Original Article

Effects of Short-Term Hypocaloric Diet on Sympatho-Vagal Interaction Assessed by Spectral Analysis of Heart Rate and Blood Pressure Variability during Stress Tests in Obese Hypertensive Patients

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We examined the effects of a short-term low-calorie diet on the activity of the autonomic nervous system during stress tests in obese patients with hypertension by analysis of heart rate and blood pressure variability. Eighteen obese inpatients with essential hypertension were given a regular-calorie diet (1,600 kcal, NaCl 7 g) for 4 days, and then a low-calorie diet (1,100 kcal, NaCl 7 g) for 11 days. During both the regular-calorie diet and low-calorie diet, power spectral analysis of heart rate and blood pressure variability at rest and during mental arithmetic test, deep breathing test, isometric handgrip test or cold pressor test was performed. Body weight and 24-h ambulatory blood pressure were significantly lower during the low-calorie diet than during the regular-calorie diet. Systolic and diastolic blood pressure significantly increased over the handgrip test and cold pressor test during both diets. The low frequency component (LF) of systolic blood pressure, a marker of sympathetic activity to the vasculature, during the deep breathing test and cold pressor test were significantly lower on the low-calorie diet than the regular-calorie diet. The blood leptin concentration was also significantly lower on the low-calorie diet than the regular-calorie diet. The decrease in body weight was positively correlated with the decrease in blood leptin concentration. The LF/high frequency component (HF) ratio of the RR interval at rest on the regular-calorie diet was negatively correlated with the decrease in blood leptin concentration. These results suggest that the autonomic nervous function assessed by analysis of heart rate and blood pressure variability during stress tests may be improved by weight loss due to a short-term low-calorie diet in obese patients with hypertension. (*Hypertens Res* 2007; 30: 1199–1203)

***Key Words*: essential hypertension, obesity, sympatho-vagal interaction, spectral analysis, leptin**

Introduction

The mechanisms underlying hypertension in obesity are not completely understood. One of the prevailing theories is that abnormal functioning of the autonomic nervous system plays a role in the pathogenesis of hypertension in obese patients (*1*). Improvement of autonomic nervous system activity may thus be one of the mechanisms of blood pressure lowering due to weight reduction.

Weight loss is recommended as the starting point in the treatment of obesity-related hypertension. Dietary calorie restriction has been reported to directly inhibit sympathetic activity in animal experiments (*2*) and humans (*3*).

The tonometric device derives systolic blood pressure (SBP) changes from the radial artery. The use of this blood pressure analysis technique has become popular because of its noninvasive nature and ease of application. Radial tonometry is used for the noninvasive acquisition of beat-to-beat blood pressure and associated autonomic analysis (*4*).

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Table 1. Characteristics of 18 Patients

	Mean	SEM
Body height (cm)	163.0	2.9
Body weight (kg)	76.8	2.2
BMI (kg/m^2)	29.1	1.0
Total cholesterol (mg/dL)	208.2	6.5
HDL cholesterol (mg/dL)	52.9	3.4
Triglyceride (mg/dL)	134.4	6.8
HbA1c (%)	6.2	0.3
Dyslipidemia	8 cases/18 cases	
Diabetes mellitus	8 cases/18 cases	
Impaired glucose tolerance	5 cases/18 cases	

BMI, body mass index; HDL, high-density lipoprotein.

In the present study, we examined the effects of a short-term low-calorie diet on the activity of the autonomic nervous system in obese patients with hypertension using analysis of heart rate and blood pressure variability before and after four kinds of stress tests.

