Thai Journal of Obstetrics and Gynaecology
April 2017, Vol. 25, pp.111-118

GYNAECOLOGY

The Correlation between Serum Estradiol Level and Body Mass Index in Postmenopausal Women: A cross-sectional study at the Menopause Clinic, Siriraj Hospital

Kitirat Techatraisak, M.D., PhD.*,
Kittiyaporn Wattayanon, M.D.*.

** Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand*

ABSTRACT

Objectives: To examine correlation between serum level of estradiol (E2) and body mass index (BMI) in postmenopausal women at a menopause clinic of a tertiary care university hospital.

Materials and Methods: A retrospective cross-sectional study was performed at the Menopause Clinic, Faculty of Medicine Siriraj Hospital, Mahidol University. One hundred and twenty five consecutive medical records of menopausal women attending the menopause clinic, including both natural and surgical menopause were reviewed. All of them never received hormonal treatment or did not receive any hormonal treatment at least one year at the time of this study. All were confirmed to have serum FSH level ≥ 40 IU/L. Baseline characteristic, data on serum level of E2, BMI, type of menopause and duration of menopause were extracted. Correlation between serum level of E2 and BMI was evaluated by the Statistics Package for the Social Sciences Program (SPSS 18.0 statistical package). Pearson correlation analysis was used to demonstrate the correlation between serum E2 level and BMI, with a p value less than 0.05 considered as statistically significant.

Results: Of all 125 patients, the majority were natural menopausal cases (81.6%). Mean E2 level and BMI were 20.38±16.61 pg/ml and 22.96±3.65 kg/m^2 respectively. No significant correlation between serum E2 level and BMI was demonstrated (r = - 0.101, p = 0.265). Also no correlation was observed in different type of menopause, different duration of menopause and different BMI classification.

Conclusion: There was no significant correlation between serum level of E2 and BMI in postmenopausal women of this study population.

Keywords: estradiol, body mass index, menopause, correlation

Correspondence to: *Kitirat Techatraisak, M.D., PhD., Head of Gynecologic Endocrinology Division, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand, Tel: +662-4194657 Mobile: +661-7711105 Fax: +662-4194658, E-mail: kitirat.tec@mahidol.ac.th*

ความสัมพันธ์ระหว่างระดับฮอร์โมนเอสตราไดออลในเลือดกับดัชนีมวลกายของสตรีวัยหลังหมดระดู: การศึกษาที่คลินิกสตรีวัยทอง โรงพยาบาลศิริราช

กิติรัตน์ เตชะไตรศักดิ์, กิตติญาภรณ์ เวทยานนท์

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ระหว่างระดับฮอร์โมนเอสตราไดออลในเลือด และดัชนีมวลกายของสตรีวัยหลังหมดระดูที่มารับบริการที่คลินิกวัยทองของโรงพยาบาลมหาวิทยาลัยแห่งหนึ่ง*

วัตถุและวิธีการ: *การศึกษานี้เป็นการศึกษาตามแนวขวางที่คลินิกวัยทอง ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ได้ทำการทบทวนประวัติของผู้ป่วยจำนวน 125 ราย ทั้งผู้ป่วยที่หมดระดูตามธรรมชาติและหมดระดูจากการผ่าตัด ผู้ป่วยทุกรายต้องไม่เคยได้รับการรักษาด้วยฮอร์โมนมาก่อนหรือไม่ได้รับฮอร์โมนชนิดใดๆ ภายในระยะเวลา 1 ปีก่อนเก็บข้อมูล และทุกรายต้องมีระดับ FSH ≥ 40 IU/L ณ เวลาที่ทำการศึกษา ทำการรวบรวมข้อมูลพื้นฐานด้านอายุ อายุที่หมดระดู ชนิดของการหมดระดู เวลานับจากวันหมดระดู และระดับฮอร์โมน FSH และเอสตราไดออลในเลือด นำผลที่ได้มาวิเคราะห์ถึงความสัมพันธ์ระหว่างระดับฮอร์โมนเอสตราไดออลในเลือดและดัชนีมวลกายของผู้ป่วย ดำเนินการวิเคราะห์ความสัมพันธ์ระหว่างระดับเอสตราไดออลในเลือดและดัชนีมวลกายโดย Pearson correlation analysis ด้วย SPSS 18.0 statistical package*

