THYROID HORMONE PROFILE IN PERITRANSPLANT PERIOD IN LIVE DONOR KIDNEY TRANSPLANTATION

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ABSTRACT

Chronic renal failure, characterised by two factors acting in opposite directions with respect to the serum thyroid hormone levels was chosen for the study. Healthy controls, donors undergoing nephrectomy and renal transplant recipients were studied. In transplant recipients, presurgical levels of total thyroxine(TT4),free triiodothyronine(FT3) and free thyroxine(FT4) were lower than controls, and immediately after the release of arterial clamps, there was an upsurge of total triiodothyronine (TT3),TT4, FT3 and FT4 due to administered and/or endogeneously secreted catecholamines. The levels of the 7th day were comparable to the presurgical levels. The changes observed in donors and recipients were similar indicating that the homonal changes observed are mostly due to surgical stress. Recovery in the homonal status did not start in the first week of posttransplant period.

KEY WORDS : Thyroid hormones, renal transplantation, nonthyroidal illness

INTRODUCTION

Significant alterations in the normal pattern of thyroid hormone indices have been described in patients suffering from a wide variety of nonthyroidal illnesses (NTI). The most common abnormality observed is a depression in both total and free serum T3 levels, a condition clinically termed the low triiodothyronine(T3) state. The serum thyroid stimulating hormone (TSH) concentrations are not usually elevated. In some critically ill patients, the low T3 state is associated with marked depression in serum thyroxine(T4) values, the low T3-T4 state. It appears likely that the low T3-T4 state usually represents an expression of extreme derangement and

is associated with increased mortality rate. The assessment of thyroid indices during the recovery phase from NTI may also provide useful information to the clinician. The persistence of low T3 state in-patients who have apparently recovered from their illness may reflect the presence of an unsuspected disease condition, malnutrition or both (1).

In chronic renal failure, most of the studies indicate decrease in thyroid hormones with normal TSH (2-4). Despite the decreased hormone levels, there are no features of hypothyroidism(5). The normal TSH level has been shown to be due to decreased sensitivity of thyrotrophs to decreased serum T4 and T3 levels(6). Our previous studies also showed a decrease in the concentration of T4 and free thyroxine (FT4) in patients with end stage renal disease on

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maintenance haemodialysis (7).

Renal replacement therapy aims at surgical implantation of functioning kidney in patients with end stage renal disease. This is expected to correct the abnormalities arising due to failure of the native kidneys. Logically, the thyroid abnormality is also expected to improve. In fact, there are reports that successful kidney transplantation improves both T3 and T4 concentrations over a period of months (8-11). But there are no reports about the changes in the immediate posttransplant period.

Also, this period is compounded by the fact that surgical stress is known to affect the serum thyroid hormone levels in a manner similar to that of nonthyroidal illness. Hence, this situation is characterised by two factors acting in opposite directions with respect to the serum thyroid hormone levels. As there are no data available in this situation, it was thought worthwhile to study the thyroid hormone profile in the immediate posttransplant period and compare the data with the changes observed in donors where in only the surgical stress exists.

MATERIALS AND METHODS

The subjects selected for the study were divided into three groups. Group I consisted of 15 healthy volunteers in the mean age of 38.2 ± 10.1 years. Group II included 10 male euthyroid end stage renal disease patients on maintenance haemodialysis who underwent live donor kidney transplantation. The mean age of this group was 45.0 ± 10.1 years. Group III consisted of 6 donors who donated their kidneys and underwent donor nephrectomy. The mean age of this group was 33.8 ± 8.6 years. All patients in group II received allografts from live related donors and underwent renal transplantation under

general anaesthesia. They received methylprednisolone 1 g i.v. injection during surgery prior to release of arterial clamps after anastomosis. The immunosuppressive treatment given to these patients includes cyclosporin, azathioprim and methylprednisolone. All patients in group III underwent donor nephrectomy, under general anaesthesia.

Blood samples were collected from controls (Group I) once after an overnight fast. For Group II patients, blood samples were collected before surgery, immediately after release of arterial clamps after the anastomosis, 6 hours, 12 hours and 24 hours after the release of clamps and on 4th and 7th postoperative days. In the case of Group III, samples were collected before surgery and on 2nd, 4th and 7th post operative days. Plasma was separated and stored at -20°C till further analysis. Creatinine was analysed on Beckman CX4 Random access analyser. total triiodothyronine (TT3), total thyroxine (TT4), thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4) were analysed by enzyme immunoassay using commercial kits on ES33 analyser (Boehringer Mannheim). Two controls run along with each batch of samples were within the assigned limits. The within run coefficients of variation (CV) were as follows: TT3-6.74%, TT4- 5.96%, TSH-2.77%, FT3-8.33 and FT4-8.42%.

The results were expressed as mean $\pm$ SD. Statistical analysis was carried out using the statistical software SPSS for windows Ver 6.0. Mann whitney U test and wilcoxon signed Rank test were employed to estimate the significance of difference between means of unpaired and paired data respectively. P value of 5×10^{-2} (0.05) was considered significant.

