We investigated the correlations between the reduction in body weight (BW) induced by calorie restriction and reductions in blood pressure (BP) and improvement in metabolic disorders in overweight women with essential hypertension. After eating a standard diet (diet-I) for 2 weeks, women in the calorie-restricted group (n = 25) received a low calorie diet for 2 weeks, and then standard diet-II for 1 week. Women in the calorie-nonrestricted group (n = 13) ate standard diet-I for 5 weeks. The calorie-restricted group exhibited a significant reduction in BP in association with loss of BW; their levels of low-density lipoprotein cholesterol, and triglycerides levels, and their fasting levels of glucose and insulin were also reduced compared with the calorie-nonrestricted group. However, there were no significant differences in the level of high-density lipoprotein cholesterol, the areas under the 2-h glucose and insulin curves (AUC<sub>2h</sub> and AUC<sub>ins</sub>), or the ratio of AUC<sub>2h</sub> to AUC<sub>ins</sub> between groups. The change in BW was significantly correlated with a reduction in BP (r = 0.62, p < 0.01), but not with an improvement in metabolic disorders. Findings suggest that the degree of BW loss, induced by short-term, severe calorie restriction is associated with BP reduction, but not with improvements in glucose and lipid metabolism in overweight hypertensive women. (Hypertens Res 1996; 19 Suppl. I: S57-S60)

Key Words: hypertension, overweight, calorie restriction, insulin resistance, hyperlipidemia

Obesity is commonly associated with hypertension, impaired glucose tolerance, non-insulin-dependent diabetes mellitus, and hyperlipidemia (1-3). Insulin resistance is believed to be the common pathogenic pathway for these diseases (4, 5). Studies (6-9) have suggested that calorie restriction can reduce the blood pressure (BP) of hypertensive overweight patients when sodium intake is kept constant. However, these studies did not include a control group of calorie-nonrestricted patients; therefore, modifications in other dietary and lifestyle habits including physical activity may have influenced BP. We previously found in a randomized, 2-week controlled study that calorie-restricted subjects experienced a significantly greater reduction in BP in association with loss of body weight (BW) compared with control subjects when dietary sodium and potassium intake and physical activity levels were standardized (10), suggesting that calorie restriction alone can cause a reduction in BP. However, the relationship between BP reduction caused by short-term calorie restriction and metabolic disorders in overweight hypertensive patients remains unclear.

Therefore, we investigated the relationship between the BW reduction induced by calorie restriction and BP reduction and glucose and lipid metabolism in overweight, hypertensive women in whom other dietary variables and physical activity levels were controlled.

Methods

We studied 38 Japanese women aged 40 to 70 years with essential hypertension who were overweight (BW, 50 to 80 kg; body mass index, 25 to 30 kg/m<sup>2</sup>). Patients were categorized as stage I or stage II according to World Health Organization classification. Antihypertensive agents were withdrawn 2 weeks before admission to study, and were withheld until the end of study. This investigation was approved by the Ethical Supervisory Committee of Iwate Medical University. All subjects were provided with detailed information about the protocol and gave informed consent before participation.

Subjects were admitted to the metabolic ward of Iwate Medical University hospital for this 5 week study. They were assigned on study entry to either...
the calorie-restricted group (n = 25) or the calorie-
nonrestricted group (n = 13). Women in the calorie-
restricted group received standard diet I for 2 weeks
(weeks 1 and 2), a low calorie diet consisting of Optifast (Sandoz Nutrition, Minneapolis, MN,
USA) and vegetables for next 2 weeks (weeks 3 and
4), and then on standard diet II for 1 week (week
5). Strenuous ex-
ertion was prohibited during this period, and extent
of exercise (walking) was measured with a pe-
dometer (HJ-7, Omron Inc., Tokyo).

