The Effect of Chronic Renal Failure on Thyroid Hormones

Layla K. Ali[*,1]

*Nursing Department , Koya Technical Institute

Abstract

Chronic renal failure (CRF) affects thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content, and increased iodine store in thyroid glands.The target of study is to find a relationship between chronic renal failure and thyroid function.In addition, we tried to study the effect of CRF on serum creatinine dependent on the level of thyroid hormones (T3 and T4) and thyroid stimulating hormones(TSH). Forty patients with chronic renal failure (20 male, 20 female) were enrolled in this study in addition to forty healthy individual as control group (20 male, 20 female). The age ranged from (25 -65) years. T_4, T_3, TSH, urea, uric acid and creatinine were measured in each of the two groups. The results revealed statistically significant reduction in T_3 and T_4 while there is elevation in TSH, urea,uric acid and creatinine in the patients group compared to the control group.

Key word : Chronic Renal Failure,Thyroid Hormones.

الخلاصة

يؤثر القصور الكلوي المزمن على فعالية الهرمونات الدرقية بطرق متعددة تتضمن قلة في تركيز هرمون الغدة الدرقية في الدم، تبدل أو تغير ايض الهرمون في الانسجة المحيطية، وإرتباطه بالبروتين الناقل، أحتمالية انخفاض مستوى الهرمونات الدرقية في الانسجة المحيطية والبلازما وكذلك زيادة خزن اليود في الغدة الدرقية. الهدف من الدراسة ايجاد علاقة بين القصورالكلوي المزمن والغدة الدرقية بالاضافة الى دراسة تاثير الفشل الكلوي المزمن اعتمادا على مستويات الهرمونات الدرقية والهرمون المحفز للدرقية. جمعت النمادج من ٤٠ مريضا" مصابا" بالفشل الكلوي بالاضافة الى ٤٠ شخصا" من الاصحاء كمجموعة سيطرة.اعمار المجاميع تتراوح بين (٢٥- ٦٥) سنة . تم قياس هرمونات الغدة الدرقية (ثلاثي يوديد الثايرونين والثايروكسين) ،الهرمون المحفز للدرقية،اليوريا ، حامض اليوريك والكرياتنين .بينت النتائج وجود انخفاض معنوي في كل من ثلاثي يوديد الثايرونين والثايروكسين في حين وجد ارتفاع ملحوظ في كل من الهرمون المحفز للدرقية ،اليوريا، حامض اليوريك والكرياتنين في مرضى القصور الكلوي مقارنة بالاصحاء.

Introduction

The thyroid gland produces two major related hormones thyroxine and triiodothyronine, commonly called T_4 and T_3, respectively, which play essential roles in the complete lack in the processes of metabolism, growth and development in most vertebrate tissue. Complete lack of thyroid secretion usually causes the basal metabolic rate to fall 40 to 50 percent below normal and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 percent above normal [1, 2] . Thyroid secretion is controlled primarily by thyroid stimulating hormone (TSH) secreted by the anterior pituitary gland. Small amount of reverse triiodothyronine (rT_3) and other compounds are also found in venous blood [1]. The synthesis of the thyroid hormones requires (150 -200 µg) of iodine daily. Most dietary iodide is reduced to iodine before absorption. Iodine after conversion to iodide in stomach is rapidly absorbed from the gastrointestinal tract and distributed in the extra cellular fluid [3].There are three thyroid hormones binding proteins in human plasma: albumin, with high capacity and low affinity; thyroxine binding globulin (TBG), with low capacity and high affinity, and transthyretin (TTR) with an intermediate capacity [4]. Thyroid hormone levels are under strict control; this is achieved mainly by feed-back inhibition through: Hypothalamic-pituitary – thyroid axis (HPTA); thyrotrpin – releasing hormone (TRH).l.Thyroid hormone regulation ,thyroid stimulating hormone (TSH) secretion or negative – feed back system on pituitary secretion of (TSH); and factors altering (TSH) secretion ,such as somatostatins dopamine and /or glucocorticoids [5]. Some changes in thyroid function test results are observed in most of the acute and chronic illnesses (i.e. renal diseases, cardiovascular diseases, inflammatory conditions and pulmonary diseases). Alteration in thyroid function test findings may reflect changes in production of thyroid hormone by effects on the thyroid itself, on the hypothalamic - pituitary thyroid – axis, on peripheral tissue metabolism of the hormones, or a combination of these effects [6] .

