The effect of medrogestone on plasma lipids and lipoproteins in postmenopausal women using conjugated estrogens: an open randomized comparative study*

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Objective: To test the hypothesis that the progestogen medrogestone has no effect on changes in lipoprotein metabolism evoked by continuous estrogen replacement therapy, paying special attention to high-density lipoproteins (HDL).

Design: Open multicenter randomized comparative trial.

Patients: Postmenopausal hysterectomized women aged 49 to 64 years.

Intervention: Continuous oral treatment with 0.625 mg daily of conjugated estrogens (CE) alone (n = 55) or CE plus 5 mg of the progestogen medrogestone orally during the last 12 days of each 28-day cycle (n = 59).

Main Outcome Measures: At baseline and at cycles 3, 6, and 13 we measured the plasma levels of apolipoprotein (Apo) A1, cholesterol in total HDL and in its subfractions HDL2 and HDL3, using density gradient ultracentrifugation.

Results: High-density lipoprotein cholesterol increased from baseline at all assessments in both treatment groups, being significantly greater in the CE group (+15% at cycle 13) than in the CE and medrogestone group (+8%). However, HDL2-cholesterol increased in both treatment groups, but with no significant difference between the two groups. High-density lipoprotein 3 cholesterol increased only in the CE group (+7% at cycle 13); there was no significant change in HDL3-cholesterol in the CE and medrogestone group. Low-density lipoprotein (LDL) cholesterol decreased from baseline at all assessments in both treatment groups (−6% and −9%, respectively, at cycle 13). The change in very low-density (VLDL) lipoprotein cholesterol was not significant in either of the two groups. Medrogestone had no significant effects on the estrogen-induced increases in apo A-1 and triglycerides nor on the decreases in ApoB and LDL-cholesterol. Neither hormone significantly affected VLDL-cholesterol or Lp(a) levels.

Conclusion: Medrogestone did not eliminate the increase in plasma HDL levels evoked by CE.

Key Words: Estrogen, Premarin, progestogen, medrogestone, lipoproteins, menopause

Postmenopausal estrogen replacement therapy is associated with a 50% reduction in the incidence of myocardial infarction (1). Although selection bias (2) and direct effects on the vessel wall and other mechanisms (3) may explain part of this apparent effect, it is plausible that the concomitant changes in lipoprotein metabolism contribute to the mechanism of protection. In postmenopausal women the plasma level of the atherogenic low-density lipoproteins (LDL) increases (4) and that of the antiatherogenic high density lipoproteins (HDL) decreases (4). Oral estrogen replacement reverses these changes (5). The addition of a progestogen to estrogen therapy currently is recommended to prevent endometrial adenocarcinoma. Progestogens have not been shown to have an untoward effect on the prevalence of ischemic heart disease, although they generally attenu-
ate the estrogen-induced increase in plasma HDL-
cholesterol levels (6). This effect is more marked
with nortestosterone-derived progestogens than
with those derived from 17-hydroxy-progesterone
(5), such as medrogestone (7–9).

Previous studies of the effect of medrogestone on
lipoprotein levels in postmenopausal women treated
with conjugated estrogens had various weaknesses:
they either were uncontrolled (8), included small
numbers of patients (7–9), or only six cycles were
analyzed (7). We studied hysterectomized postmen-
opausal women during 1 year of treatment in an open
randomized comparative multicenter trial using
semiautomated density gradient ultracentrifugation
to estimate the changes in lipoprotein subfractions.

**MATERIALS AND METHODS**

Postmenopausal women were recruited by adver-

tisement and articles in daily newspapers. Women
aged 50 to 65 years who had undergone hystere-
tomy were eligible for enrollment if they had serum
FSH levels >40 mIU/mL (conversion factor to SI
unit, 1.00) and serum E2 levels <40 pg/mL (conver-
sion factor to SI unit, 3.67).

