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ORIGINAL CONTRIBUTION

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The efficacy of dietary intervention alone or combined with hormone replacement therapy in postmenopausal women with hypercholesterolemia in Seoul, Korea

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Summary *Background* Women have an increased incidence of cardiovascular disease (CVD) due to hormone imbalance-induced changes in blood lipid profiles after menopause. *Aim of study* This study was done to compare the effects of dietary intervention and hormone replacement therapy, alone or in combination, on blood lipids and body weight in Korean postmenopausal women with hypercholesterolemia. *Method* The subjects were treated by one of three different treatments for 12 weeks: hormone replacement therapy (HRT group, n = 8), dietary intervention (DIET group, n = 8) and hormone replacement therapy combined with dietary intervention (HRT+DIET group, n = 8). *Results* Serum TC and LDL-C levels decreased by 13–16 % and 24–28 % in the HRT group, by 17–19 % and 21–23 % in the DIET group and by 19–26 % and 32–39 % in the HRT+DIET group, respectively ($P < 0.05$). Serum HDL-C levels decreased in the DIET group (–6.4 %, $P < 0.05$) but not in the HRT and HRT+DIET groups. Serum TG levels increased in the HRT group (18 %, $P < 0.05$) but decreased in the DIET group (–24.4 %, $P < 0.05$). In the HRT+DIET group, serum TG levels did not change. Body weight decreased only in the DIET group. *Conclusions* We can conclude that dietary intervention produces a considerable improvement in blood lipid profiles and body weight, even though our study is limited by the sample size. Thus, the treatment to reduce risk of CVD should be individualized on the basis of the patient's dietary intake status, and at least, HRT should not be substituted for dietary intervention.

Key words hypercholesterolemia – postmenopausal women – hormone replacement therapy – dietary intervention – lipid level

Introduction

Years of cardiovascular research focusing predominantly on males have, unfortunately, added to the impression that cardiovascular disease (CVD) is basically a male affliction. Yet, it is the leading cause of death among elderly women, especially postmenopausal women [1–3]. Women have a greater incidence of CVD after menopause. It relates to hormone imbalance-induced changes in known CVD risk factors, especially in blood lipid profiles. Estrogen began to be prescribed for the management of hypercholesterolemia in postmenopausal women, since estrogen replacement was found to have a potentially beneficial effect on CVD risk factors by lowering the low-density lipoprotein cholesterol (LDL-C) level and increasing high-density lipoprotein cholesterol (HDL-C) level [4–6].

Meanwhile, the National Cholesterol Education Program (NCEP) has emphasized that life-style modification, including diet, should be the primary treatment for lowering cholesterol levels, with drug therapy reserved for cases where life-style modification is ineffective [7]. Also, NCEP has provided the rationale for dietary change to lower blood lipid levels, and outlined the vehicles, Step-One and Step-two Diet, for that change [8].

The present study was designed to compare the effects of dietary intervention and hormone replacement therapy (HRT), alone or in combination, on blood lipid profiles and body weight in postmenopausal women with hypercholesterolemia in Korea.

Method

Subjects

Thirty-six postmenopausal women, aged 50 to 61 years, were recruited from a medical center for women in Seoul, Korea. All had hypercholesterolemia, defined as LDL cholesterol levels over 160 mg/dL, determined from the mean of two pre-study fasting samples of serum. Subjects were required to complete a semi-quantitative food frequency questionnaire (semi FFQ) that had been developed and validated to assess usual food intake of postmenopausal women in Korea [9, 10]. The results of the validation study revealed that the Pearson's correlation coefficients (r) averaged 0.41 on the semi FFQ vs. 24 h recall and 0.45 on the semi FFQ vs. biomarkers. Subjects selected for clinical trials were those who ate more than 20 % in fat intake and more than 100 mg/1000 kcal in cholesterol intake. The plausibility of reported energy intakes from the semi FFQ was assessed using the Goldberg cut-off values that were based on the ratio of estimated energy intake to predicted basal metabolic rate [11].

