THYROID HORMONES IN HEMODIALYZED PATIENTS CANDIDATE FOR RENAL TRANSPLANTATION

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SUMMARY: Chronic renal failure (CRF) may be associated with moderate to severe alteration of thyroid hormones metabolism. Dialysis does not significantly normalize these abnormalities, but transplantation leads to improve the condition. In this study to evaluate the relationship between serum levels of thyroid hormones and transplanted kidney function first thyroid hormones were measured in 30 patients under dialysis selected for renal transplantation. The results were compared with those of 40 control individuals. After renal transplantation the patients treated with Cyclosporine, Prednisolone and Azatioprine were divided into two subgroups according to their serum levels of urea nitrogen, creatinine and kidney functions: Patients with primary graft function (group I) and patients with delayed graft function (group II). The thyroid hormones were evaluated in two groups. In hemodialyzed patients, the mean levels of measured thyroid hormones were at normal range but comparing with the control, mean levels of these hormones were low except T_3 uptake (T_3 UP) which was increased. No changes were observed in the levels of TSH. Ten days after graft, reduction in the serum levels of thyroid hormones were observed and elevation of T_3 uptake was found in both groups. The alterations in group II were more than group I. In the 30th day after graft, changes in group I reached to normal levels and comparing with those of before operation marked improvement was noticed, but comparing with that of control the levels of FT_3, TT_3, TT_4 and FTI were still low. In the group II the levels of TT_3 and FTI were lower than that of normal and comparing with those of before operation reduction in the levels of TT_4, TT_3, FT_3, FT_4 and FTI was found. It was concluded that there is relationship between the levels of thyroid hormones and function of transplanted kidney and it is more significant in the cases of TT_4 and TT_3.

Key Words: Renal transplantation, FT_3, FT_4, TT_3, TT_4, FTI.

INTRODUCTION

End stage renal disease (ESRD) is a relatively common non-thyroidal illness, which induces significant morbidity and mortality (1). ESRD is a moderate to sever non-thyroid illness but nevertheless frequently alters thyroid hormone metabolism (2). In addition to metabolic and endocrine derangement induced by ESRD, these patients frequently have a multitude of non-renal non-thyroidal disorders that affect thyroid hormones metabolism including diabetes mellitus, infections and malnutrition and they are treated by a variety of pharmacological agents (3).

Low T_3 and T_4 concentration and delayed TSH responses have been described in euthyroid

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Table 1: Mean levels of BUN and creatinine in PGF and DGF patients before and after operation.

	PGF			DGF		
Variables	1	2	3	1	2	3
BUN (mg/dL)	61.2 ± 13*	20.6 ± 4.7	17.8 ± 2.4	58.5 ± 10	35.8 ± 8.9	32.9 ± 5.5
Creatinine (mg/dL)	10.1 ± 2.9	1.2 ± 0.27	1.1 ± 0.24	11.7 ± 2.9	2.5 ± 0.85	2.23 ± 0.56

* mean ± SD
1=Before renal transplantation 2 =10 days after renal transplantation 3 =30 days after renal transplantation.

patients with ESRD. Recently it has been suggested that sulphation pathway plays an important role in thyroid hormone metabolism in patients with renal disease (4).

Renal transplantation is the treatment of choice for patients with ESRD. Six months after renal transplantation return of thyroid hormones to normal concentration has been demonstrated (3). Few days after operation classic low T_3 syndrome may be observed but it can be due to stress of the operation (5).

There are no data available evaluating sequential changes in thyroid function in an early period after renal transplantation. In this study we have evaluated thyroid hormones in the immediate postoperative period after renal transplantation and the results were compared with those of obtained before operation and normal individuals. The study was performed in order to determine the relationship between improving renal function and changes in the thyroid hormone levels in serum.

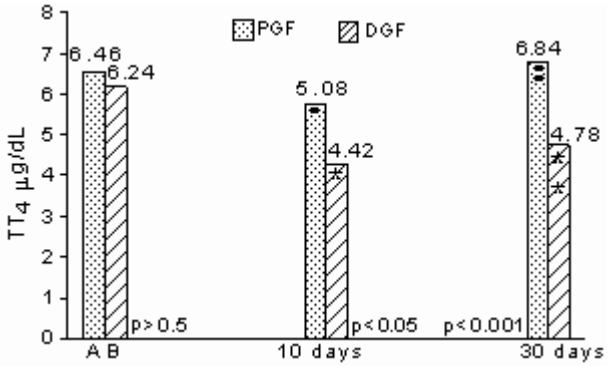
MATERIALS AND METHODS

Patients

The study was carried out on thirty patients (11 females and 19 males) with CRF, mean age 38.4±13.7 (range 24-62) years and all were candidates for renal transplantation. None of the patients had thyroid disease, nor were given thyroid-specific medication during the past 6 months. After renal transplantation the patients were divided into two groups according to their serum levels of urea, creatinine and kidney function: primary graft function (PGF) group and delayed graft function (DGF) group.

As a control thyroid hormones were also estimated in forty apparently healthy individuals (16 females and 24 males), mean age 39.4 ± 15.3 (range 14-68 years).