Those who had taken estrogens and/or progesto-
gens orally <3 months before prestudy screening or
had hypersensitivity to estrogens and/or progesto-
gens were excluded. Smoking >15 cigarettes per day
and known alcohol abuse also excluded a subject
from participating. In addition, the subjects could
not weigh >20% of their ideal weight or have blood
pressure (sitting) >160 mm Hg systolic or >90 mm
Hg diastolic, serum cholesterol >6.72 mmol/L (con-
version factor, 88.0). Other exclusion criteria were
a Papanicolaou smear of class III or
more; thrombophlebitis; thromboembolic disorders
related to estrogen therapy; ischemic heart disease;
chronic liver, renal, cerebral, or gallbladder disease;
malabsorption; evidence of estrogen-dependent neo-
plasia; and endocrine disease, except for controlled
thyroid disease.

Written informed consent was obtained before
study entry. The study was approved by the Commit-
tee of Medical Ethics of all five centers.

Two groups were formed by randomization using
a computer program. Fifty-six women used 0.625 mg
of conjugated estrogens (CE; Premarin; Wyeth Lab-
oratories, Hoofddorp, The Netherlands) continuously;
60 women took the same dosage of CE continuously
plus 5 mg medrogestone (6,17-dimethylpregna-4,6-
diene-3,20-dione, Colprone; Wyeth Laboratories)
added the last 12 days of each 28-day cycle (CE and
medrogestone).

Blood samples were obtained in the morning, after
an overnight fast (12 to 14 hours). They were centri-
fuged at 3,000 rpm for 15 minutes at 4°C to obtain
serum or plasma. Serum (from Nijmegen only) was
ultracentrifuged immediately but the plasma sam-
ple was snap-frozen in liquid nitrogen and stored
at −70°C until ultracentrifugation within 6 months.
Spare samples were kept at −20°C for measurement
of the apolipoprotein level within 18 months.

Two baseline blood samples were taken with ≥1
week in between. During the study, blood samples
were drawn between the 22nd and 28th day of the
3rd, 6th, and 13th cycles. Physical examination, rou-
tine hematologic and blood chemistry tests, and a
urinalysis were performed at baseline and at the end
of the study.

Serum FSH and E2 levels were determined using
commercial kits at each site; determinations of lipids
for screening and for scientific endpoints were per-
formed using enzymatic methods (CHOD-PAP cho-
sterol reagent and GPO-PAP triglyceride reagent;
Boehringer Mannheim, Mannheim, Germany).

The lipoprotein profile was determined in 2 mL
serum or plasma, after quick-thawing at 37°C. Den-
sity gradient ultracentrifugation was performed (10)
without previous staining using a 12-mL polypropyl-
eine tube in a SW40 Ti rotor for 18 hours at 40,000
rpm at 4°C in a Beckman L7–55 ultracentrifuge
(Beckman Instruments, Palo Alto, CA). The top 1.5
mL from the tube was removed by gentle suction
with a pipette and stored for further determinations
(cholesterol and triglycerides). Further fractionation
was performed by using a capillary placed on the
bottom of the tube, attached to a micropump and a
fraction collector, producing fractions of 250 μL each.
All fractions were weighed (Mettler PM-2000; Met-
tler-Toledo, Greifensee, Switzerland); the density
was determined using a density-measuring cell
DMA 602 M (Mettler/Paar, Graz, Austria). Both the
class and the densitometer were linked to a personal
computer to calculate the volume of each fraction
with three decimal places. A Gilson 222 (Gilson Med-
cal Electronics S.A., Villiers-le-Bel, France) sample
changer and a Dilutor 401 (Gilson Medical Electron-
ics S.A.) were used for routine purposes. The area
under the curve (AUC) comprising the fractions with
a density between 1.21 and 1.125 g/mL was used to
estimate HDL3-cholesterol; HDL2-cholesterol and
LDL-cholesterol were estimated by using the AUC
between 1.125 and 1.085 g/mL and the AUC between
1.085 and 1.019 g/mL, respectively. Apolipoproteins
(Apo) A-1 and B, and lipoprotein (Lp) (a) were deter-
mined in random fashion by rate immunonephe-
ometry using a Beckman Array Protein system
(Beckman Instruments) (11).