All subjects showed normal results in the thyroid function tests, normal fasting serum glucose levels, and no evidence of hepatic, renal, or secondary lipid disorders. None were taking supplements and/or medication that included estrogen. Informed consent was obtained from all subjects, and the consent forms and study protocol were made in accordance with the principles embodied in the Helsinki Declaration.

Study design

The subjects were randomly assigned to one of three different treatments: hormone replacement therapy (HRT group, n = 8), dietary intervention (DIET group, n = 8), or the hormone replacement therapy combined with dietary intervention (HRT+DIET group, n = 8).

Hormone replacement therapy

The HRT group and the HRT+DIET group both took a combined therapy of estrogen and progesterone, in which conjugated equine estrogen (CEE, Premarin®) 0.625 mg was prescribed for 30 days and medroxy progesterone acetate (MPA, Provera®) 5 mg was combined for the first 12 days on a monthly cyclic schedule. A prescription of HRT was accomplished with office visits at weeks 0 and 4.

Dietary intervention

NCEP Step-One and Step-Two diets for hypercholesterolemia is desirable for Americans whose fat intake levels are over 40 %, but not desirable for Koreans whose diet already coincides with the program. Therefore, the cholesterol-lowering diet for Korean postmenopausal women was designed on the basis of our previous studies [12, 13] and then implemented for both the DIET group and the HRT+DIET group. The diet was designed to approximately provide dietary cholesterol ≤ 70 mg/1000 kcal and the ratio of ingested saturated fat and cholesterol to calories (RISCC) ≤ 8, and to meet the recommended dietary allowances (RDA) for known nutrients. The RISCC is the cholesterol-saturated fat index (CSI) adjusted for energy intake [14]. The CSI was developed by Conor et al. to both easily and quickly estimate the hypercholesterolemic and atherogenic potential of food [15, 16]. Energy intake was individually tailored to maintain ideal body weight (Table 1). The diet consisted of a 10-day rotating menu to provide variety and maintain the acceptability of the diet. Extensive dietary counseling was given at the beginning of dietary intervention, and was repeated at each subsequent visit. The subjects were given dietetic scales, measuring cups and spoons, and trained in estimating portion sizes with the use of uniform food models.

The study period was a total of 12 weeks. All subjects visited the clinic at weeks 0, 4 and 12 for treatment, blood sampling and measurement of body weight. At each subsequent visit, three-day diet diaries were com-

Table 1 Basic principles of cholesterol-lowering diet

Nutrients	Principles
Energy	to maintain ideal body weight
from carbohydrate	60–65 %
from protein	15–20 %
from fat	15–20 %
Cholesterol	≤ 70 mg/1000 kcal
P/M/S	1~1.5/1~1.5/1
ω6/ω3	4~10/1
RISCC	≤ 8
Others	≥ 90 % of RDA for Korean

RISCC ((1.01 × g SFA)+(0.05 × mg Cholesterol))/kcal × 1000

pleted by all subjects to help monitor adherence to the treatment. Nutrient intake was calculated by using the Hanyang diet analysis program. We tried to encourage compliance of subjects with follow-up telephone counseling once a week during the study period.

Blood analysis

At each visit, a sample of venous blood was drawn after an overnight fast of 12 to 14 hours; it was centrifuged immediately and the serum was separated. Serum levels of total cholesterol and triglycerides were assayed enzymatically with a Hitachi 737 automated analyzer. High-density lipoprotein cholesterol (HDL-C) levels were assayed in the supernatant after the serum was precipitated with heparin-manganese. Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald equation [17]. Serum estradiol (E_2) levels were assayed by a procedure based on the competitive binding principles of radioimmunoassay using the Biodata Estradio Maia Kit (Code 12264).

Statistical analysis

All statistical analyses were performed using the statistical package for social science (SPSS). The changes in nutrient intakes of the subjects within each group were analyzed by repeated measured one-way analysis of variance (ANOVA). Repeated measured ANOVA was also used to analyze the effects of each treatment on serum E_2 level, lipids level, and body weight within and among groups during the study period. Probability levels, $P < 0.05$, were considered to be statistically significant.

