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Kronik Böbrek Yetmezliği Hastalarında Renal ve Tiroid Fonksiyon Testlerinin Değerlendirilmesi

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ÖZET

Böbreğin, normalde tiroid hormonlarının metabolizmasında, parçalanmasında ve atılmasında önemli bir rol oynadığı bilinmektedir. Bu durumda böbrek fonksiyonunda meydana gelen bir bozulmanın, tiroid fizyolojisini de etkilemesi beklenmektedir. Çalışmamızda; hemodiyaliz tedavisi gören kronik böbrek yetmezliği olan hastalarda, tek bir hemodiyaliz seansının tiroid fonksiyonuna etkisini araştırmayı ve hemodiyaliz hastalarında tiroid fonksiyon testleri ve bazı biyokimyasal parametreleri sağlıklı gruplarla karşılaştırmayı amaçladık. 29 hastadan (ortalama yaş: 46.17 ± 14.93) diyaliz öncesi ve sonrasında aldığımız kan örnekleri ile kontrol grubu olan 28 sağlıklı katılımcıdan (ortalama yaş: 40.79 ± 14.42) aldığımız kan örnekleri otoanalizör ile analiz edildikten sonra istatistiksel olarak değerlendirildi. Diyaliz öncesi ve sonrası örnekler karşılaştırıldığında TT_4, FT_3 ve FT_4 değerleri istatistiki olarak anlamlı bulundu (sırasıyla $p < 0.01$, $p < 0.05$ ve $p < 0.05$). Ayrıca; diyaliz sonrası ve kontrol grubunun örnekleri incelendiğinde, TT_3 ve TSH düzeylerinde bir anlamlılık tespit edilmezken ($p > 0.1$), aynı grubun TT_3 ($p < 0.01$), FT_3 ($p < 0.001$) ve TSH ($p < 0.05$) değerleri arasında istatistiki olarak önemli düzeyde bir anlamlılık tespit edilmiştir. Buna ek olarak, diyaliz öncesi grupta kreatinin-FT_4 ($p < 0.01$) ve diyaliz sonrası grupta kreatinin-üre ($p < 0.001$) değerlerinin de pozitif bir korelasyon gösterdiği tespit edilmiştir. Bu çalışmada kronik böbrek yetmezliği olan hastalarda tiroid bozukluklarının teşhisinde tiroid fonksiyon testlerinin önemini değerlendirerek tiroid fonksiyon testlerinin hemodiyaliz hastalarının tedavisinde önemli olabileceği kanaatine vardık.

Evaluation of Renal and Thyroid Function Tests in Chronic Renal Failure Patients

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ABSTRACT

It is known that the kidney normally plays an important role in the metabolism, degradation and excretion of several thyroid hormones. Accordingly, deterioration in renal function is expected to lead to disturbing thyroid physiology. In the study, we aimed to investigate the effect of a single hemodialysis session on thyroid function in patients with chronic renal failure that have hemodialysis treatment, and also to compare thyroid function tests and some biochemical parameters in hemodialysis patients with healthy groups. We collected blood samples which were drawn pre- and after-dialysis sessions from 29 patients (mean age: 46.17 ± 14.93) and 28 healthy participants (mean age: 40.79 ± 14.42) as control group, and analysed using an autoanalyzer followed by statistical analysis. TT_4, FT_3 and FT_4 values were found statistically significant ($p < 0.01$, $p < 0.05$ and $p < 0.05$, respectively) in comparison of pre- and post-dialysis samples. Also, the findings of the study revealed that there was a significant difference only among the parameters of TT_3 ($p < 0.01$), FT_3 ($p < 0.001$) and TSH ($p < 0.05$) for the healthy participants and dialysis group in spite of any statistically significance was not detected in the values of TT_3 and TSH parameters of the same group ($p > 0.1$). In addition, statistical results proved that creatinine - FT_4 values ($p < 0.01$) in the pre-dialysis group and creatinine-urea values in the post-dialysis group ($p < 0.001$) were correlated positively. We evaluated the significance of the thyroid function tests during the diagnosis of thyroid disorders in patients with chronic kidney failure in the present study and found that thyroid function tests could be crucial for the treatment of hemodialysis patients.