A sample size of 50 women in each treatment
group was required to detect a difference in change
Table 1 Demographya

<table>
<thead>
<tr>
<th></th>
<th>CE (n = 55)</th>
<th>CE and medrogestone (n = 59)</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>54.9 ± 3.9</td>
<td>55.3 ± 3.8</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>(49 to 64)</td>
<td>(49 to 64)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155 ± 6.3</td>
<td>164 ± 5.0</td>
<td>0.34</td>
</tr>
<tr>
<td></td>
<td>(153 to 178)</td>
<td>(156 to 178)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.1 ± 7.4</td>
<td>67.3 ± 7.1</td>
<td>0.19</td>
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<td>(54 to 86.5)</td>
<td>(50 to 81)</td>
<td></td>
</tr>
<tr>
<td>Quetelet index†</td>
<td>25.4 ± 2.8</td>
<td>25.0 ± 2.5</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>(20.2 to 32.7)</td>
<td>(18.4 to 30.8)</td>
<td></td>
</tr>
</tbody>
</table>

a Values are means ± SD with ranges in parentheses.
† Difference between the two groups.
‡ Quetelet index = (weight in kg)/ (height in m)².

in the key lipid parameters of 0.40 mmol/L in total cholesterol; 0.25 mmol/L in triglyceride; 0.20 mmol/L in HDL cholesterol and 0.38 mmol/L in LDL cholesterol with a power of 80% at a level of significance of 0.05 (two-tailed test). The adequacy of the randomization was assessed by comparing the two treatment groups at baseline using the Student's t-test or Mann Whitney U-test. The primary efficacy variables were the percentage change from baseline in HDL, total cholesterol, triglycerides, and LDL. An intent-to-treat analysis was performed for all patients assigned to treatment who received at least one dose of medication and had at least one efficacy evaluation during therapy.

Analysis of covariance (ANCOVA) was performed on the lipid parameters at each scheduled observation with the baseline value as a covariate and treatment, center, and treatment by center interaction as factors. The assumptions of normality were broken for HDL, triglycerides, and very low-density lipoprotein (VLDL), and these parameters were analyzed with the Mann Whitney U-test. Comparisons within treatment groups were made using the paired t-test or Wilcoxon matched pairs signed ranks test.

The χ² test was used for comparisons between groups of the proportion of patients who discontinued treatment, both overall and for specific reasons. Vital signs and laboratory data were analyzed by ANCOVA with the baseline value as a covariate and treatment, center, and treatment by center interactions as factors.

RESULTS

A total of 116 postmenopausal women were enrolled in this trial; none of them took any drugs affecting lipid metabolism. Fifty-six were assigned randomly to receive CE alone and 60 were assigned to receive CE and medrogestone. Tables 1 and 2 show the clinical characteristics at baseline. Except for VLDL cholesterol, the two groups did not show any statistically significant difference at baseline (Tables 1 and 2). Two patients, one from each treatment group, were excluded because of high 17-β-E₂ at baseline, leaving 55 in the CE group and 59 in the CE and medrogestone group. Thus, 114 patients commenced treatment. Eight women from the CE group and 14 from the CE and medrogestone group withdrew. The primary reasons for withdrawal in the CE group were nausea (n = 1); asthenia, depression, and dizziness (n = 1); mastodynia (n = 1); ankle edema (n = 1); and hemangioma in the liver (n = 1). In the CE and medrogestone group the primary reasons for withdrawal were vertigo (n = 1); exacerbation of depression (n = 1); headache (n = 3); weight gain and dysuria (n = 1); weight gain and itching (n = 1); mastodynia (n = 1); and thrombophlebitis (n = 1). One patient withdrew because of a non-medical event in the CE group. In the CE and medrogestone group three patients withdrew because of medical reasons not attributed to the medication, i.e., hypdrops in knee (n = 1); infection in thumb (n = 1); and cholelithiasis (n = 1). Furthermore, in this group one patient failed to return and one patient requested to withdraw because of nonmedical reasons. Fifty-two patients in the CE group and 51 in the CE and medrogestone group had at least one on-treatment lipid assessment. The full 13 cycles of the study were completed by 47 and 41 patients, respec-

