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Effect of Weight Loss on Blood Pressure and Drug Consumption in Normal Weight Patients

YUTAKA IMAI, KO SATO, KEISHI ABE, SHUICHI SASAKI, MINORU NIHEI,
KAORU YOSHINAGA, AND HIROSHI SEKINO

SUMMARY   The effect of weight loss on blood pressure and on antihypertensive drug consumption was examined in 81 nonobese subjects with essential hypertension who had been chronically treated with antihypertensive drugs. A hypocaloric diet was prescribed for 5 months. A weight loss greater than 2 kg in 5 months was considered significant. Quality and quantity of antihypertensive medications were scored according to a formula. In the subjects whose medication and weight did not change, mean arterial pressure remained unchanged, whereas it decreased significantly (-7.1 ± 1.9 mm Hg) in those who showed significant weight loss (-3.28 ± 0.34 kg) with no change in medication. Among the subjects whose antihypertensive medication remained constant during the diet program there was a significant correlation between the change in weight and mean arterial pressure ($r = 0.45$, $p < 0.01$). Mean arterial pressure increased significantly ($+5.1 \pm 1.7$ mm Hg) in subjects whose weight remained unchanged with a decrease in medication, whereas it remained significantly lower than the control (by -3.1 ± 2.0 mm Hg) in those whose weight decreased significantly (-4.57 ± 0.69 kg) with the decrease in medication. The weight loss–induced decrease in blood pressure occurred independently of the initial degree of obesity and the initial level of mean arterial pressure. Urinary sodium excretion in the control period and at the end of the diet program did not differ significantly between subgroups. These results indicate that, even in subjects of normal weight with essential hypertension, weight loss can induce a fall in blood pressure that leads to a reduction of antihypertensive medication. A 4-kg weight loss was equivalent to the amount of antihypertensive medication required for effective control of mild hypertension. (Hypertension 8: 223–228, 1986)

KEY WORDS   •   antihypertensive drugs   •   relative body weight   •   caloric restriction   •   sodium intake

CONSIDERABLE evidence has shown a direct relation between obesity and hypertension.[1-4] Many studies have also demonstrated that a weight loss in obese hypertensive subjects is associated with a fall in blood pressure. Thus, successful weight reduction is an effective treatment or adjunct to treatment for obese hypertensive patients.[1, 5-12] In a recent study on obese hypertensive patients, weight loss induced a marked fall in blood pressure levels that led to reduction or withdrawal of the antihypertensive drugs.[7, 8, 13] These results are important, since drug treatment of hypertension is costly and may have long-term adverse effects.[3, 14, 15] Indeed, the report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure emphasized the potential value of nonpharmacological management.[16]

Few studies have been conducted on the role of weight reduction in the treatment of nonobese hypertensive patients. Several reports have demonstrated that moderate weight loss affects blood pressure more or less uniformly and independently of the degree of initial overweight. Furthermore, the positive correlation between the change in weight and in blood pressure seems to be linear and is found not only in obese patients but in the population as a whole.[11, 12, 17, 18] These reports stimulated us to examine the effect of weight loss on arterial blood pressure in hypertensive patients who have gained weight but are not obese. In the present study we examined serial changes in blood pressure and drug consumption during a 5-month weight reduction program in hypertensive subjects of normal weight who had been chronically treated with antihypertensive drugs.

