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CORTISOL IN POSTMENOPAUSAL WOMEN WITH DEPRESSION

Medical Science

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ABSTRACT

Background-

Women are at a two fold greater risk for developing depression as compared to men. It has been found that women are vulnerable to depression during and after menopausal transition. Alterations in endocrine and metabolic factors including monoamine deficiency, HPA and HPT axis dysfunction and inflammation and neurodegenerative alteration can be responsible for depressive disorder. So the present study was undertaken to find out the total cortisol levels in postmenopausal women with and without depression.

Aims and objectives-

To determine the total cortisol levels in postmenopausal women with and without depression.

Materials and methods-

Fasting blood samples were analyzed for the total Cortisol levels in 30 postmenopausal females suffering from depression and 30 postmenopausal females not suffering from depression by using immunoassay technique.

Results-

Serum Total Cortisol level was significantly higher in Case group (mean-37.90) as compared to Control group (mean-29.65).

Conclusions-

Our findings support the hypothesis that hyperactivation of HPA axis leads to hypercortisolism in postmenopausal women with depression .

KEYWORDS:

HPA-Hypothalamic-Pituitary-adrenalaxis,ACTH-Adrenocorticotropic Hormon

Introduction

Depression is one of the most frequent and debilitating psychiatric disorder[1].The various community based studies conducted in India based on mental disorder found the prevalence rate of depression between 13 to 25%[2], the prevalence rate of depressive disorder between 10 to 20% in elderly population has been estimated by WHO [3]. Majority of depressive disorders remain undiagnosed and untreated because of wrong belief that it is part of aging and is a social stigma.

There is two fold greater risk for developing depression in women as compared to men[4]. Depression occurs in 21% of women over their life time[5]. Various studies found that women are at increased risk of depression during and after menopausal transition[6]. 26-33% of women develop a first episode of depression during the menopausal transition[7,8]. During postmenopausal period the mood disorders are common and women spend 30% of their lives in postmenopausal period. Perez-Lopez et al. studied that 45% women suffered from depression during postmenopausal period[9]. perimenopausal and postmenopausal women had significantly increased risk of having elevated depressive symptoms as compared to premenopausal women has been proved by SWAN study [10].HPT and HPA axis alteration or hyperactivation is responsible for depression has been proved by various studies[11,12]. Any type of stress causes release of CRH from hypothalamus which causes ACTH secreation from corticotrophic cells of anterior pituitary and cortisol from adrenal cortex[13].Various studies documented increased cortisol secretion in major depression cases[14] while lower cortisol level found in another study[15]. Normal cortisol level also observed in some studies[16]. there is so much inconsistency regarding the cortisol level in depression and also very few studies has been conducled to study cortisol level in postmenopausal women suffering from depression..So the present study was undertaken to find out the total cortisol levels in postmenopausal women with and without depression.

Materials and methods

A complete medical history and informed consent was obtained from all participants included in the study . Diagnosis of depression was done by psychiatrist by using DSM-IV criteria and Assessment of severity of depression was done by 21 items Hamilton rating scale for depression (21itemHRSD)

30 postmenopausal women diagnosed with major depression were enrolled in the study as cases and 30 normal postmenopausal women without any past history of depression were enrolled in the study as controls.

Inclusion Criteria:

1. Postmenopausal women (above 50 years of age) were selected for the study.
2. Subjects without any disorders not receiving or had not received anti-cancer medications or any thyroid drugs.
3. Thirty age matched controls with normal liver, kidney function and thyroid function belonging to the same socioeconomic background were also included as a control group used for comparison with study subjects suffering from depression.

Exclusion Criteria:

1. Postmenopausal women on hormonal treatment.
2. Patients with thyroid and adrenal gland disorder, severe liver diseases, end stage renal diseases, human immune deficiency virus infection, diabetes, hypertension and cancer.
3. Subjects on medications [therapy involving L-T4/T3, thyrostatics (carbimazole, propylthiouracil), steroid, antidepressant agent (S-adenosyl-methionine),antiepileptic agents (carbamazepine, phenytoin), Anticancer agents (6-azauridine, xanthopterin, antifolates, tamoxifen), anticonvulsant agents (GABA), and bronchodilator (theophylline)].