Table 2 Concentration of Lipids, Lipoprotein-lipids, and Apolipoproteins at Baseline in Serum or Plasmab

<table>
<thead>
<tr>
<th></th>
<th>CE (n = 55)</th>
<th>CE and medrogestone (n = 59)</th>
<th>P value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>5.78 ± 0.70</td>
<td>5.94 ± 0.73</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>(conversion factor to conventional units, 38.7)</td>
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<tr>
<td>LDL cholesterol</td>
<td>3.77 ± 0.61</td>
<td>3.80 ± 0.69</td>
<td>0.78</td>
</tr>
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<td></td>
<td>(conversion factor to conventional units, 38.7)</td>
<td></td>
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<tr>
<td>VLDL cholesterol</td>
<td>0.53 ± 0.49</td>
<td>0.67 ± 0.28</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>(conversion factor to conventional units, 88.0)</td>
<td></td>
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</tr>
<tr>
<td>Total triglycerides</td>
<td>1.17 ± 0.51</td>
<td>1.35 ± 0.58</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>(conversion factor to conventional units, 88.0)</td>
<td></td>
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</tr>
<tr>
<td>Apolipoprotein B (mg/dL)</td>
<td>1.26 ± 0.23</td>
<td>1.31 ± 0.27</td>
<td>0.29</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.47 ± 0.32</td>
<td>1.47 ± 0.28</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(conversion factor to conventional units, 38.7)</td>
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<tr>
<td>HDL2 cholesterol</td>
<td>0.41 ± 0.17</td>
<td>0.40 ± 0.19</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>(conversion factor to conventional units, 38.7)</td>
<td></td>
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<tr>
<td>Apolipoprotein A-1 (mg/dL)</td>
<td>0.99 ± 0.20</td>
<td>0.99 ± 0.16</td>
<td>0.85</td>
</tr>
<tr>
<td>Lipoprotein (a) (mg/dL)</td>
<td>1.61 ± 0.24</td>
<td>1.51 ± 0.19</td>
<td>0.98</td>
</tr>
</tbody>
</table>

b Values are medians with interquartile range in parentheses; n = 45 for CE group; n = 41 for CE and medrogestone group.

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Density (kg/L)

Density (kg/L)

0 1.00 1.10 1.20 1.30

1.00 2.00 3.00 4.00 5.00 6.00 7.00 8.00

Figure 1 Typical pattern of the cholesterol concentration as a function of the density after gradient ultracentrifugation for a patient from the CE and medrogestone group before (C) and after (○) three cycles. The AUC between 1.21 and 1.125 g/mL has been defined as HDL3-cholesterol, between 1.125 and 1.085 g/mL as HDL2-cholesterol, and between 1.085 and 1.019 g/mL as LDL.
Table 3  Percentage Change in Plasma Lipid and Lipoprotein Levels From Baseline