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Subjects and Methods

The study group included 101 subjects with essential hypertension. Diagnosis was made by history and by results of physical examination, radiological examination, and laboratory tests. The subjects were treated in the Hypertension Clinic of Tohoku University Hospital or in Kojin-kai Central Hospital. They were free of congestive heart failure, stroke, myocardial infarction, insulin-dependent diabetes mellitus, and renal failure. Of 101 subjects, 11 left the program, 7 did not comply with the prescribed regimen of antihypertensive medication, 1 had gastric cancer, and 1 acquired insulin-dependent diabetes mellitus. Two subjects with angina pectoris, three with non-insulin-dependent diabetes mellitus, and three with mild renal failure (plasma creatinine level <2.5 mg/dl) were included among the remaining 81 study subjects (average age, 50.3 ± 1.6 years; 29 women; 52 men). All were taking antihypertensive drugs at the start of the study. Sustained hypertension was confirmed in all subjects before treatment; all had blood pressure recordings consistently greater than 150 mm Hg systolic or 95 mm Hg diastolic, or both, on at least two clinic visits. The entire study was conducted over 5 years from 1980 to 1984. Subjects visited the clinic every 2 weeks so that blood pressure and weight could be measured. Weight was obtained in underwear-clad subjects with their shoes removed, and blood pressure was measured with a Dynamap type automatic oscillometric sphygmomanometer (Narco-Nippon Colin BP-203, Tokyo, Japan) by trained nurses. The sum of the diastolic pressure and one third of the pulse pressure was defined as mean arterial pressure (MAP). Compliance with antihypertensive drug regimens was evaluated by the pill count of unused medication between visits. The physician advised subjects at each clinic visit to restrict dietary salt intake to less than 8 g/day; however, he gave no particular advice concerning physical exercise during the period.

Weight Reduction Program

At the end of the control period the subjects were referred to hospital dietitians who prescribed a diet of 30 kcal/kg of ideal body weight ([height in cm − 100] kg) for weight reduction. The dietitians also advised subjects to restrict dietary salt intake to less than 8 g/day.

Study Design

The weight reduction program was conducted for 5 months. Blood pressure and weight obtained in the month before the program began were regarded as control and expressed as zero month value. Subjects were classified into two groups based on the degree of weight loss. Those who succeeded in reducing weight by over 2 kg were described as the group with weight loss. The remaining subjects were described as the group with unchanged weight. The 2-kg end point was determined by taking the yearly weight variation traced in 48 subjects whose antihypertensive medication remained constant. The average of their weight for a year was obtained, and any fluctuation in weight from the average was calculated. Mean ± 1 SD was obtained from the sum of maximum changes on the negative side in each subject. Since the maximum weight decrease was 1.31 ± 0.53 kg, a weight loss of more than 2 kg (greater than the mean + 1 SD) in 5 months was regarded as significant. Subjects in the two groups were further subdivided according to antihypertensive medication (i.e., 1 subgroup with unchanged medication and 1 with reduced medication). Subjects in the weight loss group whose antihypertensive medication remained unchanged were again subdivided into two groups according to the relative body weight (i.e., [actual body weight/standard body weight] × 100, where the standard body weight is [height in cm − 100] kg), an index of fatness or obesity. One subgroup included subjects with a relative body weight equal to or above 110 ($n = 11$), and the other subgroup included those with a relative body weight below 110 ($n = 10$). Subjects in the weight loss group whose antihypertensive medication remained unchanged also were subdivided into two groups according to initial MAP (i.e., 6 subjects with initial MAP ≥110 mm Hg, 9 with initial MAP <110 mm Hg).

The population and characteristics of each group are shown in Table 1. The quality and quantity of antihypertensive drugs were expressed collectively as a drug score. A dose of drug that effectively treats mild hypertension was arbitrarily assigned a value of 1 point. The point system is shown in Table 2. For example, a drug regimen comprising 2 mg of trichloromethiazide (1 point), 90 mg of diltiazem (0.5), and 30 mg of pindolol (2.0) has a value of 3.5 points.

Drug reduction was effected in a stepwise fashion; the drug belonging to a higher step in the stepped-care program of Joint National Committee was removed first. Drug score increased in a few subjects in the group with unchanged medication. This increase was not due to a need for further hypotensive effect or to control intractable hypertension; it resulted from the severe side effects induced by nifedipine, a potent calcium antagonistic vasodilator, or by α-blockers and β-blockers. In some of these subjects another vasodilator, β-blocker, or diuretic was substituted for nifedipine and in others a diuretic was substituted for the β-blocker or α-blocker. In such instances, drug scores were increased to adjust the antihypertensive potency of the drugs, and these subjects were included in the group with unchanged medication.

In 74 of the 81 subjects, 24-hour urine sodium was examined at 0 and 5 months. Urinary sodium excretion was estimated in comparison with the 24-hour urinary creatinine excretion and expressed as milliequivalents per gram of creatinine.