The diets administered have been previously de-
scribed (9). Standard diet I contained either 6.3,
7.1, or 8.4 MJ, with 85 to 90 g of protein, 45 to 60
g of fat, and 180 to 275 g of carbohydrates. Stan-
dard diet II contained either 3.8 or 5.0 MJ, with 65
to 70 g of protein, 30 to 40 g of fat, and 90 to 140 g
of carbohydrates. The low-calorie diet consisted of
Optifast and vegetables and contained 1.9 MJ, with
70 g of protein, 2 g of fat, and 35 g of carbohy-
drates. All diets contained equal daily amounts of
sodium (120 mmol) and potassium (60 mmol); diets
were supplemented with sodium (NaCl) and potas-
sium (Slow K®, Ciba Geigy Pharmaceuticals, Taka-
razuka, Japan) to equalize the mineral content.

Blood samples were collected at 7:00 AM after
the patients had rested for 30 minutes in the supine
position on day 4 of each study week for the deter-
minations of levels of low-density lipoprotein
cholesterol (LDL-C), high-density lipoprotein
cholesterol (HDL-C), and triglycerides (TG) as de-
scribed previously (11). Blood pressure (BP) was
measured daily, and the body weight (BW) was de-
termined daily as previously described (9). BP and
BW are expressed as the average values of 7 days in
each week. An oral glucose tolerance test (OGTT)
was performed once weekly during weeks 1 and
week 5. Blood samples were drawn 0, 60, and 120
minutes after administration of a 75-g load of glu-
cose for determinations of plasma levels of glucose
and insulin, according to previously described
methods (11).

Values are expressed as the means ± SD. Differ-
ences between the calorie-restricted and calorie-
nonrestricted groups were analyzed by the Mann-
Whitney test. Areas under the 2-hour plasma glu-
cose and insulin curves (AUC_glu and AUC_ins) dur-
ing the OGTT were calculated using the trapezoidal
rule. Correlation coefficients were calculated by
Spearman’s rank sum test. A level of p < 0.05 was
accepted as statistically significant.

Results

There were no significant differences in patient
characteristics between the calorie-restricted group
and the calorie-nonrestricted group in mean values
for age, BW, body mass index, calorie intake, exer-
cise, BP, LDL-C, HDL-C, TG, and glucose and
insulin in OGTT (Table 1).

Table 2 indicates changes from week 2 to weeks 3
and 4 between the two groups. The calorie-re-
stricted group experienced significant reductions in
systolic and diastolic BPs with BW loss, and re-
duced LDL-C, and TG levels, as compared with the
calorie-nonrestricted group. LDL-C and TG levels
in week 4 were reduced by 17% and 40%, respec-
tively, from week 2 levels. There were no significant
differences in exercise levels or the HDL-C level.

Table 3 indicates changes in plasma glucose and
insulin levels during OGTT from week 1 to week 5
between the two groups. The calorie-restricted
group experienced significant reductions in glucose
and insulin levels at week 5 and the ratio of fasting
levels of glucose to levels of insulin was significantly
higher than compared with the calorie-nonrestricted
group. However, there were no significant differ-
ences in these parameters after glucose administra-
tion between groups. There were also no significant
differences in AUC_glu and AUC_ins or the ratio of
AUC_glu to AUC_ins between groups.

In the calorie-restricted group, the reduction in
BW was significantly correlated with the reduction
in BP (r=0.62, p<0.01), but not with the change in
glucose at 0 h (r = -0.17), the change in insulin at 0
h (r = -0.02), the change in the ratio of glucose to
insulin at 0 h (r = 0.19), the change in LDL-C (r =
-0.20), or the change in TG (r = 0.19). The reduc-
tion in BP was not correlated with changes in any
glucose, insulin and lipid parameters.
Discussion

Because sodium and potassium intake and physical activity can affect the BP (12) and the metabolism of glucose (13) and lipids (14), these variables were kept constant as clinically feasible in the present study. Overweight hypertensive women who received a calorie-restricted diet for 2 weeks experienced a significantly greater BP reduction in association with BW loss compared with women in the calorie-nonrestricted group. BW loss and BP reduction were significantly correlated in the calorie-restricted group. In a meta-analysis of studies in which BW loss were accomplished by 2-5 months regimens of calorie restriction, Staessen et al. (15) found that a 1-kg loss in BW was associated with a reduction in 1.6-mmHg of systolic BP and 1.3-mmHg of diastolic BP. The results of the study are consistent with these previous findings: BW loss was associated with a 2.6-mmHg reduction in systolic BP and 1.3-mmHg reduction in diastolic BP. These results suggest that the degree of BW loss is a determinant of the degree of reduction in BP, whether the BW loss is achieved rapidly or slowly.

