Moderate Sodium Restriction Enhances the Pressor Response to Hyperlipidemia in Obese, Hypertensive Patients

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The effect of dietary sodium restriction on insulin, lipids, and blood pressure has been controversial. Evidence suggests that adverse short-term effects in response to very low-salt diets do not persist long-term with modest sodium restriction. In this study, the effects of modest dietary sodium restriction (60 and 120 mmol sodium) were measured for 3 weeks in 12 lean normotensives and 10 obese hypertensives. Blood pressure, plasma lipids, and the pressor response to an infusion of Intralipid and heparin were obtained. In contrast to previous reports concerning very low-salt diets, obese hypertensives did not manifest a pressor response or an adverse lipid effect with moderate salt restriction. Obese hypertensives were not more salt-sensitive than lean normotensives and did not manifest a different hemodynamic response to 4-hour infusion of Intralipid and heparin while on the 120-mmol/day salt diet. During the 60-mmol/day salt diet, however, plasma triglycerides increased more in obese than in lean volunteers during the Intralipid and heparin infusion (398±38 vs. 264±18 mg/dL; p<0.05), and there were greater increases in mean blood pressure (12±2 vs. 7±2 mm Hg; p<0.05) and systemic vascular resistance (111±38 vs. −25±44 dyne·sec·cm–5) as well as a larger decrease in small artery compliance (−2.5±0.6 vs. −0.4±0.6 mL/mm Hg × 100; p<0.05). These data suggest that modest dietary sodium restriction in obese hypertensives does not adversely affect baseline blood pressure or lipids, but it does magnify their adverse lipid and hemodynamic response to fat loading. (J Clin Hypertens. 2002;4:173–180) ©2002 Le Jacq Communications, Inc.

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Dietary sodium restriction has been recommended as treatment for hypertension for more than 50 years.[1] However, not all hypertensive patients are salt-sensitive, and some potentially adverse metabolic and neurohumoral changes can result from very low-salt diets, especially in the short term. We observed that a very low-salt diet (20 mmol/day) for 7 days in relatively young, obese, hypertensive, dyslipidemic subjects was associated with increases in fasting insulin, triglycerides, and low-density lipoprotein (LDL) cholesterol as well as a greater insulin response to an oral glucose load. Plasma renin and aldosterone tended to rise more, and 24-hour mean blood pressure increased, in subjects at high cardiovascular risk, relative to low-risk subjects.[2] Others have also observed that LDL cholesterol rose more during short-term exposure to a very low-salt diet in subjects with a more intense counter-regulatory response.[3–7] The notion that a low-salt diet can raise blood pressure is controversial.[8,9] The utility of continued disagreement on the merits of very low-salt diets is limited in acculturated societies, since reducing and sustaining such low levels of dietary sodium is impractical. A more useful question is whether the adverse effects observed in the short term with very low-salt diets are seen over the long term with more modest sodium restriction.[6,10–12]

Raising fatty acids appears to increase neurovascular tone and reactivity and to raise blood pressure.[13]

Table I. Blood Pressure and Heart Rate at the Qualifying Visit and 24-Hour Urinary Sodium Excretion and Weight After 3 Weeks on Low-Salt Diets

VARIABLE	OH GROUP (N=10)	LN GROUP (N=12)	*P* VALUE
Systolic BP (mm Hg)	131±4	106±3	<0.0001
Diastolic BP (mm Hg)	88±2	71±2	<0.0001
Heart rate (beats/min)	76±2	70±2	0.09
Triglycerides (mg/dL)	308±106	80±5	0.03
Total cholesterol (mg/dL)	202±14	178±7	0.05
HDL-cholesterol (mg/dL)	40±3	66±3	<0.0001
LDL-cholesterol (mg/dL)	113±13	95±6	0.21
VLDL-cholesterol (mg/dL)	41±4	16±1	<0.0001
Castelli I	5.5±0.9	2.7±0.1	0.003
Castelli II	2.6±0.3	1.5±0.1	0.0003
Urinary salt excretion (mmol/V) (60-mmol/day salt diet)	61±14	68±18	NS
Urinary salt excretion (mmol/V) (120-mmol/day salt diet)	145±21	121±19	NS
Weight (kg) (60-mmol/day salt diet)	91±5	60±3	<0.0001
Weight (kg) (120-mmol/day salt diet)	93±4	60±3	<0.0001