Statistical Analysis

All data are expressed as means ± SEM unless otherwise stated. The time course of changes in weight, blood pressure, and the drug score between the groups was compared by two-way analysis of vari-

TABLE 1.   *Characteristics of 81 Hypertensive Subjects*

Group	Sex M	Sex F	Age (yr)	Relative body weight (%)	Height (cm)	Initial MAP (mm Hg)	Initial drug score
Unchanged weight (n = 44)	23	21	51.2 ± 1.3	104 ± 2	159.2 ± 1.3	108.0 ± 1.4	2.42 ± 0.25
Unchanged medication (n = 29)	17	12	50.9 ± 1.6	107 ± 3	158.9 ± 1.4	109.1 ± 1.8	2.54 ± 0.35
Reduced medication (n = 15)	6	9	51.9 ± 2.1	101 ± 4	159.8 ± 2.0	105.8 ± 1.9	2.20 ± 0.28
Weight loss (n = 37)	29	8	49.5 ± 1.9	114 ± 2*	161.7 ± 1.4	109.3 ± 1.4	2.93 ± 0.29*
Unchanged medication (n = 21)	18	3	48.9 ± 2.5	111 ± 2	162.3 ± 1.5	111.4 ± 2.1	3.18 ± 0.46†
Reduced medication (n = 16)	11	5	51.0 ± 3.4	119 ± 4	160.9 ± 2.7	106.4 ± 1.7	2.66 ± 0.28‡

Values are means ± SEM. MAP = mean arterial pressure.
*$p < 0.005$, compared with values from unchanged weight group as a whole; †$p < 0.005$, compared with values from group with unchanged weight and medication; ‡$p < 0.005$, compared with values from group with unchanged weight and reduced medication.

TABLE 2.   *Drug Scoring*

Drug	Dose*
Diuretics	
Trichlormethiazide	2.0 mg
Methyclothiazide	2.5 mg
Meticrane	150.0 mg
Spironolactone	50.0 mg
Furosemide	40.0 mg
Vasodilators	
Diltiazem	180.0 mg
Nifedipine	30.0 mg
Verapamil	240.0 mg
Nicardipine	60.0 mg
Sympatholytics	
Clonidine	225.0 µg
Methyldopa	750.0 mg
α-blockers	
Prazosine	1.5 mg
β-blockers	
Propranolol	60.0 mg
Pindolol	15.0 mg
Carteolol	7.5 mg
Alprenolol	75.0 mg
Metoprolol	120.0 mg
Angiotensin converting enzyme inhibitors	
Captopril	37.5 mg
Enalapril	10.0 mg

*Estimated as 1 point.

ance. The values of weight, MAP, and drug score in each month were compared using Duncan's multiple range test and Student's *t* test for paired comparison. The remaining data were compared using one-way analysis of variance and Student's *t* test.

Results

As shown in Table 1, there was no significant difference in age and initial blood pressure between the groups with unchanged weight and weight loss. Rela-

tive body weight in the latter group was significantly higher than that in the former, while height was not significantly different between the two groups.

Figure 1 shows the subjects' weight change from their third decade of life. The data were obtained from the 81 subjects by recall. These subjects demonstrated a tendency to gain weight beginning in young adulthood and continuing through middle to old age.

As shown in Figure 2, the subjects in the weight loss group with unchanged medication lost weight gradually and significantly ($F_{1, 293} = 70.3$, $p < 0.001$) compared with those in the group with unchanged weight and medication. Four subjects in the latter group gained more than 1.5 kg. Subjects in the weight loss group lost 3.28 ± 0.34 kg at 5 months, and mean percentage reduction from the control weight was 4.8 ± 0.6%.

The MAP fell gradually and significantly in the weight loss group but was unchanged in the group with no weight loss ($F_{1, 293} = 30.5$, $p < 0.001$; see Figure 2). At 5 months MAP was decreased by 7.14 ± 1.91 mm Hg in the weight loss group. Among the 38 subjects whose antihypertensive medication remained constant during the program there was a significant correlation between the changes in weight and MAP at 5 months ($r = 0.45$, $p < 0.01$).

Urinary sodium excretion at 5 months was not significantly different from that at zero month in either group (see Figure 2). Neither was any significant difference in urinary sodium excretion noted between the two groups.

