Assessment of Serum TSH and Prolactin Levels among Patients with Major Depressive Disorder

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Abstract : The observational study was conducted to determine the levels of Thyroid Stimulating Hormen (TSH) and Prolactin (PRL) among patients suffering with Major Depressive Disorder (MDD). The levels were determined in 50 MDD patients and 50 age and sex matched controls. TSH and PRL levels showed significant increase in patients with MDD.

Key Words: Major Depressive Disorder (MDD), Depression, Thyroid Stimulating Hormone (TSH), Prolactin, Thyrotropin releasing hormone (TRH)

Introduction

Major Depressive Disorder or unipolar depression or Depression is a mental disorder characterize low mood, insomnia or hypersomnia, excitement or low motor activity, fatigue, feelings of guilt or/and worthlessness, lower intellectual abilities, lack of concentration as well as an inability to make decisions. It is also associated with recurrent suicidal thoughts and aversion in activities which not only causes emotional problems but also leads to decline in cognitive abilities [1,2]. Depression related disabilities exceeds in number than the disabilities caused by other diseases like cancer and diabetes mellitus, strokes and hypertensive heart diseases in India [3]. An estimated 1, 20,000 people are reported to committed suicide every year due to major depression [4]. The global burden of depression is showing increasing trend since 1990 and is projected to become second major health issue world wide by 2020 [5,6].

According to the diathesis–stress model, depression results when a pre-existing vulnerability or diathesis is activated by "social and physical stress" of the life [7, 8]. Response to stress in humans is through activation of the hypothalamic-pituitary-adrenal (HPA) axis. This activation is the consequence of activation of corticotropin-releasing factor outside the hypothalamus and activation of sympathetic nervous system through adrenaline or noradrenaline. Exhaustion of catecholamines (norepinephrine and epinephrine) is the outcome of chronic stress. This depletion of Central catecholamine in this disorder is known to have a stimulatory effect on prolactin (PRL) secretion [9]. Gomes et al reported that anxiety and depression are related to hyperprolactinemia [10].

There has been a long history of interest in the association between the hypothalamic– pituitary–thyroid (HPT) axis and mood disorders. Substantial studies have documented the effect of neurobiology of the thyroid axis in mood modulation and the role of thyroid function in the

pathophysiology of mood disorders [11,12]. Supported evidence shows role for thyrotropin-releasing hormone (TRH) as a central nervous system (CNS) homeostatic modulator [13,14]. Thyrotropin-releasing hormone (TRH) from the hypothalamus stimulates the synthesis and release of thyroid-stimulating hormone (TSH) from the pituitary thyrotrophs as well as that of prolactin (PRL) from the lactotrophs [15,16]. Extensive evidence supports relation between depression and thyroid dysregulation [17,18,19,20]. Studies show that hypothyroidism is accompanied by depression and that hyperthyroidism is accompanied by sleeplessness and agitation [21].

Objective

The study was conceived to determine and compare TSH and Prolactin serum levels in patients with major depressive disorder and healthy subjects.

Material & Methods

The study was initiated after seeking clearance from Institutional Ethical Committee, Government Medical College, Jammu. The study was conducted in Department of Psychiatry w.e.f. August 2016 to January 2017.

MDD patients were matched individually on the basis of age and gender. Age matching was done within ±3 years. All the patients presenting in psychiatry OPD and aged above 18 years were potential participants. After seeking informed consent from patients they were subjected to neuropsychiatric interview by a psychiatrist and his/her mental illness was diagnosed in accordance with Diagnostic and Statistical Manual (DSM IV). Healthy attendants attending OPD on the same day were requested to participate and were also subjected to neuropsychiatric interview and were assessed for stress level in accordance to DSM IV. The participants (MDD patients and healthy controls) on any type of medication or with any other disorder were excluded from the present study. Participant suffering from lifetime history of mania or hyper-mania or any with concurrent psychotic symptoms or pregnant females, current use of antipsychotic / any medication use that can influence prolactin secretions and co-morbid medical disorders like neuroendocrine and metabolic disorders were excluded from the study. All the patients thus diagnosed were put on medication according to the management protocol followed in the department of psychiatry and counselled for regular follow-up. They were requested to give blood sample for analysis of various parameters viz. Vitamin D, Vitamin B12, Ferritn, Insulin, TSH, Prolactin. The results of biochemical parameters except TSH and Prolactin were reported elsewhere [22]. An amount of 5 ml of fasting blood samples was drawn aseptically from the superficial veins of each of the study participants (both cases and controls) in red top vials and allowed to clot at room temperature. The clot was removed by centrifuging at 1000g for 10 minutes. Separated serum was stored at -20^{o} until the serum analysis was done.

