Effect of Weight Loss on Blood Pressure, Arterial Compliance, and Insulin Resistance in Normotensive Obese Subjects

ROSA SCHNEIDER, MD; BORIS GOLZMAN, MD; SVETLANA TURKOT, MD; JACOB KOGAN, MD; SHMUEL OREN, MD

ABSTRACT: *Background*: Obesity is characterized by insulin resistance and hyperinsulinemia that may elevate arterial pressure due to sympathetic overactivity and volume overload. The aim of the study is to measure hemodynamic parameters and metabolic variables in obese normotensive subjects. *Methods*: Twenty-four normotensive, overweight subjects from our medical staff were enrolled. They had personal and group meetings with a physician, dietician, and psychologist to improve their compliance with regard to physical activity and personal low-calorie diet. In addition, each subject was given orlistat 120 mg three times daily for 12 weeks. Noninvasive hemodynamic parameters including arterial compliance were measured using radial artery pulse wave analysis, at the beginning and 1 month after taking the last dose of Orlistat, and insulin resistance was calculated using HOMA score. *Results*: At the end of the 3-month period, the average weight was reduced from 89.5 ± 12 kg to 81.5 ± 9 kg. The systolic arterial pressure was reduced from 128 ± 12 mm Hg to 121 ± 10 mm Hg and diastolic arterial pressure was reduced from 75.4 ± 9 mm Hg to 69.6 ± 7 mm Hg. Arterial compliance measurements showed significant improvement in large artery compliance from 13 ± 4 to 15.8 ± 3.6 while no change occurred in small arteries. The insulin sensitivity assessed by HOMA score improved significantly from 6.5 ± 4.5 to 4.8 ± 3.1 with weight reduction. *Conclusions*: Our data show that weight loss is accompanied by lowering of blood pressure, even in normotensive obese patients. This weight loss brings about an improvement in insulin resistance and a rise in large artery compliance, whereas no change occurs in small artery compliance. **KEY INDEXING TERMS:** Arterial compliance; Hemodynamic parameters; Normotensive; Insulin resistance; Metabolic variables. **[Am J Med Sci 2005;330(4):157–160.]**

Overweight and obesity are the most common nutritional disorders in the United States.[1] Obesity is the main component of the metabolic syndrome and as such is characterized by insulin resistance, hyperinsulinemia, and increased frequency of diabetes mellitus, hypertension, and hyperlipidemia.[2,3] The hyperinsulinemia in obese patients may elevate arterial blood pressure, owing to sympathetic overactivity and volume overload induced by increased Na reabsorbtion in the kidneys.[4] Using various techniques, an association was found between arterial wall stiffness and insulin resistance in subjects with clustering of variables of the insulin resistance syndrome, including body mass index (BMI).[5–8] Previous studies have shown that while the obese patient is normotensive, his peripheral resistance is low.[9–10] However, once the obese patient is hypertensive, his peripheral resistance becomes inappropriately normal or even above normal.

Arterial and venous compliance were measured in obese subjects (both normotensive and hypertensive) using various methods. The data are conflicting; most of the studies showed decreases in arterial compliance in obese subjects[9,11–13] that can be improved by weight reduction[14,15]; however, few investigators suggest that obesity was associated with increased arterial compliance.[10,16–17]

There are many techniques for losing weight: behavioral, pharmacological, and even surgical, but most of them are frustrating and the success rate is very limited.

Orlistat (Xenical) is a non-systemically acting agent for the long-term management of obesity that partially blocks dietary fat absorption by inhibiting gastrointestinal lipases.[18] Orlistat in combination with a mildly hypocaloric diet promotes weight loss,

From the Department of Nephrology and Hypertension (RS) and the Department of Internal Medicine A (BG, ST, JK, SO), Faculty of Health Sciences, Ben Gurion University Barzilai Medical Center Campus, Ashkelon, Israel.

Submitted for publication December 30, 2004.

Accepted for publication June 28, 2005.

Correspondence: Shmuel Oren, Prof., Department of Internal Medicine, Barzilai Medical Center, Ashkelon 78306, Israel (E-mail: oranim@barzi.health.gov.il).

enhances long-term weight maintenance after weight loss, and improves serum lipid profiles.

