

Research Article

Estradiol Level and Psychosocial Stress in Perimenopausal Women

Kadar Estradiol dan Stres Psikososial pada Perempuan Perimenopause

Lucia L L S Hadiprodjo, Nusratuddin Abdullah, Nugraha U Pelupessy

Department of Obstetrics and Gynecology
Faculty of Medicine Universitas Hasanuddin
Dr. Wahidin Sudirohusodo General Hospital
Makassar

Abstract

Objective : To determine the relationship between estradiol levels and psychosocial stress in perimenopausal women.

Methods : Sixty perimenopausal included in a cross-sectional study from July to December 2016. Blood samples obtained from the women to measure the estradiol and the cortisol levels. Stress level measured with visual. Data presented as the mean and standard deviation (mean±SD) with p-value <.05 was considered statistically significant.

Results : There was no significant difference between the estradiol levels and the stress level ($p=0.27$) during perimenopause period. The estradiol levels were higher compared with the cortisol levels. The non-parametric correlations analysis show that the estradiol levels were not correlated with the cortisol levels ($p=0.352$). However, the cortisol levels were correlated with the stress levels ($p<0.05$).

Conclusions : Estradiol does not cause psychosocial stress during perimenopause period in our study population.

Keywords : estradiol, perimenopause, psychosocial stress.

Abstrak

Tujuan : Untuk mengetahui hubungan antara kadar estradiol terhadap stres psikososial pada perempuan perimenopause.

Metode : Enam puluh perempuan perimenopause dilibatkan penelitian potong lintang dari Juli sampai Desember 2016. Sampel darah diperoleh dari perempuan untuk mengukur kadar estradiol dan kortisol. Tingkat stres diukur dengan visual analog scale (VAS). Data yang disajikan sebagai rerata dan standar deviasi (mean±SD) dengan tingkat kemaknaan 0,05.

Hasil : Tidak ada perbedaan yang signifikan antara kadar estradiol dan tingkat stres ($p=0,27$) selama periode perimenopause. Kadar estradiol lebih tinggi dibandingkan dengan kadar kortisol. Analisis korelasi non parametrik menunjukkan kadar estradiol tidak berkorelasi dengan kadar kortisol ($p= 0,352$). Namun, kadar kortisol berkorelasi dengan tingkat stres ($p<0,05$) perempuan perimenopause.

Kesimpulan : Estradiol tidak menyebabkan stres psikososial selama periode perimenopause pada populasi penelitian kami.

Kata kunci : estradiol, perimenopause, stres psikososial

Correspondence author : Lucia Leonie L S Hadiprodjo.stephanielleonie@yahoo.com

INTRODUCTION

Perimenopause is a crucial transitional stage in a woman's life.¹ Perimenopausal stage usually begins at the end of age 40. Irregular of menstruation is an objective indicator to diagnose this period. The mean age of perimenopausal occurs at the age of 47.5 years and 51 years for menopause.² In perimenopausal period, there is an increase in FSH (follicle stimulating hormone), decreased inhibin levels, a slight increase in estradiol levels and change in luteinizing hormone (LH). In the last year before menopause, there is a decrease in estradiol levels below 40 pg /ml. Perimenopause

period is the period which the FSH levels begin to increase until postmenopausal levels above 20 IU, and LH levels remain within normal levels even though menstruation still occurs. Seventy per cent of perimenopausal and postmenopausal women experience symptoms associated with estrogen deficiency, i.e., vasomotor, psychosocial symptoms such as depression, anxiety, sensitivity, sleep disorders and decreased libido.³

Perimenopause associated with increased mood changes for depressive symptoms and increases the early onset of depression.⁴ There is research that states that during perimenopause

an increased risk of depression, including in women who have a history of depression. Alteration in estrogen levels results in depression. Perimenopausal estrogen levels affect mood and cognitive changes through alteration in acetylcholine and serotonin levels in the central nervous system. Estrogen is a steroid hormone that has a mechanism to increase the expression of genes in nucleus cells. There are two crucial estrogen receptors: alpha receptors that affect cognitive function, and beta receptors (β receptor) that affect the serotonergic system.