Results

Of the 36 subjects who entered the study, 24 completed the study period. Twelve subjects failed to complete the study: four of whom did not complete it for personal reasons, two of whom were lost during follow-up, and six of whom had problems following the dietary intervention program. There was no significant difference in the general characteristics of the subjects among the groups (Table 2).

The daily mean nutrient intakes of the subjects at the baseline are shown in Table 3. The percentages of energy intake from carbohydrate, protein and fat were 58.6 %: 15.4 %: 24.3 % in the HRT group, 59.5 %: 15.7 %: 23.1 % in the DIET group and 56.5 %: 16.8 %: 24.1 % in the HRT+DIET group. The percentage of energy intake from fat for all subjects is quite high, as compared with 65 %: 15 %: 20 %, the ratio proposed by the Korean Nutritional Society [18]. Daily mean cholesterol intake per 1000 kcal was 104.2 ± 7.6 mg in the HRT group, 109.9 ± 9.2 mg in the DIET group and 115.4 ± 8.0 mg in the HRT+DIET group. The cholesterol-saturated fat index (CSI) was 24.9 ± 1.7 in the HRT group, 25.5 ± 2.4 in the DIET group and 25.7 ± 1.4 in the HRT+DIET group. We estimated that the diet of our test subjects was as hypercholesterolemic and atherogenic as the usual Amer-

Table 2 The general characteristics of the subjects

Variables	HRT	DIET	HRT+DIET	*P*-value
Age (yrs)	51.2±1.2	52.0±2.4	52.0±2.0	0.865
Height (cm)	156.1±1.8	156.9±2.6	159.8±2.0	0.512
Weight (kg)	59.0±1.6	61.3±2.9	61.7±0.2	0.600
BMI (kg/m^2)	24.4±0.6	25.8±1.2	25.4±0.8	0.872
FBS (mg/dL)	83.7±2.6	84.5±3.6	86.3±1.8	0.830
TC (mg/dL)	254.2±6.7	252.5±4.0	256.3±8.0	0.936
TG (mg/dL)	111.2±8.0	110.3±11.6	114.0±2.7	0.965
LDL-C (mg/dL)	166.6±7.7	165.2±6.7	165.9±8.6	0.992
HDL-C (mg/dL)	65.4±2.4	65.3±3.6	67.7±5.8	0.889

mean ± SEM; *P*-value by ANOVA; *BMI* body mass index; *FBS* fasting blood sugar

Table 3 Mean nutrient intakes of the subjects at the baseline

Variables	HRT	DIET	HRT+DIET	*P*-value
Energy (kcal)	2053.8±108.6	2077.4±136.8	2043.1±139.9	0.984
% of total energy				
From carbohydrate	58.6±1.1	59.5±1.4	56.5±2.6	0.474
From protein	15.4±0.7	15.7±1.0	16.8±0.9	0.514
From fat	24.3±1.1	23.1±0.6	24.1±2.2	0.779
Dietary fiber (g)	22.3±3.9	25.0±5.4	22.3±4.8	0.899
Cholesterol (mg)	213.7±18.0	226.9±18.8	233.8±9.0	0.735
mg/1000 kcal	104.2±7.6	109.9±9.2	115.4±8.0	0.667
SFA (% of energy)	6.2±0.4	6.0±0.4	6.1±0.5	0.963
MUFA (% of energy)	6.5±0.3	6.2±0.1	6.6±0.5	0.662
PUFA (% of energy)	5.1±0.2	5.1±0.3	5.2±0.5	0.984
CSI	24.9±1.7	25.5±2.4	25.7±1.4	0.956
RISCC	12.1±0.6	12.3±0.8	12.6±0.7	0.885

mean ± SEM; *P*-value by ANOVA; *CSI* (1.01 × SFA g) + (0.05 × cholesterol mg); *RISCC* CSI/kcal × 1000

ican diet, when considering that the CSI of the usual American diet is 23 [15, 16]. There were no significant differences in the daily mean nutrient intakes among the groups at the baseline.