Analysis-

Blood Sample Collection :

1. 5 ml fasting venous blood sample was collected in plain vaccutainer under all aseptic precautions.
2. The samples were kept for 30 minutes for clotting after which they were centrifuged at 3000 rpm for 5 min to obtain clear serum.
3. Serum samples were aliquotted in micro centrifuge tubes and stored at - 20°c till further assay. The biochemical parameters to be assayed were stable at said temperature for 6 – 8 weeks.
4. Serum samples were used for the analysis of cortisol levels and A fully automated enzyme amplified chemiluminescent

immuno assay based Immulite 1000 analyzer was used for analysis

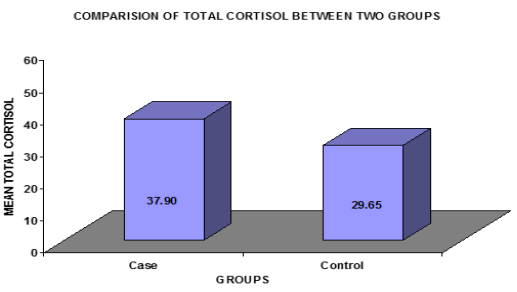
Statistical Analysis :
Numerical variables were reported in terms of mean and standard deviation. An independent sample t-test was used to compare the difference of means. In this analysis, variables showing p-value less than 0.05 were considered to be statistically significant.The SPSS software was used for data analysis.

Results-
Table No. 1 shows Mean Total Cortisol was 37.90 among Case group which was significantly more as compared to 29.65 among Control group.(table.no.1 and figure. No.1)

Table. No.1- COMPARISION OF TOTAL CORTISOL BETWEEN TWO GROUPS

Groups	Mean Total Cortisol ($\bar{x} \pm SD$)
Case	*37.90 09.40
Control	29.65 06.71

By Student t Test P = 0.01, * Significant



(Figure.No.1)

Discussion
Menopause is word developed from Greek root meaning cessation (pauses) and month (men), designing the interruption of monthly blood flow named menstruation. This state is retrospectively fixed, after the absence of menstruation for 12 consecutive months [17]. Menopause is an important period in women life.It has been defined as permant cessation of menstruation due to failure of ovarian follicular development despite of gonadotropin stimulation .The mean age of menopause is 51yrs ,but can vary from 45-55 yrs. Menopause can occur as early as30's or as late as60's in rare cases[18]. Women now spend one third to one half of their lives after menopause. Menopausal Status were classified as per the recommendation by the World Health Organization (WHO) and Stages of Reproductive Aging work-shop.[19,20].

Menopausal status was based on menstrual bleeding patterns in the previous 12 months and was categorized as
(1) premenopausal (menstrual period in the past 3 months with no change in regularity in the past 12 months);
(2) Early perimenopausal (menstrual period in the past 3 months with change in regularity over the previous 12 months);
(3) Late perimenopausal (no menstrual period within the past 3 months but some menstrual bleeding within the past 12 months); and
(4) Postmenopausal (no menstrual period within the past 12 months).

Studies has found association between depression and menopausal symptoms women during their menopausal transition suffers from various physiological menopausal symptoms which include somatic, sexual dusfunction and various vasomotor symptoms (like hot flushes and night sweats, vaginal dryness along with acnes and stiffness of joints and trouble in sleeping and lack of energy these symptoms lead to depressed mood in many females during their menopausal transition period[7]. this transition period also associated with extreme hormonal changes but it is also accompanied by changes in personal, professional and family responsibilities,stressful life events and low socioeconomic support, some studies has found depressive symptoms are associated with various health,social and demographic factors[8] while some studies has proven that risk of depression is independent of health, social and demographic factors[6]

Women during their late stage of menopausal transition has increased risk of depression because of changes in reproductive hormones like increased FSH and LH and testosterone levels along with decreased in estrogen levels[7]

Womens suffered from various physiological menopausal symptoms during and after menopause which is responsible for mental stress .and inorder to mainatain physiological stability the activation HPA axis takes place as an adaptive mechanism[21].Studies reported that directly or indirectly cortisol plays pathogenic role in depression i.e. by induction or exacerbation of disturbances in monoaminergic transmission[22].Increased FSH level causes increased secretion of estrogen from ovarian follicle as women aproches menopause and estrogen regulates CRH gene expression so hyperestrigenemia causes increased Cortisol level[23]. CRH release stimulates the synthesis and release of adrenocorticotropic (ACTH) by the anterior pituitary, which in turn stimulates the synthesis and release of cortisol by the adrenal cortex.our studies have several limitations including that we have not taken into consideration various social and demographic factors and various menopausal symptoms which may are responsible for depressive symptoms though health factors which may affect the cortisol levels has been minimized by excluding the postmenopausal women having any major disorder also with no past history of major depression and those postmenopausal women on any medicationor hormonal supplements.Our results reveled that there might be hyperactivation of HPA axis that causing CRH overdive resulting in hypercortisolemia in postmenopausal women with depression. The study might have proved very useful if we have analysed the FSH, Estrogen and ACTH level along with cortisol levels.

Conclusion-
increased cortisol level because of hyperactivation of HPA Axis is observed in postmenopausal wome n with depression and it can be used as biological marker for diagnosis of depression in postmenopausal women .

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