Serum Estradiol and Gonadotropins Level in Postmenopausal Women with or without Hormone Replacement†

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Abstract

Serum follicle stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E_2) was measured in 49 menopausal women, to assess the changing serum level in women with or without hormone replacement. Women in the study group (N=25) received estrogen with or without progestin. The control group (N=24) did not receive any hormone regimen. Serum hormone measurement was done at 0, 6 and 12 month, using time-resolved fluoroimmunoassay method. The results revealed no significant change of FSH, LH and E_2 at 0, 6 and 12 month in the control group. (FSH at 0, 6, 12 month : 55.14±22.82, 63.90±24.54, 72.81±29.58 IU/L, P=0.09; LH at 0, 6, 12 month : 35.54±19.86, 33.02±16.30, 32.33±17.37 IU/L, P=0.83; E_2 at 0, 6, 12 month : 49.28± 48.54, 37.29±39.93, 25.63±23.58 pmol/L, P=0.17). However, in the study group, FSH and LH significantly decreased but E_2 significantly increased at 6 and 12 months. (FSH at 0, 6, 12 month : 59.33±22.30, 27.23±16.31, 29.74±19.45 IU/L, P<0.05; LH at 0, 6, 12 months : 41.4± 17.02, 19.62±13.66, 15.65±8.77 IU/L, P<0.05; E_2 at 0, 6, 12 months : 47.33+41.25, 280.94± 174.11, 270.70±198.65 pmol/L, P<0.05). In conclusion, hormone replacement decreased serum gonadotrophin, though not reaching the premenopausal level. However, serum E_2 value was significantly increased close to the level in the follicular phase of normal menstrual cycle.

At present, there is increasing information that hormone replacement therapy can alleviate the symptoms of menopause and, more recently in preventing osteoporosis and reducing the risk of ischemic heart disease[1-3].

During the normal menstrual cycle, the minimal estradiol (E_2) level is approximately 40 pg/ml (147 pmol/L) with a peak of 250 pg/ml (919 pmol/L) at midcycle and 100 pg/ml (367 pmol/L) during the luteal phase[4,5]. Some suggested that these should be therapeutic guidelines for estrogen replacement therapy[5].

During menopause, E_2 level drops to less than 20 pg/ml (73 pmol/L). The response to declin-

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ing estrogen is variable from one organ system to another and from person to person[5].

In Thailand, hormone replacement therapy has been frequently prescribed for a couple of years. With the dose recommended by each pharmaceutical company, it is claimed to be adequate in elimination or attenuation of the complication incurred as a result of menopause.

Nevertheless, there is a scarcity of information concerning the serum hormone level of Thai menopausal women receiving hormone replacement. Hence, the objective of this study was to assess the changing levels of serum FSH, LH and E_2 in menopausal women with or without hormone replacement therapy.

MATERIAL AND METHOD

Subjects :

Forty nine women visiting the menopause clinic, Chulalongkorn University Hospital participated in the study. All were healthy and at least 6 months postmenopause. Postmenopausal status was confirmed by measurement of serum gonadotropins and estradiol levels. These women had not received any hormone regimen within the previous one year. These women had no chronic disease. All participants were informed of all the details before entering the study. All patients were randomly allocated to receive hormone replacement therapy or no treatment as shown in Table 1.

Study design :

This 12-month study was conducted in a prospective, open trial method. In the study group, the hormone was taken around 10.00-12.00 pm. Blood samples of both groups were collected the next morning (08.00-10.00 am.) FSH, LH and E_2 were measured in the serum sample at 0, 6 and 12 month, using time-resolved fluoroimmunoassay (FIA) method. (Wallac Oy, Turku, Finland.) A sensitivity of FSH, LH and E_2 were 0.05 IU/L, 0.05 IU/L and 13.6 pg/ml, respectively. Interassay coefficients of variation for an intermediate serum pool were 2.92 per cent for FSH, 6.55 per cent for LH and 3.89 per cent for E_2. Intraassay coefficients of variation for an intermediate serum pool were 2.15 per cent for FSH, 6.32 per cent for LH and 3.73 per cent for E_2.

Statistics :

The distribution of data was tested using Kolmogorov-Smirnov Goodness of Fit test which was found to be normal. One way ANOVA, paired and unpaired *t*-test was used where it was appropriate.