Changes in the daily mean nutrient intake during the study period are shown in Table 4. There was no significant change in any of the nutrients consumed by the HRT group, but there was a significant change in most nutrients consumed by the DIET and HRT+DIET groups. Especially, the daily mean intake of cholesterol and the RISCC decreased in the DIET and HRT+DIET groups (Fig. 1). According to analysis of standardized, quantitative dietary records, the cholesterol-lowering diet actually consumed by the subjects during the study period was close to the principles for dietary changes specified in the study protocol, with substantial differences between HRT and dietary intervention.

Table 5 shows the changes of serum lipid levels and body weight from baseline within and among the groups during the study period. After 4 weeks of treatment, there were significant reductions in mean serum total cholesterol (TC) and LDL-C levels ($P < 0.05$); approximately, –13.3 % and –24.7 % in the HRT group, –17.0 % and –21.4 % in the DIET group, and –25.7 % and –38.5 % in the HRT+DIET group, respectively. There were significant differences in the serum TC and LDL-C levels among the groups after 4 weeks ($P < 0.05$); serum TC and LDL-C levels of HRT+DIET group were lower than those of the other two groups. Serum HDL-C levels decreased in the DIET group after 12 weeks (–6.4 %, $P < 0.05$) but no significant changes were observed in the HRT and HRT+DIET groups. Thus, there were significant differences in the serum HDL-C levels among the groups after 12 weeks ($P < 0.05$); serum HDL-C levels of the DIET group were lower than those of the HRT group. Serum triglyceride (TG) levels increased in the HRT

Table 4 Changes in nutrient intakes during the study period

Variables	Study period		
	0 week	4 week	12 week
HRT			
Energy (kcal)	2053.8±108.6	1957.5±69.0	2013.2±103.2
% of total energy			
From carbohydrate	58.6±1.1	57.5±1.5	57.4±0.9
From protein	15.4±0.7	17.1±0.7	16.5±1.0
From fat	24.3±1.0	23.0±1.2	23.9±1.2
Dietary fiber (g)	22.3±3.9	21.9±2.1	22.0±3.9
Cholesterol (mg)	213.7±18.0	208.6±11.6	212.0±18.6
mg/1000 kcal	104.2±7.6	106.7±5.5	105.1±7.1
SFA (% of energy)	6.2±0.4	5.9±0.2	6.2±0.4
MUFA (% of energy)	6.5±0.3	6.4±0.2	6.9±0.3
PUFA (% of energy)	5.1±0.3	5.2±0.3	4.8±0.3
CSI	24.9±1.7	23.4±1.2	24.7±1.9
RISCC	12.1±0.6	12.0±0.5	12.2±0.6
DIET			
Energy (kcal)	2052.4±136.8	1724.4±50.4[a]	1772.4±26.7[a, b]
% of total energy			
From carbohydrate	59.5±1.4	63.5±0.7[a]	63.8±0.9[a]
From protein	15.7±1.0	18.2±0.4[a]	18.1±0.6[a]
From fat	23.1±0.6	17.1±0.3[a]	17.7±0.5[a]
Dietary fiber (g)	25.0±5.4	30.6±4.6	27.1±1.0
Cholesterol (mg)	226.9±18.8	92.1±8.3[a]	87.5±8.5[a]
mg/1000 kcal	109.9±9.2	53.7±5.8[a]	49.4±5.1[a, b]
SFA (% of energy)	6.0±0.4	4.6±0.1[a]	4.6±0.1[a]
MUFA (% of energy)	6.2±0.1	4.9±0.2[a]	5.1±0.1[a]
PUFA (% of energy)	5.1±0.3	6.0±0.5[a]	6.2±0.5[a]
CSI	25.5±2.4	9.9±0.4[a]	10.0±0.5[a]
RISCC	12.3±0.8	5.8±0.3[a]	5.6±0.3[a]
HRT+DIET			
Energy (kcal)	2043.1±139.9	1747.2±38.9[a]	1811.9±6.8[b]
% of total energy			
From carbohydrate	56.5±2.6	63.5±1.2[a]	62.5±1.1[a]
From protein	16.8±0.9	17.3±1.2	18.2±0.7
From fat	24.1±2.2	18.0±0.6[a]	17.9±0.6[a]
Dietary fiber (g)	22.3±4.8	27.9±0.3	33.7±5.1
Cholesterol (mg)	233.8±9.0	73.8±12.0[a]	91.1±7.4[a, b]
mg/1000 kcal	115.4±8.0	42.0±6.0[a]	50.3±4.2[a, b]
SFA (% of energy)	6.1±0.3	4.3±0.3[a]	4.6±0.3[a]
MUFA (% of energy)	6.6±0.5	4.3±0.5[a]	4.9±0.3[a]
PUFA (% of energy)	5.2±0.5	6.8±0.3[a]	6.9±0.1[a]
CSI	25.7±1.4	8.5±1.4[a]	10.4±0.4[a, b]
RISCC	12.6±0.7	4.8±0.7[a]	5.7±0.2[a, b]