Values are means±SEM.
OH=obese hypertensive; LN=lean normotensive; BP=blood pressure; HDL=high-density lipoprotein; LDL=low-density lipoprotein; VLDL=very low-density lipoprotin; NS=not significant

Our group has been especially interested in the role of resistance to insulin's nonesterified fatty acid (NEFA)-lowering action in obesity hypertension. Plasma NEFAs rose during very low-salt diets, despite a marked increase in fasting insulin in obese subjects with the risk factor cluster. Therefore, we examined, in lean normotensive and obese hypertensive subjects, the effects of modest dietary sodium restriction on the hyperlipidemic and hemodynamic response to an infusion of Intralipid (an emulsion of triglycerides containing mainly unsaturated fatty acids) and heparin (which activates endothelial lipoprotein-lipase and hydrolyzes fatty acids from triglycerides). This combination raises plasma NEFAs and triglycerides.

MATERIAL AND METHODS

Study Population

Twenty-two volunteers (21–49 years old) participated in this study. Twelve were lean normotensives (body mass index, >25 kg/m^2; blood pressure consistently <130/85 mm Hg) and 10 were obese hypertensives (body mass index, >27 kg/m^2; blood pressure 130–159/85–99 mm Hg). Each volunteer signed an informed consent document approved by the Office of Research Protection and Integrity at the Medical University of South Carolina.

Blood Pressure and Heart Rate Measurements

Blood pressure was measured with a mercury sphygmomanometer and an appropriately sized cuff. Systolic blood pressure was defined by the first Korotkoff sound and diastolic blood pressure by the disappearance of the last Korotkoff sound (phase 5). The qualifying blood pressure was measured in the seated position after a 5-minute rest. Blood pressure was measured in triplicate at 2-minute intervals and the mean of the last two readings was used. Heart rate was measured during screening by palpation of the radial artery pulse for 30 seconds between the 2nd and 3rd measurement of casual (seated) blood pressure.

Salt Diets

After the screening and qualifying visit, subjects were instructed to follow a 60-mmol/day and 120-mmol/day NaCl diet for 3 weeks each. Twenty-four-hour urine samples were collected for measurement of sodium after 3 weeks on the 60-mmol/day and after 3 weeks on the 120-mmol/day salt diet.

Infusion of Intralipid and Heparin to Raise Plasma NEFAs

Intralipid 20% (Baxter Healthcare Corporation, Glendale, CA) was infused at 0.8 mL/m²/min. Heparin (1000-U bolus, followed by 200 U/hr) was given to activate endothelial lipoprotein lipase and accelerate hydrolysis of fatty acids from the glycerol backbone of the triglycerides.[14]

Biochemical Measurements

Total cholesterol was measured by the colorimetric method, triglycerides were measured by the fluorometric method, and high-density lipoprotein (HDL) cholesterol was prepared from whole plasma by precipitation with phosphotungstate-$MgCl_2$.[15] The LDL cholesterol and very low-density lipoprotein (VLDL) cholesterol were calculated.[16]

Hemodynamic Variables

Arterial compliance and other hemodynamic information were obtained by analysis of the radial artery pulse waveform via the HDI/PulseWave CR-2000 (Hypertension Diagnostics, Inc., Eagan, MN).[17] The arterial tonometer was placed securely over the left radial artery, while the blood pressure cuff was placed on the right upper arm. Hemodynamic measurements were obtained at 5-minute intervals after 30 minutes of rest and at 2 and 4 hours during the Intralipid and heparin infusion.

Statistical Analysis

Data are reported as means±SEM. Blood pressure, heart rate, and biochemical data from the screening visit were assessed by means of paired and nonpaired Student *t* tests. Twenty-four-hour urine sodium and weight on the two study diets were also assessed with paired and nonpaired Student *t* tests. Changes in triglycerides and NEFAs during the Intralipid and heparin infusion on the two study diets within and between the two groups were assessed with the general linear model for repeated measures. Changes in hemodynamic variables were analyzed with the general linear model for repeated measures. All statistical analyses were performed with the SPSS/PC 10.0 statistical software package. A p value of <0.05 was accepted as statistically significant.