Methods

Eighteen obese (body mass index [BMI] ≥25 kg/m^2) inpatients with essential hypertension (11 males and 7 females; age, 62.3±2.6 years [mean±SEM]) were given a regular-calorie and low-salt diet (1,600 kcal, NaCl 7 g) for 4 days, and thereafter a low-calorie and low-salt diet (1,100 kcal, NaCl 7 g) for 11 days. Power spectral analysis of heart rate and blood pressure variability was done in the decubitus position in a quiet single room after 30 min of rest at 8:30 AM before breakfast. Patients had a tonometric device on the left wrist, a cuff for blood pressure measurement on the left arm, and used their right hand for the hand grip test and cold pressor test. In 18 patients, beat-to-beat RR interval in the electrocardiogram and beat-to-beat blood pressure measurement and power spectral analysis of heart rate and blood pressure variability at rest and during a mental arithmetic test (100−7, 93−7, 86−7, *etc*., for a total of 1.5 min), a deep breathing test (5 s deep inspiration, 5 s deep expiration, *etc*., for a total of 1.5 min), and an isometric handgrip test (one-third of maximal handgrip power for a total of 2 min) was performed using electrocardiography, automatic blood pressure measurement, tonometry (Colin BP 508 type SD; Omron Colin Co., Ltd., Tokyo, Japan), a personal computer and a Colin ANS-508 system (Omron Colin Co.) on the last days of the regular-calorie and low-calorie diet periods. A cold pressor test (placing a hand in ice water for a total of 1 min) was performed in 7 of 18 patients. Twenty-four-hour ambulatory blood pressure was measured using an A&D TM 2421 device (A&D Co., Ltd., Tokyo, Japan) on the last days of the regular-calorie and low-calorie diet periods. During the study, 8 of the 18 patients received no antihypertensive drug, while 7 patients received a

Table 2. Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and RR Interval before and during Mental Arithmetic Test, Deep Breathing Test and Hand Grip Test on Regular-Calorie Diet or Low-Calorie Diet in 18 Obese Hypertensive Patients

	Regular-calorie diet	Low-calorie diet
SBP (mmHg)		
Before test	140.6±4.5	133.7±3.8†
During mental arithmetic test	157.8±6.6***	146.7±4.8$^{\#,\dagger}$
During deep breathing test	128.9±5.9***	131.1±4.9
During hand grip test	152.9±5.8***	150.7±5.8$^{\#}$
DBP (mmHg)		
Before test	77.4±2.8	74.3±2.2
During mental arithmetic test	89.4±4.5***	82.5±3.1$^{\#}$
During deep breathing test	73.1±4.4	75.3±3.2
During hand grip test	84.6±2.9*	85.2±3.4***
RR interval (s)		
Before test	0.96±0.03	1.00±0.04
During mental arithmetic test	0.82±0.03$^{\#}$	0.84±0.04$^{\#}$
During deep breathing test	0.92±0.03	0.95±0.04
During hand grip test	0.91±0.02**	0.93±0.03$^{\#}$

Mean±SEM. *$p<0.05$, **$p<0.01$, ***$p<0.005$, $^{\#}p<0.001$ compared with before test; $^{\dagger}p<0.05$ compared with regular-calorie diet.

Table 3. HF of RR, LF/HF of RR and LF of SBP before and during Mental Arithmetic Test, Deep Breathing Test and Hand Grip Test on Regular-Calorie or Low-Calorie Diet in 18 Obese Hypertensive Patients

	Regular-calorie diet	Low-calorie diet
HF of RR(ms^2/Hz)		
Before test	43.73±17.00	70.26±26.04
During mental arithmetic test	30.18±8.90	172.42±80.17
During deep breathing test	77.65±28.77	110.22±28.05
During hand grip test	23.01±9.39	43.39±17.87
LF/HF of RR		
Before test	1.48±0.56	1.85±0.54
During mental arithmetic test	2.35±0.67	2.18±0.63
During deep breathing test	9.93±1.97*	7.69±1.17*
During hand grip test	1.89±0.44	2.28±0.50
LF of SBP (mmHg^2/Hz)		
Before test	0.81±0.35	0.40±0.07
During mental arithmetic test	1.44±0.37	1.32±0.48
During deep breathing test	11.26±2.45*	6.29±1.28*,†
During hand grip test	0.48±0.11	1.48±0.98

Mean±SEM. *$p<0.001$ compared with before test. $^{\dagger}p<0.03$ compared with regular-calorie diet. HF, high frequency component; LF, low frequency component; SBP, systolic blood pressure.

