرمون الثايروتروبين TSH الهرمون المحرض للدرقية وقياسها في مصل م ٨٠ مريضا يعانون من درجات متفاوتة بالفشل الكلوي المزمن (CRF) ومقارنتهما بـ ٤٠ شخصا من الاصحاء ، حيث قسمت الدراسة الى ثلاث مجاميع : مجموعة (I) شملت ٤٠ شخصا كمجموعة سيطرة، مجموعة (II) شملت ٤٠ مريضا في مرحلة العلاج التحفظي ،مجموعة (III) شملت ٤٠ مريضا في مرحلة الغسل الدموي.

اظهرت المجموعة الثانية والثالثة ارتفاع معنوي في مستويات اليوريا والكرياتينين عند مقارنتهما بمجموعة السيطرة وبمستوى معنوية ($p<٠,٠٠١$)، وانخفاضا معنوي في مستوى TT4 عند مستوى معنوية ($p<٠,٠١$)، وانخفاضا في مستوى TT3 بمستوى معنوية($p<٠,٠٠١$)، وانخفاضا في مستوى fT4 عند مستوى معنوية ($p<٠,٠١$) عند مجموعة العلاج التحفظي و($p<٠,٠٠١$) عند مجموعة الغسل الدموي، و انخفاض معنوي في مستوى fT3 عند مستوى معنوية ($p<٠,٠٠١$)، بيمنا قيم TSH لم تتغير معنويا .

وكان الهدف من هذه الدراسة ايجاد العلاقة بين الفشل الكلوي المزمن و وظيفة الغدة الدرقية .

Introduction

Chronic renal failure, or end- stage renal disease (ESRD) , is a progressive , irreversible deterioration in renal function in which the body ʿs ability to maintain metabolic , fluid and electrolyte balance fails , resulting in uremia or azotemia(retention of urea and other nitrogenous wastes in the blood) [1-2].

ESRD may be caused by many factors, systemic diseases, such as diabetes mellitus(leading cause); hypertension chronic glomerulonephritis ; pyelonephritis obstruction of the urinary tract ; hereditary lesion , as in polycystic kidney disease ; vascular disorders ; infections ; medications; or toxic agents.[3]

Chronic renal failure affects thyroid function in multiple way, including low circulating thyroid hormone concentration , altered peripheral hormone metabolism , disturbed binding to carrier proteins , possible reduction in tissue thyroid hormone content , and increase iodine store in thyroid glands, Both plasma triiodothyronine (T3) and Thyroxin (T4) are reduced.[4]

The thyroid function is regulated by thyrotropin (TSH) secreted from the pituitary gland .TSH secretion is in turn regulated by two opposing force: 1) By thyrotropin releasing hormone (TRH) from the hypothalamus which stimulates TSH secretion and synthesis 2) By thyroid hormones which inhibit the TSH secretary mechanism directly and also antagonizes the action of TRH Thus, homeostatic control of TSH secretion is exerted in a negative feedback manner by thyroid hormones and the threshold for feedback Inhibition in apparently set by TRH[5]

Material and Methods

This study was carried out on 80 Patients (50 men and 30 women) with end stage kidney disease. Their ages ranged from 20 to 70 year. A full clinical evaluation was done for those patients including history of disease and physical examinations. This evaluation revealed that all the patients with no previous history of thyroid dysfunction and with varying grades of chronic renal failure were included in this study. 40 Patients who had severe renal failure were on regular haemodialysis (group 3) and 40 patients with conservative managements (group 2).

Requested blood samples were taken from cubital vein and after all aseptic precautions , about 5.0 ml of blood was drawn from anterior cubital vein. Collected blood were used to estimation of serum total thyroxin (TT4),total triiodothyronine (TT3), and creatinine in the serum and Results obtained in patients with CRF. were compared with those in 40 were (group 1).

Serum levels of urea were measured by standard methods using Urea- Kit enables end point enzymatic determination of urea concentration (Urease – modified Berthelot reaction) in human urine, serum or plasma.[6,7]

$$\text{Urea} + H_2O \xrightarrow{\text{urease}} 2NH3 + CO2$$

and creatinine were measured by standard methods using creatinine kit ,creatinine in alkaline solution reacts with picrate to form a colored complex [8].

While thyroid hormones by radio immune assay techniques by hormonal Kit provides by BIOMERIEYX, France. [9]

Statistical Analysis

Data are expressed as means ± standard deviations. Statistical differences in the variables were tested using parametric and non parametric tests where appropriate. The relationship between tested variables was assessed using least significant deference LSD. Data procession software package was used SPSS for windows.