RESULTS

The 12 lean, normotensive volunteers were 38±1 years old, with a body mass index of 22.0±0.5 kg/m². Ten were women, six were Caucasian, five were African American, and one was Hispanic. The 10 obese hypertensives were 40±2 years old, with a body mass index of 31.0±1.2 mg/m². Three were women, eight were Caucasian, and two were African American.

Blood pressure, heart rate, weight, and biochemical data obtained on the qualifying visit, as well as mean 24-hour urinary sodium excretion on the 60-mmol/day and 120-mmol/day salt diets, are shown for both groups in Table I. Salt sensitivity, defined by a mean blood pressure on 120 mmol sodium/ day of ≥5 mm Hg above that on 60 mmol sodium/ day, occurred in four of the 12 lean normotensives and four of the 10 obese hypertensives. Counter-regulation,[6] defined by a mean blood pressure on 60 mmol sodium/day of ≥5 mm Hg above that on 120 mmol sodium/day, occurred in two lean normotensives and none of the obese hypertensives. Salt resistance, defined by a blood pressure difference of <5 mm Hg between the two diets, occurred in six of the 12 lean normotensives and six of 10 obese hypertensives.

Plasma NEFAs increased significantly ($p<0.05$) in both groups after 2 and 4 hours of Intralipid and heparin infusion, on both the 60-mmol/day and 120-mmol/day salt diets (Figure 1). Plasma triglycerides

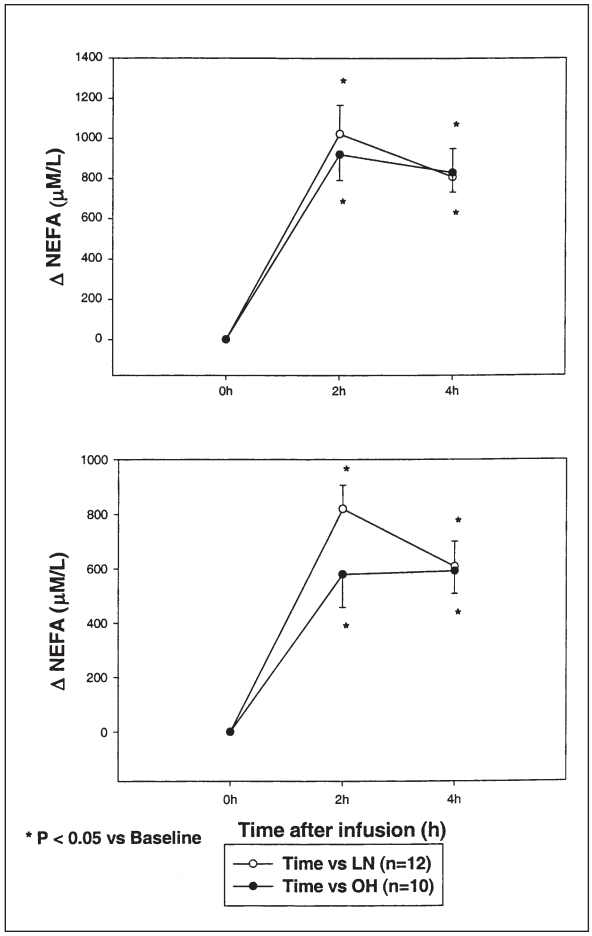

Figure 1. Changes in nonesterified fatty acid (NEFA) plasma concentration (means±SEM) after Intralipid and heparin infusion in lean, normotensive (LN, [o]) and obese, hypertensive (OH, [•]) subjects on 120-mmol/day (top) and 60-mmol/day (bottom) salt diets

