Correlation of Cortisol and Serotonin Level to the Depressive State

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Abstract:
Major Depression is a common disorder. Studies reported abnormalities in biogenic amines, among those serotonin is the most important. Besides a variety of neuroendocrine disorders mostly cortisol, which play a role in stress as a cause of depression and reflecting underlying brain damage. We examined 17 depressed patients diagnosed by ICD 10 during the depressive state and after clinical recovery. 20 healthy subjects matched for age and sex were compared as controls. They were studied for serum levels of serotonin and cortisol using Elisa technique. We found decreased serotonin level and increased cortisol levels during the depressive state, after clinical improvement assessed by HDRS, serotonin levels tend to normalize and cortisol levels decreased but both did not reach statistical significance due to the limited number of patients. Hence we can conclude that these two parameters can be considered as state markers for depression.

Introduction

Major depression is a common disorder, with a life time prevalence of about 15 – 25 percent. There is a twofold greater prevalence of major depression in women than in men due to hormonal difference, effects of childbirth, psychosocial stresses and behavioral models of learned helplessness. The incidence of major depression is now increasing in young, adults, less than 20 years with no difference from race to race. ***(Katon and Schulberg, 1992).***

Several studies reported abnormalities in biogenic amines in patients of depression Among those norepinephrine and serotonin are the two neurotransmitters most implicated in the pathophysiology of mood disorders ***(Power and Cowen, 1992)***

Depletion of serotonin may precipitate depression, and some suicidal patients have low cerebrospinal fluid (CSF) concentrations of serotonin metabolites and low concentrations of serotonin uptake sites on platelets. ***(Roy, 1993)***

A variety of neuroendocrine dysregulations have been reported in-patients with depression, these may be considered either as a cause or reflecting an underlying brain disorder. The major neuroendocrine axes of interest in depression are the adrenal, thyroid and growth hormone axes. ***(Gastpar et al, 1992)***

There is a correlation between the hypersecretion of cortisol and depression.

Normally cortisol secretions are regulated through fast feedback mechanism operating on cortisol receptors in the hippocompus and slow feedback mechanism operating through pituitary and adrenal receptors.

Depressed patients have impaired function in their fast feedback mechanism. On the other side, hypercortisolemia can damage hippocampal neurons, a cycle involving stress. ***(Hunt et al 1992).***

Objectives:

The aim of our work was to investigate plasma levels of serotonin and cortisol in

depressed patients during the depressive state and after clinical recovery.

Subjects:

17 depressed patients were recruited from inpatient and outpatient clinics of the institute of psychiatry at Ain Shams University Hospital. Two psychiatrists separately using the ICD 10 Research and Diagnostic criteria for major depression examined them.

Their age ranged between 20 – 45 years, both sexes were included. They were physically healthy and had normal physical, neurological and laboratory profile for blood sugar, renal and liver functions. All patients were drug naïve for at least 4 weeks for antidepressants, and did not receive any ECT for 6months.

Control group were formed of 20 healthy subjects participated in the study. They were screened using a semi-directive interview. They had no past or present history of medical, neurological or psychiatric disorder.

All subjects were free of any drug or alcohol misuse and gave consent after the procedure had been explained.

Method:

2 psychiatrists using the Research and Diagnostic criteria of ICD 10 for major depression examined the patient subgroup. Patient's behavior was rated with the 24 – item Hamilton depression rating scale (HDRS; Hamilton, 1960) for assessment of severity at the 1st interview and clinical improvement in follow up sessions.

Blood samples were taken at 4-5 p.m. to avoid diurnal levels in cortisol and serum being separated and examined for serotonin and cortisol levels by commercial Elisa kits during the clinical state of depression and after clinical improvement

Treatment prescribed after taking the 1st sample were tailored according to each case whether moderate, severe, with psychotic features or suicidal attempts.

Post treatment assessment focused on changes of blood levels of serotonin and cortisol in the Recovery State.

Data analysis:

Analysis of the data was performed on Statistical System Analysis (SSA). Quantitative data were summarized as means and standard deviations. Qualitative data were summarized as percentages. Comparison between group means were done using the student's t, test. ***(Armitage and Berry, 1987).***

Results:

The demographic data and clinical characteristic of the patients meeting the entry criteria and control are presented in table (I).

We found no significant difference between the patient and control group in terms of age and sex.

The patient group included 7 males and 10 females. Most of them had past history of previous depressive episodes with a mean of 2.9 ± 2.4 they were divided into moderate and server subgroups guided by ICD 10 criteria and HDRS. 6 patients had moderate depression with somatic symptoms and 11 had severe depression, 5 out of the later subgroup had psychotic symptoms. Treatment included hospitalization, pharmacotherapy and ECT. The clinical improvement was assessed

guided by HDRS and the episode duration lasted between 2-6 months.

We found significant decrease of plasma serotonin levels in depressed patients compared with controls, which tends to be more affected in severe than moderate cases.

There is significant difference between the patient and control group in cortisol levels during the depressive state.

Table IV and V show no significant changes in levels of serotonin and cortisol after clinical improvement, yet serotonin levels tend to increase while cortisol levels decreased.