Result

Table – 1 show the mean levels of blood urea and creatinine in the serum of patients were up compared with control group 25.86±11.003, ,300.10±164.971mmol/L in Conservative group respectively , and 23.385±8.194 , 338.925±182.557 m mol/L in haemodialysis group respectively ,while in control group were 4.97±1.031 , 70.35±4.588mmol/L respectively .

Table(1): Show Weight, Age and Serum levels of Urea, Creatinine in patients and control group.

Parameter	Control	Conservative	Hemodialysis
	Mean ± SD	Mean ± SD	Mean ± SD
Numbers	40	40	40
Age (yr)	41.2±17.916	55.o±14.855***	47.83±16.073
Weight(kg)	73.65±15.94[a]	71.9±14.91[a]	64.75±15.34[b]
Serum Urea (m mol/l)	4.97±1.03[a]	25.68±11.003***[b]	23.385±8.193***[b]
Serum Creatinine (mmol/l)	70.350±4.588[a]	300.10±164.971***[b]	338.925±182.557***[b]

* P < 0.05 ,**P < 0.01 ,*** P < 0.001

Comparing to the mean levels of thyroid hormones in serum of patients with those of control, significant reduction in the levels of TT4, TT3 was noticed 76.507±15.175 , 0.617±0.325 n mol/L respectively and 75.05±15.495 , 0.915±0.369 n mol/L for conservative and haemodialysis respectively, while in control group the mean levels were 86.304±12.006 , 1.376±0.322 n mol/L respectively.

Mean serum levels of fT3 values in patients were decreased comparing to the control group P < 0.001 4.774±1.006 , 2.210±1.030 and 3.035±0.963 P mol / L for conservative , haemodialysis and control groups respectively.

There was significant increase in the level of fT3 in haemodialysis compared with conservative groups.

fT4 values were also decrease in patients comparing to control group P < 0.01 but there was no significant differences between the patients groups. Mean serum TSH levels in patients were slightly higher than control group but no significant differences between groups.

Table(2): Show Serum levels of TT4,TT3,fT4,fT3 and TSH in patients and control group.

Parameters	Control	Conservative	emodialysis
	Mean ± SD	Mean ± SD	Mean ± SD
Numbers	40	40	40
TT4 (n mol/L)	86.305±12.001[a]	76.508±15.176**[b]	75.051±15.496**[b]
TT3 (n mol/L)	1.376±.322[a]	0.617±.326***[b]	0.916±.058***[c]
fT4 (P mol/L)	13.608±2055[a]	11.678±3.129**[b]	10.866±2.918***[b]
fT3 (P mol/L)	4.755±1.007[a]	2.21±1.037***[b]	3.035±.964***[c]
TSH (mlu/ml)	1.553±1.126	2.084±1.947	2.336±2.163

*P < 0.05 ,**P < 0.01 ,*** P < 0.001

Discussion

The kidney plays an important role in the metabolism , degradation and excretion of several thyroid hormones . It is not surprising , therefore , that impairment in kidney function leads to disturbed thyroid physiology.[10]

Chronic kidney disease (CKD) affects both hypothalamus – pituitary- thyroid axis and TH peripheral metabolism [11-12] .Uremia influences the function and size of the thyroid [13]. Uremic patients have an increased thyroid volume compared with subjects with normal renal function and a higher prevalence of goiter , mainly in women [14,15] Also ,thyroid nodules and thyroid carcinoma are more common in uremic patients than in the general population [16,17]

In this study the plasma concentration of thyroid stimulating hormone [TSH] is normal in patients with chronic renal failure. This results agree with previous study [18,19, 20]

This can be explain by , the TSH response to exogenous thyrotrophic - releasing hormone (TRH) is often blunted and delayed, with a prolonged time required to return to baseline levels.

The Reduced renal clearance may contribute to delayed recovery, since TSH and TRH are normally cleared by the kidney.[21]

In present study Free and total T4 concentrations are low in patients with CKD. These results agree with results of an others previous studies.[22,23,24] ,

The low total T4 values in patient with chronic renal failure may be primarily related to impaired T4 binding to serum carrier proteins. It has been reported that many inhibitors of T4 binding to serum carrier proteins are present in CRF patients and thus contributing to the decreased levels of T4

This study shows significant reduction in FT3 and TT3 concentration in patients serum with CRF compared to control group ($p<0.001$) , These results agree with results of an others studies [25,26,27] .

The decreased total T3 levels can be attributed to the increase in excretion of bound and free T4 in urine of chronic renal failure as reported in other previous study.[21] also it may be due to a decrease in the peripheral synthesis of T3 from T4.[28].

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