Table 4. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) and RR Interval before and during Cold Pressor Test on Regular-Calorie or Low-Calorie Diet in 7 Obese Hypertensive Patients

	Regular-calorie diet		Low-calorie diet	
	Before test	During test	Before test	During test
SBP (mmHg)	142.8±5.5	170.8±7.1***	138.0±4.2	171.1±5.9***
DBP (mmHg)	79.4±2.8	94.5±1.9***	72.6±1.2	88.6±3.7**
RR interval (s)	0.97±0.03	0.94±0.05	1.10±0.04†	0.99±0.04*
HF of RR (ms^2/Hz)	51.49±18.15	43.72±13.09	40.45±13.01	95.01±43.18
LF/HF of RR	0.67±0.22	0.98±0.36	0.50±0.26	0.76±0.28
LF of SBP ($mmHg^2$/Hz)	0.45±0.20	0.59±0.18	0.26±0.11	0.26±0.09†

Mean±SEM. *$p<0.05$, **$p<0.005$, ***$p<0.001$ compared with before test; †$p<0.05$ compared with regular-calorie diet. LF, low frequency component; HF, high frequency component.

constant dose of only a Ca antagonist and 3 patients received a constant dose of a Ca antagonist and an ACE inhibitor. We obtained informed consent from all patients, and the study was approved by the ethical committee at our institute. In 8 patients, blood leptin concentration was measured on the last days of the regular-calorie and low-calorie diet periods.

Statistics

Student's paired or unpaired *t*-test was used for all comparisons between groups. Values of $p<0.05$ were considered to indicate statistical significance.

Results

The characteristics of the 18 patients are shown in Table 1. Among the 18 patients, 8 patients had dyslipidemia, 8 had diabetes mellitus, and 5 had impaired glucose tolerance. Twenty-four-hour ambulatory blood pressure (141.1±3.7/84.1±3.2 mmHg for the regular-calorie *vs*. 131.2±3.4/78.8±2.4 mmHg for the low-calorie diet, $p<0.01$) and body weight (76.8±2.2 kg for the regular-calorie *vs*. 74.6±2.2 kg for the low-calorie diet, $p<0.001$) were significantly lower on the low-calorie diet than on the regular-calorie diet.

Table 2 shows the values of SBP, diastolic blood pressure (DBP), and RR interval before and during the arithmetic test, deep breathing test and hand grip test in the 18 obese hypertensive patients during the regular-calorie diet or low-calorie diet. The pre-test SBP was significantly lower on the low-calorie diet than on the regular-calorie diet. Both SBP and DBP significantly increased during the mental arithmetic test and hand grip test on both the regular-calorie and low-calorie diets. The RR interval was significantly lower during the mental arithmetic test and hand grip test than before them.

Table 3 shows the high frequency components (HF) of RR, the ratio of the low frequency component (LF) to the HF (LF/HF) of RR, and the LF of SBP before and during the mental arithmetic test, deep breathing test and hand grip test in the 18 obese hypertensive patients on the regular-calorie or low-calorie diet. Both the LF/HF of RR and LF of SBP were significantly greater during the deep breathing test than before it both on the regular-calorie diet and on the low-calorie diet. The LF values (0.04–0.15 Hz) of SBP, a marker of sympathetic activity to the vasculature, during the deep breathing test were significantly lower on the low-calorie diet (6.29±1.28 $mmHg^2$/Hz) than the regular-calorie diet (11.26±2.45 $mmHg^2$/Hz) ($p<0.03$).

Table 4 shows the values of SBP, DBP, and the RR interval before and during the cold pressor test in 7 obese hypertensive patients during the regular-calorie or low-calorie diet. SBP and DBP increased significantly during the cold pressor test on both the regular-calorie and low-calorie diets. The RR interval before the test was significantly greater while on the low-calorie diet than while on the regular-calorie diet. Furthermore, the LF values of SBP during the cold pressor test in 7 patients were significantly lower while on the low-calorie diet (0.26±0.09 $mmHg^2$/Hz) than while on the regular-calorie diet (0.59±0.18 $mmHg^2$/Hz) ($p<0.05$).