Table (1): Demographic and clinical characteristics of patients and controls

Clinical data		Patients	Controls	P
No		17	20	
Age range		20 – 45	20 – 45	
	M ± SD	32 ± 11.7	31. 1± 9.3	N.S
Sex: Male : Female		7 : 10	10 : 10	
Family history + / -		5 : 12		
Past history of similar attack				
	Range	1 – 5		
	M ± SD	2.9 ± 2.4		
Duration of present episode in months				
	Range	2 – 6		
	M ± SD	3.9 ± 2.4		
HD RS at clinical state of depression				
	M ± SD	25.8 ± 7.3		
Moderate / severe case		6 : 11		

Table (2): Serotonin levels in depressed patients and controls during depressive state:

Sub group	Patients	Control	P- value
Depression	124.7 ± 47.29	194.1 ± 10.65	< 0.001 S
Severe	113.54 ± 13.18		< 0.001 S
Moderate	124.35 ± 12.2		< 0.001 S

Table (3): Cortisol levels in depressed patients and controls during depressive states:

Sub group	Patients	Control	P- value
Depression	29.2 + 9.7	20 ± 2.7	< 0.05 S
Severe	30.5 ± 3.1		< 0.05 S
Moderate	30 ± 2.7		< 0.05 S

Table (4): Changes in serotonin levels in the depressive state and clinical recovery

Patient's subgroup	In depressive state	In clinical Improvement	P- value
Severe	113.54 ± 13.18	148.8 ± 24.64	< 0.05 IS
Moderate	124.35 + 12.2	149.51 ± 26,17	< 0.05 IS

Table (5) :Changes in cortisol levels in the depressive state and clinical recovery

Patient's subgroup	In depressive state	In clinical improvement	P- value
Severe	30.5 ± 3.1	27 ± 2.7	< 0.05 IS
Moderate	30 ± 2.7	26.3 ± 2.2	< 0.05 IS

Discussion:

In our study we found significant decrease in plasma serotonin levels in depressed patients. With the huge effect that serotonin specific reuptake inhibitors (SSRIs) have made on the treatment of depression, serotonin has become the main neurotransmitter involved in depression. ***(Workman and Short, 1993).***

Besides the effect of serotonergic drugs, other data showed that depletion of serotonin may precipitate depression. This finding go with our results and consider serotonin depletion as a cause of depression Suicidal patients have low CSF condensations of serotonin uptake sites on platelets, as measured by imipramine binding to platelets ***(Roy, 1993).***

The density of 5 HT_2 receptors studied postmortem were increased in the prefrontal cortex of suicide victims and patients who died during a major depressive episode. ***(Yates et al, 1990).***

Other studies showed different results with reduction of 5 HT_2 receptor binding in suicide victims using tracer 3 H Ketanserine ***(Gross – lssercoff et al, 1990).***

Chronic antidepressant treatments induce a down regulation of 5 HT_2 receptors ***(Peroutka – Synder, 1980)*** which might explain the different findings.

A Single photon emission computed tomography (SPECT) study indicated altered uptake of the tracer in the parietal and inferofrontal cortices of depressed patients compared with control subjected ***(D' Haenen et al, 1996).***

Using ^{18}F altanserine uptake in PET studies depressed patients showed significant changes in 5 HT_2 receptors in the right post-erolateral orbitofrontal cortex and anterior insular cortex, areas implicated in depression ***(Briver et al, 1997)***

Our finding of decreased serum level of serotonine in depressed patients is mainly related to the depressed state. These changes are inversely proportional to the severity of symptoms.

Results after clinical improvements show increased levels nearly to reach the control studies, yet these changes were not statistically significant due to the limited numbers of patients and short duration for follow up between 2-6 months according to the duration of the present episode.

The second parameter in our study is cortisol.There has been extensive interest in HPA axis function in depression, a disorder known to be associated with both stress and multiple HPA axis changes, including hypercortisolism and dexamethasone resistance in up to 70% of faces. ***(Dinan, 1994).***

We found elevated cortisol level in depressed patients compared with normal controls during the depressive episode.

Correlation between raised cortisol levels and cognitive impairments in depression subjects have been reported ***(Mitchell, 1995).***

Axelson et al, 1993 found a relationship between hypercortisolemia and reduced hippocampal volume on magnetic resonance imaging (MRI) in depressed subjects. The deleterious affects of chronic glucocorticoid secretion include ventricular dilatation, cerebral atrophy and impairments in cognition (Mauri et al, 1993). In our study cortisol levels tend to decrease after clinical improvement but still far from the control studies.

This finding can be explained by the long history of depression and repeated attacks in most of our patients. Changes as state and trait inquires about the relation of these makers need further studies to be confirmed.

Conclusion

The pathophysiology of depression may involve changes in plasma serotonin and cortisol levels that is related to the depressive state.

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العلاقة بين معدل الكورتيزول و السيروتونين بالنسبة لحالة الاكتئاب

الاضطراب الوجداني (الاكتئاب) يعتبر من الأمراض النفسية الأكثر انتشارا و من أسباب هذا المـوض عدم استقرار نسبة مادة السروتونين و الكورتيزول في الدم مما يشير إلى خلل بخلايا المخ.

لقد قمنا في هذا البحث بدراسة ١٧ حالة اكتئاب أثناء المرض و بعد التحسن بفترة من تلقى العـــلاج و تم مقارنة هذه العينة بمجموعة ضابطة حسب نسبة مادة السروتونين و الكورتيزول اثناء فترة المرض و قد تحسنت هذه النسبة مع تحسن حالة المريض بالعلاج و تعتبر هذين المادتين من العلاقات المهمـــة لمرض الاكتئاب.