Lipid metabolism was also improved in the calorie-restricted group in the present study, as indicated by significant reductions in LDL-C and TG levels. The degree of reduction in lipid levels was not correlated with BW loss. Thus, reductions in lipid levels appeared to result from calorie restriction rather than weight reduction. Osterman et al. previously reported that lipid levels were influenced by a change in the calorie intake in the absence of a change in BW (16). Calorie restriction caused no significant change in the HDL-C level in the present study, although previous studies have found that 4- to 10-weeks periods of calorie restriction resulted in significant reductions in HDL-C (17). The discrepancy between previous and present results may be related to the difference in the duration of calorie restriction.

There were no significant differences in glucose and insulin responses after the OGTT between week 1 and week 5, suggesting that insulin resistance in peripheral tissues especially in skeletal muscles, was not improved by the 3.6 kg BW loss in the present study. Su et al. (18) reported that in-

Table 2. Comparison of Changes from Week 2 (baseline) vs. Weeks 3 and 4 between Calorie-Restricted and Calorie-Nonrestricted Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calorie-restricted group</th>
<th>Calorie-nonrestricted group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 3</td>
<td>Week 4</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>-1.9 (0.6)*</td>
<td>-3.6 (0.8)*</td>
</tr>
<tr>
<td>Exercise, $10^5 \times $steps/d</td>
<td>-1 (3)</td>
<td>-2 (3)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>-5.7 (4.2)*</td>
<td>-9.6 (7.2)*</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>-2.5 (2.3)*</td>
<td>-4.6 (3.8)*</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol, $\mu$mol/l</td>
<td>-88 (421)</td>
<td>-636 (431)*</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol, $\mu$mol/l</td>
<td>-13 (91)</td>
<td>-31 (146)</td>
</tr>
<tr>
<td>Triglyceride, mmol/l</td>
<td>-1.2 (0.8)*</td>
<td>-1.3 (1.1)*</td>
</tr>
</tbody>
</table>

Individual values were obtained by subtracting values in week 2 from those in week 3 or 4. Values are means (SD) obtained from 25 patients in the calorie-restricted group and 13 patients in the calorie-nonrestricted group.

*p < 0.01 vs. week 3 in the calorie-nonrestricted group, †p < 0.01 vs. week 4 in the calorie-nonrestricted group.

Table 3. Comparison of Changes in 75-g Oral Glucose Tolerance Test from Week 1 vs. Week 5 between Calorie-Restricted and Calorie-Nonrestricted Groups

<table>
<thead>
<tr>
<th>Time after glucose intake</th>
<th>Calorie-restricted group</th>
<th>Calorie-nonrestricted group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 h</td>
<td>1 h</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>-0.8 (0.6)*</td>
<td>-0.6 (2.4)</td>
</tr>
<tr>
<td>Insulin, mU/l</td>
<td>-6.3 (5.0)*</td>
<td>-6.0 (44.6)</td>
</tr>
<tr>
<td>Glucose/insulin, mmol/U</td>
<td>87 (91)*</td>
<td>5 (10)</td>
</tr>
</tbody>
</table>

Individual values were obtained by subtracting values in week 1 from those in week 5. Values are means (SD) obtained from 25 patients in the calorie-restricted group and 13 patients in the calorie-nonrestricted group.

*p < 0.01 vs. the calorie-nonrestricted group. AUC$_{glu}$ and AUC$_{ins}$, area under the curve of glucose and insulin, respectively, after 75-g oral glucose tolerance test.
The present results suggest that the degree of BW loss is associated with BP reduction, but not with improvements in glucose and lipid metabolism in overweight hypertensive women. We emphasize that the present study involved only short-term, severe calorie restriction and that we excluded patients with organ damage from the study. Accordingly, the effects of prolonged, mild calorie restriction and the effects of organ damage on the reduction in BP induced by calorie restriction remain to be elucidated.

Acknowledgments

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References