Prolactin was determined in the serum samples by Elecsys Prolactin II assay (Roche Diagnostics GmbH, Sandhofer 116, D68305 Mannheim) and Thyroid–stimulating hormone (TSH) level was determined by ARCHITECT assay (Abbott Laboratories, Abbott Park, Illinois, US) an immunoassay using Chemiluminiscent Microparticle Immunoassay (CMIA) technology, referred to as Chemiflex.

Statistical Analysis:

The data thus collected was entered into MS-Excel and the data analysis was done using computer software Statistical Package for Social Sciences (SPSS) version 21. The TSH and Prolactin values were reported and presented as mean and standard deviation and difference in the mean values was done using student t test.

Results

Basic socio-demographic information is presented in table 1. As evident mean age of the normal subjects and patient studies was similar. The difference in average age was not statistically significant.

Table 1: Baseline Socio-demographic characteristic of studied population.

	Normal Subjects	MDD Patients	Statistical inference
Age (years)	39.12 ± 9.89	41.08 ± 11.07	t=.93 p=.35 (not significant
Female/Male	24/26	24/26	Not significant

Table 2: Comparison of mean (SD) TSH and Prolactin between normal and MDD patients among the study groups.

	Normal Subjects	MDD Patients	Statistical inference
Serum TSH (mg/dl)	1.71 ± 1.02	2.16 ± 0.95	t=2.26 p<.02 (Significant)
Serum Prolactin(mg/dl)	9.54 ± 4.79	19.46 ± 8.01	t=7.51 p<.001 (Highly Significant)

Table 2 presents the levels of TSH and Prolactin among patients with MDD and healthy controls. The mean levels of TSH and Prolactin are higher among patients with MDD as compared to healthy controls and the results are statistically significant. However, the difference is more pronounced in Prolactin levels.

Discussion

Dysregulation of Hypothalmic pituitary thyroid (HPT) axis and Hypthothalmic pituitary adrenal (HPA) axis has been recognized in patients with major depression [23,24]. The current studies further substantiate this relationship. The relationship is mediated through opposing effect of TRH on TSH and Serotonin. TRH on one hand stimulates the release of TSH while on other hand inhibits the serotonin, thereby complimenting each other in the development of MDD.

Our finding indicates significant increase in the levels of TSH levels in depressive patients when compared with normal subjects. This is consistent with the investigations carried out by Gold [25], although some studies have reported TSH levels in MDD patients in the normal range [26]. Further MDD are known to be associated with subclinical hypothyroidism [27].

TRH not only stimulates TSH but also Prolactin [16,28]. This happens through dysregulation of HPA axis owing to psychosocial stress and dissociative symptoms in the MDD patients [29]. The hyperactivity of HPA axis in depression elevates the release of glucocorticoids which inturn has an inhibitory effect on prolactin release mediated through catecholamines. The exhaustion of catecholamines stimulates the prolactin level [9]. Prolactin as it is known helps to cope the stress by altering neural circuits through activation of ion channels, modulation of signaling pathways or reduced activation of neural inputs [28]. Therefore it is not surprising that the depressive symptoms are exhibited with hyperprolactinemia.

We also observed significantly increased level of Prolactin among patients with MDD. However, the significance of PRL in MDD patients is subject to controversy. Arana *et al*. did not found any significant change of prolactin level in patients with mild depression [30] whereas others have shown significant hyperprolactinemia [31].

Therefore on the basis of above discussion it can be concluded that both TSH and PRL can be used as useful markers for diagnosis of depression. However its role in monitoring the treatment needs to be elucidated.

Conclusion

The present study aimed to investigate the endocrine parameters with respect to MDD. We observed TSH and PRL to be significantly increased among the patients studied. As described above this happens due to dysregulation of HPT axis and HPA axis. However, we suggest that the conclusions are read in the light of limitations mentioned below. Firstly, prolactin levels were measured only once which do not accurately reflect 24 hour levels. [26]. Secondly, some of the socioeconomic determinants of depression were not measured and therefore the results of the present study are opened to certain inconsistencies.

Conflicts of interest

None

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