The blood leptin concentration of 8 patients was significantly lower during the low-calorie diet (9.0±2.1 ng/mL) than during the regular-calorie diet (12.9±2.4 ng/mL) ($p<0.002$). The decrease (kg) in body weight was significantly positively correlated with the decrease in blood leptin concentration between the regular- and low-calorie diets ($r=0.876$, $p<0.005$) (Fig. 1). The LF/HF ratio of the RR interval, a marker of cardiac sympathetic activity, at rest during the regular-calorie diet was significantly negatively correlated with the decrease in blood leptin concentration between the regular- and low-calorie diets ($r=-0.785$, $p<0.03$) (Fig. 2). In these 8 patients (5 males and 3 females), the mean age was 56.6±3.6 years old, the mean body height was 166.1±4.6 cm, the mean body weight was 78.3±3.4 kg, and the mean BMI was 28.6±1.6 kg/m^2, and thus the patient characteristics were not significantly different between these 8 patients and the total 18 patients (Table 1).

Discussion

The sympathetic nervous system is activated in human obesity (*5*), and sympathetic overdrive plays a role in human obe-

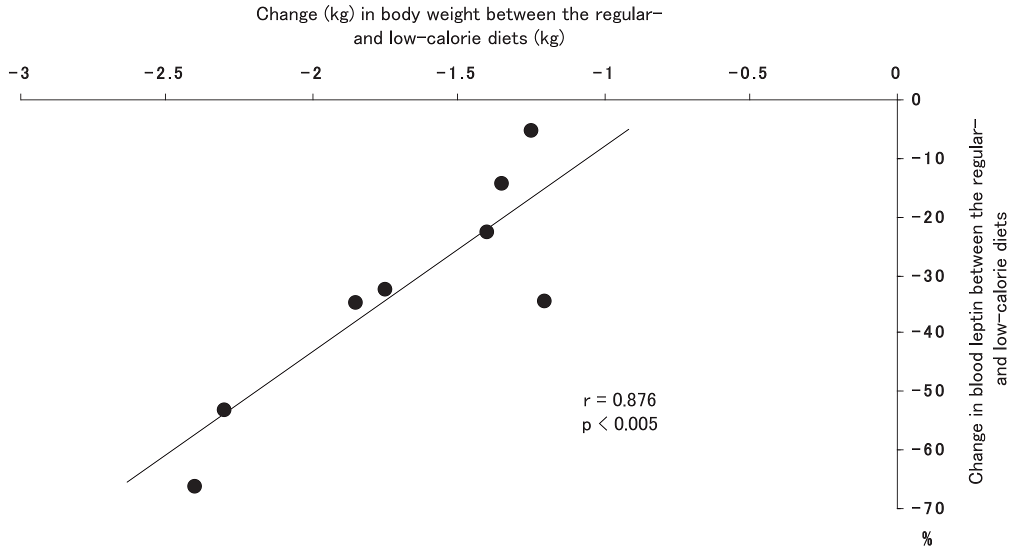

Fig. 1. *Correlation between the decrease (kg) in body weight and the decrease (%) in blood leptin concentration between the regular- and low-calorie diets.*