As shown in Figure 3, the subjects in the weight loss group with decreased medication lost weight significantly during the 5-month program ($F_{1, 179} = 96.8$, $p < 0.001$) compared with those in the group with unchanged weight but decreased medication. Subjects in the former group lost 4.57 ± 0.65 kg at 5 months, and their antihypertensive medication was reduced from 2.20 ± 0.28 to 1.26 ± 0.24 ($p < 0.01$). Medication in the group with unchanged weight was reduced from 2.66 ± 0.28 to 1.67 ± 0.30 ($p < 0.01$).

As shown in Figure 3, blood pressure in the group with unchanged weight rose gradually and significantly from the baseline with reduction of antihypertensive
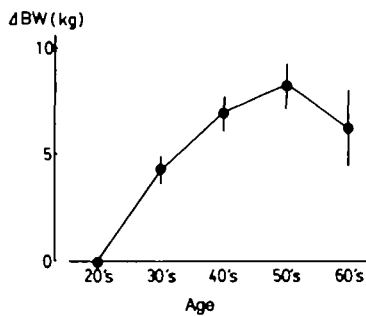
FIGURE 1. *The change in subjects' body weight (ΔBW) from their third decade of life.*

medication. Although reduction in antihypertensive medication tended to attenuate the hypotensive effect in the group with weight loss, MAP remained significantly below the baseline at 5 months. The time course of changes in blood pressure in the group with weight loss was significantly different from that in the group with unchanged weight ($F_{1, 179} = 27.2$, $p < 0.001$). Reduction in the drug score by 1.0 increased MAP by about 5.4 mm Hg in the subjects whose weight remained unchanged, and the hypotensive effect of weight reduction overrode the effect of reduced antihypertensive medication. Urinary sodium excretion at 5 months was not significantly different from that at zero month in both groups.

A weight loss in the subjects with relative body weight equal to or above 110 (3.37 ± 0.51 kg; $4.5 \pm 0.6\%$) was not significantly different from that in the subjects whose relative body weight was below 110 (3.18 ± 0.47 kg; $5.2 \pm 0.9\%$). The MAP also decreased gradually and significantly in both groups. There was no significant difference in the time course of change in MAP between the two groups ($F_{1, 119} = 3.39$, $p > 0.06$). Weight decreased significantly at 5 months by 3.01 ± 0.25 kg ($4.1 \pm 0.3\%$) in the subjects with initial MAP equal to or above 100 mm Hg and by 3.23 ± 0.52 kg ($4.7 \pm 0.8\%$) in the subjects with initial MAP below 110 mm Hg. The MAP decreased significantly in both groups, although there was no significant difference in the time course of change in MAP between the two groups ($F_{1, 83} = 0.10$, $p > 0.7$).

Discussion

The present study demonstrates that a decrease in body weight is associated with a fall in blood pressure in nonobese subjects with essential hypertension who are treated with antihypertensive drugs. Application of relative body weight, as modified for Japanese subjects, revealed only one subject with relative body weight above 130. Thus, almost all the subjects were of normal body weight.

Initial relative body weight in subjects in the weight loss group was higher than that in the group with unchanged weight. This finding suggests that weight reduction is more beneficial to overweight hypertensive persons, since it may be easier for such persons to
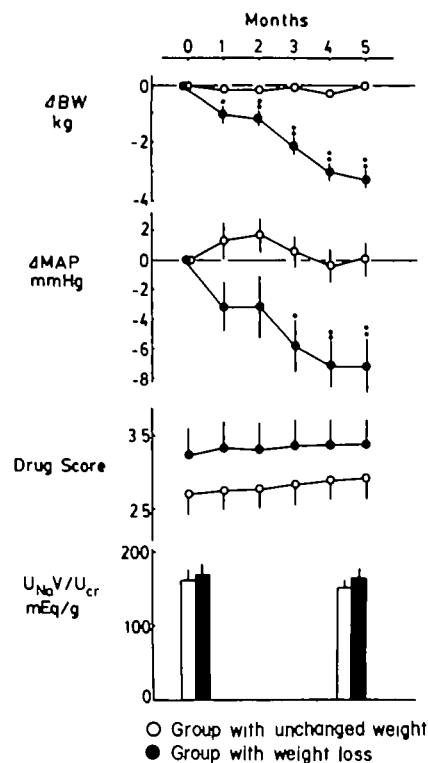