ผลการศึกษา: *จากผู้ป่วยจำนวน 125 ราย พบว่า ส่วนมากของผู้ป่วย (102 ราย, 81.6%) หมดระดูโดยธรรมชาติ ระดับค่าเฉลี่ยโดยรวมของฮอร์โมนเอสตราไดออลในเลือดเท่ากับ 20.38 ± 16.61 pg/ml และค่าเฉลี่ยมวลกายโดยรวมเท่ากับ 22.29 ± 3.65 kg/m^2 ไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติ ระหว่างระดับฮอร์โมนเอสตราไดออลและดัชนีมวลกาย ($r = -0.101$, $p=0.265$) เมื่อวิเคราะห์แยกตามชนิดของการหมดระดู เวลานับจากวันหมดระดูและดัชนีมวลกายค่าต่างๆ กัน (< 20, 20 -24.99 และ ≥ 25kg/m^2) กับระดับเอสตราไดออลในเลือดก็ไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติเช่นกัน*

สรุปผล: *ระดับเอสตราไดออลในเลือดและดัชนีมวลกายของสตรีวัยหลังหมดระดูไม่มีความสัมพันธ์กันอย่างมีนัยสำคัญทางสถิติในผู้ป่วยที่ทำการศึกษานี้*

คำสำคัญ: *เอลตราไดออล, ดัชนีมวลกาย, สตรีวัยหลังหมดระดู, ความสัมพันธ์*

Introduction

After menopause, there are many changes in sex-hormone profile. The circulating level of androstenedione is about one-half of that seen prior to menopause[1]. Most of this postmenopausal androstenedione is derived from the adrenal gland, with only a small amount secreted from the ovary. Although androstenedione is the principle steroid secreted by the postmenopausal ovary[2,3], the circulating estradiol (E2) level after menopause is approximately 10-20 pg/ml[4]. Whereas the circulating level of estrone (E1) in postmenopausal women is higher than that of E2, approximately 30-70 pg/ml[5]. Mean E2 levels started to decrease about two years before the final menstrual period, decreased rapidly after that time and plateaued by two years after final menstrual period[6]. Because the biological potency of E2 is greater than that of E1, thus E2 has more clinical importance. Secretion of E2 by the postmenopausal ovary does not appear to be an important contribution since its circulating level is similar, in postmenopause, before and after ovariectomy[7, 8].

Many studies support the concept that in postmenopausal women, the circulating E2 is derived from the peripheral conversion of E1, which in turn is the product of the peripheral aromatization of circulating androstenedione. And also the finding that obese older women were at risk for the development of endometrial cancer than thinner women, so we hypothesized that the peripheral conversion of E2 were associated with fat mass. Then, there should be some correlation between E2 level and BMI in postmenopausal women. Body weight, therefore, has a positive correlation with the circulating levels of E1 and E2, probably due to the ability of fat to aromatize androgens. Meldrum DR, et al.[1] found highly significant positive correlations of both E2 ($r = 0.472$, $p < 0.001$) and E1 ($r = 0.383$, $p < 0.001$) with percent ideal body weight. Also, Rannevik G, et al.[7] reported less significant positive correlation of E2 level ($r = 0.18$, $p < 0.03$) with body mass index (BMI). The study by Campagnoli C, et al.[9] found that overweight natural postmenopausal women suffered from hot flushes less than thinner women. Whereas the study by Burger HG, et al., in 150 natural menopausal women and followed up for six years showed no correlation between log E2 level and BMI ($p = 0.6$)[6].

In this study, we focus on the controversial correlation between serum E2 level and BMI, which is easy to obtain, in postmenopausal women that have never been reported in Thai population. Both natural and surgical menopausal women were studied because circulating E2 is mainly from the peripheral conversion of E1 as previously mentioned. The study was approved by the committee of Siriraj Review Board (SiRB)

Materials and Methods

This was a retrospective cross-sectional study. The medical records of 125 postmenopausal women attending Siriraj Menopause Clinic, Department of Obstetrics and Gynecology, Siriraj Hospital were reviewed. Sample size calculation was derived from a pilot study of 10 postmenopausal women at the Menopause Clinic and found the correlation of serum estradiol and BMI of 0.27. With $r = 0.27$, $\alpha = 0.05$ $Z\alpha/2 = 1.96$ (two tailed), $\beta = 0.2$ and $Z\beta = 0.84$, a total number of 105 cases were derived. We added approximately 20 percent more cases, so the total subjects included for analysis were 125 cases. Only cases with complete every parameter of the data were retrieved until 125 cases were achieved. The study included both natural and surgical menopausal women. Natural menopause was defined as women who had her last period at least 12 months around the time of average age of natural menopause. Premature ovarian failure was diagnosed as the cessation of ovarian function before the age of 40, with evaluated serum FSH ≥ 40 IUI/l. Surgical menopause was a selected case that had underwent bilateral oophorectomy before the time of natural menopause. All of the selected subjects must be the cases who were simultaneously tested for both serum follicle stimulating hormone (FSH) and serum E2 levels. These tests were not routinely performed in our menopause clinic. Both hormonal assays were assessed by the Electrochemiluminescense Immunoassay (ECLIA) method at the Clinical Pathology