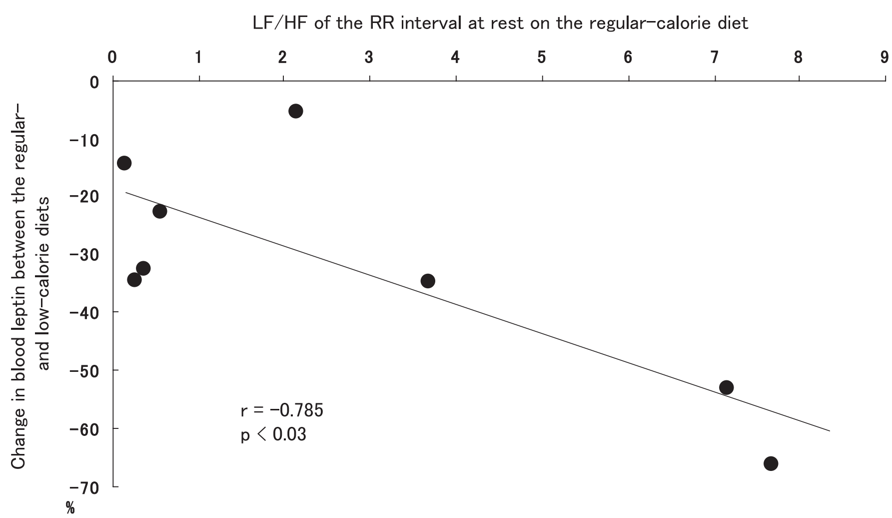

Fig. 2. *Correlation between the ratio of the low frequency components (LF) to the high frequency components (HF) of the RR interval, a marker of cardiac sympathetic activity, at rest on the regular-calorie diet and the decrease (%) in blood leptin concentration between the regular- and low-calorie diets.*

sity (*6*). Blood pressure has been shown to be decreased by weight reduction in obese patients (*7*). In another study, weight reduction by a low-calorie diet decreased blood pressure and decreased the activity of the muscle sympathetic nervous system (*8*). Thus, weight reduction by a low-calorie diet decreases the sympathetic nerve activity (*9–14*), which suggests that the decrease in sympathetic vascular constriction is one of the mechanisms of blood pressure decrease by weight reduction.

On the other hand, blood pressure decrease by weight reduction is independent of the effects of dietary salt restriction (*15*). Exercise therapy has been shown to decrease the spillover of norepinephrine, particularly in the kidney and skeletal muscle (*16*).

In the present study, we used four stress tests because we considered that it might not be easy to demonstrate a significant difference in the activity of the autonomic nervous system between the short-term regular-calorie and low-calorie diets. The results showed that the LF of SBP, a marker of sympathetic activity to the vasculature, during the deep breathing test or cold pressor test was significantly smaller on the low-calorie diet than the regular-calorie diet. This suggests that weight reduction by a low-calorie diet may improve the peripheral sympathetic activity in obese patients. In addition, the present study demonstrated that the deep breathing test and cold pressor test may be useful to show an improvement in sympathetic activity even by a short-term (11 days) low-calorie diet. As shown in Table 3, the pre-test LF of SBP was lower on the low-calorie diet than on the normal-calorie diet, and the LF of SBP during the hand grip test was higher on the low-calorie diet. However, these differences were not significant, and may have been attributable to the large variation in the LF of SBP during the hand grip test.

The RR interval before the cold pressor test was significantly greater on the low-calorie diet than on the regular-calorie diet (Table 4). That is, heart rate was decreased by the low-calorie diet. This may indicate that the low-calorie diet enhanced the parasympathetic tone. In agreement with these findings, a previous study reported that weight loss by a very low-calorie diet was associated with a decrease in heart rate, and an increase in the spectral indices of heart rate variability (*17*).

Blood leptin concentration is increased in obese hypertensive patients. Leptin is thought to increase sympathetic activity centrally or peripherally, and this is thought to be one of the mechanisms involved in the pathogenesis of hypertension in obesity (*18*). In the present study, the LF/HF ratio of the RR interval, a marker of cardiac sympathetic activity, at rest during the regular-calorie diet was significantly negatively correlated with the decrease in the blood leptin concentration between the regular-calorie and low-calorie diets (Fig. 1). This means that the decrease in the blood leptin concentration between the regular-calorie and low-calorie diets increased with increasing cardiac sympathetic activity. This in turn suggests that in obese hypertensive patients, sympathetic activity improves more by weight reduction due to a low-calorie diet, as sympathetic activity increases by a greater amount.

The present study has some limitations. There was no control group that had a regular-calorie diet period instead of a low-calorie diet period. Also, the number of patients was small, and only 7 and 8 patients of the total group underwent the cold pressor test and leptin measurement, respectively.

Conclusion

Autonomic nervous function assessed by analysis of heart rate and blood pressure variability may be improved by weight loss due to a short-term low-calorie diet in obese patients with hypertension. The analysis of heart rate and blood pressure variability during stress tests may be useful to examine the mechanism of the autonomic nervous abnormality in obese hypertension.

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