O Group with unchanged weight
● Group with weight loss

FIGURE 2. *The effect of weight loss (ΔBW) on the change in mean arterial pressure (ΔMAP) in subjects whose antihypertensive medication (Drug Score) remained unchanged. Bottom panel shows the 24-hour urinary sodium excretion ($U_{Na}V$) corrected by 24-hour urinary creatinine excretion (U_{Cr}). Asterisks represent the significant difference from control (0):* $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

complete a weight reduction program. Regardless of initial weight, however, a considerable drop in blood pressure can occur after significant weight loss. Decrease in blood pressure associated with weight reduction thus occurred in subjects of normal weight as well as in obese hypertensive subjects.

Body mass index (22.5) and relative body weight (100.8) of the Japanese population are still near ideal when compared with those of American and European countries (25–27; 115–123).[19, 20] The Japanese population has gradually gained weight during the four decades following World War II. Goto and Abe[21] reported that body mass index in all Japanese over 30 years old increased at least by 1.0 in the three decades since 1950. The report revealed a significant weight gain in those of more recent generations when they reached 40 to 50 years of age.[21] In the present study we also found that the subjects displayed a similar tendency of weight gain that commenced in young adulthood and continued through middle to old age. In comparison with their weight in young adulthood, almost all the subjects were "overweight" by ages 40 to 50 years, although they could not yet be regarded as "obese." Even normal weight or lean hypertensive subjects gained weight during the decades of adulthood. Therefore, a drop in blood pressure should be attained in subjects of almost all body types by reducing excess fat
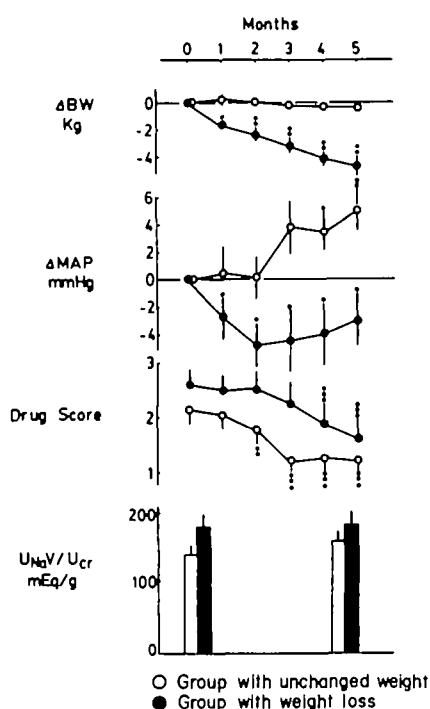
FIGURE 3. *The effect of weight loss on the change in mean arterial pressure (ΔMAP) in subjects whose antihypertensive medication (Drug Score) was decreased during the diet program. See Figure 2 for key to other abbreviations.*

gained over these decades. The regression equation we obtained from the changes in weight and blood pressure predicts a fall of 1.79 mm Hg in MAP per kilogram of weight loss. This value obtained from normal weight subjects is comparable to 1.83 mm Hg per kilogram of weight loss observed in the Evans County Study[7] and in the study by Ramsay et al.[8] of obese patients. These cumulative results suggest that, regardless of initial body weight, weight loss is associated with reduction in blood pressure.

Present results also revealed that, regardless of the initial level of blood pressure, moderate weight loss uniformly influenced blood pressure reduction. Since the drug score in the weight loss group was significantly higher than that in the group with unchanged weight, despite approximately similar initial blood pressure between the two groups, severity of hypertension in the former was at least equal to or higher than that in the latter. Therefore, it is evident that a fall in blood pressure associated with weight loss occurs over a wide range of hypertension. Reisin et al.[9] and Tuck et al.[12] also supported such results as they demonstrated that all obese hypertensive patients, at any level of blood pressure, whether treated with antihypertensive drugs or not, showed similar depressor responses in blood pressure to weight loss.