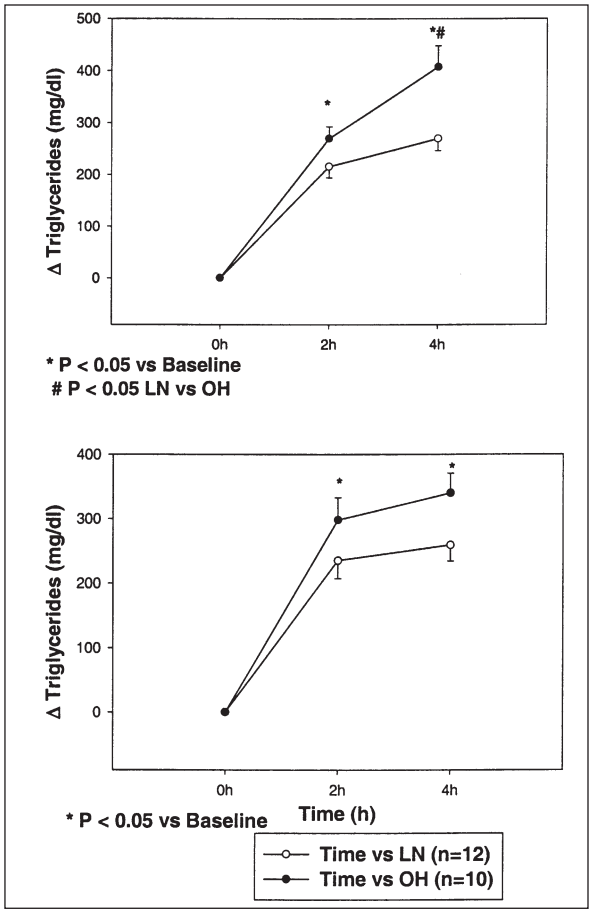

Figure 2. Plasma triglycerides in lean, normotensive (LN, [o]) and obese, hypertensive (OH, [•]) subjects after Intralipid and heparin infusion on 60-mmol/day (top) and 120-mmol/day (bottom) salt diets (means±SEM)

increased significantly (p<0.05) more in obese hypertensives than in lean normotensives after 4 hours of Intralipid and heparin infusion during the 60-mmol/day salt diet (Figure 2). Baseline systolic, diastolic, and mean blood pressures, heart rate, cardiac output, cardiac index, systemic vascular resistance, total vascular impedance, cardiac ejection time, stroke volume, and large as well as small artery elasticity indices were not different between the two diets within the lean normotensive and obese hypertensive groups (Table II). The obese hypertensive group, however, showed higher systolic, diastolic, and mean blood pressures as well as higher cardiac output and stroke volume than the lean normotensive group (Table II) on both diets. Mean blood pressure and systemic vascular resistance increased, while the small artery elasticity index decreased significantly more (p<0.05) in obese hypertensives than lean normotensives after 4 hours of Intralipid and heparin infusion on the 60 mmol/day salt diet (Figure 3). The decline in small artery elasticity in obese hypertensives correlated inversely with the increase in plasma triglycerides from baseline to the 4th