mean ± SEM; *CSI* (1.01 × SFA g) + (0.05 × cholesterol mg); *RISCC* CSI/kcal × 1000; [a] significantly different from the initial value in the same group at $P < 0.05$ by repeated measured design; [b] significantly different from the 4th week's value in the same at $P < 0.05$ by repeated measured design

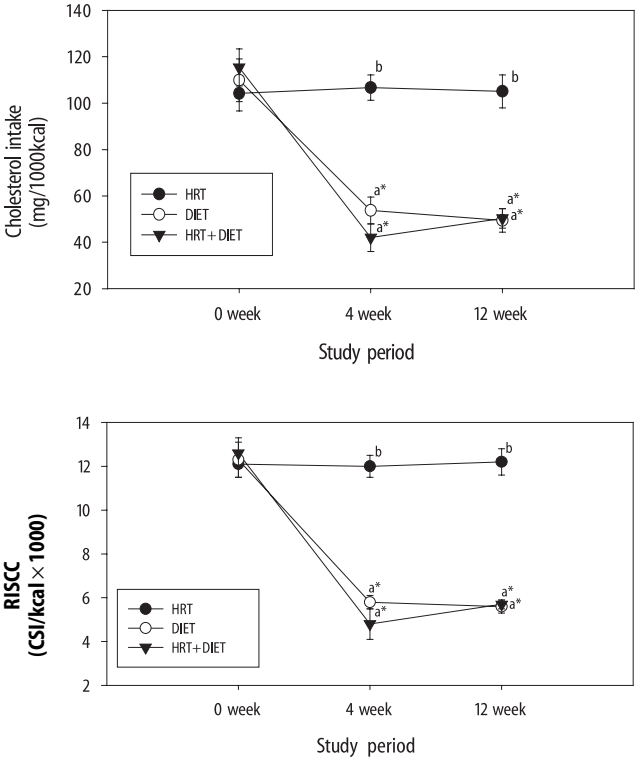

Fig. 1 Changes in cholesterol intake and RISCC during the study period. * significantly different from the initial value in the same group at $P < 0.05$ by repeated measured design; [a, b] values with different characters within the same week are significantly different among groups based on the initial value at $P < 0.05$ by repeated measured design.

Table 5 Changes in serum lipid levels and body weight during the study period

Variables	Study period		
	0 week	4 week	12 week
TC (mg/dL)			
HRT	254.20±6.66	219.60±2.15[b, c]	213.60±3.75[c]
DIET	252.50±4.00	209.75±8.53[b, c]	207.50±6.29[c]
HRT+DIET	256.33±8.01	190.67±9.82[a, c]	206.33±17.82[c]
LDL-C (mg/dL)			
HRT	166.56±7.65	123.92±2.63[b, c]	118.12±2.40[c]
DIET	165.20±6.74	130.75±12.28[b, c]	129.85±9.80[c]
HRT+DIET	165.87±8.64	102.07±7.05[a, c]	112.67±14.27[c]
HDL-C (mg/dL)			
HRT	65.40±2.35	70.00±1.57	69.20±2.34[b]
DIET	65.25±3.64	62.75±3.47	61.00±3.08[a, c]
HRT+DIET	67.67±5.78	68.00±6.93	68.33±5.33[a, b]
TG (mg/dL)			
HRT	111.20±8.01	128.40±7.47[b]	131.40±14.44[b, c]
DIET	110.25±11.60	81.25±13.38[a, c]	83.25±11.76[a, c]
HRT+DIET	114.00±2.65	103.00±3.51[a, c]	126.67±12.35[b, d]
AI			
HRT	2.92±0.19	2.14±0.07[a, b, c]	2.13±0.12[c]
DIET	2.91±0.24	2.39±0.28[b, c]	2.42±0.24[c]
HRT+DIET	2.84±0.33	1.84±0.22[a, c]	2.04±0.29[c, d]
CI			
HRT	3.92±0.19	3.14±0.07[a, b, c]	3.13±0.12[c]
DIET	3.91±0.24	3.38±0.28[b, c]	3.42±0.24[c]
HRT+DIET	3.84±0.33	2.84±0.22[a, c]	3.04±0.29[c, d]
Body weight (kg)			
HRT	59.03±1.60	59.40±1.87	59.33±1.88
DIET	61.25±2.89	59.75±5.56[c]	60.11±2.56[c]
HRT+DIET	61.70±0.20	60.80±0.53[c]	61.17±0.44

