Effect of Hormone Therapy on Lipid Profile in Menopausal Women

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Objective: *To study lipid profile of menopausal women with hormone therapy.*
Material and Method: *Two hundred and sixty eight menopausal women in good health conditions, separated into natural and surgical menopause group, received service at Menopausal clinic in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University since 1996-2004. They regularly took a single type of hormone therapy for about 12 months and obtained blood cholesterol levels for pre- and post-hormone therapy of about 12 months period. The data were analyzed with SPSS v. 10.0.5.*
Results: *The average age of the sample groups were 50.91 ± 5.93 years and 52.83 ± 5.28 respectively. Both sample groups have similar mean level of cholesterol levels during pretreatment period. Surgical menopausal group has greater HDL level than the naturally menopausal group with the average level of 64.24 ± 15.32 mg/dl. and 58.80 ± 17.20 mg/dl. respectively. However, after taking hormone therapy, blood cholesterol level was significantly changed in both groups. The mean level of LDL decreased (8.59% and 11.49% respectively) and mean level of HDL increased (15.43% and 6.89% respectively).*
Conclusions: *Hormone therapy in menopausal women can improve cholesterol levels by decreasing LDL and increasing HDL with statistical significance ($p < 0.05$).*

Keywords: *Menopause, Hormone therapy, Lipid profile*

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Changes in lipoproteins have been associated with a 30% decline in atherosclerotic cardiovascular disease (ASCVD) risk[1,2]. The important mechanism raises high density lipoprotein cholesterol (HDL) and lowering low density lipoprotein cholesterol (LDL). This change in this lipoprotein is associated with a decreased risk of ASCVD and might be associated with a decline in death from ASCVD in postmenopausal women.

Previous results from several observational studies of hormone therapy in postmenopausal women with established ASCVD have suggested that hormone therapy is associated with a decreased risk of ASCVD[1,2]. The results of the Heart and Estrogen/progesterone Replacement Study (HERS) randomized trial, published in 1998, reported that the risk of ASCVD was increased in hormone recipients during the first year of trial[1,2]. The Woman's Health Initiative (WHI) was a large-scale, Randomized controlled trial (RCT) with longer-term follow-up. It demonstrated that conjugated equine estrogens (CEE) 0.625 mg/day with medroxyprogesterone acetate (MPA) 2.5 mg/day increase the risk of ASCVD[1,2]. However the important notes from both studies were the population had a mean age of more than 60 year old, and high risk factors of ASVCD such as smoking, obesity, and hypertension. Both HERS and WHI were not evaluated in younger population[2].

The Nurses' Health Study (NHS) was a large-scale prospective observational study. That population was younger than both WHI and HERS. It demon-

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strated that CEE 0.3 mg/day can lower the risk of ASCVD [RR = 0.58(95%CI 0.37-0.92)] as similarly as CEE 0.625 mg/day [RR = 0.54(95%CI 0.44-0.67)][3]. The effects of hormone therapy on lipid profile and ASCVD were still controversial thus further studies still go on.

WHI demonstrated that hormone therapy lowered both cholesterol and LDL, and increased HDL[4,5]. At the end of the first year, lower dose of CEE can increase HDL and lower LDL to significant level. MPA used in combination with CEE, increase HDL, but not as much as when CEE is used alone. The LDL decreased, while triglyceride (TG) level increased[4-10].

Most studies were published in USA and Europe. Few studies have been published in Asia where the population, the socioeconomic and cultural, the body mass index, and the smoking behavior are different from the populations of USA and Europe. From our review, there were some publication from Turkey[10] Taiwan[11] and Japan[12] that had similar result as the studies in USA and Europe. In Thailand, there was no study done, so we designed this study to collect data for further clinical research that may have benefit for control and prevention of ASCVD in postmenopausal Thai women.

The objective of this study was to study the change in lipid profile of menopausal women with hormone therapy at Srinagarind Hospital.

Material and Method

This study was approved by the Human Ethical Committee of Faculty of Medicine, Khon Kaen University. This is a retrospective descriptive study. We enrolled 268 healthy postmenopausal women, both surgical and natural menopause, who received service at Menopausal clinic in Srinagarind Hospital, Khon Kaen University, since 1996-2004. They regularly took hormone therapy with only one type for about 12 months and obtained blood cholesterol levels for pre- and post-hormone therapy of about 12 months period. Thirty-three surgical menopausal women received conjugated equine estrogen (Premarin) 0.625 mg/day, while 235 natural menopausal women received conjugated equine estrogen (Premarin) 0.625 mg/day and medroxyprogesterone (Provera) 2.5 mg/day.