Department of Faculty of Medicine Siriraj Hospital. We extracted data of age, age at menopause, type of menopause, duration of menopause, weight, height, serum FSH and serum E2 levels. Only those with completed data were included for analysis. All of them had a serum FSH level of 40 IU/L or more which indicated a menopausal range, never received any hormonal treatment or did not receive any hormonal treatment at least one year prior to this study and with no history of any other endocrine disorder. BMI was calculated as weight in kilograms divided by the square of height in meters then classified to < 20 kg/m^2, 20-24.99 kg/m^2 and ≥ 25kg/m^2 groups.

Calculations and statistic analysis

The Statistics Package for the Social Sciences Program (SPSS 18.0 statistical package) was used to perform the data analysis. Age, age at menopause, duration of menopause, weight, height, BMI, serum FSH and serum E2 levels were demonstrated as percentage and mean ± S.D. Pearson correlation analysis was used to demonstrate the correlation between serum E2 level and BMI, with a p-value less than 0.05 considered as statistically significant.

Results

Overall demographic characteristics and hormonal profiles of the study population in both the natural and the surgical menopause subgroups are shown in Table 1. Of all 125 postmenopausal women, 102 cases were natural menopausal (81.6 %) and 23 cases (18.4%) were surgical menopausal patients. A total number of 18 premature ovarian failure patients were also included in the natural menopausal group. Most of them (71.2%) attended the menopausal clinic before 60 month duration after menopause. The majority of our study population had normal BMI (n=72, 57.6 %), with a nearly normal distribution when tested (Skewness = 0.608). Nearly 60 percent had a normal BMI and one fourth had BMI ≥ 25 kg/m^2

Table 1. Demographic characteristics and baseline laboratory results of the overall 125 cases and the two subgroups of the natural and the surgical menopausal groups. All data are shown in mean ± SD.

Character	Overall (N=125)	Natural (N=102)	Surgical (N=23)
Age (year)	49.12 ± 9.23	49.48 ± 9.86	47.52 ± 5.58
Age at menopause (year)	44.23 ± 7.51	44.95 ± 7.84	41.69 ± 5.22
Duration of menopause (month)	56.74 ± 60.22	53.79 ± 60.83	69.78 ± 56.84
Serum FSH level (IU/L)	81.75 ± 27.60	83.33 ± 28.29	74.75 ± 23.56
Serum E2 level (pg/ml)	20.38 ± 16.61	20.38 ± 15.98	20.37 ± 19.71
BMI (kg/m^2)	22.96 ± 3.65	22.72 ± 3.49	24.02 ± 4.18

BMI = Body Mass Index, E2 = Estradiol, FSH = Follicular Stimulating Hormone
Range of serum FSH level for 40 - 175 IU/L, Range of serum E2 level 0.2 - 84.06 pg/ml

The comparison data in both groups are shown in Table 2. Overall mean ages was 49.12±9.23 years. The average age of natural menopausal group was approximately two years older than the surgical menopausal one. Interestingly, longer duration of menopause before attending the clinic was seen in the surgical group. The average BMI was 22.96 ±3.65 kg/m^2 which was in a normal range. Higher BMI was seen in the surgical menopausal group than the natural menopause (24.0 and 22.72 kg/m^2, respectively). Mean serum FSH and mean serum E2 levels were 81.75±27.6 IU/L and 20.38±16.61 pg/ml. Higher FSH was observed in the natural group although time since menopause was shorter, while serum E2 levels were comparable. Scattered plots of BMI and serum E2 are shown in Fig. 1.

Table 2. Comparison of mean serum E2 levels in different type, duration of menopause and different BMI classification groups.