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INTRODUCTION

The relationship between kidney and thyroid function is a well-known phenomenon for many years [1]. Chronic renal failure (CRF) is characterized by the progressive and irreversible loss of nephrons. CRF has become an epidemic due to its increasing incidence and prevalence worldwide with adverse health outcomes and high costs [2,3]. A part of the metabolic wastes originated from various organ and/or system disorders are removed by hemodialysis procedure. The endocrine abnormalities are commonly observed in CRF patients. Kidneys play an important role in the metabolism, degradation and excretion of thyroid hormones. Thyroid hormones are very crucial in the CRF patients by reason of their influence on the homeostasis of body fluids, vascular resistance and blood pressure [4,5]. Renal function of the patients with chronic kidney disease is affected by various reasons such as decreased thyroid hormone concentration in the circulation, damaged peripheral hormone metabolism, deficient binding to carrier proteins, reduced thyroid hormone content in the tissue and increased iodine deposition in the thyroid glands [6,7]. Chronic renal disease affects the hypothalamus-pituitary-thyroid triangle and the peripheral metabolism of thyroid hormones. Even though most hemodialysis patients are euthyroid [8], subclinical hyperthyroidism and reduced T_3 levels are the most common findings in these patients [9]. And, possible loss of hormone via hemodialysis fluid and heparin used for hemodilution during the procedure could affect serum lipids and thyroid hormones. The aim of this study is to compare the urea, creatinine, and thyroid function indicators and reveal the significance of these parameters in hemodialysis patients.

MATERIAL AND METHODS

29 hemodialysis patients who were followed and treated in the Hemodialysis Unit of Eskişehir State Hospital, Eskişehir, Turkey and 28 healthy individuals were included in the study. This study was performed within the guidelines of the Helsinki Declaration. All participants were informed about the objective of this research. Patient group was checked up before the blood samples were taken whether the existence of any disorder except CRF or not. Cases with any additional disorder to CRF were not included in the study group. 10-12 ml of blood samples were drawn into vacutainer tubes from arm vein with avoiding any formation of stasis or hemolysis and centrifuged at 4000 rpm for 5 minutes. The parameters of urea, creatinine, total T_3 (TT_3), total T_4 (TT_4), free T_3 (FT_3), free T_4 (FT_4) and thyroid stimulating hormone (TSH) were analyzed in Roche Hitachi 7180 clinical autoanalyzer (Hitachi, Tokyo, Japan; reagents from Roche Diagnostics, Mannheim, Germany) by using commercial kits of the same brand. All our analyses from the samples obtained were carried out immediately.

Any differences in parameters between control group and dialysis groups were tested for significance by two-tailed unpaired t-test. And, paired t-test was used for any differences in parameters between patients before dialysis (BD) and after dialysis (AD) groups. $p < 0.05$ was considered to be statistically significant. Also, Pearson's correlation analysis was achieved measure the strength of a linear association between parameters. The statistical analysis of our findings was carried out by using “GraphPad Prizm 3.03” program.

RESULTS

The study group consisted of 14 female (43.64 ± 13.77) and 15 male (48.53 ± 16.05) patients and the control group consisted of 14 healthy women (35 ± 10.57) and 14 healthy men (46.57 ± 15.75) who have normal kidney function tests, have no known disease, do not smoke and use alcohol, and are suitable for the same age average (Table 1). The results of analyzed blood samples which were taken before and after the dialysis session were compared with the control group (Table 2 and Table 3).

Statistical results of pre- and post-dialysis data of the patient group reveals that TT_4, FT_3 and FT_4 values were significantly increased ($p < 0.0001$) after dialysis session in comparison of pre-dialysis samples.

Table 1. *Demographic distribution of the cases.*

	Hemodialysis Group		Control Group	
	Men	*Women*	*Men*	*Women*
n* (Population)	15	14	14	14
Age Average	48.53 ± 16.05	43.64 ± 13.77	46.57 ± 15.75	35 ± 10.57
Σ Age average	46.17 ± 14.93		40.79 ± 14.42	
Number of years on dialysis	7.57 ± 4.95	7.28 ± 4.51		
Number of days of dialysis per week	3 ± 0.65	2.86 ± 0.36		

n***:** Number of cases participating in the study.

