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LEPTIN: A DRIVING FORCE BEHIND THYROID PROBLEMS

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ABSTRACT

Introduction: Apart from diabetes mellitus, thyroid dysfunction is one of the most common endocrine disorders encountered in adults, affecting up to 10% of the UK population Leptin is a 16kDa protein hormone that plays a key role in regulating energy intake and energy expenditure, including appetite and metabolism.

Aim: The aim of this study was to estimate thyroid hormones and Serum Leptin levels in patients with thyroid disorders and to find their correlation with each other.

Material & Methods: 50 diagnosed patients of thyroid disorders and 30 healthy controls were recruited in our study. Serum Leptin Levels, Serum T_3, T_4, TSH levels were estimated in both cases and controls using ELISA method.

Results: There was significant negative correlation between Serum Leptin and Serum T_3. There was no significant but negative correlation between Serum Leptin and Serum T_4. A very significant positive correlation was seen between Serum TSH and Serum Leptin levels.

Conclusion: Leptin problems are a driving force behind thyroid problems. Leptin triggers the decreased production of thyroid hormones. Improving leptin problems and losing weight will improve thyroid function.

Key Words: Leptin, Thyroid, TSH- Thyroid Stimulating Hormone, T4- Thyroxine, T3- Triiodothyronine

INTRODUCTION

Thyroid dysfunction is one of the most common endocrine disorders encountered in adults. The two most common thyroid diseases are inadequate thyroid function i.e. hypothyroidism & excessive thyroid function i.e. hyperthyroidism. [1] Thyroid hormones are essential for the regulation of important processes involved in thermogenesis, energy consumption & many other metabolic reactions. Leptin, the ob gene product is a peptide hormone, secreted by adipocytes. [2] It circulates at levels proportional to body fat. Leptin enters the central nervous system in proportion to plasma concentration. It controls food intake and energy expenditure by acting on receptors in mediobasal hypothalamus. [3]

In human, leptin concentrations are elevated in the obese when compared with lean subjects, and their levels are positively correlated to the degree of obesity. In addition administration of leptin to rats deprived of food corrected many of the neuroendocrine changes (e.g. the decrease in the release of thyroid hormone) that occur as a result of food deprivation. [4]

There are three general ways in which alterations of the leptin regulatory loop could lead to obesity. a) Failure to produce leptin as occur in ob/ob mice, would result in obesity b) inappropriately low leptin secretion for a given fat mass c) Obesity could result from relative or absolute insensitivity to leptin at its site of action. [5]

Both thyroid hormones and leptin have effects on similar aspects of body homeostasis, but their potential interaction is controversial. [2]

Aims and Objectives

1. To study the serum leptin levels in various disorders of thyroid gland.
2. To evaluate thyroid hormone levels in various disorders of thyroid gland.
3. To study the correlation of serum leptin with thyroid hormones in various disorders of thyroid gland.

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MATERIALS AND METHODS

The present study was conducted in Department of Biochemistry at Govt. Medical College, Patiala on 50 diagnosed cases of thyroid disorder referred by Department of Medicine, Rajindra Hospital, Patiala from October, 2011 to May, 2012. For comparison 30 age and gender matched healthy individuals constituted the control group. Patients with history of any drug intake, history of any infection/illness, pregnant females, diabetic patients, cancer including thyroid cancer were excluded from the study. Informed consent of all subjects and detailed history were taken at the beginning of the study. Fasting venous blood samples were collected under all aseptic conditions, and subsequently, Serum Leptin Levels, Serum T_3, T_4, TSH levels were estimated in both cases and controls. Serum Leptin, Serum T_3, T_4, TSH were estimated by ELISA method. ERBA-thyrokit was used for Serum.T_3, T_4 and TSH whereas AviBion Human Leptin ELISA Kit [6] was used for Serum Leptin. Although the patients were known cases of thyroid disorders but when their hormonal status was assessed they were divided into 3 categories: euthyroid, hypothyroid and hyperthyroid. Out of the 50 cases, 20 cases were of euthyroidism, 20 cases were of hypothyroidism and 10 cases were of hyperthyroidism.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS).Means and Standard Deviations (SD) were calculated for all parameters. The independent sample *t*-test was used to compare the means of different variables in the two groups. In addition, the Pearson correlation coefficient **(*r*)** was used for correlation analysis. *P* value <0.05 was considered significant.