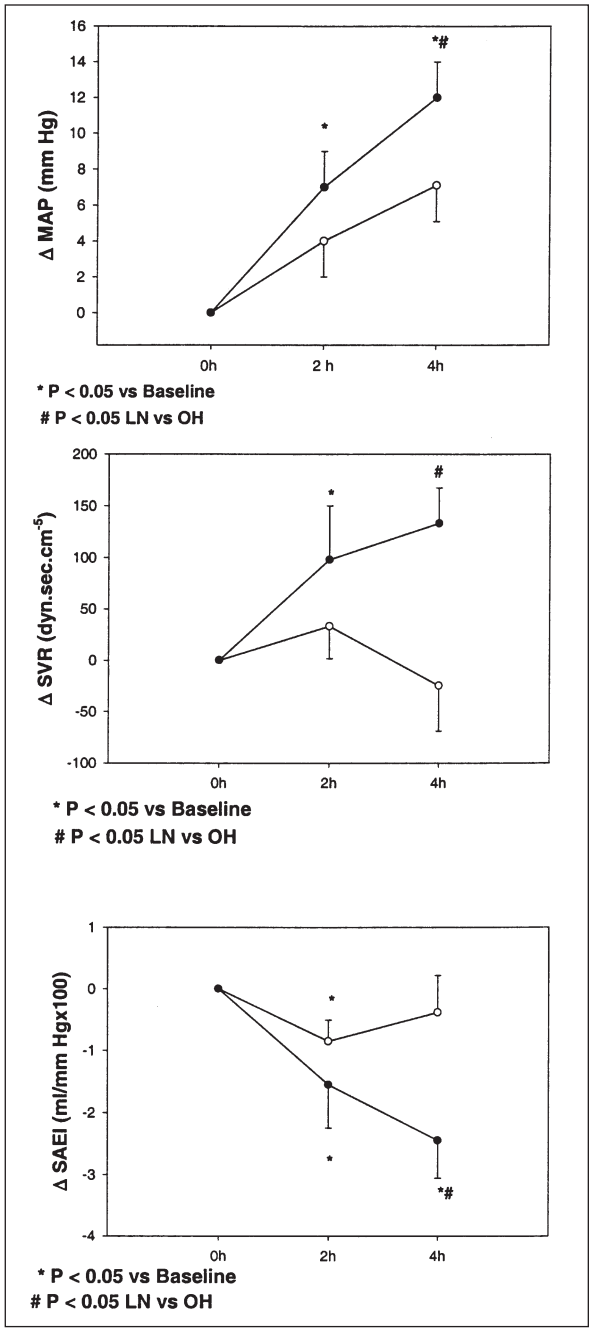

Figure 3. Changes in mean arterial pressure (MAP), systemic vascular resistance (SVR), and small artery elasticity index (SAEI) in lean, normotensive (LN, [o]) and obese, hypertensive (OH, [•]) subjects during Intralipid and heparin infusion after 3 weeks on the 60-mmol/day salt diet (means±SEM)

hour of the Intralipid and heparin infusion on the 60-mmol/day salt diet (Figure 4). Furthermore, the obese hypertensives showed a positive correlation between stroke volume and the increase in plasma triglycerides between baseline and the 4th hour of the Intralipid and heparin infusion while on the 60-mmol/day salt diet (Figure 4). Heart rate, cardiac output, cardiac index,