The mechanism by which blood pressure is reduced by weight loss has not been elucidated. Sodium restriction has been proposed as one of the factors in obese hypertensive persons.[22, 23] Dahl et al.[22] suggested that salt intake is ordinarily reduced pari passu with food

intake in hypertensive patients who are also on a weight reduction diet. However, present results demonstrated that urinary sodium excretion at the start and at the end of the weight reduction program was similar in all the study groups. Two recent studies have also reported that sodium restriction is not a prerequisite for a fall in blood pressure in the course of weight loss in obese patients.[9, 11]

Our results suggest strong additional evidence that the hypotensive effect of weight reduction occurs independently of sodium intake. Our subjects actually had excessive salt intake, although they were instructed to maintain a low salt diet. The northeastern part of Japan, where the study was conducted, is noted for having the highest salt intake in the world.[24, 25] Comparison of urinary sodium excretion at the start and the end of the program with that at the initial attendance in the outpatient clinic (238 ± 35 mEq/g creatinine; $n = 81$) reveals that these subjects were actually on a relatively low salt diet during the study; however, they did not succeed in reducing salt intake to below 10 g/day, which indicates that sufficient salt restriction is extremely difficult in the northern area of Japan. Thus, the subjects had a great surplus of salt over their set point for sodium homeostasis[26] in the control as well as in the weight reduction period, although they were on a low salt diet regimen.

Extreme dietary restriction of sodium to below 10 mmol/day is known to reduce blood pressure in hypertension.[27, 28] An intake below 100 mmol/day is expected to control hypertension[27] and below 35 mmol/day to eliminate it[28]; however, salt intake in our subjects was quite excessive when compared with levels of 10 to 100 mmol/day. Even if these subjects achieved some reduction in salt intake during the weight reduction program, the amount would be too small to make up for the excessive daily salt intake. Furthermore, a heterogeneous blood pressure response was observed when hypertensive patients were treated by sodium restriction.[29-31] Even in the most convincing study of the effect of sodium restriction, blood pressure either remained unchanged or rose in one third of the patients during a low sodium diet.[28] On the other hand, we found that weight reduction induced a homogeneous blood pressure response in the hypertensive subjects. Thus, we conclude that the hypotensive effect of weight reduction occurs independently of sodium intake. However, an indirect effect of weight reduction on blood pressure through a sodium mechanism cannot be ruled out, since fasting is well known to cause natriuresis and fat loss may decrease total exchangeable sodium, thereby inducing decreases in blood volume and cardiac output and modification of a centrally mediated cardiovascular control mechanism or peripheral vascular reactivity.

In the present study, 46% of the subjects lost more than 2 kg through moderate caloric restriction, while the remaining subjects' weight was either unchanged or increased slightly. Although it is possible that the subjects who lost over 2 kg during the weight reduction program also complied with their antihypertensive

medication regimens while the remaining subjects were noncompliant, certain findings negate such a possibility. First, although blood pressure in the group with unchanged weight revealed sustained hypertension before treatment, it was well controlled at the start of the program. Second, a decrease in antihypertensive medication in the group with unchanged weight elevated blood pressure, which would not have happened if the subjects had been noncompliant with antihypertensive medication regimens.

An important question in the care of hypertensive patients whose blood pressure is controlled by drugs is whether the drugs are still needed.[32] Since the reduction of antihypertensive medication resulted in elevated blood pressure in the present study, we conclude that most patients still need drugs to control blood pressure. This result is consistent with that of Dustan et al.,[33] who found that relatively few hypertensive subjects could sustain a reduction of blood pressure without medication. However, it is apparent that drug treatment is costly and may have long-term adverse effects.[3, 14, 15] Therefore, our finding that after significant weight loss nonobese subjects could maintain desirable blood pressure levels even after reduction of antihypertensive medication is important. In obese patients, weight loss induced a fall in blood pressure that led to reduction or withdrawal of antihypertensive drugs.[7, 8, 13] The present results clearly demonstrated that, even in normal weight hypertensive subjects, weight loss can induce a fall in blood pressure that leads to a reduced need for antihypertensive drugs; the effect of a 4-kg weight loss was equivalent to that of antihypertensive medication amounting to a 1.0 drug score.

Acknowledgments

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