RESULTS

The mean age in the present study was 42.2±15.30 years (Table I). There were 40 females and 10 males and male: female ratio was 1:4(Table II). Although the patients were known cases of thyroid disorders but when their hormonal status was assessed they were divided into 3 categories: euthyroid, hypothyroid and hyperthyroid. Out of the 50 cases, 20 cases were of euthyroidism, 20 cases were of hypothyroidism and 10 cases were of hyperthyroidism (Table IV). Serum T_3, T_4, TSH and Serum Leptin was measured in both study and control group and their correlation was studied with statistical analysis (Table III,V). There was significant negative correlation between Serum Leptin and Serum T_3 (Table VI).There was insignificant but negative correlation between Serum Leptin and Serum T_4 (Table VI). There was a statistically very significant positive correlation between Serum Leptin and Serum TSH (Table VI).

There were total 20 (40%) cases of euthyroidism out of total 50(100%) cases. Among those 20(40%) cases, 12(60%) were having normal leptin levels, 6(30%) cases were having increased leptin levels and 2(10%) cases were having decreased leptin levels. In total 20 (40%) cases of hypothyroidism, 4(20%) were having normal leptin levels, 14(70%) cases were having increased leptin levels and 2(10%) cases were having decreased leptin levels. In total 10 (10%) cases of hyperthyroidism cases, 2(20%) cases were having normal leptin levels and 8(80%) cases were having decreased leptin levels (Table VII).

DISCUSSION

Mean age for the study group was 42.2±15.30years and for control group was 36.07±14.24 years. There was no significant difference in the mean age of patients among the two groups.

Yoshida et al observed the mean age of 38.4±1.8 years in his study. [10] Tene Perez et al found the mean age of 35 years in his study. [11]

In this study there were 40 females and 10 males and male: female ratio was 1:4. Zimmermann Belsing et al had a similar type of sex distribution among his patients i.e. 2 males and 8 females.[9]

In the present study, there was significant (p=0.026) but negative correlation (r=-0.314) between Serum Leptin and Serum T_3. Al-shoumer et al gave significant (p=0.003) negative correlation between Serum Leptin and Serum T_3. [4] Azza M Abdu Allah also reported negative correlation between Serum Leptin and Serum T_3 with significant p value (p=0.000). [12]The possible reason for significant p value between Serum Leptin and Serum T_3 may be that the T_3 induced alternation in adipocyte sensitivity to catecholamines can give rise to altered serum leptin levels (decreased in hyper thyroid patients).[7] There was no significant but negative correlation between Serum Leptin and Serum T_4. A study by Ozata et al supported the present study and gave the negative but insignificant correlation between Serum Leptin and SerumT_4.[13] Hseih et al reported significant negative correlation between Serum Leptin and Serum T_4 [14] The reason is that leptin affects thyroid deiodinase activities with activation of T_4 to T_3 conversion. [8,9]

There was positive and very significant correlation between Serum Leptin and Serum TSH levels. Iacobellis et al gave the positive correlation between Serum Leptin and Serum TSH with significant p value (p=0.01). [15] Siemienska et al shows the positive correlation between S. Leptin and S. TSH with significant p value (p<0.01).[16] Azza M. Abdu Allah et al did a similar study and gave positive correlation

between Serum Leptin and Serum TSH with significant p value ($p<0.01$).[12] The reason for significant correlation between Serum Leptin and Serum TSH is because TSH receptors have been identified in adipose tissues and therefore we cannot deny the possibility that TSH might directly regulate leptin gene expression. [7]