<table>
<thead>
<tr>
<th></th>
<th>CE</th>
<th>CE and medrogestone</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>Cycle 3: 52</td>
<td>Cycle 6: 49</td>
<td>Cycle 13: 47</td>
</tr>
<tr>
<td>Total cholesterol*</td>
<td>Cycle 3: -0.89 ± 1.37</td>
<td>Cycle 6: 0.77 ± 1.62</td>
<td>Cycle 13: 1.46 ± 1.41</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: -6.45 ± 1.39$</td>
<td>Cycle 6: -5.32 ± 1.60$</td>
<td>Cycle 13: -3.76 ± 1.66$</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: -11.77 ± 1.74$</td>
<td>Cycle 6: -12.38 ± 2.08$</td>
<td>Cycle 13: -9.07 ± 2.28$</td>
</tr>
<tr>
<td>VLDL cholesterol</td>
<td>Cycle 3: 13.19 (-25.32; 43.48)</td>
<td>Cycle 6: -9.43 (-35.53; 44.68)</td>
<td>Cycle 13: -5.89 ± 1.65$</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: -7.25 (-35.53; 44.68)</td>
<td>Cycle 6: -2.75 (-35.53; 44.68)</td>
<td>Cycle 13: -2.75 (-35.53; 44.68)</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: 8.15 (-2.97; 16.13)$</td>
<td>Cycle 6: 8.88 (-0.93; 21.17)$</td>
<td>Cycle 13: 7.63 (-0.87; 21.05)$</td>
</tr>
<tr>
<td>HDL2 cholesterol†</td>
<td>Cycle 3: 40.19 (14.16; 94.29)</td>
<td>Cycle 6: 44.44 (17.14; 75.76)</td>
<td>Cycle 13: 46.16 (21.21; 75.76)</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: 27.27 (5.40; 62.86)$</td>
<td>Cycle 6: 33.77 (-1.36; 60.34)$</td>
<td>Cycle 13: 30.30 (0.00; 56.00)$</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: -1.55 (10.20; 9.09)</td>
<td></td>
<td>Cycle 6: 2.88 (-7.32; 11.37)</td>
</tr>
<tr>
<td>Triglycerides†</td>
<td>Cycle 3: 12.44 (-9.09; 36.40)</td>
<td></td>
<td>Cycle 6: 19.30 (-8.46; 55.91)</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: 8.55 (-13.48; 42.42)</td>
<td></td>
<td>Cycle 6: -1.55 (-35.53; 44.68)</td>
</tr>
<tr>
<td>Apo A-I*</td>
<td>Cycle 3: 15.3 ± 1.4$</td>
<td>Cycle 6: 16.0 ± 1.6$</td>
<td>Cycle 13: 16.1 ± 2.0$</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: 11.6 ± 1.6$</td>
<td>Cycle 6: 12.5 ± 1.6$</td>
<td>Cycle 13: 13.6 ± 1.5$</td>
</tr>
<tr>
<td>Apo B*</td>
<td>Cycle 3: -3.3 ± 1.7</td>
<td>Cycle 6: -0.2 ± 2.4</td>
<td>Cycle 13: 1.8 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>Cycle 3: -4.9 ± 1.8$</td>
<td>Cycle 6: -4.9 ± 2.0$</td>
<td>Cycle 13: -1.7 ± 2.0$</td>
</tr>
<tr>
<td>Lp(a)†</td>
<td>Cycle 3: -1.9 (-28.3; 13.1)</td>
<td>Cycle 13: -9.2 (-38.1; 14.5)</td>
<td></td>
</tr>
</tbody>
</table>

* Values are means ± SEM.
† Values are medians with interquartile ranges in parentheses.
‡ Change from baseline significantly different from zero, P < 0.001.
§ Change from baseline significantly different from zero, P < 0.001.
|| Change from baseline significantly different from zero, P < 0.05.

rise in plasma levels of HDL cholesterol and those of other lipoproteins. Several lines of evidence suggest that HDL inhibits atherogenesis directly or indirectly or even enhances the regression of plaques: HDL is involved in cholesterol reverse transport (12); given IV, HDL inhibits plaque formation in cholesterol-fed rabbits (12); transgenic mice containing multiple copies of Apo A-1 develop less fatty streaks than mice without the extra genes (13); and primary Apo A-1 deficiency in human subjects is associated with early ischemic heart disease (14). The plasma level of HDL cholesterol is the sum of the cholesterol content of two subfractions, the less-dense HDL2 and the denser HDL3. Generally the former is more variable (15) and more sensitive to sex steroids (6) than the latter. This subfractionation does not provide more information on cardiovascular risk than the total HDL cholesterol level (15, 16). However, to gain more insight into the possible mechanisms behind the changes, subfractionation of HDL can be worthwhile. The hepatic triglyceride lipase activity is involved in the conversion of HDL2 into HDL3, and this enzyme is inhibited by estrogens (17). That would explain the increase in HDL2 but not that in HDL3. On the other hand, androgenic side effects of a progestogen may enhance hepatic triglyceride lipase activity (6, 17). Thus, if medrogestone would have had any androgenicity it probably would have become visible as a prevention of the increase of HDL2 in the CE and medrogestone group. In fact
the rise in HDL2 was not significantly smaller in the CE and medrogestone group than in the CE group. Thus, the inhibition of hepatic triglyceride lipase activity by estrogens in the presence of medrogestone may have been similar to that in the CE group. The HDL3 subfraction showed a greater increase in the CE group than in the CE and medrogestone group, suggesting that other factors besides hepatic triglyceride lipase activity were effective, e.g., a difference in the estrogen-induced Apo A-1 synthesis rate (18). In later cycles this difference in change diminished. Fahreus and Wallentin (19), using sequential ultracentrifugation for the estimation of HDL2 and HDL3, also found an increase in HDL3 level, but only with the high dosage of 4 mg of oral micronized 17-β-E2. Two other factors involved in HDL cholesterol levels are known, i.e., lecithin:cholesterol acyltransferase, which adds cholesterol to the payload of HDL, causing transition from HDL3 to HDL2. Cholesterolester transfer protein transfers cholesterol ester from HDL to triglyceride-rich lipoproteins like VLDL in exchange for triglycerides, causing a decrease in HDL2. However, neither of these two factors has been reported to be affected by sex steroids.

