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Editorial board

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Salivary cortisol level as psychological disorders marker that assessed according to menopause rating scale on perimenopausal women in Indonesia-Medan

SIREGAR M.F.G.
Division of Reproductive Endocrinology and Fertility Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine Universitas Sumatera Utara, Medan, Indonesia

Introduction
Perimenopause as the beginning of a transition that began 5 years before menopause and 2 years after menopause occurs. During perimenopause, especially during pre-menopause irregularity of the menstrual cycle occurs. This period begins around the age of 40 years. During perimenopause marked by decrease in estrogen hormone levels often cause symptoms that are debilitating the lives of women and even threaten the household life. The symptoms include hot flushes (a burning sensation from the chest to the face), night sweat, memory loss, depression, stress, fatigue and insomnia (1).
According to Proverawati and Sulistyawati (2010) factors that influence the symptoms of premenopause include: psychological factors, socio-economic, cultural and environmental, other factors such as unmarried women, career women who have or have not been married and first menstruation (1).
Psychological factor closely is related to the levels of cortisol. Where, the state of stress associated with the neuroendocrine system. The cortisol hormone as a product of this mechanism is often used as a biomarker for studying stress. Physiologically, the HPA (Hypothalamus-Pituitary Axis) is associated with changes in the physiological adaptation to the effects of external environment, so that secretion of hypothalamic releasing factor corticotrophin releasing hormone (CRH) can be activated by psychological events with varying levels of activation. CRH relationship with adrenocorticotropic hormone (ACTH), activation of the neurotransmitters and autonomic nervous systems are very complex. Cortisol secreted by the adrenal gland through a feedback response on the body. Cortisol is a powerful chemical substance that, along with the adrenaline is very effective in protecting the body during times of stress (2, 3).
Previous research by Siregar and Permata (2015) found that cortisol levels may be a marker for menopausal symptoms disorders that were assessed with the menopause rating scale (MRS), which in this study was obtained sensitivity and specificity of 77 and 85% respectively (4).
Diagnosis of menopausal symptoms is still limited to the complaints that tend to be subjective, so it is necessary a study of the parameters that are objective in assessing the severity of menopausal symptoms, so it can be used as a marker and perhaps even follow-up in the treatment of menopausal symptoms, in this case cortisol is expected to be a diagnostic tool for menopausal disorders.

Methods
This study is an analytic study with cross-sectional design and diagnostic test. The variables were analyzed in univariate and multivariate, using comparative and correlative analyze. The study was conducted in RSUP. H. Adam Malik Medan. The study began from July 2015 to September 2015. Samples were perimenopausal women aged 45-52 years who worked as a paramedic in H. Adam Malik Hospital outpatient clinic. Inclusion criteria in this
study includes no menstruation for 12 months, has passed the L-MMPI (Lie-Minnesota Multiphasic Personality Inventory) with a raw score of < 5, never underwent hysterectomy or bilateral removal of ovaries, not receiving hormone replacement therapy, no history of psychiatric disorder, no history of malignant disease, no history of heart disease, no history of diabetes mellitus and high blood pressure, no history of osteoporosis, not drinking and smoking. Exclusion criteria were withdrew from the study.

The research variables divided into independent variable and the dependent variable. Independent variables is salivary cortisol levels. While the dependent variable is a psychological disorder.

Giving questionnaires to perimenopause women paramedic who meet the inclusion and exclusion criteria.

All participants in this study were interviewed and recorded in the status of research include: age, parity, married status, history of long menopause, surgical history, education level, history of the use of hormonal therapy, history of heart disease, history of suffering from osteoporosis, history of diabetes mellitus and hypertension, history of thyroid, history of liver problems, history of drinking alcohol.

Then the subjects fill the L - MMPI scale (Minnesota Multiphasic Personality Lie- Inventory Scale). L - MMPI scale is part of the scale validity of MMPI (Minnesota Multiphasic Personality Inventory), further, the subjects fill the basic health questionnaire from the Department of Health (2007) to exclude systemic disease that can affect the value of cortisol.