CONCLUSION

The present study shows that Serum Leptin levels were raised in most of the hypothyroid patients and decreased in majority of hyperthyroid patients suggesting that leptin triggers the decreased production of thyroid hormones. Leptin problems are a driving force behind thyroid problems. Problems in the leptin are often the primary cause of many hypothyroid symptoms in overweight individuals. There is relationship between leptin and thyroid gland probably via an influence of leptin on negative feedback of thyroid hormones as well as influence on thermogenesis. Improving leptin problems and losing weight will improve thyroid function. But surely a larger study group is required to prove this relationship.

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Table I: Comparison of age distribution of study and control group

Age (in years)	Study group	Control group	P value
Mean±SD	42.2±15.30	36.07±14.24	0.0789

Table II : Distribution of study and control group according to sex

Sex	Study Group		Control Group	
	Number of cases	%age	Number of cases	%age
Male	10	20	7	13
Female	40	80	23	77
Total	50	100	30	100

Table III: Comparison of Serum T3, T4 and TSH in study group and control group

Hormone	Group	Number of patients	Range	Mean ±SD	P value
Serum T3	Study	50	0.1-4.6	0.99±0.73	0.651
	Control	30	0.5-2.0	1.05±0.41	
Serum T4	Study	50	3.76-19.8	8.5±3.34	0.011
	Control	30	4.1-9.3	6.85±1.20	
Serum TSH	Study	50	0.09-44.6	5.88±8.74	0.0321
	Control	30	0.6-4.2	2.38±1.04	

Table IV: Distribution of Serum T_3, T_4 and TSH in the study group on the basis of their hormonal status

Hormone	Hormonal Status	Range	Mean±SD
	Euthyroidism	0.1-2.59	1.44±1.82
S. T_3 (ng/ml)	Hypothyroidism	0.1-1.9	0.71±0.43
	Hyperthyroidism	0.1-4.6	1.41±1.22
	Euthyroidism	6.7-13.5	8.62-1.77
S. T_4 (μg/dl)	Hypothyroidism	3.76-13.56	7.24±3.10
	Hyperthyroidism	4.52-19.56	10.75±4.63
	Euthyroidism	0.6-3.09	2.02±1.80
S. TSH (μIU/ml)	Hypothyroidism	3.9-44.6	12.93±10.42
	Hyperthyroidism	0.09-0.41	0.25±0.10

Table V: Comparison of Serum Leptin in study and control group

Hormone	Group	Number of patients	Range	Mean ± SD	P value
Serum Leptin(pg/ml)	Study	50	744-29280	8078.1±6054.3	0.786
	Control	30	1600-14600	7741.6±3929.47	

Table VI: Correlation between Serum Leptin and Serum T3, T4 and TSH in study and control group

Correlation	Group	r	P value
Serum Leptin and Serum T3	Study	-0.314*	0.026
	Control	-0.148	0.435
Serum Leptin and Serum T4	Study	-0.251*	0.078
	Control	0.048	0.801
Serum Leptin and Serum TSH	Study	0.416*	0.0027
	Control	0.081	0.67

Table VII: Leptin levels in study group on the basis of their hormonal status

Hormonal Status	T3	T4	TSH	Total Cases		Normal Leptin Levels		Increased Leptin Levels		Decreased Leptin Levels	
				Number	% age	Number	% age	Number	% age	Number	% age
Euthyroidism	N	N	N	20	40	12	60	6	30	2	10
Hypothyroidism	↓	↓	↑	20	40	4	20	14	70	2	10
Hyperthyroidism	↑	↑	↓	10	20	2	20	-	-	8	80
Total				**50**	**100**	**18**	**100**	**20**	**100**	**12**	**100**

N = Normal, ↑ = increase, ↓ = decrease