Table 2. *The comparison of kidney function results in the study and control groups.*

Parameters [1]	**Group** [2]	**Mean ± SD** [3]	**t** [4]	**p** [5]
Urea (mg/dL)	CG	28.44 ± 6.22	17.39	p < 0.001***
	BD	124.6 ± 28.59		
	CG	28.44 ± 6.22	5.02	p < 0.0001****
	AD	41.88 ± 12.77		
	BD	124.6 ± 28.59	21.83	p < 0.0001****
	AD	41.88 ± 12.77		
Creatinine (mg/dL)	CG	0.84 ± 0.21	14.64	p < 0.0001****
	BD	7.6 ± 2.45		
	CG	0.84 ± 0.21	12.98	p < 0.0001****
	AD	3.01 ± 0.86		
	BD	7.6 ± 2.45	11.04	p < 0.0001****
	AD	3.01 ± 0.86		

[1]: Biochemical parameters; [2]: Groups; AD: after dialysis, BD: before dialysis, CG: control group; [3]: mean and standard deviation of results; [4]: t test values; [5]: p significance values. *: * borderline, ** normal, *** high, **** very high

Besides, any significance was not detected on TT_3 and TSH levels of the same group ($p > 0.1$). Contrary to this, TT_3, FT_3 and TSH levels were statistically significant ($p < 0.01$, 0.0001 and $p < 0.05$; respectively) in comparison of post-dialysis group with healthy volunteers. TT_3, TT_4, FT_3 and FT_4 results of pre-dialysis samples of the patient group were found statistically significant ($p < 0.01$, $p < 0.001$, $p < 0.0001$ and $p < 0.001$; respectively) when they compared with healthy volunteers. Moreover, creatinine - FT_4 values of pre-dialysis samples and creatinine - urea values of the post-dialysis samples of patient group were positively correlated ($p < 0.01$ and $p < 0.001$, respectively) (Table 2 and Table 3).

As seen on Table 2, statistically significance was found on the Urea and Creatinine parameters when pre- and post-dialysis values of patients compared with the control group ($p < 0.001$; $p < 0.0001$ $p < 0.0001$; $p < 0.0001$; respectively).

In our correlation analysis between obtained results of all three groups, a statistically positive correlation was found between urea-TSH, creatinine-FT_3 and creatinine-FT_4 values in our control group ($p < 0.01$ and $p < 0.001$, $r = -0.445$ and $r = 0.461$, $r = 0.579$). In our pre-dialysis group, there was a statistically positive correlation between creatinine-FT3 ($p < 0.04$ and $r = -0.382$). Also, a positive correlation between creatinine-urea values in our post-dialysis group ($p < 0.0001$ $r = 0.0713$) has been identified.

DISCUSSION

Various studies have demonstrated that TT_3, TT_4 and TSH levels decrease in both CRF [10–13] and hemodialysis patients similarly [14,15]. Most hemodialysis patients are considered euthyroid according to common opinion, hence, hypothyroidism is rarely seen in these patients [16]. Hemodialysis is associated with the change in the concentration of thyroid hormones in the circulation. The decrease of TT_3 and FT_3

Table 3. *The comparison of thyroid function results in the study and control groups.*

Parameters [1]	Group [2]	Mean ± SD [3]	t [4]	p [5]
TT_3 (ng/mL)	CG	1.18 ± 0.21	2.99	p < 0.01**
	BD	0.99 ± 0.25		
	CG	1.18 ± 0.21	3.16	p < 0.01**
	AD	0.99 ± 0.22		
	BD	0.99 ± 0.25	0.077	p > 0.1
	AD	0.99 ± 0.22		
TT_4 (µg/dL)	CG	8.35 ± 1.57	5.22	p < 0.001***
	BD	6.13 ± 1.63		
	CG	8.35 ± 1.57	0.40	p > 0.1
	AD	8.15 ± 2.23		
	BD	6.13 ± 1.63	8.83	p < 0.0001****
	AD	8.15 ± 2.23		
FT_3 (pg/mL)	CG	3.17 ± 0.58	7.36	p < 0.0001****
	BD	2.23 ± 0.36		
	CG	3.17 ± 0.58	5.09	p < 0.0001****
	AD	2.50 ± 0.39		
	BD	2.23 ± 0.36	4.95	p < 0.0001****
	AD	2.50 ± 0.39		
FT_4 (ng/mL)	CG	1.24 ± 0.20	3.29	p < 0.001***
	BD	1.04 ± 0.26		
	CG	1.24 ± 0.20	0.66	p > 0.1
	AD	1.20 ± 0.27		
	BD	1.04 ± 0.26	8.46	p < 0.0001****
	AD	1.20 ± 0.27		
TSH (IU/mL)	CG	2.67 ± 1.13	1.29	p > 0.1
	BD	2.20 ± 1.55		
	CG	2.67 ± 1.13	1.81	p < 0.05*
	AD	2.06 ± 1.38		
	BD	2.20 ± 1.55	1.62	p > 0.1
	AD	2.06 ± 1.38		

