THE RELATIONSHIP OF SERUM CORTISOL LEVELS WITH SEVERITY OF DEPRESSION AND AGE IN MAJOR DEPRESSION
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ABSTRACT

Hormones play an essential role in the development and expression of a series of behavioral changes. Recent theories associate depression with physiological changes in the functioning of the Hyperactivity of the Hypothalamo-Pituitary Axis (HPA) and serotonergic neurotransmission. The high cortisol levels found in plasma is some of the most consistent findings in psychiatry. Objective: We measured blood levels of cortisol in patients with major depression according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM- V) and compared results with levels found in healthy people considering the effect of age and the severity of the depression. Method: Thirty patients meeting the DSM-V criteria for major depressive disorder. The severity of depression was assessed by the Hamilton Rating of Depression Scale (HAM-D17). Serum cortisol levels were determined by using ELISA. Results: There is a significant increase in serum plasma level of cortisol among patients with major depression Moreover, there is a significant correlation between age and serum cortisol level among patients with depression while the relation is insignificant among control group.

Keywords: Depression, cortisol, DSM-V criteria.

INTRODUCTION

The World Health Organization estimates that depression will be the second leading cause of global illness by 2020. Severe depression may significantly decrease quality of life and lead to death by suicide. It may also increase mortality associated with general medical conditions, most notably cardiovascular disease (Lisanby, 2007).

Cortisol (17-hydroxyl-11-dehydrocorticosterone) is a steroid hormone secreted from adrenal gland (Andersen, 2002). CRH (Corticotropin-Releasing Hormone) secreted from Hypothalamus,ACTH (Adreno-Cortico-Trophic Hormone) secreted from corticotrophs of the Anterior Pituitary, Glucocorticoids (cortisol particularly) secreted from Zona Fasciculata and Zona Reticularis.Cortisol is converted in peripheral tissue into Cortisone by 11beta-steroid hydrogenase enzyme (Beishuizen et al, 2001).

Studies about HPA axis activity in patients with depression found an increased cortisol response to ACTH stimulation, decreased cortisol response to hypoglycemia, decreased ACTH response to stimulation with CRH and resistance to cortisol suppression by dexamethasone response (Murphy, 1991, Zobel et al., 1999).

Depression is associated with Hyperactivity of the Hypothalamo-Pituitary Axis (HPA) in 30-50% of patients, Older patients are the most likely to manifest increased HPA activity (Pariante and Lightman, 2008). Psychotic depression is more closely associated with hypercortisolism and non suppression of cortisol( Nelson and Davis 1997). According to Saraiva et al (2005), there are two models of association between depression and changes in physiological cortisol levels. In one model primary factors contribute to the primary event of hypercortisolism. These factors are trauma and harmful effects in the hippocampus, such as inhibition of neurogenesis and hippocampal volume loss. In the second model the triggering element of the cognitive effects may be hypercortisolism (Sapolsky, 2001).

AIM OF THE WORK

To study the serum cortisol level in patients with major depression considering the effect of age and the severity of the depression.

PATIENT AND METHODS

The study was conducted in Department of Neuropsychiatry at Al-Azhar University Hospital (Assiut branch) on patients with major depression attending psychiatry clinic from January 2014 to January 2015 after approval from the ethical committee of the Faculty of Medicine Al-Azhar University, Assiut Branch.

Patient Group

The present study included a thirty population of major depressed out patients who were compared with thirty population of control.
Patients aged 15—45 years selected upon strict fulfillment of criteria for major depressive disorder according to DSM-V. Diagnosis was confirmed by two psychiatrists assessing the patients independently. We assessed the severity of depression by using the Hamilton Depression Rating Scale (HAM-D17), this scale applied by the researchers.

Exclusion Criteria
1. Significant psychiatric co-morbidity
2. Organic mental disorder
3. Intellectual disability
4. Anxiety disorder if primary and/or predominant
5. Drug abuse during the last 12 months
6. Patients who used psychotropic drugs or had been administered ECT two months prior to the study.

Hamilton Depression Rating Scale (HAM-D17)
The Hamilton Depression Rating Scale (HAM-D17) is a 17-item, clinician-administered scale published in 1960. It assesses the level of depression and its change in severity (each item can be scored from 0 to 4). The validity and reliability study of the Arabic version of the HAM-D17 was performed by lotfy (Lotfy, 1997). A total score of between 0 and 7 indicates no depression; while scores between 8 and 15 indicate mild depression; scores between 16 and 28 indicate moderate depression; and a score greater than 29 indicates severe depression.

Serum samples
Serum samples for cortisol level measurement using electrochemiluminescence immunoassay Accu-Bind ELISA microwells, product code 3625-300.

The blood samples were collected with Serum tubes with increased Silica Act Clot Activator. All blood samples were centrifuged within 30 minutes after collection at 1100-1300 rpm for 15 minutes. The samples did not run in duplicate. They were not diluted.

Control Group
Apparent thirty volunteers interviewed by psychiatrists to exclude any psychiatric disorder were age and sex matched to the depressed patient.