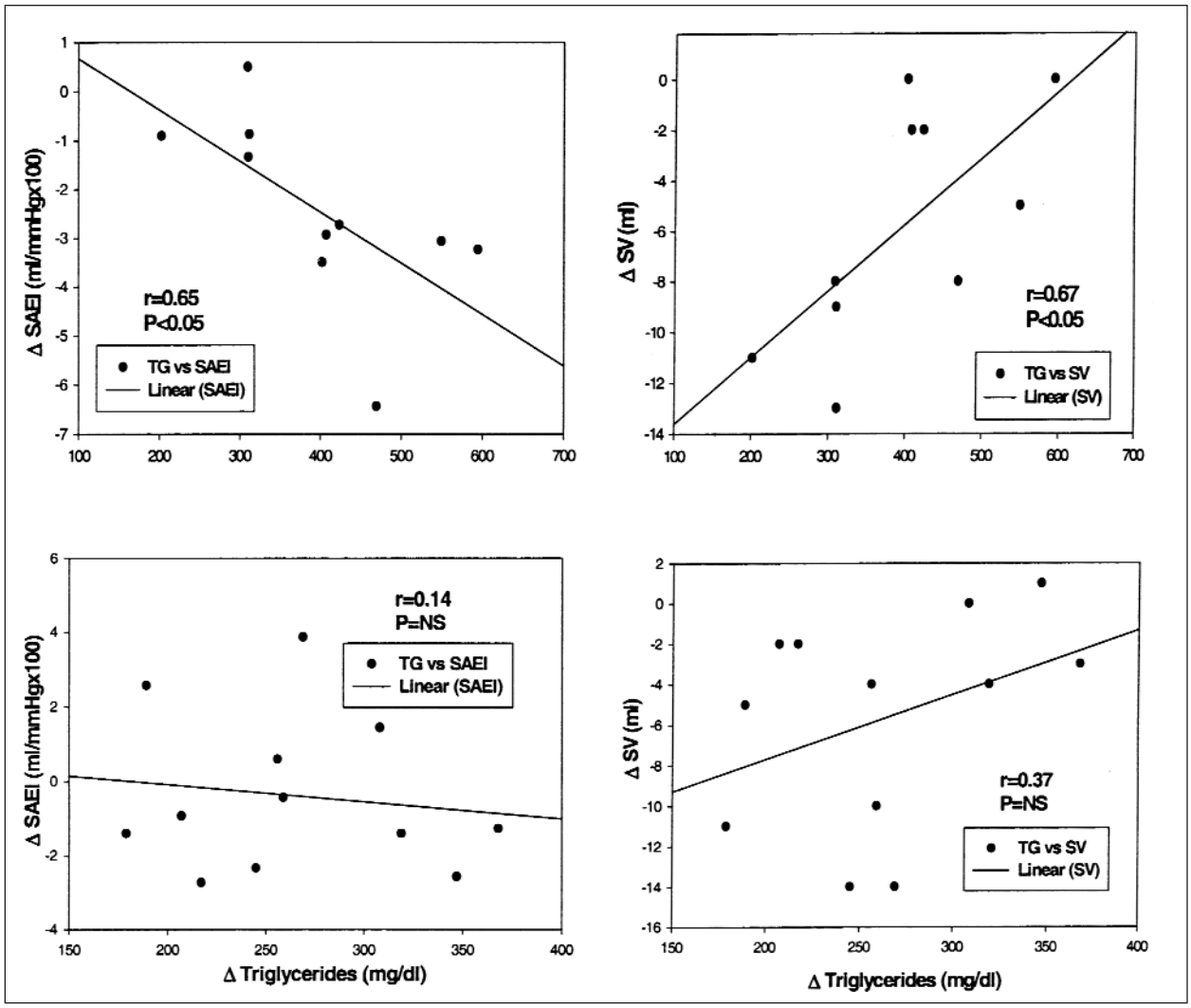

Figure 4. Correlations between small artery elasticity index (SAEI, left side), stroke volume (SV, right side), and triglycerides (TG) in obese, hypertensive patients (top, [•]) and lean, normotensive controls (bottom, [o]) after 4 hours of Intralipid and heparin infusion on the 60-mmol/day salt diet

total vascular impedance, cardiac ejection time, stroke volume, and the large artery elasticity index did not differ between groups during Intralipid and heparin infusion on either the 60-mmol/day or 120-mmol/day salt diet (data not shown).

DISCUSSION

The "high" sodium diet in this study was defined as 120 mmol daily. This was based on the fact that participants in the Dietary Approaches to Stop Hypertension (DASH) study consumed an average of 120 mmol of sodium daily.[18] While on this level of sodium intake, systolic blood pressure declined significantly in hypertensive patients on a diet high in fruits and vegetables, with low-fat dairy products. However, the more recent DASH sodium trial has shown that blood pressure declines even more when sodium intake is limited to ≈50–60 mmol/day.[19] In light of these important considerations, we assessed the dietary effects of 120 as compared to 60 mmol/day of sodium on baseline hemodynamic and metabolic variables, as well as the response to an infusion of Intralipid and heparin.

The obese, hypertensive subjects were not more salt-sensitive than the lean, normotensive volunteers in this study, as assessed by differences in blood pressure between the 120-mmol/day and 60-mmol/day sodium diets for 3 weeks each. These findings are consistent with previous work in our laboratory in which blood pressure responses to a very low-salt diet were measured after 7 days.[2] However, unlike subjects with evidence of the risk factor cluster who had a pressor response to a very low-salt diet for 7 days,[5] we did not observe an increase in blood pressure among any obese subjects with longer-term adherence to moderate salt restriction in this study.

Table II. Hemodynamic Data for Lean, Normotensive (LN) and Obese, Hypertensive (OH) Subjects After 3 Weeks on Each Salt Diet

Variable	OH Group (N=10)		*P* Value	LN Group (N=12)		*P* Value
	60 mmol/d Salt Diet	120 mmol/d Salt Diet		60 mmol/d Salt Diet	120 mmol/d Salt Diet	
SBP (mm Hg)	130±5	131±5	NS	108±3*	109±3*	NS
DBP (mm Hg)	77±3	79±2	NS	63±2*	65±2*	NS
MBP (mm Hg)	95±3	99±3	NS	79±2*	81±2*	NS
Heart rate (beats/min)	60±3	61±3	NS	61±1	61±1	NS
Cardiac output (L/min)	6.1±0.3	6.1±0.3	NS	5.1±0.1*	5.1±0.1*	NS
Cardiac index ($L/min/m^2$)	3.0±0.1	3.0±0.1	NS	3.1±0.1	3.2±0.1	NS
Total vascular impedance ($dyne{\cdot}sec{\cdot}cm^5$)	118±10	123±16	NS	138±8	138±15	NS
Large artery elasticity index (mL/mm Hg × 10)	18±1	18±2	NS	16±1	16±1	NS
Small artery elasticity index (mL/mm Hg × 100)	8±1	7±1	NS	6±0.6	7±1	NS
SVR ($dyne{\cdot}sec{\cdot}cm^5$)	1312±72	1354±82	NS	1291±49	1316±60	NS
Stroke volume (mL/beat)	97±3	97±2	NS	85±2*	85±3*	NS
CET (msec)	360±7	357±9	NS	364±5	366±6	NS