[1]: Biochemical parameters; [2]: Groups; AD: after dialysis, BD: before dialysis, CG: control group; [3]: mean and standard deviation of results; [4]: t test values; [5]: p significance values. *: * borderline, ** normal, *** high, **** very high

concentrations in blood can cause a number of serious disorders such as systemic acidosis, dialysis, endothelial damage, cardiac dysfunction and inflammation [17]. In our study, TT_3, TT_4, FT_3 and FT_4 results of pre-dialysis samples of the patient group were lower and statistically significant compared to the healthy individuals.

Concentrations of TT_3, TT_4, FT_3 and FT_4 are usually normal in CRF patients, however, they might be lower than normal in some cases. The decrease in T_3 concentration due to decline in peripheral synthesis of T_3 from T_4 is the most common thyroid change in hemodialysis patients.

Chronic metabolic acidosis associated with CRF may contribute to the emergence of this decline. In addition to this, drugs used for anti-coagulation during hemodialysis have been reported to affect thyroid function test results [17,18].

In this study, we found that TT_4 levels were raised significantly in post-dialysis group while the difference between pre- and post-dialysis values of TT_3 was not significant. The difference in the levels of TT_3 between pre-dialysis and healthy individuals was also statistically significant. When levels of post-dialysis samples and healthy individuals were compared, the difference according to pre-dialysis results was smaller but meaningful statistically. While TT_4 levels of healthy individuals and pre-dialysis were statistically very significant, any

significance was not detected in the post-dialysis group.

Many researchers have indicated that CRF patients exhibit normal TSH levels and classified them as euthyroid [8,19,20]. Conversely, in one study, patients were classified as subclinical hypothyroidism due to minor changes in TSH levels [21]. In our study, any statistical significance was not found even though TSH levels of patient group were lower than the healthy individuals.

Plasma FT_3 levels are low in patients with end-stage renal disease. Besides, it has been stated that FT_3 ranges acutely and reversibly during the inflammatory process triggered by various infections that may occur in individuals with chronic renal disease [17–19]. The FT_3 values in our study are consistent with these findings. In comparison of the healthy individuals, both the pre and after dialysis groups were statistically significant. While FT_4 values of our control group compared with pre- and post-dialysis results were not statistically significant, whereas FT_4 results of the pre- and post-dialysis groups were significant.

CONCLUSION

As a result; from a clinical point of view, testing for thyroid function is usually sufficient in patients with kidney disease, but the effects of hypothyroidism and hyperthyroidism on renal function should be considered for the removal of the diagnostic errors. Since the drugs used in the treatment of thyroid and kidney diseases may lead to changes in the pathophysiology of these organs, the differences that may be encountered in thyroid function tests in acute or chronic renal diseases should also be considered.

REFERENCES

[1] A.I. Katz, D.S. Emmanouel, M.D. Lindheimer, Thyroid hormone and the kidney, *Nephron*. 15 (1975) 223–249.

[2] G. Süleymanlar, Kronik böbrek hastalığı ve yetmezliği: tanımı, evreleri ve epidemiyolojisi, *Türkiye Klinikleri Dahili Tıp Bilimleri Dergisi*. 3 (2007) 1–7.

[3] A.S. Levey, J. Coresh, E. Balk, A.T. Kausz, A. Levin, M.W. Steffes, R.J. Hogg, R.D. Perrone, J. Lau, G. Eknoyan, National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification, *Annals of Internal Medicine*. 139 (2003) 137–147.

[4] W.J. Kalk, J.E. Morley, C.H. Gold, A. Meyers, Thyroid function tests in patients on regular hemodialysis, *Nephron*. 25 (1980) 173–178.

[5] M.C. Pagliacci, G. Pelicci, F. Grignani, C. Giammartino, L. Fedeli, C. Carobi, U. Buoncristiani, I. Nicoletti, Thyroid function tests in patients undergoing maintenance dialysis: characterization of the 'low-T4 syndrome'in subjects on regular hemodialysis and continuous ambulatory peritoneal dialysis, *Nephron*. 46 (1987) 225–230.

