ABSTRACT. Forty-eight morbidly obese patients were placed on a very low calorie (800 kcal) formula diet (OPTIFAST®) for a 10-week period with the goal of achieving 10% weight loss within this time. Weekly serum leptin measurements were performed to determine whether changes in this adipose protein would serve as a useful marker of acute and chronic weight loss compliance. In the basal state, serum leptin averaged 56.9±5.8 ng/ml (SE) in the 24 successful (S) patients, and 67.7±6.7 ng/ml in the non-successful (N-S) group. During the first week of weight loss there was little change in leptin despite an average weight loss of 2.2%, but after 4 weeks serum leptin decreased by 36% in the S group, and 20% in the N-S group. After 10 weeks, the S group averaged 13.6% weight loss and the serum leptin decreased to 50% of starting levels. In the 24 N-S patients, the mean weight loss was 7.0%, and serum leptin decreased by 22%, remaining unchanged in the final 6 weeks despite a weight loss of 3.6% in this time. On a week-to-week basis serum leptin changed concordantly with weight loss only two-thirds of the time. In a subgroup of 14 patients (8 S+6 N-S), serial assessments of serum leptin, insulin and tumor necrosis factor-α (TNF-α) were performed. Serum insulin levels decreased with weight loss similar in magnitude to that noted for leptin; however, the insulin changes occurred more rapidly. Serum TNF-α also decreased with weight loss, but the weekly changes were more erratic, with a concordance rate of only 48%. In summary, serum leptin, insulin and TNF-α all decreased during a rapid weight loss program but at differing rates and variability, precluding their usefulness as markers of week-to-week weight loss compliance.

INTRODUCTION

Since the identification of the ob gene product, leptin, there has been intense interest in this adipose tissue protein and its potential regulatory role in human obesity (1-6). Considine et al. and others reported elevated serum leptin in obesity and a good correlation between serum leptin and BMI, total fat composition and other parameters of obesity (2, 4, 7-11). The association of obesity with hyperinsulinemia and insulin resistance has long been known (12-14) and more recently tumor necrosis factor-α (TNF-α) has been shown to be produced in adipose tissue (15, 16). Starvation has been reported to drastically lower leptin levels (16, 17) and insulin resistance within hours, and several studies have shown that chronic calorie restriction is associated with lowered serum leptin concentrations (10, 11, 18-21), decreased insulin (9) and TNF-α levels (15). In the present study, we explored whether weekly leptin measurements could serve as a useful marker of weight loss compliance in a population of morbidly obese patients undergoing rapid weight loss with a very low calorie formula diet (VLCD). In a randomly selected subset of this population, serum insulin and TNF-α were measured along with serial leptin levels. Our results confirm decreases in serum leptin, insulin and TNF-α with weight loss, but at differing rates. Variability of these 3 measurements on a week-to-week basis precluded their usefulness as markers of weight loss compliance.

MATERIALS AND METHODS

Data were analyzed from 48 consecutive morbidly obese patients (37 women and 11 men) who completed a 10 week course of a VLCD program using OPTIFAST® (22). The patients’ characteristics are presented in Table 1. Patients were recruited from an inner-city indigent population and were provided services and VLCD free of charge. The population stud-
Leptin, insulin and TNF-α in weight loss

The study was for two-thirds African-American and one-third Hispanic and Caucasian patients. Exclusion criteria were minimal and included: age below 18 years, severe anemia, active cancer, active inflammatory disease (i.e. lupus, enteritis, arthritis), chronic renal or hepatic failure, recent myocardial infarction or cerebrovascular incident. Patients were accepted after completion of a physical examination ECG, blood count (CBC), and chem screen analysis. Patients were instructed to have a light breakfast and to skip lunch prior to their initial visit. Consent was obtained to draw 1 red top tube for leptin measurement in the basal week and at the time of weekly visits held between 14:00-17:00 h, having withheld a mid-day feeding. Thus, weekly blood studies were obtained 6-8 hours after a morning 160-kcal meal. The study was approved by our Institutional Review Board (IRB). Patients were seen by a physician weekly to monitor the progress of the weight loss, and to evaluate potential problems, which proved to be minimal. Only patients who completed the 10-week course were included in this study. Patients who missed visits and/or dropped out during the 10-week period (62%) were not included. There were no significant differences in starting weight, age, basal leptin levels, or gender distribution between patients who completed vs patients who did not complete the 10-week course. The clinical features of these patients are presented in a separate publication (23).

Patients were considered as successful (S) if they lost 10% of their initial weight (24) within the 10-week program, and unsuccessful (N-S) if they did not lose 10% of their starting weight within this time. Serum samples were centrifuged and stored at -80°C until assayed. Leptin assay was performed using RIA Kit (Linco, St. Louis, USA) (25). Intra-assay variation was 6.0% and inter-assay variation was 7.2%. During a 3-month period, samples were split at the time of freezing and assayed for TNF-α and insulin as well as leptin in a subset of 14 patients under study at that time. In this group of patients, 8 were assessed as S and 6 N-S. TNF-α was assayed via enzyme immunoassay technique, using a kit (R&D Systems, Minneapolis, MN, USA). Intra-assay variation for TNF-α assay was 4.8% and inter-assay variation was 6.5%. For the insulin assays, intra-assay variation was 5.7% and inter-assay variation was 7.5%. All samples were defrosted only once, for assay.

Statistical analyses were performed using Student’s t-test. Gender differences in serial leptin values were compared using lesser squares means, and were shown to be not significant (courtesy of Dr. Stanley Von Hagen, Department of Pharmacology, UMDNJ- New Jersey Medical School.

RESULTS

Figure 1 plots basal serum leptin vs BMI in our 48 obese patients along with values obtained from the 4 less obese Authors of this paper. The correlation coefficient of +0.63 confirms studies of Considine et al. (2) and others (8-10) showing increased basal leptin levels with increasing parameters of obesity. The clinical features of the 24 S and 24 N-S patients are presented in Table 1. The S group consisted of 8 men and 16 women, and the N-S group had 3 men and 21 women. This difference was not significant. Age, starting weights, BMI, and co-morbid illnesses were comparable in both groups except for dyslipidemia that was present in 6 S patients but was found in 18/24 of the N-S group. Basal leptin levels in the S group averaged 56.9±5.81 (SE) vs 67.7±6.7 ng/m in the N-S group. This difference was not statistically significant despite the larger proportion of men in the S group. When leptin levels were tracked separately by gender during...