RESULTS

Of the 49 menopausal women who participated in the study, 25 women were randomly allocated to the study group and 24 were in the control group. The patients' characteristics are shown in Table 2. The mean serum levels of FSH, LH and estradiol at 0, 6 and 12 month in the control and study group are illustrated in Fig. 1-3. In the study group, FSH and LH levels significantly decreased from baseline value at 6 and 12 month ($P<0.01$). However, there was no statistically significant difference of FSH, LH and E_2 at 6 and 12 month.

Table 1. Regimen of hormonal replacement therapy.

Group	Type of menopause	Regimen used
HRT	1. Natural	1. Cyclic : EV (2 mg) + Norgestrel (0.5 mg)
		2. Cyclic : CEE (0.625 mg) + Medrogestone (5 mg)
		3. Combined continuous regimen : CEE (0.625 mg) + MPA (2.5 mg)
	2. Surgical	1. Cyclic : CEE (0.625 mg)
		2. Cyclic : 17 Beta-estradiol 15 mg
Non-HRT		Calcium 1,000 mg/d ± parasympatholytics as needed

HRT = Patients receiving hormonal replacement therapy
Non-HRT = Patients not receiving hormonal replacement therapy
Cyclic = Estrogen on days 1-21 ± progestin on day 12-21
EV = Estradiol valerate
CEE = Conjugated equine estrogen
MPA = Medroxy progesterone acetate
Combined continuous regimen = estrogen and progestin daily

Table 2. Population characteristics.

Characteristics (Mean±SD)	Control (N=24)	Study (N=25)	P-value P<0.10
1. Age (yr)	49.38±3.93	50.29±4.15	NS
2. BW (kg)	62.75±14.96	54.20±3.05	NS
3. Height (cm)	154.83±3.67	154.00±4.64	NS
4. T-men (yr)	3.58±2.70	4.10±3.19	NS

BW = Body Weight
T-men = Time since menopause
yr = year

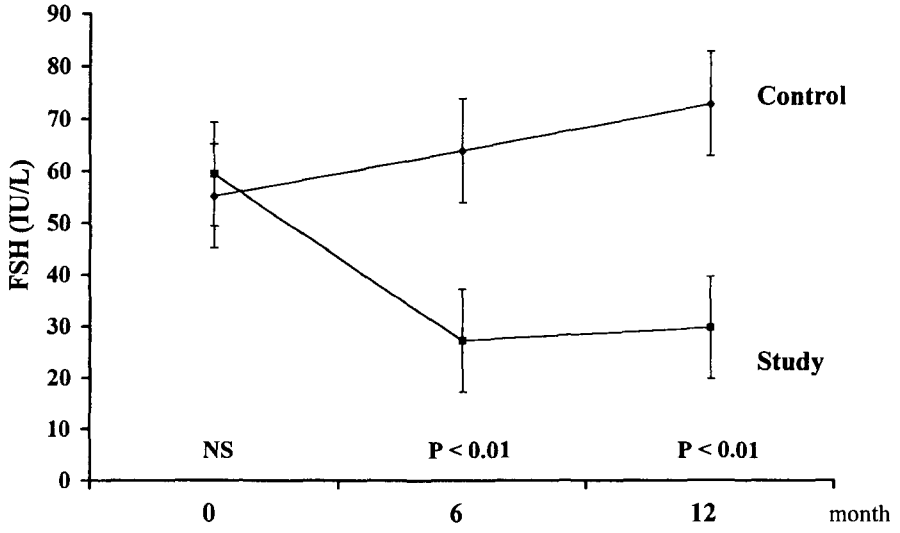

Fig. 1. Comparison of the mean value of serum follicle-stimulating hormone (FSH) at 0, 6 and 12 month.