Statistical analysis
Statistical analysis was done using SPSS version 11.0. Comparisons between case and control groups were done using T-test and P value was considered significant at ≤ 0.05 level and highly significant at ≤ 0.01. Results were expressed as Mean ± SD.

Ethics and confidentiality

Patients followed up for 3 months. All information of the patient is secret by using Code number and Hidden names for all patients. Informed written consent obtained from all patients.

RESULTS

Table (1): Demographic characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Patients</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.8 ± 3</td>
<td>43.5 ± 1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Marital Status</td>
<td>83.7 ± 4.2</td>
<td>76.8 ± 2.9</td>
<td>0.3</td>
</tr>
</tbody>
</table>

There is no statistically significant difference between the two groups regarding the age and marital status.

Table (2): Cortisol Level

<table>
<thead>
<tr>
<th>Chorotsol level</th>
<th>Cases</th>
<th>Control</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14.2 ± 1.64</td>
<td>11.5 ± 1.3</td>
<td>&lt;0.001**</td>
</tr>
</tbody>
</table>

** Statistically significant difference (p<0.01)

There is statistically significant difference between the patient and control group, higher values observed among patients with major depression.

Age effect on cortisol level

Table (3): The relation between serum cortisol levels and age in major depression

<table>
<thead>
<tr>
<th>Chorotsol (M ± S)</th>
<th>15-&lt;25 years</th>
<th>25-&lt;35 years</th>
<th>35-&lt;45 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.4 ± 1.56</td>
<td>15.0 ± 0.75</td>
<td>15.9 ± 0.58</td>
</tr>
<tr>
<td>P. value</td>
<td>&lt;0.001</td>
<td>0.85</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pearson correlation</td>
<td></td>
<td>0.85</td>
<td></td>
</tr>
</tbody>
</table>

There is statistically significant correlation between the age and the serum cortisol level in patients with major depression while the correlation is statistically insignificant in control group.

Figure 1: Cortisol serum level in depressed patients considering the effect of age

Table (4): The Relation between Serum Cortisol Levels and severity of Depression

<table>
<thead>
<tr>
<th>Severity of Depression</th>
<th>Mild</th>
<th>Moderate</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol level</td>
<td>14.67 ± 1.53</td>
<td>14.08 ± 1.74</td>
<td>0.606</td>
</tr>
</tbody>
</table>

According to severity of depression there were two groups' mild and moderate. There is statistically insignificant correlation between the
severity of depression and the serum cortisol level in patients with major depression.

**DISCUSSION**

The present study included a thirty population of major depressed outpatients who were compared with age- and sex-matched controls.

The results go with (Wolkowitz .1999) who reported higher serum cortisol level among patients with depression .as regard to Wolkowitz & Reus, hypercortisolism is frequent in patients with major depression, various behavioral changes has been associated, such as sleep disorders, decreased attention, loss of libido, psychomotor disorders, anxiety and suicide ideation.

However, the results are against Vythilingam et al., (2010), who reported low early morning plasma cortisol level in patients with depression.

The interpretation of these data is difficult because analysis of many studies demonstrate that not all patients with depression have hypercortisolism, and not all patients with hypercortisolism have depression.

As regard to the Relation between Serum Cortisol Levels and age in major Depression. The results go with Keller et al (2004) who reported high cortisol levels in depression, and levels are higher in elderly individuals with depression. The results go against Molchan et al., (1990), who concluded that age has no effect on cortisol level in patient with depression.

Physiological aging is associated with a relative increase in the activity of the HPA axis associated with a reduction of mineralocorticoid and glucocorticoid receptors.

This is not a simple aging effect because it is absent in healthy volunteers. The potentiating or additive effect of age in conjunction with depression on pituitary adrenocortical activity was suggested by other studies.

Von Cauter et al. and Harman suggest that ACTH and cortisol secretions are age-related, as mean 24 hour serum cortisol level is 20% to 50% greater in men and older women, and that serum cortisol levels have similar increases in response to fasting in elderly men and young people. Serum cortisol responses to stress are prolonged in older individuals, possibly due to changes in glucocorticoid receptors.

The answer to whether depression is the cause of consequence of hypercortisolism is hard. Depression has been associated with chronic high cortisol levels because of the deregulation of the HPA axis and the reduction of hippocampal volume in humans after recurrent episodes of depression. (Harman 2014 and Young 1991)

**The severity of depression and Cortisol Level:**

There is insignificant correlation between the severity of depression and the serum cortisol level in patients with major depression, the results go against Keller et al. who reported that the patients with depression who attempt suicide violently have higher cortisol levels than patients with depression and non-violent suicide attempts, and suggested that deregulation of the HPA axis may be a factor of violent suicide behavior.

In our study no relationship was determined between the serum cortisol levels and depression severity in outpatients.

Close reading of the literature show there is striking that HPT axis alterations and hypercortisolism have almost exclusively been described in in-patients (Weber 2000), and to a much lesser extent in outpatients.

Young et al and Sullivan suggest that the in/outpatient status is an important factor in the presence of endocrine alterations in major depression.

**CONCLUSION**

There is a significant increase in serum plasma level of cortisol among patients with major depression. Moreover, there is a significant correlation between age and serum cortisol level among patients with depression while the relation is insignificant among control group.

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