Our results partly confirm those of Sonnendecker et al. (7), who performed a randomized, placebo-controlled, double-blind crossover study with 22 participants for six cycles. They found no additional effect on HDL subfractions of cyclic 5 mg medrogestone plus 0.625 mg CE when compared with 0.625 mg CE alone, whereas we did. However, this group used a precipitation technique to separate HDL2 from HDL3. Teichmann et al. (8) performed an uncontrolled study of the effect of 5 mg medrogestone plus 1.25 mg CE on lipoprotein lipids and apolipoproteins in 20 oophorectomized patients during 12 cycles. They used a quantitative electrophoretic method to estimate lipoproteins, which did not allow for estimation of HDL subfractions.

Plasma total cholesterol level decreased in both groups and significantly more in the CE and medrogestone group than in the CE group in the first three cycles, whereas the decrease in LDL was not significantly different in the two groups. Obviously the explanation for this discrepancy should be that total cholesterol, being the sum of cholesterol all different classes of lipoproteins, reflects the change in all these classes. Beyond any doubt, changes in LDL cholesterol levels and Apo B levels can be interpreted in terms of cardiovascular risk. The similar decrease in the average LDL cholesterol level and in the Apo B level in both treatment groups therefore is reassuring. The clearance of LDL is mainly receptor dependent, and the LDL receptor activity is enhanced by oral estrogen treatment (20). Apparently in this study, 5 mg of medrogestone in a cyclic regimen did not attenuate this estrogen effect on the LDL receptors to an extent sufficient to interfere with the lowering of the plasma LDL levels by estrogens. If medrogestone exerted any androgenic effect in the liver, lower VLDL production (21) and, consequently, decreased LDL synthesis and lower plasma LDL levels would have resulted. However, that has not been found. In fact, fasting plasma triglyceride levels, which reflect the VLDL concentration and VLDL production, were not significantly different between the two groups throughout the treatment period. Finally, the LDL production rate might have been lowered by an increased clearance of VLDL remnants just before their conversion into LDL. This explanation is given for the observation in female patients with Familial Dysbetalipoproteinemia, in whom accumulated VLDL remnants in plasma can be lowered by oral estrogen therapy (22).

The Lp(a) levels did not differ significantly from baseline at cycle 13. This is in contrast to the observational study of Nabulsi et al. (23) who found 13% lower Lp(a) levels among current estrogen users than among nonusers and with a persistent decrease of Lp(a) from baseline during another study of hormone replacement therapy (24). It should be remembered that the effect of sex steroids on Lp(a) may be transient (25) and that we may have missed an eventual decrease in Lp(a). We found no significant correlation between Lp(a) and either LDL cholesterol or Apo B.

We conclude that medrogestone given in the dose regimen of this study has little effect on estrogen-induced changes in lipoprotein metabolism and that in these terms no objection can be made against the use of this 17-hydroxyprogesterone-derived progestogen for adjunct treatment in postmenopausal hormone replacement therapy.

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