Data are means±SEM.
SBP=systolic blood pressure; DBP=diastolic blood pressure; MBP=mean blood pressure; SVR=systemic vascular resistance; CET=cardiac ejection time; NS=not significant; *$p<0.05$, between-group comparison on 60-mmol/day and 120-mmol/day salt diet

Obese, hypertensive subjects had higher values for total cholesterol, very LDL cholesterol, and triglycerides and lower levels of HDL cholesterol than lean, normotensive subjects at baseline, and these values did not change in either group after modest dietary sodium restriction. Grey and colleagues[11] found no changes in lipid metabolism after moderate salt restriction in normal subjects. In contrast, we and many others have reported adverse changes in total and LDL cholesterol after an average of 7 days on very low-salt diets.[2–4,20] There is, however, one report[12] of a direct correlation between the decline in urinary sodium excretion and the decrease in HDL cholesterol in hypertensive patients following moderate dietary salt restriction.

Changes in plasma triglycerides and NEFAs were measured at fasting baseline and during the 4-hour infusion of Intralipid and heparin on both diets. Plasma NEFAs at baseline were higher in obese hypertensives. However, plasma NEFAs rose similarly in both groups during the infusion of Intralipid and heparin on the 120-mmol/day and 60-mmol/day salt diets (Figure 1). Plasma triglycerides increased significantly more in obese hypertensives than in lean normotensives during the infusion of Intralipid and heparin on the 60-mmol/day salt diet (Figure 2). Mean blood pressure increased significantly more in obese hypertensives than in lean normotensives in response to short-term hyperlipidemia during the 60-mmol/day salt diet. The greater rise in blood pressure in obese hypertensives probably resulted from the larger increase in systemic vascular resistance and the larger decline in small artery elasticity (Figure 3). These data are consistent with evidence from our laboratory and others' indicating that raising blood lipids can acutely affect the function of blood vessels.[13,21]

Small artery compliance fell more in obese hypertensives than in lean normotensives during the infusion of Intralipid and heparin. The greater decline in the small artery distensibility of hypertensives probably reflected their larger increase in plasma lipids, since the changes were inversely correlated. Inhibition of nitric oxide synthase with N^G-monomethyl-L-arginine significantly reduces small artery compliance.[22] Therefore, the rise in plasma NEFAs may have reduced small artery compliance during the infusion of Intralipid by inhibiting nitric oxide synthase and reducing endothelium-dependent dilation. This point notwithstanding, our data indicate that modest dietary sodium restriction can impair lipid clearance in response to a fat load and adversely affect vascular function in obese subjects with evidence of the insulin resistance syndrome.

While the utility of our findings is limited by the short-term nature of the intervention, Neutel a nd colleagues[23] reported a positive correlation between proximal and distal vascular compliance and multiple components of the metabolic syndrome, including plasma insulin, triglycerides, total cholesterol, and HDL cholesterol, in hypertensive and normotensive subjects on their usual diets. Collectively, the observations from all of these studies raise the possibility that elevated lipids have adverse short- and long-term effects on vascular compliance.

We proposed that dietary sodium restriction achieved through changes in food selection, which typically include more low-fat foods, is strongly supported by the literature. However, we expressed reservations about the long-term benefits of removing only sodium from foods that are high in fat and sugar.[24] This study does not resolve that question. However, the findings raise the possibility that modest sodium restriction may exacerbate the exaggerated postprandial lipemia after a high-fat meal in subjects with the metabolic syndrome (low HDL cholesterol, increased triglycerides, obesity, and hypertension)[25] and adversely affect vascular function. Until the question is resolved, it seems prudent to recommend salt restriction in combination with a low-fat diet for obese, hypertensive patients.