Figure 1: Comparison of mean levels of TT_4 in PGF and DGF groups.



TT_4: Total thyroxine
DGF: Delayed graft function
PGF: Primary graft function
A and B: Groups before graft
• p<0.001 versus group A
•• p<0.05 versus group A
*p<0.001 versus group B
** p<0.001 versus group B

Table 2: Comparison mean levels of serum thyroid hormones and TSH in patients under dialysis and control.

	Control		Patients			
Variables	N	Mean ± SD	N	Mean ± SD	t value	p value
TT_4 (mg/dL)	40	8.85 ± 1.75	30	6.39 ± 0.8	-7.79	<0.001
TT_3 (ng/dL)	40	141.6 ± 18.64	30	98.13 ± 19.9	-9.37	<0.001
FT_4 (p.mol)	40	17.32 ± 2.2	30	15.59 ± 2.44	-3.07	<0.05
FT_3 (p.mol)	40	4.01 ± 0.85	30	2.67 ± 0.30	-9.24	<0.001
TSH (mu/l)	40	1.29 ± 0.62	30	1.53 ± 0.53	1.69	>0.05
T_3 Up (%)	40	29.16 ± 1.5	30	30.33 ± 1.95	2.84	<0.05
FTI (mg/dL)	40	2.6 ± 0.5	30	1.93 ± 0.26	-7.06	<0.001

Three samples were collected from the patients; (1) before graft and last dialysis, (2) ten days and (3) one month after graft.

Methods

Serum levels of urea and creatinine were measured by standard methods using COBAS MIRA autoanalyzer and thyroid hormones by radio immunoassay techniques.

RESULTS

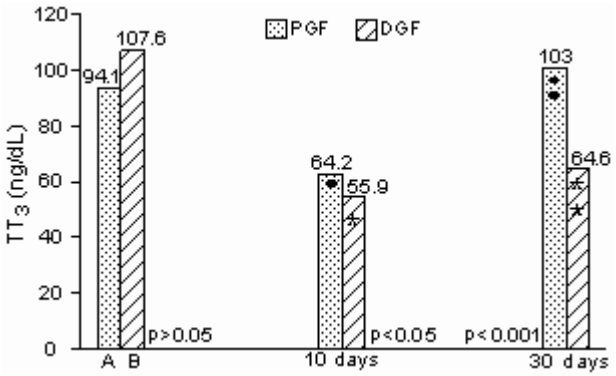
Mean levels of BUN and creatinine in the serum of patients (PGF and DGF) are shown in Table 1. After 10 and 30 days of the graft, reduction in the levels of both parameters in PGF was more than that of DGF.

Comparing the mean levels of thyroid hormones in serum of patients under dialysis with those of control significant reduction in the levels of TT_4, TT_3, FT_3 and FTI in the patients was noticed ($p<0.05$ in all cases).

Marked increase of T_3 uptake was observed ($p<0.05$) but in the case of TSH no differences were found (Table 2).

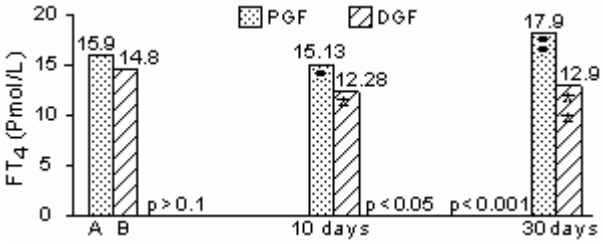
Mean levels of TT_4, TT_3, FT_4, FT_3, TSH, T_3UP and FTI in serum of the PGF and DGF patients before renal transplantation, 10 and 30 days after operation are shown in Figures 1-7. Comparing with those of control 10 days after graft, reduction in serum levels of thyroid hormones and TSH and

Figure 2: Comparison of mean levels of TT_3 in PGF and DGF groups.



TT_3: Total triiodothyronine
DGF: Delayed graft function
PGF: Primary graft function
A and B: Groups before graft
• p<0.001 versus group A
•• p<0.05 versus group A
*p<0.001 versus group B
** p<0.001 versus group B

Figure 3: Comparison of mean levels of FT_4 in PGF and DGF groups.



FT_4: Free thyroxine
DGF: Delayed graft function
PGF: Primary graft function
A and B: Groups before graft
• p<0.05 versus group A
•• p<0.001 versus group A
*p<0.05 versus group B
** p>0.1 versus group B

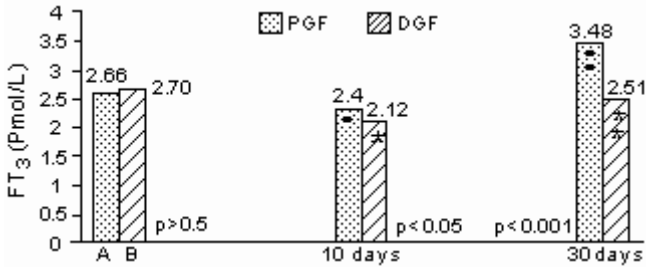
elevation of the T_3 uptake were found in both groups. The changes in DGF were more than PGF. Thirty days after graft alteration in PGF reached to normal levels and comparing with those of before operation marked improvement was noticed, but comparing with that of control the levels of FT_3, TT_3, TT_4 and FTI were still low. In the DGF the levels of TT_3 and FTI were lower than that of normal and comparing with those of before operation, reduction in the mean levels of TT_4, TT_3, FT_4 and FTI was found.