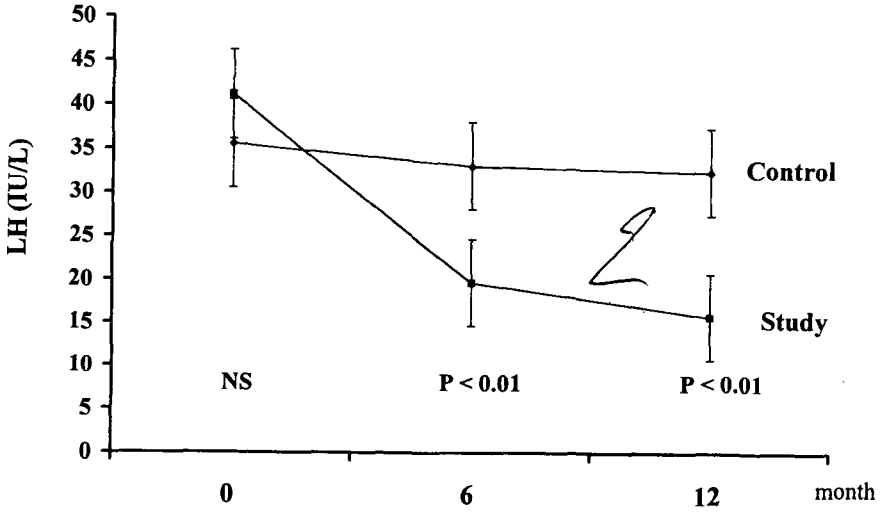

Fig. 2. Comparison of the mean value of serum luteinizing hormone (LH) at 0, 6 and 12 month.

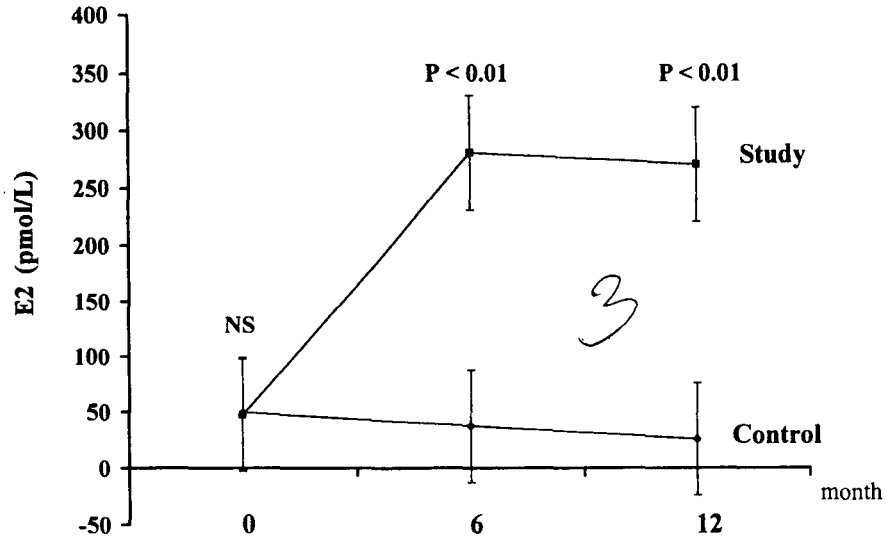

Fig. 3. Comparison of the mean value of serum estradiol (E_2) at 0, 6 and 12 month.

Table 3. Comparing serum levels of FSH, LH and E_2 at 0, 6 and 12 month between the control and study group.

Serum hormone (Mean ± SD)		Control (N=24)	Study (N=25)	P-value
FSH	0	55.14±22.82	59.33±22.30	NS
(IU/L)	6	63.90±24.94	27.23±16.31	P <0.01
	12	72.81±29.58	29.74±19.45	P <0.01
LH	0	35.54±19.86	41.14±17.02	P = 0.293
(IU/L)	6	33.02±16.30	19.62±13.66	P <0.01
	12	32.33±17.37	15.65±8.77	P <0.01
E_2	0	49.28±48.54	47.33±41.25	P = 0.492
(pmol/L)	6	37.29±39.93	280.94±174.11	P <0.01
	12	25.63±23.58	270.70±198.65	P <0.01

NS = Non-significant

On the contrary, estradiol level significantly increased from baseline value at 6 and 12 month (P<0.01), though there was no significant difference of the serum level at 6 and 12 months. Considering the control group, there was no statistically significant difference of FSH, LH and E_2 at 0, 6 and 12 months. However, it was found that serum FSH level significantly increased and serum estradiol significantly decreased at 12 months from the baseline value (P<0.01). When comparing all the serum levels between the study and control group, the result is shown in Table 3.

DISCUSSION

It was shown in this study that without HRT, Thai menopausal women tend to have rising FSH and decreasing E_2 levels as time went by, though there was no noticeable changes in LH level. Nevertheless, HRT, FSH and LH levels decreased significantly, though not reaching the premenopausal levels at 12 month. This is probably because before entering menopause, the ovary not only secretes estrogen, progesterone and androgen, but also produces inhibin which suppress FSH level to the premenopausal range[6].