[6] G. Lippi, M. Montagnana, G. Targher, G.L. Salvagno, G.C. Guidi, Relationship between thyroid status and renal function in a general population of unselected outpatients, *Clinical Biochemistry*. 41 (2008) 625–627.

[7] G. Rajeev, W.D.S.C. Rayappa, R. Vijayalakshmi, M. Swathi, S. Kumar, Evaluation of thyroid hormone levels in chronic kidney disease patients, *Saudi Journal of Kidney Diseases and Transplantation*. 26 (2015) 90.

[8] M.W. Szkudlinski, V. Fremont, C. Ronin, B.D. Weintraub, Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships, *Physiological Reviews*. 82 (2002) 473–502.

[9] G. Basu, A. Mohapatra, Interactions between thyroid disorders and kidney disease, *Indian Journal of Endocrinology and Metabolism*. 16 (2012) 204.

[10] J. Punekar, A.A. Singh, M.K. Malav, Study of thyroid function in patients with chronic kidney disease, *Int J Health Sci Res*. 7 (2017) 68–72.

[11] P.B. V Vivek, S. Kirubakaran, K. Elavarasan, S. Natarajan, A Prospective Study on the Evaluation of Thyroid Function Status in Patients with Chronic Kidney Disease, *Journal of Medical Science and Clinical Research*. 5 (2017) 28007–28014. doi:https://dx.doi.org/10.18535/jmscr/v5i9.107.

[12] V. V Deokar, S.S. Patil, K. Babu, J. Patel, Evaluation of thyroid function status in patıents with chronic kidney disease, *Journal of Critical Reviews*. 7 (2020) 535–538.

[13] P. Iglesias, J.J. Díez, Thyroid dysfunction and kidney disease, *European Journal of Endocrinology*. 160 (2009) 503–515.

[14] J. Horacek, S.D. Sulkova, M. Kubisova, R. Safránek, E. Malírova, M. Kalousová, I. Svilias, J. Malý, L. Sobotka, P. Zák, Thyroid hormone abnormalities in hemodialyzed patients: low triiodothyronine as well as high reverse triiodothyronine are associated with increased mortality, *Physiological Research*. 61 (2012) 495.

[15] S.E.S. Farag, Functional and Morphological Thyroid Disorders in Hemodialysis Patients, *J Thyroid Disord Ther*. 2 (2013) 2–5.

[16] S. Jusufovic, E. Hodzic, Functional thyroid disorders are more common in patients on chronic hemodialysis compared with the general population, *Materia Socio-Medica*. 23 (2011) 206.

[17] E.O. Kim, I.S. Lee, Y.A. Choi, S.J. Lee, Y.K. Chang, H.E. Yoon, Y.S. Jang, J.M. Lee, H.S. Kim, C.W. Yang, Unresolved subclinical hypothyroidism is independently associated with progression of chronic kidney disease, *International Journal of Medical Sciences.* 11 (2014) 52.

[18] S. Sakurai, Y. Hara, S. Miura, M. Urabe, K. Inoue, T. Tanikawa, M. Yanagisawa, M. Iitaka, J.U.N. Ishii, Thyroid functions before and after maintenance hemodialysis in patients with chronic renal failure, *Endocrinologia Japonica*. 35 (1988) 865–876.

[19] K. Yonemura, T. Nakajima, T. Suzuki, S. Ando, R. Genma, H. Nakamura, A. Hishida, Low free thyroxine concentratios and deficient nocturnal surge of thyroid-stimulating hormone in haemodialysed patients compared with undialysed patients, *Nephrology Dialysis Transplantation*. 15 (2000) 668–672.

[20] J. Malyszko, J. Malyszko, S. Wolczynski, M. Mysliwiec, Adiponectin, leptin and thyroid hormones in patients with chronic renal failure and on renal replacement therapy: are they related?, *Nephrology Dialysis Transplantation*. 21 (2006) 145–152.

[21] M. Tarakçıoğlu, E. Algün, R. Şekeroğlu, S. Alıcı, S. Topal, İ. Meral, Hemodiyaliz Hastalarında Tiroid Hormon Düzeyleri ve Bir Hemodiyaliz Seansının Bu Değerlere Etkisi, *Van Tıp Dergisi*. 4 (n.d.) 201–204.