Character	Number	(Percent)	E2 level (pg/ml)	p value
Type of menopause				0.998
Natural	102	(81.6)	20.37 ± 19.71	
Surgical	23	(18.4)	20.38 ± 15.95	
Duration of menopause (month)				0.311
< 24	45	(36.0)	23.40 ± 16.22	
24-60	44	(35.2)	18.44 ± 17.99	
> 60	36	(28.8)	18.97 ± 15.21	
BMI (kg/m^2)				0.107
< 20	22	(17.6)	24.04 ± 19.23	
20-24.99	72	(57.6)	21.50 ± 17.67	
≥ 25	31	(24.8)	15.16 ± 10.09	
Total	**125**	**(100.0)**		

BMI = Body Mass Index, E2 = Estradiol

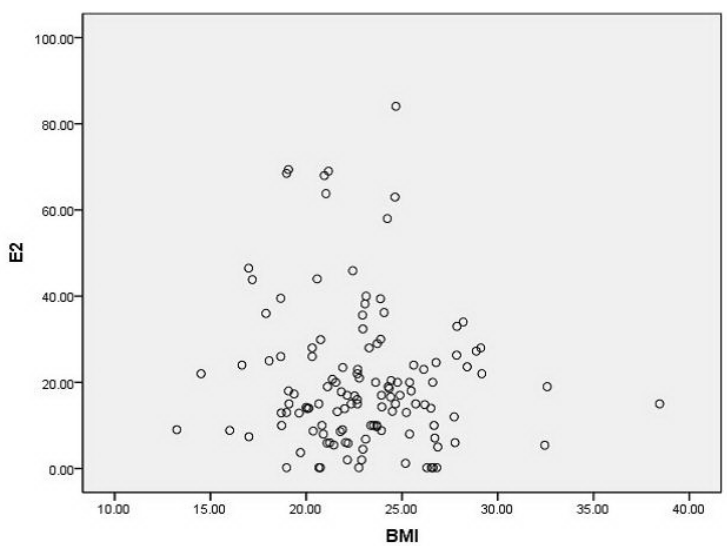

Fig. 1. Scattered plots between BMI and E2 of 125 cases.
BMI = Body Mass Index, E2 = Estradiol

No differences between serum E2 levels and type, duration of menopause and different BMI groups were demonstrated. Subsequent analysis showed no correlation between overall serum E2 level and BMI (r = - 0.101, p = 0.265) as shown in Table 3. Also, no significant correlations were seen between mean serum E2 and different type, duration of menopause and BMI classification groups.

Table 3. Correlation between BMI and serum E2 level.

Parameter	Correlation	p value
Overall	-0.101	0.265
Type of menopause		
Natural	-0.086	0.392
Surgical	-0.150	0.494
Duration of menopause (months)		
< 24	-0.073	0.636
24-60	-0.068	0.662
> 60	-0.145	0.400
BMI (kg/m^2)	22	
< 20	0.087	0.700
20-24.99	0.145	0.225
≥ 25	0.145	0.437

BMI = Body Mass Index, E2 = Estradiol

Discussion

In this report, the overall mean age at menopause was about 44 years old. The mean age at menopause was relatively younger in this study when compared with other previous general investigations such as that reported by Rannevik G, et al., who reported the age at natural menopause of 51-52 years[7]. This finding can be explained by the characteristic of the study population that we also included surgical menopause patients and 18 cases of premature ovarian failure in the natural menopausal group. The mean serum estradiol level was in the previously reported postmenopausal range. In this study, no correlation was demonstrated between E2 and BMI. Moreover, subgroup analysis also did not show correlation when we categorized and examined in different type and duration of menopause and different BMI. The study of Burger HG, et al.,[6] in a longitudinal study of a population-based cohort women aged 45-55 years and pre- or perimenopausal at baseline with annual record and experienced the menopausal transition, no correlation between circulating log E2 level and BMI was demonstrated which showed no effect of BMI. Gold EB, et al.[10], also studied perimenopausal women aged 42-52 years and also found the risk of vasomotor symptoms was higher in heavier women and there were no increase in estrogen level in obese women. They explained that increase in body fat provided more insulation, increased core body temperature and prevented aromatization in adipose tissue. The similar finding was found in this study.

The result was difference from the report by Meldrum DR, et al[1], who found positive correlation between percent ideal weight and circulating E2 level, as well as the report of Rannevik G, et al[7], that positive correlation between BMI and serum E2 level was demonstrated. The later study by Freeman EW, et al[11], who found that women who had heavier weight, would have higher E2 levels than thinner women. This made the thinner women encountered longer duration of vasomotor symptoms than those with heavier weight (BMI > 30kg/m^2, P = 0.003). One previous cross-sectional report by Schwingel PJ, et al[12], on natural menopausal women aged between 40-60 years with vasomotor symptoms found that thin, smoking women during the premenopausal period were more likely to experience vasomotor symptoms than the obese women. But this finding was not significant for non-smokers. Whiteman MK, et al[13], studied women aged 40-60 years and found that BMI higher than 30 kg/m^2 was associated with an increased risk of moderate to severe hot flashes. They explained the fact that

adipose tissue produced hormones (e.g. leptin, tumor necrosis factor) which inhibited ovarian steroid production and resulted in a slight level of estrogen in obese women.