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REFERENCES

1 Kempner W. Treatment of hypertension vascular disease with rice diet. *Am J Med*. 1948;4:545–577.
2 Egan BM, Weder AB, Petrin J, et al. Neurohumoral and metabolic effects of short-term dietary NaCl restriction in men. Relationship to salt-sensitivity status [see comments]. *Am J Hypertens*. 1991;4:416–421.
3 Iwaoka T, Umeda T, Ohno M, et al. The effect of low and high NaCl diets on oral glucose tolerance. *Klin Wochenschr*. 1988;66:724–728.
4 Masugi F, Ogihara T, Hashizume K, et al. Changes in plasma lipids and uric acid with sodium loading and sodium depletion in patients with essential hypertension. *J Hum Hypertens*. 1988;1:293–298.
5 Egan BM, Stepniakowski K, Goodfriend TL. Renin and aldosterone are higher and the hyperinsulinemic effect of salt restriction greater in subjects with risk factors clustering. *Am J Hypertens*. 1994;7:886–893.
6 Ruppert M, Overlack A, Kolloch R, et al. Effects of severe and moderate salt restriction on serum lipids in nonobese normotensive adults. *Am J Med Sci*. 1994;307(suppl 1):S87–S90.
7 Sharma AM, Arntz HR, Kribben A, et al. Dietary sodium restriction: adverse effect on plasma lipids. *Klin Wochenschr*. 1990;68:664–668.
8 MacGregor GA, Markandu ND, Best FE, et al. Double-blind randomised crossover trial of moderate sodium restriction in essential hypertension. *Lancet*. 1982;1:351–355.
9 Longworth DL, Drayer JI, Weber MA, et al. Divergent blood pressure responses during short-term sodium restriction in hypertension. *Clin Pharmacol Ther*. 1980;27:544–546.
10 de Wardener HE, Kaplan NM. On the assertion that a moderate restriction of sodium intake may have adverse health effects [editorial]. *Am J Hypertens*. 1993;6:810–814.
11 Grey A, Braatvedt G, Holdaway I. Moderate dietary salt restriction does not alter insulin resistance or serum lipids in normal men. *Am J Hypertens*. 1996;9:317–322.
12 McCarron DA, Weder AB, Egan BM, et al. Blood pressure and metabolic responses to moderate sodium restriction in isradipine-treated hypertensive patients. *Am J Hypertens*. 1997;10:68–76.
13 Stojiljkovi MP, Lopes HF, Lee CG, et al. Hemodynamic effect of lipids in humans. *Am J Physiol*. 2001; 280:R1674–R1679.
14 Haastrup AT, Stepniakowski KT, Goodfriend TL, et al. Intralipid enhances alpha1-adrenergic receptor mediated pressor sensitivity. *Hypertension*. 1998;32:693–698.
15 De Bruin TW, Brouwer CB, Gimpel JA, et al. Postprandial decrease in HDL cholesterol and HDL apo A-I in normal subjects in relation to triglyceride metabolism. *Am J Physiol*. 1991;260:E492–E498.
16 Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499–502.
17 McVeigh GE, Bratteli CW, Morgan DJ, et al. Age-related abnormalities in arterial compliance identified by pressure pulse contour analysis: aging and arterial compliance. *Hypertension*. 1999;33:1392–1398.
18 Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med*. 1997;336: 1117–1124.
19 Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001;344:3–10.
20 Midgley JP, Matthew AG, Greenwood CM, et al. Effect of reduced dietary sodium on blood pressure: a meta-analysis of

randomized controlled trials. *JAMA* 1996;275:1590–1597.
21 Bulow J, Madsen J, Hojgaard L. Reversibility of the effects on local circulation of high lipid concentrations in blood. *Scand J Clin Lab Invest*. 1990;50:291–296.
22 Gilani MK, Rajala S, Bank AJ, et al. Differences in large and small artery response to acute inhibition of nitric oxide synthase in human subjects. *Am J Hypertens*. 2000;13:187.
23 Neutel JM, Smith DH, Graettinger WF, et al. Dependency of arterial compliance on circulating neuroendocrine and metabolic factors in normal subjects. *Am J Cardiol*. 1992;69:1340–1344.
24 Egan BM, Lackland DT. Biochemical and metabolic effects of very-low-salt diets. *Am J Med Sci*. 2000;320:233–239.
25 Meijssen S, Cabezas MC, Twickler TB, et al. In vivo evidence of defective postprandial and postabsorptive free fatty acid metabolism in familial combined hyperlipidemia. *J Lipid Res*. 2000; 41:1096–1102.