Estrogen regulates neuroendocrine, autonomy, and response to stress. Therefore, estrogen proved to regulate related functions of inflammatory processes, pain, anxiety, depression, and cognitive function.⁵ Mood and cognition are affected by estrogen on the central nervous system. Estrogens increase serotonin levels by decreasing monoamine oxidase that metabolised the serotonin.²

Perimenopausal period is a long period so that it is important to comprehend the role of estradiol in psychosocial stress symptoms because mood changes and psychosocial stress can reduce the quality of life of women during this period. This study aims to determine the relationship between estradiol levels and psychosocial stress in perimenopausal women.

METHODS

A cross-sectional study was conducted in RS. Dr. Wahidin Sudirohusodo and affiliated hospitals at the Department of Obstetrics and Gynecology at Universitas Hasanuddin from July to December 2016. The study involved perimenopausal women with the criteria: aged 40-50 years, irregular menstruation and FSH levels >20 IU. Blood samples obtained from the women to measure the estradiol and the cortisol levels. Stress level measured with visual. The study protocol was approved by analogue scales (VAS). The study protocol was approved by the Health Research Ethics Committee of Medicine Faculty Hasanuddin University Makassar. Data presented as the mean and standard deviation (mean \pm SD) with p-value $<.05$ was considered statistically significant.

RESULTS

The perimenopausal women in the current study were 28(46.7%) aged 45-49 years old, 36(60%) multiparous, 40(67%) normal BMI and all of them were smokers. The characteristics of the perimenopausal women listed in Table 1.

Table 1. Subject Characteristics

Characteristics (N=60)	n	%
Age (years)		
40-44	21	25
45-49	28	46.7
>50	11	18.3
Parity		
Nulliparous	7	11.7
Primiparous	6	10
2-3	36	60
>3	11	18.3
Body Mass Index (kg/m²)		
<18.5	8	13.3
18.5-25	40	66.7
>25	12	20
Smoking status		
Yes	60	100
No	0	0
Education (years)		
<9	10	16,66
>9	50	83,33

There was no significant difference between the estradiol levels and the stress level ($p=0.27$). The estradiol levels were higher compared with the cortisol levels (Table 2). Further analysis using the non-parametric correlations show that the estradiol levels were not correlated with the cortisol levels ($p=0.352$) (Table 3). However, the cortisol levels were correlated with the stress levels ($p<0.05$) (Table 4).

Table 2. Psychosocial Stress and Oestradiollevels

Psychosocial stress	n	Estradiol levels (mean \pm SDpg/ml)	P-value
Stress	30	76.1 \pm 97.6	0.27
Not stress	30	95.2 \pm 112.8	

Table 3. Correlation between Estradiol Levels and Cortisol Levels in the Perimenopausal Women

Variables	n	Mean±SD (pg/ml)	Median (pg/ml)	P-value
Estradiollevels	60	85.63±105.01	44.31	0.352
Cortisollevels	60	5.11±4.58	4.27	

Table 4. The Cortisol Levels and the Stress Level in the Perimenopausal Women

	n	Mean±SD	Median	P-value
Cortisollevels (pg/ml)	60	5.11±4.58	4.27	0.04
Stress level	60	18.32±5.58	19.5	

DISCUSSION

Stress occurs when an individual is under pressure beyond the adaptability. Stress is often caused by the surrounding environment which involves the ability of the individual to respond to any event that exceeds the capacity of the individual.⁶ Estradiol levels affect the mood changes in perimenopausal women⁷, and low levels of estradiol are one of the factors on depression in perimenopausal women. Transdermal estradiol administration may decrease depressive symptoms in perimenopausal women.⁷ Heisler and colleague suggested that serotonin may affect the hypothalamic-pituitary-adrenal (HPA) axis through the 5HT_{2CR3} receptor as the receptor of corticotropin-releasing hormone (CRH) neurons in the brain.⁸ In addition, the current study also shows no significant differences between estradiol levels and cortisol levels in perimenopausal women. Our result is consistent with a study by Avis that found no direct effect of estradiol with the depression in perimenopausal women. Perimenopausal women who experience depression is not caused by the direct effect of low levels of estradiol but due to vasomotor symptoms that interfere with the quality of life of women.⁹