DISCUSSION

The hypothalamic-pituitary-thyroid hormone axis as well as peripheral thyroid hormone metabolism are altered in ESRD patients without concurrent thyroid diseases. All patients showed low T_3 and T_4 concentrations in the presence of low TSH in up to 10 days after renal transplantation. TT_3 seems to be a reliable marker reflecting graft function, because in PGF, T_3 concentrations returned to normal within 30 days after renal transplantation whereas in DGF, T_3 levels remained in the hypothyroid range. Moreover, there was a negative correlation of T_3 and serum levels of creatinine and urea. Similar results have been reported by others (6).

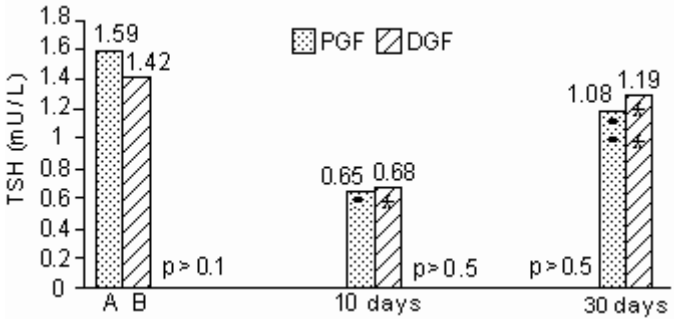
T_4 decreased significantly postoperatively but returned to normal in patients with PGF on day 30. Patients with DGF continued to have significantly decreased T_4 concentrations. T_4 binding inhibitors and low TSH may contribute to this state (7).

Figure 4: Comparison of mean level of FT_4 in PGF and DGF groups.



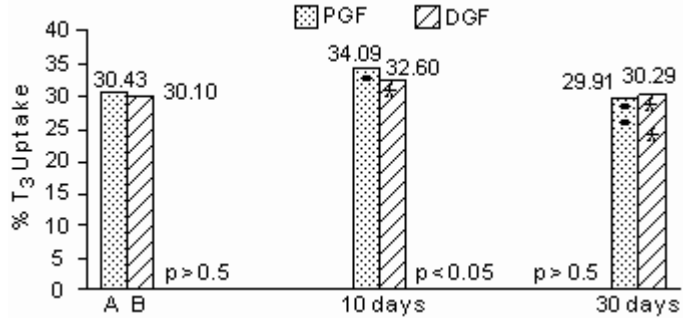
FT_3: Free triiodothyronine
DGF: Delayed graft function
PGF: Primary graft function
A and B: Groups before graft
• p<0.05 versus group A
•• p<0.001 versus group A
*p<0.05 versus group B
** p>0.1 versus group B

Figure 5: Comparison of mean levels of TSH in PGF and DGF groups.



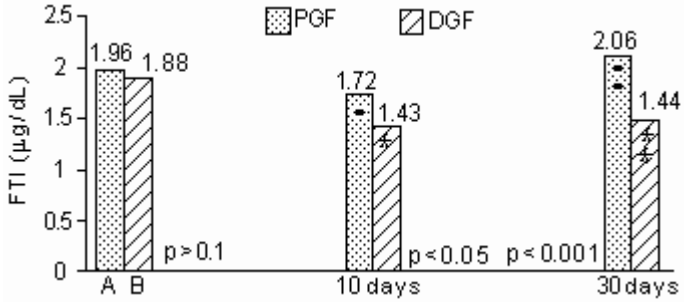
TSH: Thyroid stimulatinghormone PGF: Primary graft function • p<0.01 versus group A *p<0.05 versus group B
DGF: Delayed graft function A and B: Groups before graft •• p>0.05 versus group A ** p>0.05 versus group B

Figure 6: Comparison of mean levels of T_3UP in PGF and DGF groups.



T_3 Up:Triiodothyronine uptake PGF: Primary graft function • p<0.001 versus group A *p<0.05 versus group B
DGF: Delayed graft function A and B: Groups before graft •• p>0.5 versus group A ** p>0.05 versus group B

Figure 7: Comparison of mean levels of FTI in PGF and DGF groups.



FTI: Free thyroxine index PGF: Primary graft function • p<0.05 versus group A *p<0.05 versus group B
DGF: Delayed graft function A and B: Groups before graft •• p<0.05 versus group A ** p<0.001 versus group B

Serum TSH levels fall on the first day after renal transplantation and this is a well-known phenomenon after surgery (8). TSH is also a marker of recovery.

Comparing the other measured parameters it was concluded that there is relationship between thyroid hormones and function of transplanted kidney and it is more significant in the case of TT_4 and TT_3.

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