The exclusion criteria were use of any hormone therapy six weeks before enrolled, changed the hormone therapy formula within 12 months of studies, can not continue and/or follow-up for 12 months, or concomitant use of medications that might interfere in lipid metabolism (thiazides, corticosteroids, beta-blocker, cyclosporine)

We collected the study data from their medical records. This data included age, body weight, height, parity, occupation, education, marital status, history of gynecological surgery, underlying diseases, use of lipid lowering drugs, duration used of hormone therapy, pre- and post-hormone therapy level of total cholesterol, triglyceride, LDL, and HDL.

We used SPSS v. 10.0.5 software for Windows (SPSS Inc., USA) for data processing and analysis. Results were reported as means, standard deviations (SD), and mean differences by paired t-test with 95% confidence interval (CI).

Results

The study included 268 postmenopausal women, thirty-three were surgical menopause women (Group I), and 235 were natural menopause women (Group II). Group I received CEE 0.625 mg/day, while group II who received CEE 0.625 mg/day and MPA 2.5 mg/day. The mean age of both groups were 50.91 $\pm$ 5.93 year old and 52.83 $\pm$ 5.28 year old respectively (Table 1). Both groups had similar mean height, mean weight, and mean BMI. Mean duration used of hormone therapy in group I was 14.91 $\pm$ 4.99 months, and in

Table 1. Characteristic of studies woman: (Mean $\pm$ SD)

Parameter	CEE (n = 33)	CEE + MPA (n = 235)
Age (years)	50.91 $\pm$ 5.93	52.83 $\pm$ 5.28
Weight (kg)	54.59 $\pm$ 6.20	56.77 $\pm$ 7.97
Height (cm)	151.32 $\pm$ 5.93	152 $\pm$ 4.79
BMI (kg/m^2)	23.90 $\pm$ 2.88	24.42 $\pm$ 3.16
Duration (months)	14.91 $\pm$ 4.99	15.91 $\pm$ 5.12

Data are expressed as mean $\pm$ SD. CEE, conjugated equine estrogen; MPA. medroxyprogesterone acetate

Table 2. Lipid profiles of the patients (Mean ± SD)

Parameter	Baseline	After using hormone therapy	Level change
Group I CEE (n = 33)			
Cholesterol	221.45 ± 38.38	218.61 ± 29.83	↓ 1.29%
HDL	64.24 ± 15.32	74.15 ± 18.91	↑ 15.43%*
LDL	129.73 ± 38.69	118.58 ± 32.22	↓ 8.59%*
Triglycerides	130.30 ± 56.79	126.48 ± 53.45	↓ 2.91%
Group II CEE ± MPA (n = 235)			
Cholesterol	226.48 ± 40.82	214.91 ± 36.57	↓ 5.11%*
HDL	58.80 ± 17.20	62.85 ± 16.19	↑ 6.89 %*
LDL	142.45 ± 41.07	126.08 ± 34.16	↓ 11.49%*
Triglycerides	127.47 ± 74.94	130.42 ± 59.77	↑ 2.31%

Data are expressed as mean ± SD (mg/dL). CEE, conjugated equine estrogen; MPA. medroxyprogesterone acetate; HDL. high-density lipoprotein; LDL, low-density lipoprotein

* $p < 0.05$ vs pretreatment values by paired t-test

group II 15.91 ± 5.12 months. Both groups were healthy postmenopausal women and no one smoke.

Both groups had similar mean level of pretreatment lipid level (Table 2). There was significant change in lipid level in both groups. Mean level of LDL decreased by 8.59% in group I and 11.49% in group II, while the mean level of HDL increased by 15.43% in group I and 6.89% in group II. Mean level of total cholesterol in group I decreased by 1.29%, an insignificant change, while in group II this value was decreased with 5.11% a significant change. Meanwhile the mean level of Triglyceride in both groups were insignificantly changed (decreased 2.91% and increased 2.31% respectively).

Discussion

We found that the surgical menopausal women who received only CEE had decreased mean level of LDL by 8.59% and increased mean level of HDL by 15.43%. Both were significantly changed with $p < 0.05$. We also found that the natural menopausal women who received CEE+MPA had decreased mean level of LDL by 11.49% and increased mean level of HDL by 6.89% (significantly with $p < 0.05$), while mean level of triglyceride was increased by 2.31%. This is an insignificant change. Our results were similar to the studies of Godsland IF[4] Folsom AR[5] and Lobo RA[6] that hormone therapy in postmenopausal women could decrease level of total cholesterol and LDL and increase level of HDL, while the usage of MPA combined with CEE could rise the level of HDL less than when it is used of CEE alone.

The change in lipid profile in both groups of this study was similar to the study of Wakatsuki Akihiko[12] in 1996 that reported that hormone therapy in postmenopausal women could significantly reduce the level of LDL and raise the level of HDL. Additionally, the study of WHI found that estrogen therapy could lower the level of LDL and raise the level of HDL.