mean ± SEM; *AI* atherogenic index, (TC – HDL-cholesterol)/HDL-cholesterol; *CI* cardiac index, TC/HDL-cholesterol; [a, b] values with different characters within the same column are significantly different among groups based on the initial value at $P < 0.05$ by repeated measure design; [c] significantly different from the initial value in the same group at $P < 0.05$ by repeated measured design; [d] significantly different from the 4th week's value in the same at $P < 0.05$ by repeated measured design

group (16.8% at 4 weeks and 18.0% at 12 weeks, $P < 0.05$) but decreased in the DIET group (–26.7% at 4 weeks and –24.4% at 12 weeks, $P < 0.05$). In the HRT+DIET group, serum TG levels decreased after 4 weeks (–9.7%, $p < 0.05$) but tended to increase over its initial value after 12 weeks.

Body weight did not change significantly in the HRT group but decreased in the DIET group ($P < 0.05$). In the HRT+DIET group, body weight decreased significantly after 4 weeks but returned to its initial value after 12 weeks.

Discussion

CVD, the leading cause of mortality in many countries including Korea, is a multi-factorial disease that is associated with non-modifiable risk factors, such as age, gender, and genetic background, and with modifiable risk factors, including elevated total cholesterol and LDL-C levels. There is convincing evidence to show that lowering serum lipid levels will slow the progression or even induce regression in atherosclerotic lesions. In our study we observed that HRT and dietary intervention produced a considerable improvement in blood lipid profiles. HRT lowered TC and LDL-C levels by 13–16% and 24–28%, respectively, and dietary intervention lowered TC and LDL-C levels by 17–19% and 21–23%, respectively during the study period. HRT combined with dietary intervention lowered TC and LDL-C levels by 19–26% and 32–39%, respectively. This shows that a combination of HRT and dietary intervention has better effects than each treatment on its own. These results were more significant than we expected, and may be attributable to the subjects' good adherence to the cholesterol-lowering diet. Another probable reason for the success of dietary intervention was the high baseline level of fat and cholesterol intake of the subjects. Fat and cholesterol content of the diet at the baseline was low compared to the typical American diet, but high compared to the usual Korean diet. It is known that hypercholesterolemia patients who are on high fat or high cholesterol diets respond quite well to dietary intervention [7, 19, 20].

It is generally accepted that estrogen increases serum HDL-C levels [4, 5], while there are inconsistent results with regards to the effect of diet on serum HDL-C levels [21]. In our study, serum HDL-C levels significantly decreased in the DIET group (–6.4%) after 12 weeks, but not in the HRT and HRT+DIET groups. A few studies [13, 22] have suggested that the benefit of diet in decreasing LDL-C levels could be offset by the accompanying reduction in HDL-C levels. High HDL-C is a negative risk factor of CVD in populations on high-fat diets because it reflects the ability to handle dietary fats. However, low HDL-C found in many populations or groups on low-fat diets, such as that in the present study, lose its role as an indicator of risk because the challenge of fat loads is lacking [23, 24]. Moreover, the serum HDL-C levels of the DIET group in the present study were still in the normal range, despite the significant reduction after 12 weeks, because all subjects were relatively high in serum HDL-C levels at the baseline. Thus, the reduction of serum HDL-C levels observed in the DIET group does not indicate a high risk.