RESULTS AND DISCUSSION

The mean $\pm$ SD of various parameters studied are given in table 1. Fig. 1 depicts the changes in the hormones with time in group II. Fig. 2 compares the changes in hormones in groups II and III.

after the release of clamps during transplant surgery. This is usually transient but some times requires administration of catecholamines. The upsurge of the hormones observed can be explained to be the result of administered and/or endogeneously secreted catecholamines. Then, the levels started decreasing till the 7th day. The levels of the hormones on 7th day were comparable to the presurgical levels pointing to

Table I Mean $\pm$ S.D. of parameters studied in different groups

Group		Creatinine (mg%)	TT3(nmol/L)	TT4(nmol/L)	FT3(pmol/L)	FT4(pmol/L)	TSH(μ U/ml)
I control		0.9 $\pm$ 0.3	1.9 $\pm$ 0.4	86.8 $\pm$ 19.2	6.8 $\pm$ 1.3	16.1 $\pm$ 4.6	2.0 $\pm$ 1.2
	before surgery	6.3 $\pm$ 1.5*	1.7 $\pm$ 0.4	66.0 $\pm$ 22.2*	4.7 $\pm$ 1.0*	11.8 $\pm$ 2.0*	1.6 $\pm$ 0.8
	after release of clamps	6.7 $\pm$ 1.7*	2.4 $\pm$ 0.6*#	72.6 $\pm$ 16.0	7.3 $\pm$ 2.8#	21.9 $\pm$ 6.7*#	1.5 $\pm$ 0.8
	6 hrs	4.0 $\pm$ 1.1*#	1.5 $\pm$ 0.5*	67.0 $\pm$ 40.0	4.9 $\pm$ 1.6*	12.5 $\pm$ 5.4*	0.7 $\pm$ 0.5*#
II transplant reciepiant	12 hrs	2.7 $\pm$ 0.9*#	1.3 $\pm$ 0.4*	67.4 $\pm$ 39.2	3.5 $\pm$ 0.9*#	12.7 $\pm$ 3.9*	0.7 $\pm$ 0.3*#
	24 hrs	1.8 $\pm$ 0.9*#	1.5 $\pm$ 0.3*	62.2 $\pm$ 39.0*	3.4 $\pm$ 1.2*#	12.0 $\pm$ 3.5*	0.4 $\pm$ 0.4*#
	4th day	1.3 $\pm$ 0.7#	1.8 $\pm$ 0.5	66.4 $\pm$ 24.2*	4.4 $\pm$ 2.0*	12.0 $\pm$ 4.4*	0.6 $\pm$ 0.4#
	7th day	1.2 $\pm$ 0.7#	1.7 $\pm$ 0.7	67.6 $\pm$ 41.5*	4.7 $\pm$ 2.5*	13.4 $\pm$ 3.6*	1.1 $\pm$ 0.7*#
	before surgery	-	2.0 $\pm$ 0.6	82.9 $\pm$ 18.8	7.0 $\pm$ 2.5	12.5 $\pm$ 4.2	2.9 $\pm$ 1.7
III donors	2nd day	-	1.2 $\pm$ 0.5#	70.1 $\pm$ 12.7	4.5 $\pm$ 1.2#	9.8 $\pm$ 2.3	3.2 $\pm$ 4.6
	4th day	-	1.6 $\pm$ 0.5	75.2 $\pm$ 19.8	5.4 $\pm$ 2.1#	12.9 $\pm$ 5.8	3.2 $\pm$ 1.2
	7th day	-	1.9 $\pm$ 0.6	84.1 $\pm$ 40.4	6.2 $\pm$ 3.1	15.3 $\pm$ 7.9	4.6 $\pm$ 2.6#
IV reference range		0.6 - 1.5	1.2 - 2.8	58 - 151	4.1 - 9.2	10.0 - 25.0	0.3 - 0.5

* statistically significant difference with respect to 'control' ($p < 0.05$), # statistically significant difference with respect to 'before surgery' ($p < 0.05$)

In transplant recipients. (Group II) the presurgical levels of TT4, FT3 and FT4 were found to be significantly lower than the control group. These findings are in accordance with the previous reports(2-4). During surgery, immediately after the release of arterial clamps, there was an upsurge of TT3, TT4, FT3 and FT4 reaching or even crossing the levels of control group. Hypotension is known to occur immediately

the possibility that whatever changes occurred in the first week after surgery are most probably due to surgical procedure and the changes expected due to recovery of renal function did not start at least till the end of one week. Presurgical serum TSH levels in these patients were lower than the control group but the difference was not statistically significant. Thereafter the levels fell throughout the study period except for a little improvement on 7th day. However

Fig. 1 Change in thyroid hormones in group II patients

even on 7th day, the TSH levels were still significantly lower than the presurgical levels. This may be explained by the methylprednisolone infusion given just before the release of clamps.

In group III donors, who underwent donor nephrectomy, the basal levels of all the parameters were within the normal range and there was no statistically significant difference between this group and controls. By 2nd day, all the hormones except TSH decreased. But the decrease in TT3 and FT3 only was statistically significant. This was followed by a rise to presurgical levels by 7th day. These findings suggest the occurrence of low T3 state after surgery in otherwise healthy individuals which is transient and improves within 7 days.

Fig. 2 Comparison of hormonal changes in groups II and III

The changes observed in group II and group III are similar but for the fact that the basal levels of TT4, FT3 and FT4 were lower. The graph showing the trend of changes reveals the same trend in both the groups for TT3, FT3, TT4 and FT4 (Fig 2). This further supports the idea that the changes observed in group II patients are as a result of surgical procedure. Further lowering of thyroid hormones in group II

patients during the postoperative period and the finding that the hormone levels did not improve over the presurgical levels on 7th day indicates that the effect of surgical procedure as a cause of NTI is additive and independent of the existing factor i.e. chronic renal failure. Further studies including regular long term follow up are required to understand fully the process of normalisation of thyroid hormone indices in patients undergoing successful renal transplantation.

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