This study was a retrospective descriptive study of 8 years of data. The design of the study limits the interpretation of the differences in serum lipids between formulations. However, the difference with respect to LDL and HDL found in both groups in our study are in line with the differences found in the WHI study.

In conclusion, our study was designed to be used as baseline for further studies. By using tight control on all environmental factors, populations and proper study disciplines, the result of those studies could lead to good practice of hormone therapy in postmenopausal women. This could help to use hormone therapy with safety and may prevent risks of cardiovascular disease as well as the risk of death from other disease in menopausal women.

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การเปลี่ยนแปลงของระดับไขมันในเลือดในสตรีวัยหมดประจำเดือนที่ได้รับการรักษาด้วยฮอร์โมน

วัชระ ศรัณย์รัตน์, ชวนชม สกนธวัฒน์, ทรงขวัญ ศิลารักษ์, สุกรี สุนทราภา, ศรีนารี แก้วฤดี

วัตถุประสงค์: *เพื่อศึกษาถึงการเปลี่ยนแปลงของระดับไขมันในเลือด ในสตรีวัยหมดประจำเดือนที่ได้รับฮอร์โมนรักษา*
วิธีการศึกษา: *เป็นการวิจัยเชิงพรรณนา (Descriptive study)*
วัสดุและวิธีการ: *สตรีวัยหมดประจำเดือนที่มีสุขภาพดี ทั้งที่หมดประจำเดือนโดยธรรมชาติและที่หมดประจำเดือนจากการผ่าตัด มารับบริการที่คลินิกวัยทอง โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ตั้งแต่ปี พ.ศ. 2539 ถึง พ.ศ. 2546 ซึ่งเป็นผู้ที่ได้รับฮอร์โมนรักษาเพียงรูปแบบเดียวโดยสม่ำเสมอ เป็นระยะเวลาประมาณ 12 เดือน และได้รับการตรวจหาระดับไขมันในเลือดก่อนและหลังได้รับฮอร์โมนรักษาครบตามระยะเวลา*
ผลการศึกษา: *จากการรวบรวมข้อมูลผู้มารับบริการจำนวน 268 ราย แบ่งเป็นสตรีวัยหมดประจำเดือนโดยการผ่าตัด จำนวน 33 ราย และสตรีวัยหมดประจำเดือนโดยธรรมชาติ จำนวน 235 ราย พบว่าอายุเฉลี่ยของกลุ่มประชากรเท่ากับ 50.79 $\pm$ 5.00 ปี และ 52.83 $\pm$ 5.28 ปีตามลำดับ ทั้งสองกลุ่มมีค่าเฉลี่ยระดับไขมันในเลือด ก่อนได้รับฮอร์โมนรักษาใกล้เคียงกัน กลุ่มสตรีวัยหมดประจำเดือนจากการผ่าตัดมีค่า HDL สูงกว่ากลุ่มสตรีวัยหมดประจำเดือนโดยธรรมชาติเล็กน้อย คือมีค่าเฉลี่ยเท่ากับ 63.12 $\pm$ 17.48 มก./ดล. และ 58.74 $\pm$ 17.21 มก./ดล. ตามลำดับ แต่ภายหลังได้รับฮอร์โมนรักษา พบว่า ทั้งสองกลุ่มมีค่าเฉลี่ยของระดับไขมันในเลือด เปลี่ยนแปลงอย่างมีนัยสำคัญทางสถิติ คือ ค่าเฉลี่ยของระดับ LDL ลดลงร้อยละ 15.25 และร้อยละ 12.48 ตามลำดับ ในขณะที่ค่าเฉลี่ยของระดับ HDL เพิ่มขึ้นร้อยละ 14.88 และร้อยละ 5.91 ตามลำดับ ค่าเฉลี่ยของระดับ total cholesterol กลุ่มสตรีวัยหมดประจำเดือนจากการผ่าตัดลดลง ร้อยละ 5.95 แต่ไม่มีนัยสำคัญทางสถิติ ส่วนกลุ่มสตรีวัยหมดประจำเดือนโดยธรรมชาติลดลงอย่างมีนัยสำคัญทางสถิติคือลดลงร้อยละ 6.28 ค่าเฉลี่ยของระดับ triglyceride ของกลุ่มสตรีวัยหมดประจำเดือนโดยธรรมชาติลดลง ร้อยละ 8.54 ส่วนกลุ่มสตรีวัยหมดประจำเดือนจากการผ่าตัดมีค่าเฉลี่ยเพิ่มขึ้นร้อยละ 0.53 แต่ทั้งสองกลุ่มมีการเปลี่ยนแปลงแบบไม่มีนัยสำคัญทางสถิติ*
สรุป: *การใช้ฮอร์โมนรักษาในสตรีวัยหมดประจำเดือน ช่วยทำให้ระดับไขมันในเลือดเปลี่ยนแปลงไปในทางที่ดีขึ้น*