The current study also shows that higher stress levels were correlated with cortisol levels in the study group. Otherwise produced by adrenals, cortisol is also produced by adipose cells by converting the inactivated 11 β -Hydroxysteroid dehydrogenase type 1 (HSD11 β 1), and estrogens can up-regulate the expression of mRNA HSD11 β 1 in female adipose tissue.¹⁰ The stress levels in the current study was comparing with the cortisol serum levels as hormonal stress, in addition, to interview using questionnaire. Combining this measurement, the results show that the level of stress measured with questionnaires significantly corresponds to the levels of cortisol.

Factors that affect psychological stress include smoking, body mass index, previous history of depression and hot flushes. In the current study, all the women not smoking and the previous history of depression was excluded. Smoking status can affect the onset of menopause. Study show women who smoke will experience early menopause.¹¹

The limitations of the current study were blood sampling for the examination of the hormone estradiol performed only once. Hormone levels have a wide range of variability during the perimenopausal period so that the results might not be represented the true levels of estradiol in our study group. This limitation affects the current study findings that different from the previous studies.

CONCLUSION

In conclusion, the psychosocial stress during perimenopause was not affected by the estradiol levels.

REFERENCES

1. Gyllstrom ME, Schreiner PJ, Harlow BL. Perimenopause and depression: strength of association, causal mechanisms and treatment recommendations. *Best Pract Res Clin Obstet Gynecol.* 2007;21(2):275-92.
2. Gungor BB, Gungor M, Taymur I, Askin R, Demirci H, et al. The effect of perimenopausal estrogen levels on depression and anxiety: a pilot study. *Eur Res J.* 2015;1(1):8-14.
3. Fritz MA, Speroff L. Menopause and the perimenopause. In *Clinical Gynecologic Endocrinology and Infertility*. 8theds. Lippincott Williams & Wilkins. Philadelphia, 2011:673-771.
4. Dumas JA, Kutz AM, Naylor MR, Johnson JV, Newhouse PA. Estradiol treatment altered anticholinergic-related brain activation during working memory in postmenopausal women. *Neuroimage.* 2012;60(2):1394-403.

5. Handa RJ, Mani SK, Uht RM. Estrogen receptors and the regulation of neural stress responses. *Neuroendocrinol*. 2012;96(2):111-8.
6. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA*. 2007;298(14):1685-7.
7. Soares CN, Almeida OP, Joffe H, Cohen LS. Efficacy of Estradiol for the Treatment of Depressive Disorders in Perimenopausal Women: a Double-Blind, Randomized, Placebo-Controlled Trial. *Arch Gen Psychiatry*. 2001;58(6):529-34.
8. Heisler LK, Pronchuk N, Nonogaki K, Zhou L, Raber J, et al. Serotonin inactivates the hypothalamic-pituitary-adrenal axis via serotonin 2C receptor stimulation. *J Neuro Sci*. 2007;27(26):6956-64.
9. Avis NE, Crawford S, Stellato R, Longcope C. Longitudinal study of hormone levels and depression among women transitioning through menopause. *Climacteric*. 2001;4(3):243-9.
10. Mattsson C, Olsson T. Estrogens and glucocorticoid hormones in adipose tissue metabolism. *Curr Med Chem*. 2007;14(27):2918-24.
11. Randolph JF Jr, Zheng H, Sowers MR, Crandall C, Crawford S, et al. Change in follicle-stimulating hormone and estradiol across the menopausal transition: effect of age at the final menstrual period. *J Clin Endocrinol Metabol*. 2011;96(3):746-54.