The effect of HRT, the combined therapy of estrogen and progesterone, on serum TG levels has been controversial, but many studies [25–27] have suggested that HRT may, if anything, increase serum TG levels. During the present study, serum TG levels decreased in the DIET group, but, conversely, increased in the HRT group. A few studies have suggested that the positive effects of estrogen on the blood lipid profiles could be offset by combined progesterone [28, 29]. On the basis of these studies, it is noteworthy that there was a slight but significant

decrease in serum TG levels in the HRT+DIET group after 4 weeks. It was supposed that the accompanying dietary intervention would undercut the HRT-induced increase in serum TG levels. During this study it was also observed that the levels of blood lipids, including TG, tended to return to their initial values after 12 weeks in the DIET and HRT+DIET groups. It is possible that subjects were progressively less adherent to the prescribed cholesterol-lowering diet, but failed to report this behavioral change in their diet records, as reported by Bae et al. [30].

Weight reduction has been cited as an important method for the control of CVD because obesity is associated with increased levels of LDL-C and with decreased levels of HDL-C [22, 31]. It has also been shown that the hypocholesterolemic effect of dietary intervention is obvious, especially it is accompanied by a reduction in body weight [22]. In the present study, there was a significant reduction of body weight in the DIET and the HRT+DIET groups after 4 weeks, but only in the DIET group after 12 weeks. The reduction of the serum TC and LDL-C levels observed in the two groups could be attributed to weight reduction during the study period. However, significant correlations were not observed between changes in the serum TC and LDL-C levels and weight changes during the study period (data not shown). Also, our results did not demonstrate a significant increase of serum HDL-C levels by weight reduction, which was reported in a few studies [31, 32]. In the present study there was rather a positive correlation between changes in the serum HDL-C levels and weight changes ($r = 0.488$, $p = 0.029$). This could be explained by the differences in responses for men and women. Brownell [33] already reported that weight reduction for men seems to produce beneficial changes in the levels of HDL-C and LDL-C, but a beneficial decrease in LDL-C levels for women may be counteracted by a negative decrease in HDL-C levels. In addition, subjects participating in the present study had a high baseline level of serum HDL-C, as already described above, so weight reduction may not necessarily accompany increases in serum HDL-C levels. Moreover, weight reductions observed in the DIET and HRT+DIET groups were considerably lower than expected in comparison to energy intake during the same period. This is probably due to the overestimation of basal dietary intake levels of the subjects because of the limitations of the semi-quantitative food frequency questionnaire, or perhaps due to a reduction of adherence to the diet as described above. When considering these things, the importance of weight reduction in improving blood lipid profiles should not be ignored, although a correlation between weight reduction and improvement in the serum lipid levels was not observed in this present study.

It is well known that there are often striking variances between subjects in the response of serum lipids level to diet. Recently, many studies have examined that serum lipoprotein response to dietary manipulation has a significant genetic component, and they suggest that treatment based on the hyperlipidemic patient's genetic background is needed [34–36]. Although we did not consider the subjects' genetic backgrounds, dietary intervention and HRT produced a considerable improvement in blood lipid profiles and in the body weight of the subjects. Also, the effects of the two treatments are independent and additive. However, the results obtained by the dietary intervention groups of this present study may slightly overestimate the average effect of diet prescribed in routine clinical practice because of following reasons. First, this study was composed of subjects whose diet contained more fat and cholesterol than the average Korean diet. Second, only the subjects who satisfactorily conformed to dietary intervention were included for analysis. Third, this study devoted considerable effort to encouraging dietary compliance and this remains a difficult task in routine clinical practice. Nevertheless, it is very stimulating to note that individual patients who have a high fat/cholesterol diet, and who are highly motivated, may achieve results that are much better than average in improving hypercholesterolemia by means of dietary intervention. Thus, dietary intervention should remain as the primary treatment for lowering cholesterol levels in patients having problems with dietary intake – especially with fat and cholesterol intake.

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