1Corresponding author E- mail : Nergzkarem@yahoo.com
Received : 13/12/2009
Accepted : 27/4/2010

A general conviction exists that patients with thyroid function test abnormalities do not have hypothyroidism despite the low serum hormone levels in blood and low T_3 in most of the tissues. Many patients with non- thyroid illness (NTI) also receive drugs-that affect thyroid hormone regulation and metabolism. This discussion does not consider pharmacological interference an intrinsic part of the spectrum of changes in hypothalamic – pituitary thyroid function that occur in (NTI)[6] . Assessment of thyroid function in patients with non- thyroid illness is difficult. Many of them have low serum concentrations of both T_4 and T_3 and their serum (TSH) concentration may also have been low. Previously, these patients were thought to be eurthyroid, and the term eurthyroid – sick syndrome was used to describe the laboratory abnormalities. It is possible that the changes in thyroid function during severe illness are protective in that they prevent excessive tissue catabolism [7]. There are two important general principles in laboratory assessment of thyroid: thyroid function should not be assessed in seriously ill patients unless there is strong suspicion of thyroid dysfunction. When Thyroid dysfunction is suspected uncritically ill patients, measurement of serum(TSH) alone is inadequate for the evaluation of thyroid function [7]. Chronic kidney disease is defined as either kidney damage or a decreased kidney glomerular filtration rate(GFR) of less than 60 ml / min / 1.73 m^2 for 3 or more months [8]. The causes of the chronic kidney disease could be due to primary and secondary glomerular disease, tubulointerstial disease and vascular disease [9]. Previous studies on thyroid function tests indicate lower thyroid hormone concentration (T_3, T_4) with normal TSH in heaemodialysed patients compared with normal subjects[10] . Thyroid gland produces T_4 but only 20% of the most metabolically active thyroid hormone T_3 and 5% to 8% as the calorgenically inactive reverse t_3 (rT_3) hormone and T_4 in tissues such as liver,kidneys and muscles[11]. Haemodialysis employs the process of diffusion across a semi permeable membrane to remove toxic products and excess fluid from the blood, while adding desirable components [12] .The aim of this work is to evaluate thyroid gland function in chronic renal failure patients as an attempt to find a relationship between chronic renal failure and thyroid dysfunction.

Materials and Methods

-Selection of Subjects &Blood Collection

Forty patients with chronic renal failure (20 male, 20 female) were enrolled in this study in addition to forty healthy individual as control group (20 male, 20 female). The age ranged from (25 -65) years.To compare the significance of the difference in the mean values in comparison groups, student t - test was applied; $P \leq 0.05$ was considered statistically significant. Patients with ischemic heart disease, diabetes mellitus and thyroid disease (such as hypothyroidism, hyperthyroidism and goiter) were excluded [13] . Five ml of venous blood were aspirated from control group and CRF patients at 8:00 - 9: 00 am. Blood samples were collected into plain test tubes and centrifuged after 30 minutes of collection for 10 minutes at 3000 rpm.Serum was frozen at -20 C^0 till used in determination of T_3, T_4, TSH ,urea , uric acid and creatinine.

- Determination of T3, T4 and TSH

Total triiodothyronine (tT_3), total thyroxin (tT_4) and thyroid stimulating hormone (TSH) were evaluated using VIDAS (T_3) REF, 30403, VIDAS (T_4) REF 304041 and VIDAS (TSH) REF. 30400 from biomerix (France) respectively.The principle of the quantitave determination of T_3, T_4 and TSH combines an enzyme immunoassay competition method with a final fluorescence detection (EIFA).

-Determination of Urea

Urea concentration levels were determined in serum by using enables end point enzymatic (Urease – modified Berthelot reaction) in which urease hydrolyzes urea in an alkaline medium.The ammonium ions react with the salicylate and hypochlorite to form a green colored indophenol.The reaction is catalyzed by the sodium nitroprusside [4].

-Determination of Uric Acid

Uric acid concentrations were determined by using uricase- peroxidose - chromogen sequence in which hydrogen peroxide is formed and reacts as Tinder type reaction[4] .

-Determination of Creatinine

Creatinine levels were evaluated according to Jaffes method.The production of orange color after the addition of alkaline picrate. The color is proportional to the concentration of creatinine[4] .

Results and Discussion

Table (1) shows the (mean ± SD) of T_3, T_4, TSH, urea, uric acid and creatinine concentrations in sera of patients with chronic renal failure and control group,in which $P \leq 0.05$ was considered significant .

Table 1: levels of T_3, T_4, TSH, urea, uric acid and creatinine concentrations in sera of patients with renal failure and control group.

Subjects	Control (n=40)	Patients (n=40)	t -Test
T_3(ng/ml)	1.55 ± 0.54	0.63±0.05	$P \leq 0.05$
T_4(µg/ml)	9.13±2.84	3.32±1.99	$P \leq 0.05$
TSH (µIU/ml)	2.41± 0.52	6.22±3.31	$P \leq 0.05$
Urea (mg/dl)	35.27±5.94	120.81±20.62	$P \leq 0.05$
Uric acid (µmol/L)	300.7± 85.05	1220.6±24.1	$P \leq 0.05$
Creatinine (mg/dl)	0.94 ± 0.19	7.42 ±1.94	$P \leq 0.05$