Also, there were reported differences in the relation between BMI and the percentage of body fat across ethnic groups by body composition analyses. Large variations were observed among Asian populations. Hong Kong Chinese, Indonesians, Singaporeans, urban Thai and young Japanese had lower BMI at a given body fat compare with Europeans. On the other hand, in some Asian populations a specific BMI reflects a higher percentage of body fat than in white or Europeans populations. There were also reported differences in the relation between BMI and the percentage of body fat among white people[15]. These data encouraged overweight women who smoke and have more severe vasomotor symptoms to lose weight and refrain from smoking[12-14]. The study population included both natural and surgical menopause with unequal numbers and the numbers in both groups might be too small for comparing to see a difference. These factors might be limitation factors of this study. Possibly, the individual variation in the aromatase activity that until now still no enough information was explored. Controversial data on the association between BMI and serum E2 level still exists. So further studies are needed to clarify for association.

Conclusion

The data failed to show significant correlation between serum E2 level and BMI. Also, for different type of menopause, time since menopause and different groups of BMI, the circulating E2 levels showed variations but the data failed to show significant correlation with BMI. A larger number of subjects, the effect of aromatase activity which affects conversion of serum androgen to E2 in different BMI group of menopausal women should also be further studied.

Acknowledgments

The authors thank Mr. Suthipon U-dompunturak, a statistician of the Clinical Epidemiology Unit, Faculty of Medicine Siriraj Hospital, Mahidol University, for statistical analysis.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Meldrum DR, Davidson BJ, Tataryn IV, Judd HL. Changes in circulating steroids with aging in postmenopausal women. Obstet Gynecol 1981;57: 624-8.
2. Grodin JM, Siiteri PK, MacDonald PC. Source of estrogen production in postmenopausal women. J Clin Endocrinol Metab 1973;36:207-14.
3. Fritz MA, Speroff L. Menopause and the perimenopausal transition. In: Fritz MA, Speroff L, editors. Clinical Gynecologic Endocrinology and Infertility. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2011:673-784.
4. Judd HL, Shamonki IM, Frumar AM, Lagasse LD. Origin of serum estradiol in postmenopausal women. Obstet Gynecol 1982;59:680-6.
5. Judd HL, Judd GE, Lucas WE, Yen SS. Endocrine function of the postmenopausal ovary: concentration of androgens and estrogens in ovarian and peripheral vein blood. J Clin Endocrinol Metab 1974;39:1020-4.
6. Burger HG, Dudly EC, Hopper JL, Groome N, Guthrie JR, Green A, et al. Prospective measured levels of serum follicular stimulating hormone, estradiol, and the dimeric inhibins during the menopausal transition in a population-based cohort of women. J Clin Endocrinol Metab 1999;84:4025-30.
7. Rannevik G, Jeppsson S, Johnell O, Bjerre B, Laurell-Borulf Y, Svanberg L. A longitudinal study of the postmenopausal transition: altered profiles of steroid and pituitary hormones, SHBG and bone mineral density. Maturitas 1995;21:103-13.
8. Vermeulen A, Verdonck L. Factors affecting sex hormone levels in postmenopausal women. J Steroid Biochem 1979;11:899-904.
9. Campagnoli C, Morra G, Belforte P, Prelato TL. Climacteric symptoms according to body weight in woman of different socio-economic groups. Maturitas 1981;3:279-87.
10. Gold EB, Block G, Crawford S, Lachance L, Fitzgerald G, Miracle H, et al. Lifestyle and demographic factor in relation to vasomotor symptoms: baseline results from the study of women's health across the nation. Am J Epidemiol 2004;159:1189-99.
11. Freeman EW, Sammel MD, Lin H, Liu Z, Gracia CR. Duration of menopausal hot flashes and associated risk factors. Obstet Gynecol 2011;117:1095-104.
12. Schwingl PJ, Hulka BS, Harlow SP. Risk factors for menopausal hot flashes. Obstet Gynecol 1994;84:29-34.

13. Whiteman MK, Staropoli CA, Largenberg PW, McCarter RJ, Kjerulff KH, Flaws JA. Smoking, body mass, and hot flashes in midlife women. Obstet Gynecol 2003;101: 264-72.
14. Gold EB, Sternfeld B, Kelsey JL, Brown C, Mouton C, Reame N., et al. Relation of demographic and lifestyle factors to symptoms in a multi-racial/ethnic population of women 40-50 years of age. Am J Epidemiol 2000; 152:463-73.
15. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.