Objective

Our objectives in the present study were to assess insulin resistance using the HOMA score and to examine hemodynamic variables and arterial compliance in obese normotensive subjects during a weight management program, including behavioral and pharmacological treatment.

Methods

Our medical center headed a program aimed at encouraging weight reduction among obese members of the medical staff. Our study was part of this program, and 24 obese subjects who wished to participate made up the study group. The subjects underwent physical examination, blood tests, and a medical history. Subjects with a history of coronary artery disease or peripheral vascular or cardiovascular disease based on symptoms, physical signs, and electrocardiogram (ECG) were excluded, but no imaging tests were done specifically for the study. The study subjects had fasting glucose level lower than 126 mg/dL according to American Diabetic Association diagnostic criteria[19] and blood pressure lower than 140/90 mm Hg according to the JNC7 Report.[20]

No subjects took any cardiovascular drugs during the study period. All the obese subjects were instructed on a nutritionally balanced low-calorie diet containing 30% of calories as fat. They were also instructed by the dietician on uniform sodium intake of no more than 80 m/Eq sodium per day. The energy content of the diet of individual patients was calculated from estimated total daily energy expenditure minus 600 kcal/day. The lowest energy intake allowed was 1200 kcal/day. Patients were encouraged to take three main meals per day. The patients met a dietician to assess dietary compliance at randomization and at week 4, 8, and 12. They also participated in group and individual meetings and were encouraged to perform physical activity to improve their success rate. All the subjects were treated with orlistat 120 mg three times daily for 12 weeks. They had the telephone number of the investigator and they visited the clinic every 2 weeks; the pills were counted to assess compliance with the study protocol. The subjects received medication for the next 2 weeks and were asked about any possible side effects. Fasting plasma glucose and fasting plasma insulin were measured and HOMA score was calculated with the following formula: fasting serum insulin (μU/mL) $\times$ fasting plasma glucose (mmol/L)/22.5, as described by Matthews and coworkers.[21]

Arterial Compliance Measurements

All of the hemodynamic measurements were performed in a silent room, by the same observer between 7:00 AM and 9:00 AM according to the guidelines of the JNC7 Report.[20] The pulse wave analysis was performed twice, before beginning the medication and at the end of the study period, at least 1 month after cessation of orlistat treatment.

The method was previously described in detail.[22,23] Patients were studied while fasting in the morning and having abstained from smoking or from consuming caffeine or alcohol in the previous 12 hours. Radial arterial waveforms were recorded for 30 sec for each subject in the supine position. The pressure transducer amplifier system was connected to a specially designed device (Model CR-2000, hypertension Diagnostics Inc., Eagen, MN). The passive transient response of the arterial vasculature to the initial loading conditions was determined by analyzing the diastolic portion of the pressure pulse waveform. This technique, which has been used extensively,[22–24] was used with a simple noninvasive radial pulse wave recording and a computer analysis of the diastolic decay. This provides separate assessment of the large artery or capacitive compliance (C_1) and small artery reflective or oscillatory compliance (C_2). Studies have demonstrated an age-dependent decline in both C_1 and C_2 parameters, reflecting structural or functional changes in the large conduit arteries as well as in the smaller reflective sites.

Pulse contour analysis of diastolic pressure decay utilizes modified Windkessel model, a well-established electrical system analogue. Components of the diastolic waveform are mapped to the modified Windkessel model equation, comprising components matched to the arterial circulation, namely cardiac output, capacitive and oscillatory compliance, and systemic vascular resistance.[23,24]

Systemic vascular resistance is calculated as mean arterial pressure divided by cardiac output. The mean arterial pressure is derived from waveform analysis, integrating the area under the curve and calculating the mean area of recordings during 30 sec.

The study was approved by the ethics committee of our institute, and all the participants signed a consent form.

Statistics

Data are reported as mean $\pm$ SD and were analyzed using paired samples *t*-test.

Results

Twenty-four overweight subjects were included in the study; only 3 of them were male. Their average age was 44 $\pm$ 11 years; 6 of them were physicians