Approaching menopause, the ovary secretes less and less inhibin causing FSH level to be rising before E_2 level starts to drop, which is the early sign of menopause[6]. With HRT, eventhough FSH can be suppressed by the hormone used, it does not reach the premenopausal range. This is probably due to the lack of inhibin.

Considering the E_2 level in this study, it was found that in the HRT group, serum E_2 level rose nearly to the normal range of the follicular phase of normal menstrual cycle. E_2 of this level can relieve menopausal symptoms and prevent significant bone loss[5,7]. However, the changing hormone level in this study reflected the effect of HRT in a broad sense. This is because the studied population used various hormone regimens with different doses and routes of administration. Besides this, the interval of blood sample collection in this study was between 8-10 hours from the time of hormone administration. Since the peak serum estrogen level after estrogen used was reported to be 4-10 hours,[8-11] it depends on the type, dose and route of estrogen used to determine the time interval from estrogen administration to the peak level. Hence, further study with specific regimen of HRT is needed to reveal exactly the changing value of serum hormone level in menopausal women receiving HRT.

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ระดับฮอร์โมนในกระแสเลือดในสตรีวัยหมดระดูที่ได้รับหรือไม่ได้รับฮอร์โมนทดแทน

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สตรีวัยหมดระดู 49 รายได้รับการตรวจหาระดับของฮอร์โมน Follicle stimulating hormone (FSH) , luteinizing hormone (LH) และ estradiol (E_2) เพื่อดูการเปลี่ยนแปลงของระดับฮอร์โมนในกระแสเลือดในสตรีที่ได้รับหรือไม่ได้รับฮอร์โมนทดแทน โดยสตรีในกลุ่มศึกษาจำนวน 25 ราย ได้รับฮอร์โมนเอสโตรเจนอย่างเดียวหรือร่วมกับฮอร์โมนโปรเจสติน ในกลุ่มควบคุม จำนวน 24 ราย ไม่ได้รับฮอร์โมนใด ๆ สตรีทั้งสองกลุ่มจะได้รับการตรวจระดับของฮอร์โมนดังกล่าวในเดือนที่ 0, 6 และ 12 ด้วยวิธี Time-resolved fluoroimmunoassay ผลการศึกษาพบว่า ในกลุ่มควบคุมไม่พบการเปลี่ยนแปลงของ FSH, LH และ E_2 ในกระแสเลือดอย่างมีนัยสำคัญทางสถิติ (FSH ที่ 0, 6, 12 เดือน : 55.14$\pm$22.82, 63.90$\pm$24.54, 72.81$\pm$29.58 IU/L , P=0.09 ; LH ที่ 0, 6, 12 เดือน : 35.54$\pm$19.86, 33.02$\pm$16.30, 32.33$\pm$17.37 IU/L, P=0.83 ; E_2 ที่ 0, 6, 12 เดือน : 49.28$\pm$48.54, 37.29$\pm$39.93, 25.63$\pm$23.58 pmol/L, P=0.17) อย่างไรก็ตามในกลุ่มศึกษาพบว่า ระดับ FSH และ LH ลดลงในขณะที่ E_2 เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติที่ 6 และ 12 เดือน (FSH ที่ 0, 6, 12 เดือน : 59.33$\pm$22.30, 27.23$\pm$16.31, 29.74$\pm$19.45 IU/L , P<0.05 ; LH ที่ 0, 6, 12 เดือน : 41.4$\pm$17.02, 19.62$\pm$13.66, 15.65$\pm$8.77 IU/L, P<0.05 ; E_2 ที่ 0, 6, 12 เดือน : 47.33$\pm$41.25, 280.94$\pm$174.11, 270.70$\pm$198.65 pmol/L, P<0.05) กล่าวโดยสรุปการได้รับฮอร์โมนทดแทนทำให้ระดับฮอร์โมน FSH และ LH ลดลงแม้จะไม่ลดลงจนถึงระดับเฉลี่ยปกติในสตรีที่ยังไม่หมดระดูก็ตาม อย่างไรก็ดีพบว่า ระดับ E_2 เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติใกล้เคียงกับระดับของฮอร์โมนในระยะ Follicular ของรอบระดูปกติ

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