Measurement of psychological complaints in accordance with the Menopause Rating Scale were filled solely by the subject. Then this examination includes measuring blood pressure, weight and height, laboratory tests conducted by measuring the levels of cortisol in saliva, take at least 1.5 cc saliva of a subject by means of the subjects lowered his head and let his own saliva to flow into the tube of polypropylene.

In conducting the study, researchers have received permission from the Research Ethics Committee of the Faculty of Medicine, University of Sumatera Utara.

**Results**

In this study, MRS total scores were obtained for each group. 44 subjects were positive for psychological disorders, and 52 subjects were found without psychological disorders.

<table>
<thead>
<tr>
<th>Psychological Disorders</th>
<th>Salivary cortisol levels (ng / ml)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;10 ng / ml</td>
<td>&gt;10 ng / ml</td>
</tr>
<tr>
<td>Negative</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>Positive</td>
<td>8</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Based on Table 1, most subjects with positive psychological disorders were having salivary cortisol level of >10 ng/ml (43 subjects; 82.6%); P-Value <0.01.

Based on Figure 1 and Figure 2, salivary cortisol cut off value is 9.02 ng/ml, with a sensitivity of 90.4% and a specificity of 86.4%.

**Discussion**

Perimenopause is a transition between premenopause and postmenopause. This phase is characterized by irregular menstrual cycles. In most women the menstrual cycle > 38 days and the remaining < 18 days. As many as 40% of women experience anovulatory menstrual cycles. In some women, it manifested as vasomotor complaints, or premenstrual syndrome complaints. But climacteric complaints can occur not only in women with the low level of hormone (5).

There are two types of symptoms: (a) Vasomotor disorder, which consists of hot flushes and night sweats, occur in 75% of postmenopausal women with varying degrees of severity; (b) Urogenital symptoms, estrogen deficiency causes atrophy of the urethra and vagina. Vagina wall will thinning and atrophy of vaginal glands will occur, so that lubrication is reduced and cause dyspareunia. The effect of estrogen deficiency on the urethra and bladder is associated with urethral syndrome such as frequency, urgency and dysuria (6).

Menopause Rating Scale (MRS) is a quality of life scale that was developed in the early 90s to assess the severity of menopausal complaints as a response to the lack of a standardized scale to measure the severity of the symptoms of aging and its effects on quality of life (7).

The emergence of psychological symptoms in menopause cannot be separated between organ-biological aspects, social, cultural and spiritual life of
the woman. Some prominent psychological symptoms when menopause arrives are irritability, depression, nervousness, loneliness, impatience, tension, anxiety, stress, and depression. Stress is a physical and mental strain or emotional because the body responds to the demands, pressures and distractions that surround us (8).

Stress is a condition or challenge beyond one's ability, therefore, stress is very individual in nature. Stress during menopause may be accelerated by the instability of the hormone and vice versa (9).

A state of physical stress such as injury, infection, trauma, extreme temperatures, as well as the state of emotional stress such as anxiety and depression lead to the body's reaction to a stress-response pathway in the form of general adaptation syndrome/GAS and generate stimulus in the limbic system that involves the hippocampus and amygdala. Adaptation to stress is mediated by the autonomic nervous system to the neuroendocrine adrenal gland, which eventually cause secretion of cortisol. Through a mediator which is neurotransmitter: Gamma Amino Butyric Acid (GABA), serotonin (5-HT), catecholamines, dopamine, cause changes in homeostasis involving intercellular signaling and stimulates neurons in the hypothalamus. Excitation is passed through the median eminence (ME) until it reaches a certain neuroendocrine cells in the hypothalamus that causes secretion of CRH (Corticotropin Releasing Hormone) and AVP (arginine vasopressin) by the paraventricular nucleus (PVN) of the hypothalamus. In this way, the stimulus is forwarded to the anterior pituitary that causes the secretion of ACTH (Adrenocorticotropic Hormone) into the systemic circulation.
ACTH then reaches the adrenal cortex hormone and causes the secretion of corticoid hormone, especially glucocorticoids such as: cortisol or corticosterone (10).

Conclusions

Salivary cortisol level can be used as a marker to determine psychological disorder in perimenopausal subjects. Further research is needed to apply salivary cortisol in clinical setting.

References

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