This study shows highly significant reduction in T_3 and T_4 concentration in patients serum with CRF compared to control group ($P \leq 0.05$) . Intensive studies revealed that renal insufficiency affects thyroid function in multiple ways, including altered peripheral hormone metabolism, disturbed binding to proteins, reduction in tissue thyroid hormone content, and iodine accumulation in thyroid gland [14,15].Another explanation is that the reason for the decrease in T_4 could be attributed to multiple factors such as deficiency of thyroxine binding - globin (TBG) [16,17]. In the present study serum TSH was measured in CRF and control groups.CRF group had TSH above normal range. Some authors interpret this TSH elevation as a sign of recovery from a hypothyroid state despite the distortion of TSH in some euthyroid patients with NTI, who have significant elevation of TSH due to underlying primary hypothyroidism[18] . Highly significant elevation was found in urea, uric acid and creatinine in serum of CRF patients compared to control group.Increase in urea in renal failure are caused by impaired ability to excrete proteinaceous catabolites because of marked reduction in glomerular filtration rate(GRF).Increases in serum creatinine are also a result of decreased renal excretion[19] .

References

1. Guyton A.C. and Hall J. E.: "Text Book of Medical Physiology",11 th ed, Sanders, Elsevier Inc 1600 John F. kenedy Blvd, Philadelphia,2006, 2-9.
2. Iwasaki y., Morishita M., Asai M. , Onish: A., Yoshida M., Oiso y. and Inoue k. :Effects of hormones targeting nuclear receptors on transcriptional regulation of the growth hormone gene in the MtT/S rat somatotrope cell line . Neuroendocrinology, 2004, 79, 229 – 236.
3. Andreoli, Bennett, Carpenter:" Cecil Essentials of Medicine", 4th ed, W. B. Saunders Company, New York,1997,111-116.
4. Benvenga S.: "The Thyroid, Fundamental of Clinical Text Books", 9th ed. Le,Utiger RD(Eds),Lippincot Williams and Willkins, Philadelphia ,2005, 97.
5. Zoeller R. T., Tan S.W. and Tyl R. W:"General background on the hypothalamic-pituitary-thyroid(HPT)axis", Crit Rev Toxical. ,2007 ,37 (1-2),11 - 53.
6. Serhat Aytug MD., Lawrence E and Shapiro MD :Euthyroid Sick Syndrome,EMedicine Specialties,Endocriology,Thyroid,2007,18 ,55.
7. Douglas S. Ross:Thyroid Function in non –thyroid Illness,: Up to Date CME, 2007,134,1-7.
8. Levey As, Coresh J and Bake E.:National kidney foundation practice guidelines for chronic kidney disease:evaluation,classification,and stratification, Ann Intern Med.,2003, 139(2),137-147.
9. Chobanian AV, Bakris GL, Black HR, Cushman WC: Green LA and Izzo JL:The seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure, JAMA,2003, 289 (19),2560 – 2572.
10. Goffin E., Oliveira DBG, Raggatt P. and Evans DB:Assessment of the thyroid function of patients undergoing regular haemodialysis, Nephron.,1993,65, 568–572.
11. Shamsadini S. , Darvish and Abdollah H.:Blood urea nitrogen and thyroid hormone levels before and after haemodialysid, Health Journal,2006,12,55.
12. Hakim RM and Lazarus JM. :Medical aspects of haemodialysis,In:Brenner BM,Rector FC,eds. The

kidney.Philadelphia, Saunders ,1986 ,5,1791.

13. Lisandro lrizarry MD. , Nadine A. and Jeffry G.:Toxicity,Thyroid Hormone ,Medicine specialties, Emergency Medicine,Toxicology,2008,65,44-50.

14. Lim Vs:Thyroid function in patients with chronic renalfailure, Am J. kidney Discase,2001,38(1), S80 – S84.

15. Kaptein EM , Quion – Verde H., ChoolJian CJ, Tany ww , Friedman PE , Rodriquez HJ and Massry SG:The thyroid in end –stage renal diseases, Medicine (Baltimore),1988,67,187 – 197.

16. Biff F. palmer : Metabolic disturbances in chronic renal failure,Saudi Journal of Kidney disease and Transplantation,2002,13(3),273-280.

17. Boelen A, Mass MA, Lowik CW., Platvoet MC. and Wiersinga WM:Induced interleukin-6 (IL-6) knock-outmice:A causal role of IL-6 in the Development of the low 3,5,3-triiodothyronine syndrome, Endocrinology,1996,137,5250 – 5254.

18. Michalak M. , Vagenakis AG. , and Makri: M:Dissociation of the early decline in serum (T3) concentration and serum IL-6 rise and TNFalpha in nonthyroidal illness syndrome induced by abdominal Surgery,J. Clin. Endocrinol Metab.,2001,86 (9),4198 – 4205.

19. Shivananda Nayak B.: "Manipal Manual of Clinical Biochemistry", 3 rd ed., Medical publishers LTD., New Delhi,2007,182 – 186.